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ACC: Brilinta Effective in Long-Term DAPT

— Fewer heart attacks and strokes, but more bleeding with extended DAPT.

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SAN DIEGO -- Patients who took ticagrelor (Brilinta) plus aspirin for almost 3 years after a myocardial infarction were less likely to have a second heart attack or stroke or to die from cardiovascular disease, but were more likely to have a major bleeding event.

On the other hand, there was no increase in fatal bleeding events, said Marc S. Sabatine, MD, MPH, principal investigator for the PEGASUS TIMI-54 study. Sabatine reported the results at a late-breaking clinical trial session at the American College of Cardiology meeting here. The findings were also simultaneously published in *The New England Journal of Medicine*.

Richard A. Chazal, MD, ACC vice president and medical director of the heart and vascular institute at Lee Memorial Health System in Fort Myers, Fla., told *MedPage Today* the only thing that can be gleaned from PEGASUS is that "both doses of the drug are effective."

He added that the finding cannot be extrapolated to a comparison with clopidogrel and that the data were unlikely to support a change in practice.

The findings were not, however, unexpected since AstraZeneca, which markets ticagrelor, released the topline results in January.

The study recruited 21,162 myocardial infarction patients and evenly assigned them to 90 mg or 60 mg ticagrelor twice daily or placebo. All patients received low-dose aspirin at doses ranging from 75 mg to 150 mg. Patients were followed for a median of 33 months.

The primary efficacy endpoint was a composite of recurrent MI, stroke, or cardiovascular death, and the safety endpoint was TIMI major bleeding, Sabatine said.

Although both ticagrelor doses reduced ischemic events and cardiovascular death compared with placebo, Sabatine said the 60-mg dose is probably the better choice because it was better tolerated and the bleeding rate was less with it. Moreover, the efficacy benefit was largely driven by a reduction in recurrent MI.

The composite efficacy endpoint was reached by 7.85% of patients in 90-mg ticagrelor group (HR versus placebo 0.85, 95% CI 0.75-0.96, P=0.008) and 7.77% of the 60-mg group (HR versus placebo 0.84 95% CI 0.74-0.95, P=0.004), Sabatine said.

"Rates of TIMI major bleeding were higher with ticagrelor (2.60% with 90 mg and 2.30% with 60 mg) than with placebo (1.06%) (P<0.001 for each dose

versus placebo); the rates of intracranial hemorrhage or fatal bleeding in the three groups were 0.63%, 0.71%, and 0.60%, respectively," he wrote.

Ticagrelor was once touted for its blockbuster potential because it appeared to have a better safety profile than Plavix (clopidogrel) and it had the advantage of being faster acting but also faster to turn off. But its associated bleeding risk did become a problem.

It stumbled on the way to FDA approval and then, in 2013, reports surfaced about problems with the data from the pivotal PLATO trial.

These new findings, while not spectacular, may breathe new life into the drug and appear to make a case for its use in secondary prevention. Yet much of the enthusiasm for extended dual antiplatelet therapy has waned in recent years as data have continued to confirm the bleeding risk, counterbalancing the reduction in thrombotic events also consistently shown with extended therapy.

In an editorial that accompanied the PEGASUS results in *NEJM*, John F. Keaney Jr., MD, of the University of Massachusetts Medical School in Worcester, raised that concern, noting that the data prompt speculation as to whether dual platelet inhibition with high-potency agents is "approaching the point of diminishing returns."

Keaney wrote, "On the basis of the 60-mg ticagrelor dose, treating 10,000 patients for 1 year would prevent approximately 42 primary endpoint events and produce approximately 31 TIMI major bleeding events -- close to an even proposition."

And economics may also play into the equation since clopidogrel has a demonstrated track record and an off-patent price tag of less than $10 for a month's supply versus $350 for ticagrelor.

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