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http://dx.doi.org/10.1016/j.jacc.2015.01.055

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REPLY: Is CABG Superior to DES for Repeat Revascularization in Patients With Isolated Proximal LAD Disease?

We thank Dr. Matsoukis and colleages for their letter expressing an interest in our recent study (1).

Regarding the type of drug-eluting stents (DES) (first vs. second generation), 72% of the stents used in the propensity-matched DES/coronary artery bypass graft (CABG) pairs were second-generation DES, with the others being first-generation DES. When the pairs were limited to second-generation DES compared with CABG surgery, there were still no significant differences for mortality or for mortality/myocardial infarction/stroke. Repeat revascularization rates were again lower for CABG surgery, and the adjusted hazard ratio (AHR) was very similar to the AHR for all pairs (0.60 vs. 0.54 for all pairs).

It is possible that our results could have been different if we had used cardiac mortality instead of all-cause mortality, but unfortunately we did not have access to that measure.

It is not true that CABG surgery was associated with a significantly lower rate when we looked at the composite endpoint of mortality/myocardial infarction/stroke. As the letter states, we found the AHR to be 0.96 (95% confidence interval: 0.86 to 1.06), which is not significant because the confidence interval includes the number 1.

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http://dx.doi.org/10.1016/j.jacc.2015.02.030

Please note: Dr. Sharma has reported that he receives research grant support from Boston Scientific, Inc.; and serves on the Speakers' Bureau of Boston Scientific Inc., Abbott Vascular, Lilly, and The Medicines Company. Dr. King has reported that he receives royalties from Cordis; and serves as an Advisory Board member of Medtronic. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Has Prasugrel Been Compared Correctly With Clopidogrel in Non–ST-Segment Elevation Acute Coronary Syndrome?

We read with great interest the paper by Montalescot et al. (1) and the editorial by Ibanez and Dangas (2) about prasugrel in non-ST-segment myocardial infarction (NSTEMI), and we appreciate the research on this interesting issue. The ACCOAST (A Comparison of Prasugrel at PCI or Time of Diagnosis of Non-ST Elevation Myocardial Infarction) trial demonstrated that pre-treatment with prasugrel in NSTEMI adds no benefit compared with initiating the drug after angiography and also was associated with an increase in bleeding events (3). In the same way, in the subgroup of patients analyzed in the ACCOAST-PCI, the results are concordant with the main study in terms of same clinical outcome as well as a higher rate of bleeding events (1).

As is pointed out in the editorial, both the recent American College of Cardiology/American Heart Association and the European Society of Cardiology guidelines recommend prasugrel in NSTEMI only after angiography, and this fact places prasugrel as a second-line agent. Although prasugrel showed benefit over clopidogrel in the TRITON (Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel), the design of the trial was criticized due to the 300-mg loading dose of clopidogrel and also the administration after angiography instead of earlier, probably limiting the effect of clopidogrel, the effect of which takes longer to act.

In our opinion, the right comparison between prasugrel and clopidogrel in NSTEMI has still not been carried out. If we review both the results of the CREDO (Clopidogrel Maintaining Dosage in Acute Coronary Syndrome After Drug Eluting Stent Implantation) and ACCOAST, we can assume that the best moment to initiate clopidogrel would be as soon as possible after admission and just after the initial angiography for prasugrel. Both drugs have theoretical advantages such as an unrestricted spectrum of patients (4,5), fewer bleeding events, more experience with the drug, and lower cost of clopidogrel versus more rapid onset and action, a reduction in nonfatal coronary events and stent thrombosis, and avoiding the administration of the drug in patients who would need surgery once the anatomy is known for prasugrel. Although it is highly improbable that a prospective and adequately powered study will be designed 8 years after the publication of the TRITON trial and with the presence of ticagrelor in the market, we believe that the only way to have the correct answer for prasugrel and clopidogrel in NSTEMI would be to compare in ischemic and bleeding events the pre-treatment with clopidogrel with the administration of prasugrel after the initial angiography, and it would probably be the only way for prasugrel to once again become a first-line treatment for these patients.

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http://dx.doi.org/10.1016/j.jacc.2015.01.056

Please note: Dr. Lozano has received honoraria for lectures about ticagrelor. The other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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REPLY: Has Prasugrel Been Compared Correctly With Clopidogrel in Non–ST-Segment Elevation Acute Coronary Syndrome?

We thank Dr. Lozano and colleagues for their interest in our paper. However, they misinterpret the results of the ACCOAST (Comparison of Prasugrel at PCI or Time of Diagnosis of Non-ST Elevation Myocardial Infarction) and of the preceding trials. Placing the new $P2Y_{12}$ antagonists in general and prasugrel in particular as a second-line treatment in non-ST-segment elevation myocardial infarction (NSTEMI) does not reflect the superiority demonstrated by these new drugs over clopidogrel in 2 pivotal trials. It does not comply with the current guidelines, especially for the patients undergoing percutaneous coronary intervention, as both prasugrel and ticagrelor have a class I recommendation, whereas clopidogrel should be given "only when prasugrel or ticagrelor are not available or are contraindicated" (1). So the first error is to believe that clopidogrel is still the gold standard for the treatment of NSTEMI.

The second error is to believe that pre-treatment with a $P2Y_{12}$ antagonist is of benefit to NSTEMI patients. Pre-treatment is a treatment given to the patients while they wait to undergo coronary angiography. Although Dr. Lozano thinks that this is the right thing to do with clopidogrel, it has never been validated by a randomized study. This question of clopidogrel pre-treatment was not evaluated in the CURE (Clopidogrel in Unstable Angina to Prevent Recurrent Events) study because the majority of patients did not have coronary angiography performed in this study. It was also not addressed by the CREDO (Clopidogrel for the Reduction of Events During Observation) study because the coronary status of the majority of patients was known at the time of randomization (2). No study