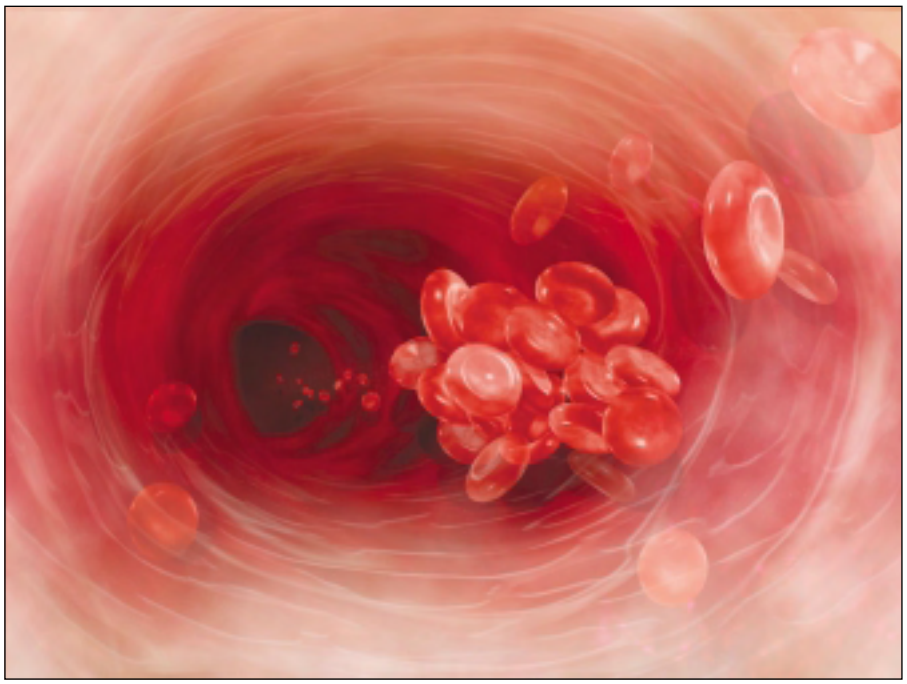
CHARISMA

CHARISMA (Clopidogrel for High Atherothrombotic Risk, Ischemic Stabilization, Management, and Avoidance) is the first clinical trial to evaluate long-term effectiveness of clopidogrel plus aspirin in a population of high-risk patients, including symptomatic individuals with documented disease. Principal investigator Deepak Bhatt, MD, of the Cleveland Clinic Cardiovascular Coordinating Center, presented results from more than 15,000 study participants followed for a median of 2.3 years.

The median patient age in CHARISMA was 65, with women constituting 30% of the study population. Risk factor profiles were categorized as "two major," "three minor," or "one major/two minor," with major risk factors including diabetes, diabetic nephropathy, an ankle brachial index (ABI) <0.9 (consistent with peripheral arterial disease), or asymptomatic carotid stenosis >70% (or 1 or more carotid atheroma identified by intima-media thickness measurement).

Minor risk factors included male gender 65 years or older, females 70 years or older, systolic blood pressure >150 mm Hg despite antihypertensive therapy for at least 3 months, primary hypercholesterolemia, and smoking >15 cigarettes a day.



The study population was randomized to either clopidogrel (75 mg daily) or placebo. All study participants took aspirin (75-162 mg daily).

Study data indicated that clopidogrel plus ASA failed to demonstrate a statistically significant reduction in the primary endpoints of non-fatal MI, stroke, or CV-related death compared to ASA alone in a broad patient population with either established atherothrombotic disease or multiple risk factors for atherothrombotic events.

While patients with risk factors but no clinical evidence of disease saw no benefit in the primary endpoints, the subgroup of patients with documented cardiovascular disease at enrollment demonstrated some benefit with clopidogrel plus ASA for the primary endpoints (6.9% for clopidogrel/ASA vs 7.9% for placebo, RR 0.88, p=0.046).

These findings suggest that dual antiplatelet therapy (clopidogrel plus aspirin) may not be useful as a primary prevention strategy. But in those individuals with established disease, dual therapy may be effective in reducing events. (CHARISMA's findings in regard to the study's secondary endpoints are consistent with other major trials—CURE, COMMIT and CLARITY-TIMI 28—that have demonstrated efficacy for dual antiplatelet therapy in the context of PCI and acute coronary syndromes.) Therefore the results of CHARISMA do not alter the established efficacy of dual therapy in patients with acute coronary syndrome and/or PCI.

In presenting results of the CHARISMA trial, Dr. Bhatt noted that "by strict statistical terms, our primary endpoint was negative. But the secondary endpoints dig a little deeper, and actually raise questions that we now need to answer. It's clear that the question of dual antiplatelet therapy demands further study."