FAST FACTS: EVIDENCE FOR GENOTYPE-GUIDED ANTIPLATELET THERAPY IN PATIENTS WITH CORONARY ARTERY DISEASE

Pre-emptive pharmacogenomic testing has been proven to reduce adverse drug reactions.

Dual antiplatelet therapy with aspirin and a $P2Y_{12}$ receptor inhibitor (clopidogrel, prasugrel, or ticagrelor) remains the standard of care for the prevention of ischemic events in patients with coronary artery disease, in particular those with acute coronary syndrome (ACS) or in patients undergoing percutaneous coronary intervention (PCI). Clopidogrel is the most commonly prescribed $P2Y_{12}$ inhibitor because of its favourable safety profile, low cost, and broad indications for use.

Approximately 30% of patients treated with clopidogrel have high on-treatment platelet reactivity (HPR), an established marker of thrombotic risk in patients undergoing PCI. More potent $P2Y_{12}$ inhibitors like prasugrel and ticagrelor can overcome this limitation, but are more expensive and have a higher risk of bleeding complications.

One important reason for clopidogrel response variability is genetic polymorphisms of the *CYP2C19* enzyme. Carriers of loss-of-function (LoF) alleles for *CYP2C19* are characterised by reduced generation of clopidogrel's active metabolite, leading to increased rates of HPR and enhanced risk for thrombotic complications.

A meta-analysis published in JACC in 2021 reviewed results of seven randomised controlled trials involving 15 949 patients. The authors concluded that the selective use of prasugrel or ticagrelor among *CYP2C19* LoF carriers, combined with the selective use of clopidogrel among non-carriers of LoF alleles, results in a clinically significant reduction in bleeding complications while avoiding the increased ischemic risk associated with unselected use of clopidogrel (see diagram on next page).

Meta-Analysis results:
Individualising oral $P2Y_{12}$ inhibitor therapy

Indications: Coronary Artery Disease - Acute Coronary Syndrome
± Percutaneous Coronary Intervention
7 RCTs - 15 949 patients - 98% (ACS), 77% (PCI)

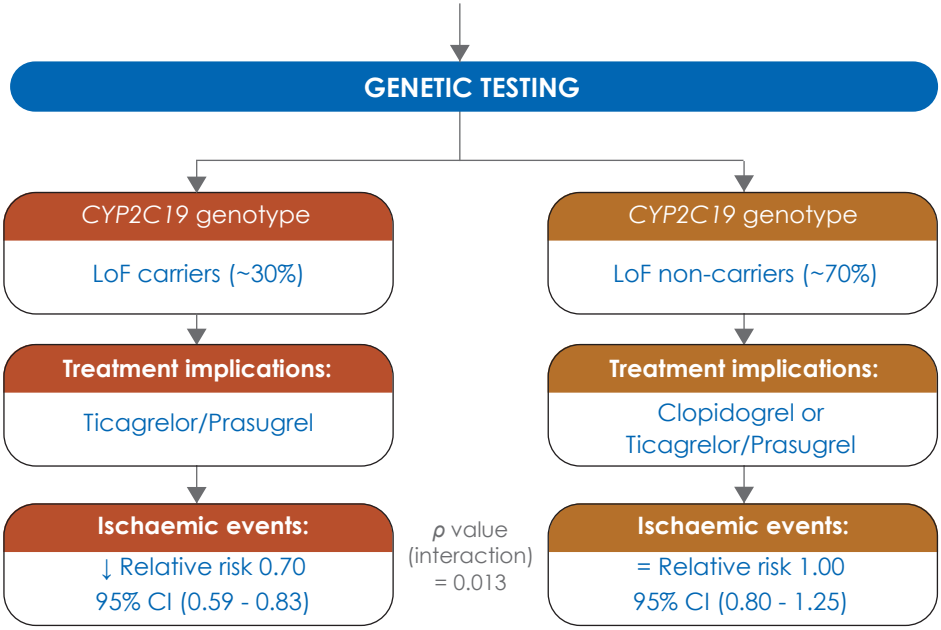

Diagram adapted from: Pereira, N.L. et al. J Am Coll Cardio Intv. 2021;14(7):739-50

- *CYP2C19* genotyping is performed as part of our comprehensive pharmacogenomics panel (Test Mnemonic: **PHARMA**).
- Results are available within 10 working days.

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