Stroke prevention is another important therapeutic goal for patients with AF. Vitamin K antagonists, such as warfarin, are currently the treatment of choice for the prevention of stroke in high-risk patients with AF. In the ACTIVE W trial, warfarin reduced the risk of thrombotic events without raising the risk of major bleeding compared with dual antiplatelet therapy with clopidogrel and aspirin [Connolly SJ et al. *Circulation* 2008]. Despite the clear benefits of warfarin therapy in stroke prevention, many patients with high-risk AF are suitable candidates for oral anticoagulation therapy due to bleeding risk, patient preference, or an inability to maintain warfarin within the therapeutic range. Therefore, patients with AF require new options for long-term stroke prevention.

Dabigatran is a novel antithrombotic agent that reversibly binds to free and fibrin-bound thrombin. In the Randomized Evaluation of Long-Term Anticoagulant Therapy (RE-LY) trial, once-daily dabigatran 150 mg reduced the risk of stroke and systemic embolism by 33% ($p<0.001$) compared with warfarin. The net clinical benefit, which incorporated the absence of stroke or systemic embolism, death, myocardial infarction, pulmonary embolism, and major bleeding, favored treatment with dabigatran [Connolly SJ et al. *N Eng J Med* 2009].

In summary, treatment options AF are expanding. New antiarrhythmic options may improve long-term cardioversion and enhance clinical outcomes in patients with AF. In addition, novel anticoagulants may reduce the risk of thrombotic events while minimizing the risk of bleeding, particularly in high-risk populations.

RAAS Inhibitors and the Prevention of Vascular Damage in Patients with Prehypertension

Hypertension is a primary mechanism that is responsible for the progression of cardiovascular and renal damage in patients with elevated blood pressure (BP). In particular, functional and structural changes in the vessel wall may represent the key pathological event in the development of hypertension. Within this disease model, prehypertension may be a marker for subclinical vascular disease. In this session, Carlos M. Ferrario, MD, Wake Forest University School of Medicine, Winston-Salem, North Carolina, USA, reviewed evidence that supports the treatment of patients with prehypertension, which is defined as a systolic BP (SBP) from 120 mm Hg to 139 mm Hg or a diastolic BP (DBP) from 80 mm Hg to 89 mm Hg.

The Trial of Preventing Hypertension (TROPHY) was designed to evaluate whether early treatment of patients with high-normal BP levels could slow or prevent the development of hypertension (≥140/90 mm Hg) [Julius S et al. *N Engl J Med* 2006]. In TROPHY, 809 patients with prehypertension were randomly assigned to treatment with the angiotensin receptor blocker (ARB) candesartan at a dose of 16 mg or a matching placebo for 2 years; then, all patients were treated with placebo for an additional 2 years. Data for analysis were available for 772 patients at the end of the study. Compared with those in the placebo group, patients in the candesartan group were 66.3% less likely to progress to stage 1 hypertension after 2 years ($p<0.001$) and 15.6% less likely to develop hypertension after 4 years ($p<0.007$) [Julius S et al. *N Engl J Med* 2006].

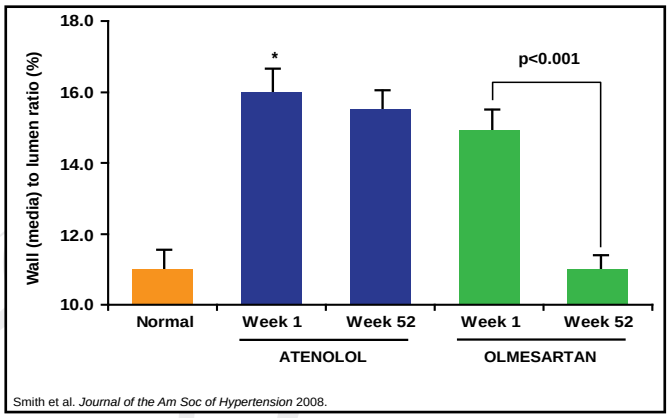
In the Prevention of Hypertension with the Angiotensin-Converting Enzyme Inhibitor Ramipril in Patients with High-Normal Blood Pressure (PHAROA) study, ramipril reduced the 3-year risk of progression from prehypertension to hypertension by 34.4% compared with placebo (42.9% vs 30.7%; $p=0.0001$) [Lüders S et al. *J Hypertens* 2008]. Together, findings from TROPHY and PHAROA indicate that a large proportion of patients with untreated high-normal BP will develop hypertension within 2 to 3 years. Moreover, treatment with a renin-angiotensin-aldosterone system (RAAS) inhibitor significantly reduced the risk of progressing to hypertension within the follow-up period that was studied [Julius S et al. *N Engl J Med* 2006; Lüders S et al. *J Hypertens* 2008].

