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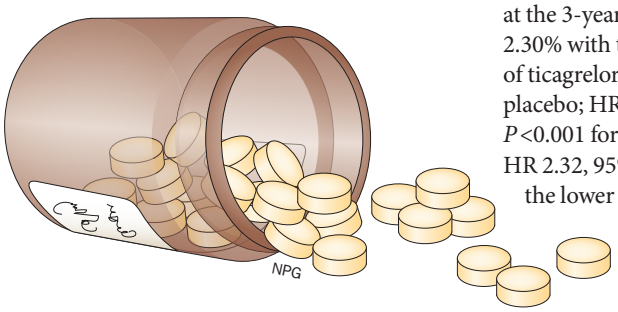
ANTIPLATELET THERAPY

Long-term ticagrelor use in patients with history of MI

European and US guidelines recommend use of a $P2Y_{12}$-receptor antagonist for up to 1 year after myocardial infarction (MI). The PEGASUS-TIMI 54 trial was designed to assess whether long-term addition of ticagrelor to low-dose aspirin treatment confers benefit in patients who have a history of MI. In total, 21,162 patients who had experienced an MI 1–3 years before enrolment, and who were taking 75–150 mg aspirin daily, were randomly assigned to placebo or to one of two doses of ticagrelor—the previously studied dose of 90 mg twice daily, and a lower dose of 60 mg twice daily.



At the 3-year follow-up, the primary efficacy end point—a composite of cardiovascular death, MI, or stroke—was reduced with both the 90 mg and the 60 mg dose of ticagrelor, compared with placebo (7.85% and 7.77% with the 90 mg and 60 mg doses of ticagrelor, respectively, vs 9.04% with placebo; HR 0.85, 95% CI 0.75–0.96, $P = 0.008$ for the higher dose vs placebo; HR 0.84, 95% CI 0.74–0.95, $P = 0.004$ for the lower dose vs placebo). This effect of ticagrelor was apparent for all major patient subgroups assessed.

The primary safety end point—TIMI major bleeding—was significantly increased with both doses of ticagrelor at the 3-year follow-up (2.60% and 2.30% with the 90 mg and 60 mg doses of ticagrelor, respectively, vs 1.06% with placebo; HR 2.69, 95% CI 1.96–3.70, $P < 0.001$ for the higher dose vs placebo; HR 2.32, 95% CI 1.68–3.21, $P < 0.001$ for the lower dose vs placebo). The rates of fatal bleeding or nonfatal intracranial haemorrhage were similar for the three treatment groups. The PEGASUS-TIMI 54 investigators caution that "the study protocol excluded patients with recent bleeding, prior stroke, or the need for oral anticoagulation therapy. Therefore, the safety profile of long-term ticagrelor that we observed should not be generalized to other populations at heightened risk for bleeding."

"The results of the present trial provide prospectively defined evidence affirming the hypothesis that long-term, intensive platelet inhibition with ticagrelor reduces ischaemic events in patients with prior MI," concluded the investigators. They speculate that "the 60 mg dose may offer a more attractive benefit–risk profile," but point out that the differences between the effects of the two doses of ticagrelor used in their study were not statistically signficant.

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Original article Bonaca, M. P. *et al.* Long-term use of ticagrelor in patients with prior myocardial infarction. *N. Engl. J. Med.* doi:10.1056/NEJMoa1500857