Circulation Journal
doi:10.1253/circj.CJ-22-0826

ORIGINAL ARTICLE

Clopidogrel Use in *CYP2C19* Loss-of-Function Carriers With High Bleeding Risk After Percutaneous Coronary Intervention

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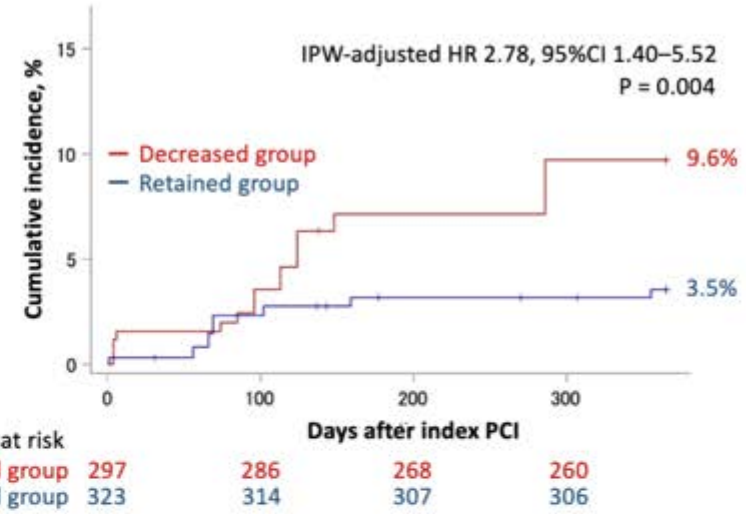
Background: It is not known whether clopidogrel use in cytochrome P450 (CYP) 2C19 loss-of-function (LOF) carriers with high bleeding risk (HBR) contributes to adverse outcomes after percutaneous coronary intervention (PCI).

Methods and Results: This retrospective observational study included 618 consecutive patients with available *CYP2C19* polymorphism information who underwent PCI between September 2014 and August 2021. Patients with HBR (319 [52%] met the Academic Research Consortium definition) were divided into 2 groups according to $P2Y_{12}$ inhibitor action, namely decreased (i.e., clopidogrel in *CYP2C19* LOF carriers) and retained (i.e., clopidogrel in *CYP2C19* LOF non-carriers or prasugrel regardless of *CYP2C19* polymorphisms), and clinical outcomes at 1 year were compared using inverse probability-weighted Cox proportional hazard regression. The primary ischemic outcome (a composite of cardiovascular death, myocardial infarction, or ischemic stroke) was significantly higher in the decreased than retained group (10.2% vs. 3.0%; adjusted hazard ratio [aHR] 2.78; 95% confidence interval [CI] 1.40–5.52; P=0.004). The primary bleeding outcome (Bleeding Academic Research Consortium 3 or 5) did not differ significantly between the decreased and retained groups (3.4% vs. 6.9%, respectively; aHR 0.48; 95% CI 0.22–1.01; P=0.054). There were no interactions between the treatment groups and HBR status in primary ischemic and bleeding outcomes.

Conclusions: Among patients with HBR, clopidogrel use in *CYP2C19* LOF carriers was significantly associated with increased ischemic events after PCI.

Key Words: *CYP2C19*; High bleeding risk; Percutaneous coronary intervention

(A) Ischemic events (CVD/MI/stroke)



(B) Bleeding events (BARC 3 or 5)