Ticagrelor for Secondary Prevention of Atherothrombotic Events in Patients With Multivessel Coronary Disease

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ABSTRACT

BACKGROUND Patients with prior myocardial infarction (MI) and multivessel coronary disease (MVD) are at high risk for recurrent coronary events.

OBJECTIVES The authors investigated the efficacy and safety of ticagrelor versus placebo in patients with MVD in the 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) trial.

METHODS Patients with a history of MI 1 to 3 years before inclusion in the PEGASUS-TIMI 54 trial were stratified in a pre-specified analysis based on the presence of MVD. The effect of ticagrelor (60 mg and 90 mg) on the composite of cardiovascular death, MI, or stroke (major adverse cardiovascular events [MACE]), as well as the composite of coronary death, MI, or stent thrombosis (coronary events), and on TIMI major bleeding, intracranial hemorrhage (ICH), and fatal bleeding were evaluated over a median of 33 months.

RESULTS A total of 12,558 patients (59.4%) had MVD. In the placebo arm, compared with patients without MVD, those with MVD were at higher risk for MACE (9.37% vs. 8.57%, adjusted hazard ratio [HRadj]: 1.24; p = 0.026) and for coronary events (7.67% vs. 5.34%, HRadj: 1.49; p = 0.0005). In patients with MVD, ticagrelor reduced the risk of MACE (7.94% vs. 9.37%, HR: 0.82; p < 0.0001) and coronary events (6.02% vs. 7.67%, HR: 0.76; p < 0.0001), including a 36% reduction in coronary death (HR: 0.64; 95% confidence interval: 0.48 to 0.85; p = 0.002). In this subgroup, ticagrelor increased the risk of TIMI major bleeding (2.52% vs. 1.08%, HR: 2.67; p < 0.0001), but not ICH or fatal bleeding.

CONCLUSIONS Patients with prior MI and MVD are at increased risk of MACE and coronary events, and experience substantial relative and absolute risk reductions in both outcomes with long-term ticagrelor treatment relative to those without MVD. Ticagrelor increases the risk of TIMI major bleeding, but not ICH or fatal bleeding. For patients with prior MI and MVD, ticagrelor is an effective option for long-term antiplatelet therapy. (Prevention of Cardiovascular Events [e.g., Death From Heart or Vascular Disease, Heart Attack, or Stroke] in Patients With Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin [PEGASUS]; NCT01225562) (J Am Coll Cardiol 2018;71:489–96) © 2018 by the American College of Cardiology Foundation.

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The 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) trial evaluated the benefit of long-term treatment with 2 doses of ticagrelor (60 mg and 90 mg twice daily) compared with placebo in patients treated with low-dose aspirin who had a history of myocardial infarction (MI) between 1 and 3 years before randomization and who also had additional risk factors for recurrent atherothrombotic events. Ticagrelor reduced the risk of major adverse cardiovascular (CV) events (MACE) (CV death, MI, or stroke), with an increase in nonfatal major bleeding (1).

Patients with multivessel coronary artery disease (MVD) have more advanced atherosclerosis, with higher rates of in-hospital events, as well as recurrent atherothrombotic coronary events and death (2–6). Significant debate has centered on revascularization strategies in MVD patients; less attention has been paid to the intensity and duration of antithrombotic therapy. Recently, data from multiple small trials have provided some evidence of reduction in major ischemic events with more intense and longer duration antiplatelet therapy in patients with MVD (7). In this pre-specified analysis from the PEGASUS-TIMI 54 trial, we evaluated the efficacy and safety of long-term ticagrelor therapy in patients with prior MI and MVD.

**METHODS**

The design and primary overall results of PEGASUS-TIMI 54 have been previously published (8). Patients with a history of MI 1 to 3 years previously and at least one additional atherothrombotic risk factor (age >65 years, diabetes mellitus requiring medication, second prior spontaneous MI, chronic renal dysfunction, or MVD) were randomized to ticagrelor (90 mg or 60 mg...
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