Ticagrelor vs Clopidogrel After Fibrinolytic Therapy in Patients With ST-Elevation Myocardial InfarctionA Randomized Clinical Trial

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Question In patients with ST-elevation myocardial infarction treated with fibrinolytic therapy, is ticagrelor noninferior to clopidogrel with respect to thrombolysis in myocardial infarction major bleeding at 30 days?

Findings In this randomized clinical trial of 3799 patients, delayed administration of ticagrelor after fibrinolytic therapy was noninferior to clopidogrel for thrombolysis in myocardial infarction major bleeding at 30 days. However, minor bleeding was increased with ticagrelor and there was no benefit on efficacy outcomes.

Meaning Because most of the included patients were pretreated with clopidogrel, these findings reflect mostly the noninferiority of switching from clopidogrel to ticagrelor in patients already fully loaded with clopidogrel.

Abstract

Importance The bleeding safety of ticagrelor in patients with ST-elevation myocardial infarction treated with fibrinolytic therapy remains uncertain.

Objective To evaluate the short-term safety of ticagrelor when compared with clopidogrel in patients with ST-elevation myocardial infarction treated with fibrinolytic therapy.
Design, Setting and Participants  We conducted a multicenter, randomized, open-label with blinded end point adjudication trial that enrolled 3799 patients (younger than 75 years) with ST-segment elevation myocardial infarction receiving fibrinolytic therapy in 152 sites from 10 countries from November 2015 through November 2017. The prespecified upper boundary for noninferiority for bleeding was an absolute margin of 1.0%.

Interventions  Patients were randomized to ticagrelor (180-mg loading dose, 90 mg twice daily thereafter) or clopidogrel (300-mg to 600-mg loading dose, 75 mg daily thereafter). Patients were randomized with a median of 11.4 hours after fibrinolysis, and 90% were pretreated with clopidogrel.

Main Outcomes and Measures  The primary outcome was thrombolysis in myocardial infarction (TIMI) major bleeding through 30 days.

Results  The mean (SD) age was 58.0 (9.5) years, 2928 of 3799 patients (77.1%) were men, and 2177 of 3799 patients (57.3%) were white. At 30 days, TIMI major bleeding had occurred in 14 of 1913 patients (0.73%) receiving ticagrelor and in 13 of 1886 patients (0.69%) receiving clopidogrel (absolute difference, 0.04%; 95% CI, −0.49% to 0.58%; \( P < .001 \) for noninferiority). Major bleeding defined by the Platelet Inhibition and Patient Outcomes criteria and by the Bleeding Academic Research Consortium types 3 to 5 bleeding occurred in 23 patients (1.20%) in the ticagrelor group and in 26 patients (1.38%) in the clopidogrel group (absolute difference, −0.18%; 95% CI, −0.89% to 0.54; \( P = .001 \) for noninferiority). The rates of fatal (0.16% vs 0.11%; \( P = .67 \)) and intracranial bleeding (0.42% vs 0.37%; \( P = .82 \)) were similar between the ticagrelor and clopidogrel groups, respectively. Minor and minimal bleeding were more common with ticagrelor than with clopidogrel. The composite of death from vascular causes, myocardial infarction, or stroke occurred in 76 patients (4.0%) treated with ticagrelor and in 82 patients (4.3%) receiving clopidogrel (hazard ratio, 0.91; 95% CI, 0.67-1.25; \( P = .57 \)).

Conclusions and Relevance  In patients younger than 75 years with ST-segment elevation myocardial infarction, delayed administration of ticagrelor after fibrinolytic therapy was noninferior to clopidogrel for TIMI major bleeding at 30 days.

Trial Registration  clinicaltrials.gov Identifier: NCT02298088.