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Ticagrelor for Prevention of Ischemic Events after Myocardial Infarction in Patients with Peripheral Artery Disease

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Abstract

Background:

Peripheral artery disease (PAD) is associated with heightened ischemic and bleeding risk in patients with prior myocardial infarction (MI).

Objectives:

This study evaluated the efficacy and safety of Ticagrelor on major cardiovascular (CV) events and major adverse limb events in patients with PAD and a prior MI.

Methods:

PEGASUS-TIMI 54 (Prevention of Cardiovascular Events in Patients with Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin-Thrombolysis in Myocardial Infarction 54) randomized 21,162 patients with prior MI (1 to 3 years) to Ticagrelor 90 mg twice daily, Ticagrelor 60 mg twice daily, or placebo, all on a background of low-dose aspirin. History of PAD was obtained at baseline. Occurrences of major adverse cardiovascular events (MACE) (defined as CV death, MI, or stroke) and major adverse limb events

(MALE) (defined as acute limb ischemia or peripheral revascularization for ischemia) were recorded in follow-up.

Results:

A total of 1,143 patients (5%) had known PAD. In the placebo arm, those with PAD (n = 404) had higher rates of MACE at 3 years than those without (n = 6,663; 19.3% vs. 8.4%; $p < 0.001$), which persisted after adjusting for baseline differences (adjusted hazard ratio: 1.60; 95% confidence interval: 1.20 to 2.13; $p = 0.0013$), and higher rates of acute limb ischemia (1.0% vs. 0.1%) and peripheral revascularization procedures (9.15% vs. 0.46%). Whereas the relative risk reduction in MACE with Ticagrelor was consistent, regardless of PAD, patients with PAD had a greater absolute risk reduction of 4.1% (number needed to treat: 25) due to their higher absolute risk. The absolute excess of TIMI major bleeding was 0.12% (number needed to harm: 834). The 60-mg dose had particularly favorable outcomes for CV and all-cause mortality. Ticagrelor (pooled doses) reduced the risk of MALE (hazard ratio: 0.65; 95% confidence interval: 0.44 to 0.95; $p = 0.026$).

Conclusions:

Among stable patients with prior MI, those with concomitant PAD have heightened ischemic risk. In these patients, Ticagrelor reduced MACE, with a large absolute risk reduction, and MALE. (Prevention of Cardiovascular Events in Patients With Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin [PEGASUS-TIMI 54]; NCT01225562).

Keywords:

Acute limb ischemia; major adverse cardiovascular events; major adverse limb events; peripheral arterial disease; Ticagrelor.

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Randomized Controlled Trial

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