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Editorial

Does Rivaroxaban Better than Vitamin K Antagonists in Atrial Fibrillation Patients Undergoing PCI?

Abbreviations

ACS: Acute Coronary Syndrome; AF: Atrial Fibrillation; DAPT: Dual Antiplatelet Therapy; INR: International Normalized Ratio; MI: Myocardial Infarction; PCI: Percutaneous Coronary Intervention; PIONEER AF-PCI: Open-Label, Randomized, Controlled, Multicenterstudy Exploring two Treatment Strategiesof Rivaroxaban and a Dose-Adjusted Oral Vitamink Antagonist Treatment Strategy in Subjectswith Atrial Fibrillation Who Undergo Percutaneous Coronary Intervention; TIMI: Thrombolysis In Myocardial Infarction; VKA: Vitamin K Antagonist

Editorial

Approximately 15% of AF patients have a history of myocardial infarction. Between 5–15% of them will require stenting at some point in their lives with the need for a triple therapy combining an oral anticoagulant, a P2Y12 Inhibitor and aspirin [1-3].

This combination requires careful evaluation of bleeding risk, stroke risk and the risk of acute coronary syndromes (ACS) to reduce the risk of major hemorrhage [4-6].

In this context, the PIONEER AF-PCI [7], trial was conducted to evaluate the effectiveness and safety of anticoagulation with rivaroxaban plus either one or two antiplatelet agents.

PIONEER AF-PCI included 2.124 patients with non-valvular AF (paroxysmal, persistent or permanent), oral anticoagulation for at least 3 months, and undergoing coronary angioplasty with stent placement. Within 3 days of the intervention, these patients were randomized to 3 antithrombotic treatments:

- Group 1: rivaroxaban at a dose of 15 mg once daily (or a dose of 10 mg once daily in moderate renal impairment with creatinine clearance of 30 to 50 ml per minute) plus clopidogrel at a dose of 75 mg once daily or ticagrelor at a dose of 90 mg twice daily or prasugrel at adose of 10 mg once daily for 12 months.

- Group 2 : rivaroxaban at a dose of 2.5 mg twice daily plus dual antiplatelet therapy (DAPT) with low-dose aspirin (75 to 100 mg per day) and clopidogrel at a dose of 75 mg once daily (or ticagrelor at a dose of90 mg twice daily or prasugrel at a dose of 10 mg once daily) for a prespecified duration of 1, 6, or 12 months followed by rivaroxaban 15 mg / d (or 10 mg / day in moderate renal insufficiency) in combination with aspirin until the end of the 12th month.

- Group 3 : Vitamin K Antagonist (VKA) warfarin once daily (with dose adjustment to achieve a targetINR of 2.0 to 3.0) plus DAPT with low-dose aspirin (75 to 100 mg per day) and clopidogrel at a dose of 75 mg once daily (or ticagrelor at a dose of 90 mg twice daily or prasugrelat a dose of 10 mg once daily for a prespecified duration of 1, 6, or 12 months followed by an VKA in association with aspirin until the end of the 12th month.

In the majority of cases, investigators chose to prolong antiplatelet therapy for 12 months and the anti-P2Y 12 used was clopidogrel.

The primary safety end point was the occurrence of clinically significant bleeding (a composite of major bleeding or minor bleeding according to Thrombolysis in Myocardial Infarction (TIMI) criteria or bleeding requiring medical attention) during the treatment period.

Secondary end points included the incidence of each component of the primary safety end point, as well as the following efficacy end points: the occurrence of a major adverse cardiovascular event (a composite of death from cardiovascular causes, myocardial infarction, or stroke), each component of

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the major adverse cardiovascular event end point, and stent thrombosis.

The results show a marked reduction in bleeding in the two groups under rivaroxaban compared to patients in the third comparator group under VKA: 16.8%, 18% versus 26.7%. The relative risks of bleeding in group 1 versus group 3 and group 2 versus group 3 were 0.59 (95% CI [0.47-0.76]), and 0.63 (95% CI [0,50-0.80]), respectively.(p<0.001).

Regarding the antithrombotic efficacy of the three protocols for prevention of thrombosis, the incidence of the composite criterion (CV death, MI, stroke) was not significantly different in the three groups: 6.5%, 5.6%, and 6% respectively. The groups do not differ in terms of CV death, MI or stroke, considered independently.

The safety of protocols 1 or 2, compared to protocol 3, therefore seems to be gained. The question that remains unresolved is that of antithrombotic efficacy, and in particular with respect to stroke, since it is nevertheless their prevention that is aimed at anticoagulation in the AF.

The study does not establish, and even does not test frankly, non-inferiority in stroke prevention, strategies based on rivaroxaban compared to the standard of care that constitutes a VKA added to the dual antiplatelet therapy.

PIONEER was not sized for efficacy since patients at high risk of stroke were relatively few.

It should be noted that the doses of rivaroxaban used in PIONEER are below the recommended 20 mg once daily in AF and that if the risk of stroke is not significantly different in group 1 versus 3 and in group 2 versus 3, the confidence intervals are considerable.

There are currently several ongoing studies on the benefits of new anticoagulants in patients with AF receiving a stent: REDUAL PCI with dabigatran, AUGUSTUS with apixaban, ENTRUST-AF-PCI with edoxaban.

However, PIONEER remains an important contribution to the data available in this field, which is in fact very limited

In conclusion, in AF patients undergoing PCI with placement of stents, the administration of either low-dose rivaroxaban plus a P2Y12 inhibitor for 12 months or very-low dose rivaroxaban plus DAPT for 1, 6, or 12 months was associated with a lower rate ofclinically significant bleeding than was standard therapy with a Vitamin K Antagonist plus DAPT for 1, 6, or 12 months. The three groups had similar efficacy rates, although thetrial was underpowered to evaluate stroke prevention.

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