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Ticagrelor is as safe and effective as clopidogrel after heart attack

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Patients given clot busters to treat a heart attack fared equally well if they were given the standard blood thinning medication clopidogrel versus the newer, more potent drug ticagrelor, according to research presented at the American College of Cardiology's 68th Annual Scientific Session.

The trial, called TREAT, is the first large, international trial to assess ticagrelor's safety and efficacy in patients taking fibrinolytic therapy, or "clot busters," a class of drugs that break up the blood clots that cause heart attacks. Clot busters are used to treat heart attacks when it is not feasible to perform percutaneous coronary intervention (PCI), a procedure to open blocked arteries that is the gold standard for treating ST-elevation myocardial infarction (STEMI), the most severe type of heart attack.

In 2018, researchers reported the trial met its primary endpoint (major bleeding at 30 days) showing comparable safety between ticagrelor and clopidogrel. The current pre-specified analysis of efficacy and safety at 12 months suggests ticagrelor and clopidogrel have comparable efficacy and offers further confirmation that ticagrelor is safe to use in this patient population, researchers said.

Ticagrelor reduces clotting by preventing platelets from aggregating. It takes effect more quickly than clopidogrel. A previous study, called PLATO, found ticagrelor was superior to clopidogrel at preventing adverse cardiac events in patients with acute coronary syndromes—a

group of conditions that includes heart attacks and unstable angina—who were not given clot busters. TREAT was designed to determine whether these benefits extend to patients given clot busters after STEMI.

"In spite of the fact that ticagrelor is more potent than clopidogrel, we found that it is safe to use ticagrelor in this population," said Otavio Berwanger, MD, Ph.D., Chair of the Steering Committee and the study's lead author. "In terms of efficacy, it is appropriate to interpret it statistically as a neutral trial, though it should be looked at in the broader context along with PLATO."

The use of clot busters is most common where PCI is not available 24 hours a day, which includes most lower- and middle-income countries as well as some higher-income countries. The trial, conducted in 10 countries on five continents, included a mix of higher-income and lower-income countries and thus has worldwide relevance, researchers said.

The trial enrolled 3,800 patients treated for STEMI at more than 180 centers. All patients had received fibrinolytic therapy within 24 hours of their heart attack. Half of the participants were randomly assigned to take ticagrelor and half took clopidogrel. Patients were given an initial loading dose of their assigned drug and then continued taking the drug for 12 months.

At 12 months, researchers assessed rates of the key endpoint for the 12-month analysis, a composite of death from vascular causes, heart attack, stroke, severe recurrent ischemia, transient ischemic attack or another arterial thrombotic event. Eight percent of patients taking ticagrelor and 9.1 percent of those taking clopidogrel suffered these events, a difference that was not statistically significant.

Researchers noted that the trial was much smaller than PLATO, which had more than 18,000 participants, and had a lower than expected

number of adverse events, limiting its statistical power. The risk reductions of ticagrelor as compared with the clopidogrel groups were identical in both studies; however, the gap was considered statistically significant in PLATO due to that trial's larger size. When the researchers analyzed pooled data combining PLATO and TREAT, they found ticagrelor significantly improved outcomes compared to clopidogrel.

"The TREAT patients are exactly the population that was excluded from PLATO," Berwanger said. "By combining both trials, we can say that ticagrelor is beneficial across the whole spectrum of patients with acute coronary syndromes, regardless of how they are managed in terms of fibrinolytic therapy."

When TREAT data were analyzed alone, researchers found no significant difference in terms of the secondary composite endpoint that included death from vascular causes, heart attack or stroke, which occurred in 6.9 percent of those on ticagrelor and 7.3 percent of those on clopidogrel. They also found no significant differences in terms of the individual components of the composite endpoint or death from any cause.

Bleeding is the most common complication from blood thinners, which are used to help prevent heart attacks and strokes by reducing the body's ability to clot blood. The TREAT researchers assessed rates of bleeding events using the criteria defined by the Thrombolysis in Myocardial Infarction (TIMI) score, as well as the Bleeding Academic Research Consortium (BARC) categories and the definition used in PLATO. Rates of the most important types of bleeding such as major bleeding and major and minor bleeding combined were low (between 1 and 2 percent) and not significantly different between the two groups, suggesting the safety of ticagrelor. However, rates of minor, non-clinically relevant bleeding (such as from a nosebleed or minor cut) were significantly higher in the ticagrelor group, with 5.9 percent reporting

such bleeds compared with 2.9 percent among those taking clopidogrel. This difference was expected and in line with previous studies, Berwanger said.

More information: Otavio Berwanger et al, Ticagrelor versus Clopidogrel in Patients with STEMI Treated with Fibrinolytic Therapy: TREAT Trial, *Journal of the American College of Cardiology* (2019). DOI: 10.1016/j.jacc.2019.03.011

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