MY TAKE

Poor Design Limits Conclusions

The value of warfarin genotyping in the real world was not established by this study. There is some doubt that warfarin has a disease-modifying effect of equal magnitude on other primary-disease etiologies. One has to assume that we are merely seeing a Hawthorne effect on a population with much closer and better follow-up.

Even when you include propensity scoring, you can control only for the baseline variables that you can see. The dynamic variables that occur by following patients with warfarin titration are not accounted for by the propensity score analysis. Also, there is considerable doubt as to whether control patients were equally managed post intervention, and there were no data on the international normalized ratio achieved.

My conclusion is that the outcome was more likely the result of closer attention and better follow-up. The trial design was not adequate to answer the question that was posed.

MANDEEP R. MEHRA, M.B.B.S., *is head of the division of cardiology at the University of Maryland in Baltimore. He has received consulting fees or honoraria from Medtronic, St. Jude/Boston Scientific, Solvay, and Geron.*

Clopidogrel Plus Aspirin Cost Effective

BY BRUCE JANCIN

ATLANTA — Adding clopidogrel to aspirin for stroke prevention in warfarin-unsuitable patients with atrial fibrillation is cost neutral, according to a new secondary economic analysis of the ACTIVE-A trial.

What this means is that the substantial cost of adding brand-name clopidogrel (Plavix) to aspirin therapy is canceled out by the resultant considerable savings resulting from fewer strokes, even after taking into account the costs related to clopidogrel-associated bleeding complications, Dr. Andre Lamy said at the annual meeting of the American College of Cardiology.

The good news for health plans is that clopidogrel will go generic in just a few months in the United States and most of the rest of the world. At that point, using clopidogrel plus aspirin instead of aspirin alone to protect against strokes in patients with atrial fibrillation who can't take warfarin will no longer be cost neutral, it will actually become cost saving, according to Dr. Lamy, a surgeon and clinical epidemiologist at McMaster University in Hamilton, Ont.

"It's very unusual to see that with a drug. Health care systems will get good value for the investment. The strokes are quite expensive," he observed in an interview.

ACTIVE-A (Atrial Fibrillation Clopidogrel Trial With Irbesartan for Prevention of Vascular Events–Aspirin) was a randomized trial involving 7,554 patients with atrial fibrillation in 33 countries who were deemed unsuitable for warfarin. The primary outcomes have previously been published: a 28% reduction in the risk of stroke with dual preventive therapy compared to aspirin alone during a median 3.6 years of follow-up, which came at the expense of a 57% increase in risk of major hemorrhage (N. Engl. J. Med. 2009;360:2066-78).

For every 1,000 patients treated with clopidogrel and aspirin for 3 years, there were 28 fewer strokes than with aspirin alone, including 17 fewer disabling or fatal ones, 6 fewer MIs, and 20 additional major bleeding episodes, 3 of which were fatal.

Dr. Lamy and coinvestigators calculated the direct medical costs associated with these outcomes using Canadian cost rates, which are similar to Medicare costs. They determined that although dual therapy cost an average of $2,114 Canadian more, this was counterbalanced by the savings achieved through strokes avoided, even after subtracting the costs associated with the major bleeding incidents. ■

Disclosures: *Dr. Lamy said that this economic analysis as well as the ACTIVE-A trial were funded by grants from Sanofi-Aventis and Bristol-Myers Squibb.*