Comparison of ticagrelor with clopidogrel in patients with a planned invasive strategy for acute coronary syndromes (PLATO): a randomised double-blind study

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Summary

Background Variation in and irreversibility of platelet inhibition with clopidogrel has led to controversy about its optimum dose and timing of administration in patients with acute coronary syndromes. We compared ticagrelor, a more potent reversible P2Y12 inhibitor with clopidogrel in such patients.

Methods At randomisation, an invasive strategy was planned for 13 408 (72·0%) of 18 624 patients hospitalised for acute coronary syndromes (with or without ST elevation). In a double-blind, double-dummy study, patients were randomly assigned in a one-to-one ratio to ticagrelor and placebo (180 mg loading dose followed by 90 mg twice a day), or to clopidogrel and placebo (300–600 mg loading dose or continuation with maintenance dose followed by 75 mg per day) for 6–12 months. All patients were given aspirin. The primary composite endpoint was cardiovascular death, myocardial infarction, or stroke. Analyses were by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT00391872.

Findings 6732 patients were assigned to ticagrelor and 6676 to clopidogrel. The primary composite endpoint occurred in fewer patients in the ticagrelor group than in the clopidogrel group (569 [event rate at 360 days 9·0%] *vs* 668 [10·7%], hazard ratio 0·84, 95% CI 0·75–0·94; p=0·0025). There was no difference between clopidogrel and ticagrelor groups in the rates of total major bleeding (691 [11·6%] *vs* 689 [11·5%], 0·99 [0·89–1·10]; p=0·8803) or severe bleeding, as defined according to the Global Use of Strategies To Open occluded coronary arteries, (198 [3·2%] *vs* 185 [2·9%], 0·91 [0·74–1·12]; p=0·3785).

Interpretation Ticagrelor seems to be a better option than clopidogrel for patients with acute coronary syndromes for whom an early invasive strategy is planned.

