Abstract

Patients are prescribed P2Y12 inhibitors as part of dual antiplatelet therapy following percutaneous coronary intervention (PCI) in the acute coronary syndrome or stable coronary artery disease settings. The P2Y12 inhibitor clopidogrel requires activation by CYP2C19 in order to exert its antiplatelet effects. The gene encoding CYP2C19 is highly polymorphic, and patients may have alleles ranging from increased function to no function. Patients carrying one no function allele and one increased or normal function allele are classified as intermediate metabolizers. Patients who carry two no function alleles are classified as poor metabolizers. Intermediate and poor metabolizers of CYP2C19 are at increased risk for ischemic events with clopidogrel as they have reduced levels of active metabolite. FDA labeling and current CPIC guidelines recommend using alternative P2Y12 therapy such as ticagrelor or prasugrel in patients who are intermediate or poor metabolizers.

Despite these recommendations, there remains controversy surrounding the use of CYP2C19 genotype information to guide antiplatelet therapy. An expert consensus statement published in the Journal of American College of Cardiology states that genotype data may provide prognostic data for cardiovascular risk prediction but is not routinely recommended to guide escalation or de-escalation of antiplatelet therapy. Different randomized controlled trials evaluated genotype-guided therapy but have failed to show superiority compared to non-genotype guided therapy. These trials, however, have been limited due to small sample size. Multiple meta-analyses as well as a real-world analysis showed that genotype-guided selection of antiplatelet therapy significantly reduced the risk of ischemic events post-PCI in both ACS and stable CAD settings. CYP2C19 metabolizer status is, therefore, an important consideration in addition to other clinical characteristics when selecting antiplatelet therapy for post-PCI.

Audience Response Questions

1. Which of the following P2Y12 inhibitors does not require activation by the liver to exert antiplatelet effects?
    a. Clopidogrel
    b. Prasugrel
    c. Ticagrelor
2. What are the clinical implications for a patient identified as a CYP2C19 poor metabolizer?
    a. Increased risk for bleeding if taking clopidogrel
    b. Increased risk of ischemic events if taking clopidogrel
    c. Decreased risk of ischemic events if taking clopidogrel
    d. No effect on risk of ischemic events if taking clopidogrel
3. True or false: CYP2C19 genotyping has been evaluated post-PCI in both ACS and stable CAD settings
    a. True
    b. False

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