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Acute Coronary Syndromes

GREATER EFFICACY OF TICAGRELOR COMPARED TO CLOPIDOGREL IN ACUTE CORONARY SYNDROME IS NOT DRIVEN BY OUTCOMES IN POOR METABOLIZERS OF CLOPIDOGREL

ACC Moderated Poster Contributions
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Background: Ticagrelor is superior to clopidogrel for prevention of the combined rate of cardiovascular (CV) death, myocardial infarction (MI) and stroke in acute coronary syndromes (ACS).(1) Patients with two loss-of-function (LOF) alleles at CYP2C19, the main genetic factor affecting clopidogrel PK/PD, are classified as poor metabolizers (PM) of clopidogrel. We used the PLATO genetic sub-study to assess the impact of PM on the overall PLATO result.

Methods: 10,285 DNA samples from PLATO, which randomized 18,624 ACS patients to ticagrelor or clopidogrel for 6 - 12 months, underwent CYP2C19 genotyping for wildtype (*1); LOF alleles *2, *3, *4, *5, *6, *7, & *8; and gain of function allele *17 as previously described.(2) Patients with any combination of two LOF alleles were denoted as PM. Analysis of PLATO primary efficacy and safety outcomes proceeded after excluding PM from both treatment groups.

Results: PMs constituted 121 of 5,137 ticagrelor patients and 125 of 5,148 clopidogrel patients. After exclusion of PMs, the remaining cohort (n=10,039) showed a significant reduction in the primary endpoint (myocardial infarction, stroke, or CV death) with ticagrelor compared to clopidogrel (8.8% vs 10.4%/yr; hazard ratio [HR] 0.85, 95% confidence interval 0.74- 0.96, P=0.01), consistent with the primary PLATO findings. Total major bleeding did not differ between treatments, with 10.7%/yr rates for each; non-CABG major bleeding trended higher with ticagrelor (4.0%/yr) than with clopidogrel (3.3%/yr). Ticagrelor similarly reduced the primary endpoint in the PM group (8.8% v 9.7%/yr, HR=0.87), although there were only 22 events.

Conclusions: In PLATO, ticagrelor reduced the primary endpoint of CV death, MI or stroke in ACS patients compared to clopidogrel. These results were not driven by patients who are poor metabolizers of clopidogrel.

1. Wallentin L et al. NEJM 2009; 361: 1045-57.

2. Wallentin L et al. Lancet 2010; 376:1320-8.