Comparative safety and effectiveness of standard doses of apixaban versus dabigatran, rivaroxaban, and VKAs in non-valvular atrial fibrillation patients in France: the NAXOS study

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Topic(s):
Oral Anticoagulation

Funding Acknowledgements:
The Alliance Bristol-Myers Squibb/Pfizer

BACKGROUND:
Real-world data comparing all available oral anticoagulants (OAC) on a nationwide scale (i.e. in France: apixaban, rivaroxaban, dabigatran and vitamin K antagonists - VKAs) are lacking. In everyday practice, oral anticoagulants are often underdosed, which may render comparisons between agents difficult.

PURPOSE and METHODS:
NAXOS is a French real-world study comparing the safety (major bleeding), effectiveness (stroke, systemic thromboembolic events (STE)) and all-cause mortality for apixaban, dabigatran, rivaroxaban, and VKAs, in adult patients with non-valvular atrial fibrillation (NVAF) initiating a given OAC between 2014 and 2016. The French national health insurance data (SNIIRAM) were used. Analyses were performed with adjustment on propensity scores. To avoid bias potentially related to underdosing, the present analysis included only patients receiving standard doses of apixaban (5mg bid), rivaroxaban (20mg od), and dabigatran (150 mg bid), or VKAs. Only OAC naïve patients were included.

RESULTS:
In the OAC-naïve cohorts treated with apixaban, rivaroxaban, and dabigatran, 54,575 (62.3%), 65,208 (65.2%), and 9,000 (42.4%), respectively, had the standard dose at the index dispensation, and 112,628 patients received VKAs. After adjustment on propensity scores, apixaban 5 mg was associated with a lower risk of major bleeding, compared to VKAs (Hazard Ratio: 0.47; 95%CI: 0.43-0.51) and rivaroxaban 20mg (HR: 0.64; 0.59-0.71), but not to dabigatran 150 mg (HR: 0.97; 0.79-1.18). Apixaban was associated with a lower risk of stroke and STE, compared to VKAs (HR: 0.62; 0.56-0.69) but not to rivaroxaban (HR: 1.03; 0.92-1.16), and dabigatran (HR: 0.96; 0.76-1.21). Apixaban showed a lower risk of all-cause mortality compared to VKAs (HR: 0.44; 0.41-0.47) and rivaroxaban (HR: 0.87; 0.81-0.94) but not to dabigatran (HR: 1.10; 0.92-1.32).

CONCLUSIONS:
The NAXOS population-based country-wide observational study shows that 42% to 65% of patients were treated with standard doses of OACs. Analyses of standard doses confirmed the superiority of apixaban compared with VKAs for the three studied outcomes and suggests better safety profile of apixaban compared to rivaroxaban but similar to dabigatran.
Abstract: P1255
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Figure: Forest plot presenting the results of the standard dose analysis (PS adjusted)