Effectiveness and safety of reduced dose non-vitamin K antagonist oral anticoagulants in Asian patients with atrial fibrillation: A nationwide population-based study in Korea

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**Introduction**: It has been reported that physicians tend to prescribe reduced-dose NOACs to Asian patients with non-valvular atrial fibrillation (NVAF). However, real world evaluation to assess the effectiveness and safety of reduced-dose NOACs when compared to warfarin in the Asian population is limited. The objective of this study was to compare the risk of stroke/systemic embolism (S/SE), and major bleeding (MB) in patients treated with reduced-dose NOACs versus warfarin.

**Methods**: A retrospective study was conducted using Health Insurance Review & Assessment Service (HIRA) claims database in Korea. NVAF patients who initiated OACs (apixaban, dabigatran, rivaroxaban, warfarin) from 01JAN2015- 30NOV2016 were included. Patients who used any oral anticoagulants (OACs) within 1 year prior to the index date were excluded. Cox models with one to one propensity score matching (PSM) was used to estimate hazard ratio (HR) with 95% confidence intervals (95% CI) of S/SE and MB identified by inpatient diagnosis and CT/MRI records.

**Result**: Of 48,389 patients with NVAF who initiated NOACs or warfarin, patients with apixaban, dabigatran, rivaroxaban, and warfarin were 10,548, 11,414, 17,779, and 8,648, respectively. Patients treated with reduced-dose NOACs were older, had higher CHA2DS2-VASc and HAS-BLED scores compared with patients treated with standard-dose NOACs and warfarin. After PSM, the numbers of reduced-dose NOAC patients (matched to the same number of warfarin patients) were: 2.5 mg BID apixaban (4,774), 110mg BID dabigatran (5,221), and 15mg QD rivaroxaban (5,746). When comparing reduced-dose NOACs versus warfarin, all reduced-dose NOACs showed significantly lower risk of S/SE (HRs [95% CI], 0.63 [0.52-0.75] for apixaban; 0.51 [0.42-0.61] for dabigatran; 0.67 [0.57-0.79] for rivaroxaban) and MB (0.54 [0.45-0.65] for apixaban; 0.58 [0.49-0.69] for dabigatran; 0.73 [0.63-0.85] for rivaroxaban).

**Conclusion**: In the real-world practice among Asians with NVAF, potential confounding may still be present due to unmeasured variables and it cannot be ascertained whether dose selection matches indicated criteria from the data source, however, all reduced-dose NOACs were associated with
significantly lower risk of S/SE and MB compared to warfarin.