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Proton Pump Inhibitors and Antiplatelet Drugs Can Be Used Together Following Careful Consideration of the Risks and Benefits

For patients at high risk of GI bleeding who require antiplatelet therapy for heart disease, the balance of risk and benefit favor concomitant use of acid suppressing drugs (PPIs)

(Washington, DC) – November 8, 2010 — Using proton pump inhibitors (PPIs) and antiplatelet drugs (thienopyridines) together is an appropriate way of treating patients with cardiovascular (CV) disease who are at high risk of upper gastrointestinal (GI) bleeds, despite recent concerns about an adverse interaction between these two types of drugs, according to an Expert Consensus Document released jointly today by the American College of Cardiology Foundation (ACCF), the American College of Gastroenterology (ACG), and the American Heart Association (AHA).

The potential benefits of antiplatelet therapy for patients with atherosclerotic CV disease have been amply demonstrated, especially among patients at higher risk of CV events. However, use of antiplatelet drugs increases the risk of upper GI bleeding from pre-existing ulcers, lesions and other tissue breaks in the GI tract. Those at highest risk for GI bleeding are patients with a history of previous GI bleeding, as well as patients with multiple risk factors for upper GI bleeding, including: a history of peptic ulcer disease; advanced age; use of anticoagulants, steroids, or NSAIDs; and *H. pylori* infection.

"PPIs are prescribed together with antiplatelet drugs for one reason — to reduce the increased risk of GI complications caused by antiplatelet drugs," according to the new expert consensus document. PPIs suppress gastric acid production, which helps heal the pre-existing lesions and NSAID- and aspirin-related ulcers.

"Our goal was to carefully evaluate recent studies that suggested a potential dangerous interaction between PPIs and thienopyridines, in order to provide clinicians with a pragmatic evidence-based approach for safer prescribing of antiplatelet drugs, especially among patients in whom the risk-benefit ratio requires a careful assessement," said Neena S. Abraham, M.D., MSCE, FACG, a gastroenterologist at the Michael E. DeBakey VAMC and Baylor College of Medicine, the chair of the document's writing committee. "The document summarizes the best evidence and incorporates the expert clinical viewpoints of both cardiologists and gastroenterologists, who face this dilemma on a daily basis."

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Conflicting Data Clouded Clinical Picture for PPIs and Antiplatelet Drugs

Following the publication of the organizations' 2008 document recommending simultaneous prescription of a PPI in high-risk patients, new research suggested an adverse interaction between the two drugs that may lessen the antiplatelet effects of thienopyridines and thereby place patients at an increased risk of CV events. Experts from the ACCF, ACG and AHA observe that it has been difficult for physicians to assimilate this flood of information and to develop optimal treatment strategies for managing patients who might benefit from antiplatelet therapy, yet who might suffer from GI bleeding.

"The flurry of conflicting data published following the 2008 Expert Consensus Document left many practitioners confused," Abraham commented. "However, much of the published data used results of platelet function tests as surrogate markers of cardiovascular risk. The differences in drug levels and in platelet function studies caused concern about an adverse drug interaction, but the clinical significance of these laboratory test results has not been substantiated when held to the higher scientific standard of large patient studies with clinically relevant endpoints, such as heart attacks or strokes."

Moreover, the recent publication of a randomized trial (COGENT) of 3761 patients with cardiovascular disease demonstrated a substantial decrease (56 percent) in GI bleeding, with no significant difference in cardiac events, among the patients randomized to concomitant use of clopidogrel and a PPI compared with patients randomized to clopidogrel alone. "This study is of particular importance as it is the only published randomized controlled trial specifically designed to assess the clinical occurrence of GI bleeding, heart attacks and strokes associated with the prescription of clopidogrel alone versus clopidogrel with a PPI," noted Dr. Abraham.

New Recommendations Clarify Appropriate Therapy by Weighing Risk-Benefit

The new recommendations include:

- The use of PPIs is recommended for patients with a history of upper GI bleeding or for those with multiple risk factors for upper GI bleeding, including a history of peptic ulcer disease; advanced age; use of anticoagulants, steroids, or NSAIDs; and *H. pylori* infection.

- PPIs are not recommended to reduce upper GI bleeding in patients who have a lower risk of upper GI bleeding, and who have much less potential to benefit from prophylactic therapy.

- Future studies are required to assess the impact of concomitant PPI and antiplatelet use among the small subset of high-risk cardiac patients with an impaired ability to metabolize antiplatelet drugs.

"Use of PPIs and antiplatelet drugs must be individualized, not done as a matter of routine," said Mark A. Hlatky, M.D., FACC, a cardiologist at Stanford University School of Medicine and vice-chair of the writing

group. "The risk of GI bleeding varies among individuals, as does the risk of cardiac events. In patients at high risk of GI bleeding who require antiplatelet therapy for heart disease, the balance of risk and benefit favor use of PPIs together with antiplatelet drugs. In patients at low risk of GI bleeding, however, the balance of risk and benefit tips away from using PPIs together with antiplatelet drugs. We need additional research to determine whether genetic testing or platelet function testing are useful in individualizing treatment with antiplatelet drugs."

Full text of this report will be published in the *Journal of the American College of Cardiology, The American Journal of Gastroenterology*, and *Circulation: Journal of the American Heart Association.* It will also be available on the ACC (www.cardiosource.org), AHA (www.heart.org), and ACG (www.acg.gi.org) web sites.

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