Time Course for Benefit and Risk of Ticagrelor and Aspirin in Acute Ischemic Stroke or Transient Ischemic Attack

Yongjun Wang, MD, Yuesong Pan, PhD, Hao Li, PhD, et al.

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Study Question
Do the benefits and risks of ticagrelor plus aspirin compared with aspirin alone in patients with mild-moderate ischemic stroke or high-risk TIA change over time?

What Is Known and What This Paper Adds
Dual antiplatelet therapy started within 24 hours after symptoms onset is a recommended treatment for patients with minor stroke or TIA. The Acute Stroke or Transient Ischemic Attack Treated With Ticagrelor and ASA for Prevention of Stroke and Death (THALES) trial demonstrated that, compared with aspirin alone, 30 days of ticagrelor-aspirin reduced the risk of stroke and death but was associated with an increase in severe bleeding in patients with mild to moderate acute ischemic stroke or TIA. This investigation further assessed the time course of benefit and risk of ticagrelor plus aspirin. This study provides Class II evidence that, for patients with mild-moderate ischemic stroke or high-risk TIA, the ischemic benefit of ticagrelor-aspirin outweighs the risk of major hemorrhage throughout the 30-day treatment period.

Methods
For this exploratory time-course analysis, the investigators used data from the THALES trial, which was an international, randomized, double-blind, placebo-controlled, parallel-group trial that compared ticagrelor plus aspirin with aspirin alone for preventing recurrent stroke in patients with mild to moderate acute ischemic stroke or TIA who presented ≤24 hours after symptom onset. Recruitment occurred through 414 sites in 28 countries between January 22, 2018, and December 13, 2019. These analyses focused on 5,523 patients who received ticagrelor plus aspirin and 5,493 patients who received aspirin alone. The investigators evaluated the cumulative incidence of irreversible efficacy outcome of major ischemic events and safety outcome of major hemorrhage at different time points during the 30-day treatment period.

Results and Study Limitations
The reduction of major ischemic events by ticagrelor occurred in the first week (4.1% vs 5.3%; absolute risk reduction 1.15%, 95% CI 0.36%–1.94%) and remained throughout the 30-day treatment period. An increase in major hemorrhage was seen during the first week and remained relatively constant in the following weeks (absolute risk increase ≈0.3%). Cumulative analysis showed that the net clinical impact favored ticagrelor-aspirin in the first week (absolute risk reduction 0.97%, 95% CI 0.17%–1.77%) and remained constant throughout the 30 days. The limitations of the present study include a lack of power for exploratory landmark analysis on treatment pattern over time and somewhat high treatment discontinuation.

Registration, Study Funding, and Competing Interests
This study was registered with ClinicalTrials.gov (NCT03354429). This study is supported by AstraZeneca. Some authors reported support from pharmaceutical and biotechnology companies. Four authors reported employment by AstraZeneca. Go to Neurology.org/N for full disclosures.
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