Efficacy and safety of uninterrupted periprocedural edoxaban in patients undergoing catheter ablation for atrial fibrillation: Prospective KYU-RABLE study

Authors:
N Takahashi¹, Y Mukai², K Okumura³, ¹Oita University Faculty of Medicine - Oita - Japan, ²Kyushu University, Cardiovascular Medicine - Fukuoka - Japan, ³Saiseikai Kumamoto Hospital Cardiovascular Center, Division of Cardiology - Kumamoto - Japan,

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Daiichi Sankyo Co. Ltd.

Background/Introduction
Catheter ablation (CA) has been established as a first-line therapy in the treatment of non-valvular atrial fibrillation (NVAF), and uninterrupted direct oral anticoagulants (DOACs) have become mainstream for the management of periprocedural thromboembolic events. Since 2014, edoxaban has been used for anticoagulation therapy for AF in Japan. However, evidence for uninterrupted use of edoxaban during the periprocedural period of CA in NVAF patients is limited.

Purpose
KYU-RABLE is a prospective, multicenter, single-arm interventional study, conducted in 23 institutions in Japan to evaluate the efficacy and safety of uninterrupted periprocedural oral edoxaban in patients undergoing CA. The plasma concentration of edoxaban and its relation with plasma coagulative biomarker levels during the periprocedural period were also evaluated.

Methods
A total of 537 Japanese NVAF patients were enrolled in Japan from December 2017 to September 2018. Edoxaban 60mg (30 mg in patients indicated for dose adjustment) was administered once daily in the morning for at least 4 weeks before CA and continued for at least 4 weeks after CA. On the day of CA, edoxaban was administered immediately after confirmation of hemostat. The primary endpoint was the composite incidence of thromboembolism and major bleeding events during 4 weeks from the procedural day. Plasma concentration of edoxaban and its relation with plasma coagulative biomarker levels during the periprocedural period were also evaluated.

Results
Among the total 513 patients who underwent CA, 75.2% had radiofrequency CA and 23.0% had cryoballoon CA. The majority of CA patients (65%) received edoxaban 60mg/day, while others (35%) received 30mg/day. As for the primary endpoint, one major bleeding (cardiac tamponade) event was observed and no thromboembolism occurred. Clinically relevant non-major bleeding events occurred in six patients (1.2%), the most were puncture site hemorrhage. The plasma concentration of edoxaban at CA was dependent upon the duration from last administration of edoxaban before CA. However, plasma levels of coagulative biomarkers (D-dimer, SFMC, F1+2) were maintained within appropriate range during the periprocedural period, irrespective of the edoxaban concentration. We also report changes of plasma levels of coagulative biomarkers in sub group analyses by CHADS2 scores and types of AF.

Conclusion
The KYU-RABLE study demonstrated the first evidence of the efficacy and safety of uninterrupted periprocedural edoxaban administered once daily on the morning for NVAF patients underwent CA. Edoxaban treatment was associated with a low risk of periprocedural bleeding and thromboembolic complications. Furthermore, these low event risks were considered to be associated with the maintained plasma level of coagulative biomarkers, regardless of the change in edoxaban plasma concentration.