

“Optimal Dose of NOACs in JAPAN”

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East Asian patients have reduced anti-ischemic benefits and increased bleeding risk during antithrombotic therapies compared with Caucasian patients, so-called “the East Asian paradox.” As direct oral anticoagulants (non-vitamin K antagonist oral anticoagulants; NOACs) are commonly used for atrial fibrillation (AF) patients in contemporary practice, the unique risk-benefit trade-off in East Asians has been a topic of emerging interest.

Previous studies have shown that East Asians with AF have a low risk of atherothrombotic events, including cardiovascular mortality and different active metabolite levels of direct oral anticoagulants compared to Caucasians. Complex interactions between these findings could make a separate therapeutic window of antithrombotic treatment among East Asian versus Caucasian patients. Accordingly, the ethnicity-tailored antithrombotic strategy would be essential to minimize severe complications in East Asian patients.

In the ROCKET AF study, Japanese AF patients were not enrolled because of the following two reasons; 1) Pharmacokinetic modeling data indicated that the distribution of both the maximum concentration and area under the curve from 0 to 24 h of rivaroxaban in Japanese patients with AF who received a 15 mg o.d. dose of rivaroxaban would be comparable to those in Caucasian patients with AF who received a 20 mg o.d. dose, 2) Japanese physicians tend to favor lower levels of anticoagulation, resulting lower anticoagulation targets in clinical practice. Then, a phase 3 trial of J-ROCKET AF was performed. Also, phase 3, a multicenter, randomized, double-blind, placebo-controlled, event-driven trial, was conducted to compare a once-daily 15-mg dose of edoxaban with a placebo in elderly Japanese patients (≥ 80 years of age) with nonvalvular atrial fibrillation who were not considered to be appropriate candidates for oral anticoagulant therapy at doses approved for stroke prevention.

On the contrary, in the real-world setting, a significant proportion of AF patients received NOACs doses inconsistent with drug labeling (AFIRE subanalysis from Japan/ Data from Korean National Health Insurance Service database). Those studies suggested that NOAC underdosing was not significantly associated with an increased risk of stroke. However, there might be no safety benefit compared to label-adhered NOAC dosing.

In this session, we will review the recent evidence above on this intriguing topic and propose future directions for antithrombotic treatment in East Asian patients.