Letters to the Editor

Risk of ticagrelor versus clopidogrel discontinuation

Riesgo de interrupción del ticagrelor frente al clopidogrel

To the Editor,

In their recent article, Almendro-Delia et al.[1] concluded that the association between nonadherence to ticagrelor vs clopidogrel and the risk of major adverse cardiac events (MACE) was not modulated by the choice of $P2Y_{12}$ receptor inhibitor. Nonetheless, 60 of the 1078 patients on ticagrelor (5.5%) stopped using this drug, while almost twice as many (114/1102 patients, 10.4%) stopped using clopidogrel. In the analysis of factors associated with premature cessation of dual antiplatelet therapy (DAPT), ticagrelor (vs clopidogrel) had an adjusted hazard ratio of 0.97 (95%CI, 0.93-1.01) and a *P* value of .080, suggesting that the association between nonadherence to DAPT and MACE can in fact be modulated by choice of inhibitor. That said, previous studies have shown an increased risk of bleeding with ticagrelor compared with clopidogrel,[2–4] whereas the data presented by Almendro-Delia et al.[1] seem to suggest that patients on clopidogrel have a lower risk of DAPT cessation than those on ticagrelor. These findings warrant further discussion and clarification.

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STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

Artificial intelligence was not used for this work.

CONFLICTS OF INTEREST

None.

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REFERENCES

1. Almendro-Delia M, Padilla-Rodríguez G, Hernández-Meneses B, et al. Nonadherence to ticagrelor versus clopidogrel and clinical outcomes in patients with ACS. Results from the CREA-ARIAM registry. *Rev Esp Cardiol.* 2023 https://doi.org/10.1016/j.rec.2023.05.011.
2. Navarese EP, Khan SU, Kołodziejczak M, et al. Comparative Efficacy and Safety of Oral P2Y12 Inhibitors in Acute Coronary Syndrome: Network Meta-Analysis of 52 816 Patients From 12 Randomized Trials. *Circulation.* 2020;142:150–160.
3. Gimbel M, Qaderdan K, Willemsen L, et al. Clopidogrel versus ticagrelor or prasugrel in patients aged 70 years or older with non-ST-elevation acute coronary syndrome (POPular AGE): the randomised, open-label, non-inferiority trial. *Lancet.* 2020;395:1374–1381.
4. Mullen L, Meah MN, Elamin A, et al. Risk of Major Bleeding With Potent Antiplatelet Agents After an Acute Coronary Event: A Comparison of Ticagrelor and Clopidogrel in 5116 Consecutive Patients in Clinical Practice. *J Am Heart Assoc.* 2021;10:e019467.

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Risk of ticagrelor versus clopidogrel discontinuation. Response

Riesgo de interrupción del ticagrelor frente al clopidogrel. Respuesta

To the Editor,

In reference to the article published in *Revista Española de Cardiología,*[1] it is accurate to note that the overall unadjusted treatment interruption rate was higher with clopidogrel than with ticagrelor due to greater physician-guided discontinuation ($P = .003$, Table 4 of the supplementary material)[1], and was not associated with a higher risk of major adverse cardiovascular events (MACE) ($P = .079$). In contrast, the rate of disruptions was proportionally higher with ticagrelor ($P = .003$, Table 4 of the supplementary material)[1], especially in the 90 days following the index acute coronary syndrome ($P < .001$, Table 4 of the supplementary material). Taking this into consideration, disruption was indeed associated with a higher risk of MACE ($P = .001$), particularly when it occurred within the first 90 days of treatment (adjusted hazard ratio, 3.83; $P < .001$, Figure 7 of the supplementary material), unlike what was seen with physician-guided discontinuation. Therefore, after adjustment for potential differential nonadherence based on the $P2Y_{12}$ receptor inhibitor used, the time to interruption (earlier with ticagrelor than clopidogrel: 22 vs 53 days; $P = .035$, Table 5 of the supplementary material)[1], and the interaction between these 2 variables on an additive scale, the association between mode/timing of treatment interruption and MACE risk according to the type of $P2Y_{12}$ receptor inhibitor did not reach statistical significance (Table 5 of the