Intolerance to aspirin in patients undergoing percutaneous coronary intervention in the setting of chronic coronary syndromes: perspectives from the ESC 2019 Chronic Coronary Syndromes guidelines

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Bianco *et al* draw attention to the therapeutic challenge that aspirin intolerance not uncommonly presents to interventional cardiologists. In the ESC 2019 Guidelines on Chronic Coronary Syndromes, we describe several relevant points in this regard.[1] Firstly, we state that other nonselective non-steroidal anti-inflammatory drugs are not suitable as an alternative to aspirin in view of their adverse cardiovascular risk profile. Secondly, we provide a class IIb recommendation for using prasugrel or ticagrelor in patients who cannot tolerate aspirin. We don't suggest an alternative to aspirin as part of a dual therapy strategy with prasugrel or ticagrelor but do describe the results of the GEMINI ACS study in which rivaroxaban 2.5 mg b.i.d. in combination with an oral $P2Y_{12}$ inhibitor was compared with standard DAPT and shown to have similar efficacy, albeit in stabilized patients after uncomplicated percutaneous coronary intervention (PCI) in the presence of aspirin.[2] This presents the possibility of using such a regimen in patients where there are concerns about the risk of stent thrombosis with prasugrel or ticagrelor monotherapy. However, currently there is insufficient evidence on which to base any recommendations for such a strategy, particularly since, as we indicate, the safety of performing PCI without aspirin pre-treatment is uncertain.

Desensitization is routinely used in many PCI centres to deal with patients who have sensitivity to aspirin,[3,4] as pointed out by Bianco *et al*, and we were not able to include exhaustive details about pharmacotherapy for PCI in the guidelines. Providing concise guidance in this area is complicated by the marked variability in the severity of the different adverse reactions to aspirin, such that the safety of aspirin desensitization likely relates to the severity of previous adverse reaction. Many patients may report a history of intolerance to aspirin that cannot be confidently attributed to an allergic or other adverse response to aspirin. Non-life-threatening adverse reactions such as urticaria, mild angioedema and mild bronchospasm are probably more suited to a desensitization strategy whereas it may be preferable to avoid aspirin in those with a history of aspirin-associated Samter's triad, severe bronchospasm, anaphylaxis or anaphylactoid reactions, in which case prasugrel or ticagrelor, with or without rivaroxaban 2.5mg b.i.d. (depending on the stent thrombosis risk), may be a preferable strategy pending further evidence in this area.

A further consideration is that, although studies of aspirin desensitisation show generally favourable short-term tolerability outcomes in small cohorts with wide heterogeneity in aspirin intolerance, longer-term outcomes for a desensitization strategy are less certain, which further prohibited any recommendation for this in preference to alternative antithrombotic strategies. Further work is required

on the safety and efficacy of different approaches to managing patients with aspirin intolerance so that this can be addressed in future guidelines.

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