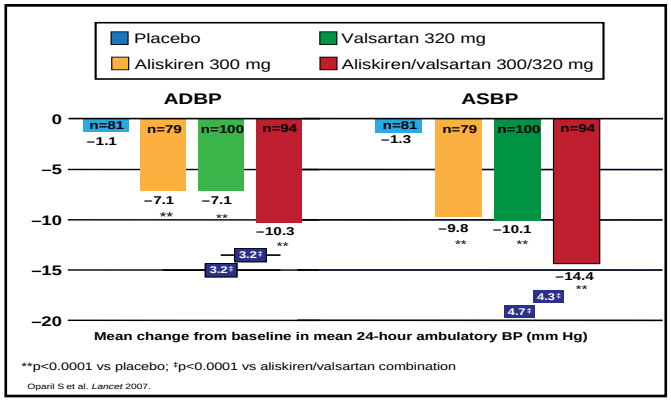
inhibition in patients with hypertension, diabetes, and other CV risk factors. These studies may show whether combining a renin inhibitor with other RAAS blockers provides additional incremental benefits in blood pressure control and CV risk reduction.

**Figure 1. Combination Therapy with Aliskiren and Valsartan Improves Blood Pressure Control Compared with Either Component as Monotherapy.**

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## A New Focus on Genetics and Individualized Management Approaches for CAD

There are many factors that increase the risk of developing coronary artery disease (CAD), including hypertension, dyslipidemia, inflammation, health behaviors, and genetics. Robert Chilton, DO, FACC, Professor of Medicine, University of Texas Health Science Center, San Antonio, Texas, USA, highlighted recent evidence concerning CAD treatment and described the clinical shift in therapeutic concentration from vulnerable plaque to genomics and metabolomics to improve drug risk benefit.

Recent studies have revealed an association between certain genetic phenotypes and CAD risk. In a meta-analysis by Schunkert and colleagues, genetic variants at chromosome 9p21.3 were associated with a 30% increase in CAD per copy of the 9p21.3 risk allele for heterozygote mutation [Schunkert H et al. *Circulation* 2008]. This study supported previous findings that mutations within this genetic locus conveyed a higher risk of CAD [Nilesh J et al. *N Engl J Med* 2007]. Additionally, a Trp719Arg polymorphism within the KIF6 gene, which encodes for a kinesin, also predicts development of CAD [Iakoubova OA et al. *J Am Coll Cardiol* 2008]. These results begin to elucidate the role of genetics in the risk of developing CAD and may prove to be useful predictive markers in the future.

In a population-based study, reductions in short-term fatality rates from myocardial infarction (MI) between 1999 and 2008 were associated, in part, with the use of effective therapeutics, such as statins, renin angiotensin aldosterone system (RAAS) blockers, and β-blockers [Yeh RW et al. *N Engl J Med* 2010]. However, genes also play a role in treatment response, and more individualized strategies may be warranted, based on varying gene polymorphisms and therapeutic interactions. In the PROVE IT-TIMI 22 trial, carriers of 719Arg demonstrated significantly greater benefit from intensive statin therapy compared with noncarriers (41% relative risk reduction [RRR] in death/MI; p=0.018) [Iakoubova OA et al. *J Am Coll Cardiol* 2008]. Similar evaluations that were performed in the CARE and WOSCOPS trials also showed that pravastatin therapy effectively reduced the risk of coronary events in KIF6 719Arg carriers, with a 54% RRR in coronary heart disease and a 41% RRR in acute MI [Iakoubova OA et al. *J Am Coll Cardiol* 2008]. Alternatively, variants that were identified within SLCO1B1 (rs4363657) were strongly associated with an increased risk of statin-induced myopathy [SEARCH Collaborative Group. *N Engl J Med* 2008]. Thus, the need to consider genetics when determining an appropriate treatment strategy has become more apparent.

There has been increasing evidence of interactions between gene polymorphisms and therapies that are associated with variability in coronary risk. Pharmacogenomics and variable therapeutic responses have altered views on treatment approaches and may lead to more emphasis on genetic predictors of risk and therapeutic response moving forward. While previous strategies have focused on factors, such as inflammation, lipids, glucose, and other risk measurements, future approaches may incorporate additional factors, such as individual risk profile, genomics, and biomarkers.

## Stroke Prevention in Atrial Fibrillation: Novel Agents Versus the Gold Standard

Stroke prevention is a priority for clinicians who treat patients with atrial fibrillation (AF). Warfarin has been the gold standard therapy for patients with AF who are at moderate or high risk of stroke. However, there are concerns about the limitations of warfarin, such as adherence issues, bleeding risk, narrow therapeutic window, vigilant monitoring requirements, and drug-drug/food-drug interactions that make it difficult to