Comparative effectiveness and safety between non-VKA oral anticoagulants in non-valvular atrial fibrillation patients with differential duration of treatment: an analysis of the ARISTOPHANES study

Authors:
S Deitelzweig¹, A Keshishian², A Kang³, A Dhamane³, X Luo⁴, X Li³, N Balachander³, L Rosenblatt³, J Mardekin³, J Jiang³, M Di Fusco⁵, A B Garcia Reeves⁶, H Yuce⁷, GYH Lip⁸, ¹Ochsner Clinic Foundation, Department of Hospital Medicine - New Orleans, LA - United States of America, ²STATinMED - Ann Arbor, MI - United States of America, ³Bristol-Myers Squibb Company - Lawrenceville, NJ - United States of America, ⁴Pfizer, Inc. - Groton, CT - United States of America, ⁵Pfizer, Inc. - New York, NY - United States of America, ⁶University of North Carolina - Chapel Hill, NC - United States of America, New York College of Technology, City University of New York - New York, NY - United States of America, ⁷New York City College of Technology, City University of New York - New York, NY - United States of America, ⁸University of Liverpool and Liverpool Heart & Chest Hospital, Liverpool Centre for Cardiovascular Science - Liverpool, UK - United States of America.

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BACKGROUND: The ARISTOPHANES (Anticoagulants for Reduction In STroke: Observational Pooled analysis on Health outcomes ANd Experience of patientS) study showed that apixaban was associated with lower risks of stroke/systemic embolism (S/SE) and major bleeding (MB) versus dabigatran and rivaroxaban; dabigatran was associated with similar risk of S/SE and lower risk of MB compared to rivaroxaban.

PURPOSE: To assess long-term use of non-VKA oral anticoagulants (NOACs) in ARISTOPHANES by evaluating the risk of S/SE and MB among non-valvular atrial fibrillation (NVAF) patients receiving different NOACs by duration of treatment (<1 and =1 year).

METHODS: In the ARISTOPHANES study, NVAF patients initiating apixaban, dabigatran, and rivaroxaban from 01/01/2013-09/30/2015 were identified from the CMS Medicare data and four US commercial claims databases, covering >180 million beneficiaries annually (~56% of US population). After 1:1 propensity score matching (PSM) in each database between NOACs (apixaban-dabigatran, apixaban-dabigatran, and dabigatran-rivaroxaban), the resulting patient records were pooled. Treatment duration was defined as time between the day after the index treatment date and discontinuation (defined using a 30-day gap in the prescription), treatment switch, death, end of study period, or end of continuous medical and pharmacy enrollment, whichever occurred first. Matched patients with observed treatment duration <1 or =1 year were separately examined. Cox models were used to estimate hazard ratios of S/SE and MB (identified by inpatient claims) during observed treatment duration. S/SE included ischemic stroke, hemorrhagic stroke, and SE; MB included gastrointestinal (GI) bleeding, intracranial hemorrhage (ICH), and other MB.

RESULTS: The mean treatment duration for patients with shorter (<1 year) vs longer (=1 year) duration was ~4 months vs 18-21 months across the three matched cohorts. All the matched baseline variables remained balanced. The incidence rates of S/SE and MB and the proportion of patients with treatment discontinuation were higher in patients with shorter treatment duration. Regardless of treatment duration, apixaban and dabigatran had a lower risk of MB versus rivaroxaban; and dabigatran had a similar risk of S/SE versus rivaroxaban. Compared to dabigatran patients, apixaban patients with treatment duration <1 year had a lower risk of S/SE and MB, while those with treatment duration =1 year had similar S/SE and MB risk. Compared to rivaroxaban patients, apixaban patients with treatment duration <1 year had a lower risk of S/SE, while those
with treatment duration =1 year had similar S/SE risk.

CONCLUSIONS: Across NVAF patients with duration of treatment <1 and =1 year in the ARISTOPHANES study, both apixaban and dabigatran were associated with a lower risk of MB compared to rivaroxaban. These findings indicate varying long-term safety outcomes among different NOACs.