Studies of RAAS blockade in patients with established hypertension demonstrate that it is possible to slow or even reverse vascular damage that is associated with elevated BP. In the Vascular Improvement with Olmesartan Study (VIOS), treatment with an ARB provided greater reversal of vascular hypertrophy compared with beta blockade after 1 year in patients with essential hypertension (Figure 1) [Smith RD et al. *J Am Soc Hypertens* 2008]. The improvements in vascular resistance were independent of the magnitude of BP reduction that was achieved by ARB or β-blocker therapy.

The Multicentre Olmesartan Atherosclerosis Regression Evaluation (MORE) study was designed to compare the effects of olmesartan and atenolol on the progression of atherosclerotic plaques in 165 patients with hypertension and established atherosclerosis [Stumpe KO et al. *Ther Adv Cardiovasc Dis* 2007]. Patients were randomly assigned to treatment with olmesartan or atenolol for 2 years, and ultrasound evaluations were performed at 28, 52, and 104 weeks to monitor the progression of atherosclerosis and changes in common carotid intima-media thickness (CC-IMT) and plaque volume (PV). Olmesartan and atenolol produced similar reductions in blood pressure levels and

CC-IMT at Weeks 28, 52, and 104. Atenolol was associated with a steady, but nonsignificant, increase in PV compared with baseline at each follow-up evaluation. In contrast, olmesartan significantly reduced PV compared with baseline levels at each time period, including 28 weeks (p=0.044), 52 weeks (p=0.038), and 104 weeks (p=0.014), and significantly reduced PV compared with atenolol at 52 weeks (p=0.032) and 104 weeks (p=0.023) [Stumpe KO et al. *Ther Adv Cardiovasc Dis* 2007].

Figure 1. Reversal of Vascular Hypertrophy with Olmesartan Versus Atenolol in Patients with Prehypertension.



Reproduced with permission from C. Ferrario, MD.

The VIOS and MORE trials reinforce the role of RAAS inhibitors in reducing structural damage in patients with hypertension. New models of the vascular disease continuum, which note the onset of vascular remodeling prior to the development of hypertension, highlight the potential benefits of the RAAS blockade in patients with prehypertension as well.

ACAOS: An Update on Imaging and Revascularization Techniques

Congenital coronary artery anomalies are rare, with an incidence of about 0.3% to 1.3% of all patients undergoing cardiac angiography. Although many anomalies are asymptomatic and benign, more serious defects can cause significant morbidity and mortality. The structure of the anomalous vessel, particularly its origin and course, often determines patient prognosis.

Anomalous coronary artery originating from the opposite sinus of Valsalva (ACAOS) is an under-recognized anomaly that can cause syncope, MI, and sudden cardiac death (SCD) without appropriate intervention. Howard Bush, MD, Cleveland Clinic Florida, Weston, Florida, USA, described contemporary options for imaging and revascularization in patients with ACAOS.

ACAOS is a defect in which both coronary arteries arise from the same aortic sinus. One subtype of ACAOS occurs when the left coronary artery arises from the right aortic sinus. This form of ACAOS represents approximately 1.3% of all coronary anomalies, and has been reported in 0.017% to 0.03% of the general population undergoing coronary catheterization. Young athletes with this defect have a high risk of SCD either during or immediately after physical exercise. Another type of ACAOS occurs when the right coronary artery (RCA) arises from the left aortic sinus. This is a more common defect that accounts for approximately 8.1% of serious coronary anomalies. Prognosis is very poor, with a 25% incidence of SCD in patients with RCA from the left aortic sinus.

Given the low prevalence of ACAOS, new options for diagnosis and treatment are described primarily in individual case reports. Several recent case reports suggest that advanced imaging techniques may improve the detection of ACAOS. For instance, 64-slice computed tomographic angiography (CTA) complements traditional imaging with coronary arteriography in the assessment of the functional anatomy in patients with ACAOS. Evaluation with CTA allows cardiologists to confirm the anatomical course of the aberrant coronary arteries, as well as their relationship to surrounding cardiac structures. CTA imaging also enhances percutaneous coronary intervention, an emerging treatment for anomalous RCA arising from left sinus. By improving the timely recognition, evaluation, and management of rare coronary anomalies, advanced imaging may contribute to improved outcomes in patients with ACAOS.