Letters

I read with interest Dr. Gurbel's article "Transitioning to Generic Clopidogrel" in the May/June 2012 issue of *Cardiac Interventions Today*. While I respect the work of platelet experts to the field of interventional cardiology, the topic of "clopidogrel nonresponders" is much more complex than presented. While 30% of the PCI population may be pharmacologic nonresponders to clopidogrel, the clinical relevance of this phenomenon is nebulous at best. Even if we assume that only one-third of these "nonresponders" actually have clinical events (ie, stent thrombosis), that would amount to approximately 5 million patients with stent thrombosis in the United States alone, which is hardly the case. This "exaggerated threat" of clopidogrel nonresponders was evident in GRAVITAS[1] and TRIGGER-PCI.[2] Which leads me to the question, "How many patients who are compliant with clopidogrel actually present with stent thrombosis?" Not many. In GRAVITAS, the stent thrombosis rate was < 0.8%; in TRIGGER-PCI, it was 0%. Considering that perhaps the biggest factor affecting medication compliance is cost, adopting the practice of picking newer antiplatelet drugs "regardless of cost" is irresponsible not only to the patient but also to society as a whole.

Payam Fallahi, MD, FACC, FSCAI
Interventional Cardiology
Hagerstown Heart, PA
Hagerstown, Maryland

1. Price MJ, Berger PB, Teirstein PS, et al. Standard- vs high-dose clopidogrel based on platelet function testing after percutaneous coronary intervention: the GRAVITAS randomized trial. JAMA. 2011;305:1097-1105.
2. Trenk D, Stone GW, Gawaz M, et al. A randomized trial of prasugrel versus clopidogrel in patients with high platelet reactivity on clopidogrel after elective percutaneous coronary intervention with implantation of drug-eluting stents: results of the TRIGGER-PCI (Testing Platelet Reactivity In Patients Undergoing Elective Stent Placement on Clopidogrel to Guide Alternative Therapy With Prasugrel) study. J Am Coll Cardiol. 2012;59:2159-2164.

RESPONSE

We are glad that Dr. Fallahi is interested in the issue of stent thrombosis and clopidogrel nonresponsiveness. It is a very important subject, with highly significant clinical implications. The recent prospective ADAPT-DES study[1] (n = 8,349) clearly demonstrated the relation of high platelet reactivity (HPR) to stent thrombosis and will help address any confusion. In this very large study, stented patients with HPR (PRU > 208) had a four-times greater risk for 30-day stent thrombosis; 50% of stent thrombosis occurrence was solely attributable to HPR by multivariate analysis.

The observations from ADAPT-DES clearly indicate that this risk is far from "exaggerated" and is far greater than the risk of myocardial infarction occurrence associated with diabetes according to epidemiologic data (eg, Framingham study). We certainly don't ignore the increased cardiovascular risk in the patient with diabetes, so how can we rationalize ignoring an even greater thrombotic risk in the patient with HPR? Moreover, in the patient-based meta-analysis of Brar et al[2] (n = 3,059), there was an eight-fold increased occurrence of 2-year stent thrombosis in patients with the highest quartile of platelet reactivity compared to the lowest quartile.

The data from ADAPT-DES, Brar et al, and others involving many thousands of patients conclusively demonstrate that stent thrombosis is not as rare as Dr. Fallahi suggests, and indeed, it is a "real threat" in patients with HPR. Identifying patients with HPR on clopidogrel who have an increased risk for stent thrombosis and treating them selectively with a new $P2Y_{12}$ inhibitor appears to be a cost-effective and rational approach to us rather than a nonselective, "one-size-fits-all" strategy. We believe it is irresponsible to administer a drug that is pharmacodynamically unpredictable to a patient with high-risk coronary artery disease when we clearly know the increased risk carried by HPR. Moreover, it is wasteful to administer a drug that is pharmacodynamically ineffective in up to 30% to 40% of patients. We strongly encourage everyone to read our recent review article in *Circulation*[3] for detailed coverage of personalized antiplatelet therapy. ■

Paul A. Gurbel, MD
Udaya S. Tantry, PhD
Sinai Center for Thrombosis Research
Cardiac Catheterization Laboratory
Baltimore, Maryland

1. Stone GW. Assessment of Dual-AntiPlatelet Therapy with Drug-Eluting Stents A Large-Scale, Prospective, Multicenter Registry Examining the Relationship Between Platelet Responsiveness and Stent Thrombosis After DES Implantation. Presented at: Transcatheter Therapeutics meeting; November 7-11, 2011; San Francisco, CA.
2. Brar SS, Ten Berg J, Marcucci R, et al. Impact of platelet reactivity on clinical outcomes after percutaneous coronary intervention; a collaborative meta-analysis of individual participant data. J Am Coll Cardiol. 2011;58:1945-1954.
3. Gurbel PA, Tantry US. Do platelet function testing and genotyping improve outcome in patients treated with antithrombotic agents? Platelet function testing and genotyping improve outcome in patients treated with antithrombotic agents. Circulation. 2012;125:1276-1287.