of IPA will result in better clinical outcome is valid, then every prasugrel regimen will be superior to clopidogrel, and there is no need to choose too aggressive prasugrel dosing risking higher bleeding rates. Conventional wisdom suggests that clopidogrel replaced ticlopidine not because of the superior efficacy, more potent IPA, or less ‘non-responders’ rates, but because of the better safety profile. Moreover, the incidence of bleeding in JUMBO, in contrast to the ‘similar rates’ stated in Introduction, was in fact 30% higher in the combined prasugrel arms (1.7%) when compared with the clopidogrel group (1.2%).2 Last but not least, it seems not appropriate to declare ‘no conflict of interest’ when most the authors are industry representatives, whose careers and stock option values are dependent heavily on the success of prasugrel.

References


3. Chen Z, Jiang LX, Chen YP, Xie JX, Pan HC, Peto R, Collins R, Liu LS; COMMIT (ClOpidogrel in Heart Disease) Investigators. Comparison of a 60 mg loading dose of prasugrel (Study Limitations). At both sites, compliance with study drug was closely monitored and aggregometry was performed using similar methods in two experienced laboratories. The potential for non-compliance to explain the inter-site IPA variability is discounted by the results obtained at the two sites with loading doses (administered to patients under direct supervision) and by the consistent dose-response pattern observed during maintenance dosing. Rather, the higher IPA levels at one site appear more likely related to different aggregometers and/or differing subject population responses. The lack of non-responders at the US site on day 28 is not surprising because only four subjects were randomized to clopidogrel at that site. Of these patients, one (23% IPA; Figure 3B) approached the non-respondent criteria (20% IPA to 20 μM ADP).

Further, the authors acknowledge that debate continues on how best to characterize clopidogrel response variability. However, clopidogrel resistance and its association with adverse clinical outcomes in PCI has been reported.3 The present study demonstrates for the first time in subjects with coronary artery disease that prasugrel has far fewer non-responders than clopidogrel, regardless of the criteria selected to define poor response.6

A statement regarding any conflict of interest was indeed submitted to the journal with the report, which unfortunately was not acknowledged in the published manuscript. However, information concerning institutional affiliations of the authors was clearly expressed in the manuscript itself.

We thank Dr Serebruany for highlighting that the current study provides new findings that clearly support the superior platelet inhibition achieved with prasugrel vs. clopidogrel. However, validation of the hypothesis that the improved antiplatelet profile of prasugrel will result in superior efficacy and acceptable safety in ACS subjects undergoing PCI must await the results of TRITON-TIMI 38.

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Tomas Jernberg
Department of Medical Sciences,
Cardiology
Uppsala Clinical Research Center
University Hospital
751 85 Uppsala
Sweden

Lars Wallentin
Department of Medical Sciences,
Cardiology
Uppsala Clinical Research Center
University Hospital
751 85 Uppsala
Sweden
Tel: +46 18 611 00 00
Fax: +46 18 50 66 38
E-mail address: lars.wallentin@ucr.uu.se