

ALTERNATIVE VIEWPOINTS

PPIs and Plavix: So, What To Do Now?

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Kreutz and colleagues should be commended for their publication entitled “Impact of Proton Pump Inhibitors on the Effectiveness of Clopidogrel after Coronary Stent Placement: The Clopidogrel Medco Outcomes Study.”¹ Unfortunately, there is little discussed in the original article or accompanying editorial in terms of guidance when there are no alternatives to using a proton pump inhibitor (PPI) with clopidogrel (e.g., failing/intolerance of H2 antagonists, Barrett’s esophagus, thrombocytopenia, *Helicobacter pylori* infection, etc...). We suggest that further clarification on the role of rabeprazole may help to ease concern with this tenuous drug-drug interaction (DDI).

While Kreutz and colleagues do mention that rabeprazole has demonstrated a lower inhibitory potential towards CYP2C19, the use of rabeprazole as an option for patients on clopidogrel was not thoroughly discussed.¹

Various sources have mentioned the possible use of rabeprazole in clopidogrel patients. Li and colleagues showed that rabeprazole has the least inhibitory effects compared to lansoprazole, omeprazole, and esomeprazole.² The rabeprazole thioether metabolite has a greater inhibitory effect on CYP2C19 than the parent compound but less than that of omeprazole.^{2,3}

Ishizaki and colleagues introduced an

intriguing topic; that patients at the highest risk for this DDI may actually have the lowest risk of a DDI when using rabeprazole.³ Poor S-mephenytoin 4'-hydroxylase metabolizers will have significantly high omeprazole AUCs when compared to extensive metabolizers. Poor metabolizers also have higher AUCs of rabeprazole's parent compound which has lower inhibitory potential on CYP2C19.⁴ In contrast, Furuta and colleagues analyzed different CYP2C19 genotypes and found that the combination of clopidogrel and the PPIs (specifically omeprazole, lansoprazole, and rabeprazole) on poor CYP2C19 metabolizers varies.⁵ So, what to do now?

It is generally accepted that inhibitory effect on CYP2C19 plays a significant role in the PPI/clopidogrel DDI. Therefore, a medication that has less potential inhibition of CYP2C19, like rabeprazole, would be reasonable to use in a situation that requires the concomitant use of a PPI and clopidogrel.

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Authors' Reply

The authors appreciate Dr. Riche's insightful thoughts; we reiterate the call to make sure that a Proton Pump Inhibitor is absolutely required before prescribing with clopidogrel, and that while rabeprazole may represent a rational option, further prospective/retrospective data would be needed to say anything further.