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INVITED EDITORIAL

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De-escalation of antiplatelet therapy after acute coronary syndrome — a way to improve medication adherence?

According to European Society of Cardiology (ESC) guidelines [1–3], dual antiplatelet therapy (DAPT) with a P2Y12 inhibitor and aspirin is recommended for 12 months after acute coronary syndrome (ACS) to prevent adverse thrombotic events. Earlier DAPT termination is justified only in high bleeding risk patients [1–3]. Recently, Kubica et al. [4] proposed a DAPT de-escalation strategy based on the pathophysiological premises providing a rationale for a randomized clinical trial. They designed the Evaluation of safety and efficacy of two ticagrelor-based de-escalation antiplatelet strategies in acute coronary syndrome — a randomized clinical trial (ELECTRA-SIRIO 2), to assess the influence of ticagrelor dose reduction with or without continuation of aspirin versus DAPT with standard-dose ticagrelor in reducing clinically relevant bleeding and maintaining anti-ischaemic efficacy in ACS patients [4]. The authors stressed that an increased ischaemic risk occurs in the early period after ACS, with elevated rates of clinical events clustering during the first month, while the bleeding risk is related to the duration and dose of the antiplatelet treatment and the majority of bleeding events occur after 30 days post-ACS [5]. Therefore, in the earliest phase after ACS potent antiplatelet treatment is justified, whereas after the clinical stabilization occurs, de-escalation of the antiplatelet therapy may be a better option. Previously published studies showed that reduction of ticagrelor bioavailability significantly decreases the antiplatelet effect of ticagrelor in patients with acute myocardial infarction (MI), but not in the stable setting [6–8].

Moreover, a pharmacodynamic randomized study provided evidence that reduced ticagrelor maintenance dose of 60 mg b.i.d. provides comparable antiplatelet effect to the standard 90 mg b.i.d. dose in stable patients one month after MI [9, 10]. This observation was in line with results of the PEGASUS-TIMI 54 sub-study showing similar platelet inhibition with reduced (60 mg b.i.d) and standard (90 mg b.i.d) maintenance doses in stable patients more than 1 year after MI [11]. It should be underlined that in the PEGASUS-TIMI 54 study both ticagrelor doses showed comparable clinical efficacy, however, better tolerability of treatment with the lower dose of ticagrelor resulting in better adherence to medication was observed [12, 13].

According to the results of the TWILIGHT study, replacement of standard DAPT (ticagrelor plus aspirin) with ticagrelor alone resulted in a substantially lower bleeding rate than in the DAPT arm, without an increase of ischaemic events over a 1 year of follow-up [14, 15]. Moreover, adherence to ticagrelor treatment one year after randomization was slightly better in the ticagrelor-plus placebo arm than in the ticagrelor-plus-aspirin arm (87.1% and 85.9%, respectively) [14].

The ELECTRA-SIRIO 2 trial has been designed taking into account all these premises [4]. Patients with ACS will be randomised in a 1:1:1 ratio into one of three arms: standard-dose ticagrelor (90 mg b.i.d) with aspirin (100 mg q.d.) for 12 months; low-dose ticagrelor (dose reduction to 60 mg b.i.d. after one month) with aspirin group, low-dose ticagrelor (dose reduction to 60 mg b.i.d. after one month) with the placebo group (aspirin cessation after three months). The primary safety composite endpoint of this trial is the first occurrence of type 2, 3 or 5 bleeding according to the BARC criteria within 12 months after ACS. The primary efficacy endpoint is the composite of death from any

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cause, first nonfatal MI, or first nonfatal stroke [4]. To date, the de-escalation of antiplatelet therapy in ACS patients based on lowering the dose of ticagrelor with or without discontinuation of aspirin has never been tested in a large randomised clinical trial. It should be highlighted, that this groundbreaking trial has been made possible thanks to the support of financial support from the Medical Research Agency.

The primary hypothesis of the ELECTRA-SIRIO 2 trial is that monotherapy with low-dose ticagrelor will lead to improved safety (reduction of clinically relevant bleeding) with the same efficacy (no increase of adverse ischaemic events) in comparison to standard-dose ticagrelor with aspirin in ACS patients [4].

Both strategies applied in the trial — ticagrelor dose decrease and aspirin cessation are expected to improve adherence to treatment [16–33]. This effect is expected to be enhanced by the Multilevel Educational and Motivational Intervention in Patients After Myocardial Infarction (MEDMOTION) project, including assessment with the Readiness for Hospital Discharge after Myocardial Infarction Scale (RHD-MIS) at the end of hospitalization, and with the Functioning in Chronic Illness Scale (FCIS) during follow-ups [34–41]

In summary, the tested antiplatelet strategy, which is expected to be safer in comparison to standard treatment may also be more effective in the prevention of ischaemic events due to better adherence to study medication.

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