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Letters

TO THE EDITOR

Lights and Shadows of Antiplatelet Therapy in Primary Percutaneous Coronary Intervention

We have read with great interest the paper written by Zeymer et al. (1), and the authors should be praised for the investigation into this relevant issue. Ticlopidine was rapidly displaced by clopidogrel because the new drug solved the risk of bone marrow aplasia, and consequently, it became the drug of choice during the last decade. After the publication of the TRITON (Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel) and PLATO (Platelet Inhibition and Patient Outcomes) trials, both the European and American College of Cardiology/American Heart Association guidelines recommended the 3 agents in primary percutaneous coronary intervention (PPCI) with Class I, Level of Evidence: B, with the comment in the European document that both prasugrel and ticagrelor, unless contraindicated, should be the first-line agents over clopidogrel. In the present study, Zeymer et al. randomized 62 subjects to 600 mg of clopidogrel versus 60 mg of prasugrel scheduled for PPCI, and because prasugrel achieves a lower platelet reactivity index, the authors concluded that prasugrel should be preferred to clopidogrel in PPCI. In our opinion, there are no doubts about the faster and more powerful effect in platelet inhibition with prasugrel, but this fact should not be directly translated into a recommendation of utilization. Antithrombotic therapy in acute coronary syndromes (ACS) should always be dictated by an essential balance between ischemic and bleeding risks, and we should keep in mind that the main limitation of the new drugs is their risk of bleeding. In the TRITON study, although prasugrel was superior to clopidogrel in the whole cohort of patients with ST-segment elevation myocardial infarction, the dose of clopidogrel was suboptimal and the benefit was due to the patients with secondary PCI, without significant differences in the subgroup of PPCI (2). In the same way, in the 7,544 patients with ST-segment elevation myocardial infarction in the PLATO trial, ticagrelor was superior to clopidogrel in all the endpoints with the exception of a significant increase of cerebrovascular accidents that finally placed the p value at a level of 0.07 (3). We believe that because the guidelines give the same level of recommendation to the 3 agents, none of them has demonstrated a definitive benefit over the other, and although the new drugs have shown more powerful effect, there are still shadows in the decision about the preferred drug. The fact that clopidogrel has no contraindications and prasugrel is limited in a significant percentage of patients (4) could mean that maybe with the former, we have reached the safest possible balance between ischemia and bleeding. Because it has been suggested that the benefits of ticagrelor in ACS with even a discrete reduction in mortality and fewer contraindications would be mediated, not only by $P2Y_{12}$ antagonism, but also by its adenosine-like effect (5), maybe we should assume that in the future, we should focus the research in ACS on drugs with a well-balanced $P2Y_{12}$ antagonism but with an additional way of platelet inhibition.

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Please note: Dr. Lozano has lectured about ticagrelor for AstraZeneca. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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REPLY: Lights and Shadows of Antiplatelet Therapy in Primary Percutaneous Coronary Intervention

We thank Lozano et al. for their thoughtful comments on our ETAMI (Early Thienopyridine Treatment to Improve Primary PCI in Patients With Acute Myocardial Infarction) trial (1) and fully agree with their statement that in antithrombotic therapy, there should always be a balance between efficacy and safety. Our study has investigated the very acute phase of primary percutaneous coronary intervention (PCI) in ST-segment elevation myocardial infarction (STEMI) in which a faster onset of action of a platelet inhibition effect is desirable to reduce ischemic complications of the procedure. In the recently published ATLANTIC (A 30 Day Study to Evaluate Efficacy and Safety of Pre-hospital vs. In-hospital Initiation of Ticagrelor Therapy in STEMI Patients Planned for Percutaneous Coronary Intervention) trial, a very early initiation of ticagrelor in the pre-hospital phase leading to clinical relevant difference in platelet inhibition 1 h after PCI was associated with a reduction in stent thrombosis compared with the same loading dose started on average 31 min later in the hospital (2). In addition, there are several reports linking inadequate platelet inhibition at the time of PCI to ischemic complications, underscoring the importance of an effective platelet periprocedural inhibition during primary PCI (3). In the TRITON (Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel) trial, patients with STEMI have especially benefited from prasugrel compared with clopidogrel without an increase in bleeding complications (4). These results were confirmed by recent reports from real-life experience of registries. Bleeding complications in TRITON accumulated over time but were not statistically different between clopidogrel and prasugrel in the primary PCI group at 30 days as well as at 15 months (4). The net clinical benefit was clearly in favor of prasugrel. The statement about a differential effect of prasugrel between secondary and primary PCI in STEMI is not correct, and this reference indicated no statistical heterogeneity between the 2 groups (4). This has been now well evaluated, and there is no significant interaction for the primary and secondary endpoints and a consistent effect of prasugrel across all types of PCI performed in STEMI patients (5). The numerical differences are related to the difficulties in measuring periprocedural MI in primary PCI versus secondary PCI and not related to the efficacy of prasugrel (5). The statement about contraindications against prasugrel majorly relates to patients with prior stroke, which is present in up to 3% of STEMI patients. Elderly or patients with low body weight <60 kg might be treated with the same loading dose of 60 mg and a lower maintenance dose of 5 mg to reduce bleeding complications.

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Triple Antithrombotic Therapy Following Anterior ST-Segment Elevation Myocardial Infarction

We would like to commend LeMay et al. (1) for their work addressing the important clinical conundrum of whether to provide triple antithrombotic therapy (TATT) for patients presenting apical akinesis/