Naxos study: risk of bleeding with oral anticoagulants in non-valvular atrial fibrillation patients in France

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Background: In patients with non-valvular atrial fibrillation (NVAF), oral anticoagulants reduce the risk of stroke and systemic embolism, at the expense of an increased risk of bleeding.

Purpose: To compare the risk of bleeding and sites of bleeding according to the type of oral anticoagulant used in NVAF patients.

Methods: NAXOS is a population-based, historical cohort study including all patients aged ≥18 years with NVAF and newly initiating one of the OACs available in France between 2014 and 2016, aiming to compare safety, effectiveness, and all-cause mortality, according to the type of oral anticoagulant used. The French national health insurance reimbursement database, cross-linked with the hospitalisation database and civil status registry (SNIIRAM) was used to identify first users of oral anticoagulants and outcomes over their follow-up.

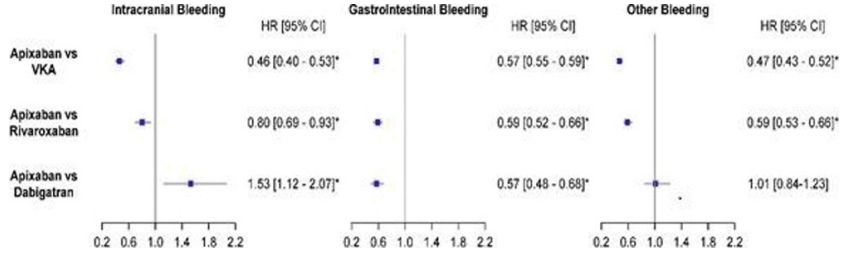
Major bleeding events were identified through main diagnoses of hospital stays, with a specific focus on bleeding site. Apixaban was used as the reference treatment.

Analyses were performed on crude data and with adjustment on propensity scores calculated separately for each of the comparators (VKAs, rivaroxaban and dabigatran).

Results: Overall, 321,501 NVAF patients were included: 87,565 (27.2%), 112,628 (35.0%), 100,063 (31.1%), and 21,245 (6.6%) initiated apixaban, VKAs, rivaroxaban, and dabigatran, respectively. The crude risks of intracranial bleeding were 0.45 [0.40–0.50], 1.23 [1.16–1.30], 0.48 [0.44–0.53], and 0.26 [0.19–0.34] per 100 patient-year, for apixaban, VKA, rivaroxaban, and dabigatran, respectively. The respective figures for gastrointestinal bleeding were: 0.67 [0.61–0.74], 1.73 [1.64–1.81], 1.01 [0.94–1.08], 1.02 [0.89–1.17]; and those for non-intracranial and non-gastrointestinal but other bleeding were: 0.84 [0.78–0.92], 2.22 [2.13–2.32], 1.24 [1.17–1.31] and 0.71 [0.60–0.84].

After adjustment on propensity-scores, patients initiating apixaban were at a lower risk of all major bleeding vs. VKA, rivaroxaban and dabigatran (HR=0.49 [0.46–0.52], 0.63 [0.58–0.67]) and 0.85 [0.76–0.95]). Apixaban was associated with a decreased risk of intracranial bleeding compared with VKAs (HR=0.46 [0.40–0.53]) and rivaroxaban (HR=0.80 [0.69–0.93]), and an increased risk compared with dabigatran (HR=1.53 [1.12–2.07]). The risk of gastro-intestinal bleeding was lower with apixaban than with VKAs (HR=0.57; [0.55–0.59]), rivaroxaban (HR=0.59; [0.52–0.66]), and dabigatran (HR=0.57; 0.48–0.68]). For other bleedings, apixaban was associated with a lower risk compared with VKAs (HR=0.47; [0.43–0.52]), and rivaroxaban (HR=0.59; [0.53–0.66]), and with a similar risk compared with dabigatran (HR=1.01; [0.84–1.23]).

Conclusion: In this large, real-world, population-based cohort, apixaban was associated with a lower risk of all types of bleedings requiring hospitalisation, compared with vitamin K antagonists. Differences between direct oral anticoagulants were also observed.



Results of the comparative analyses