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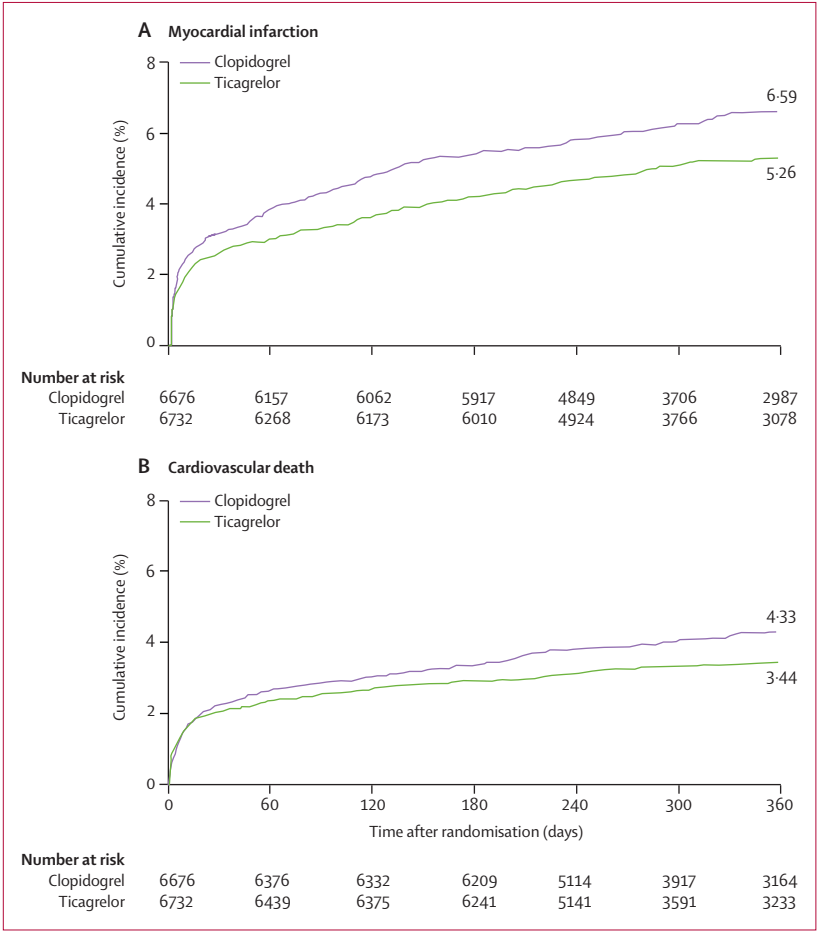
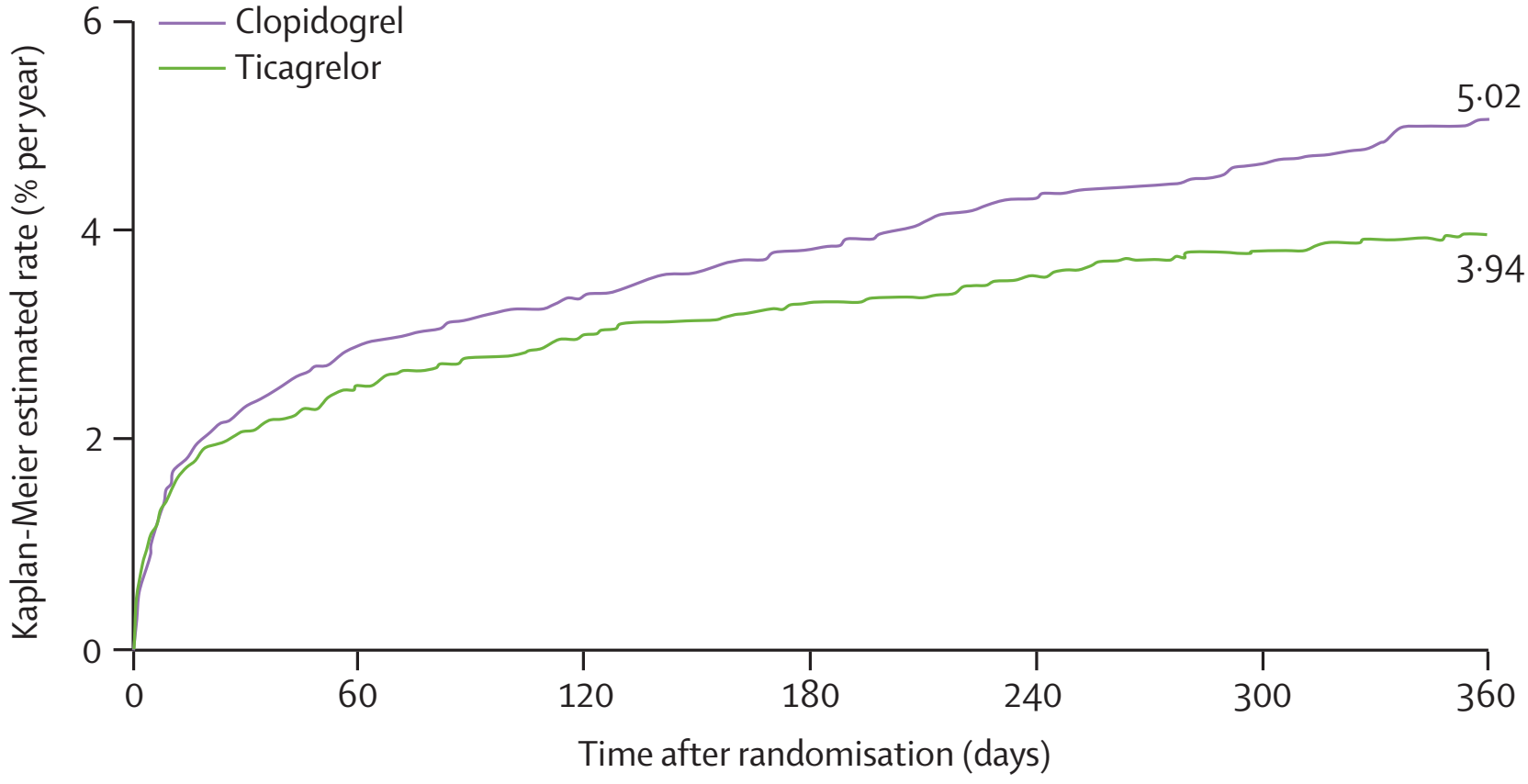


Figure 3: **Cumulative Kaplan-Meier estimates of time to myocardial infarction (A) or cardiovascular death (B) in patients intended to undergo an invasive strategy**



Number at risk

Clopidogrel	6676	6376	6331	6209	5114	3917	3164
Ticagrelor	6732	6439	6375	6241	5141	3951	3233

Figure 4: **Cumulative Kaplan-Meier estimates of time to all-cause mortality in patients intended to undergo an invasive strategy**