Non-vitamin K antagonist oral anticoagulation agents in anticoagulant naïve atrial fibrillation patients

Torben Bjerregaard Larsen¹,²*

¹Department of Cardiology, Aalborg AF Study Group, Aalborg University Hospital, Aalborg DK-9000, Denmark; and
²Thrombosis Research Unit, Department of Clinical Medicine, Faculty of Health, Aalborg University, DK-9000 Aalborg, Denmark

Received 31 July 2014; accepted after revision 2 August 2014; online publish-ahead-of-print 23 October 2014

This editorial refers to ‘Non-vitamin K antagonist oral anticoagulation agents (NOACs) in anticoagulant naive atrial fibrillation patients: Danish Nationwide Descriptive Data 2011–2013’ by J.B. Olesen et al., on page 187–193.

Atrial fibrillation (AF) is the commonest cardiac rhythm disorder and is associated with an increased risk of mortality and morbidity from stroke and thromboembolism. Stroke prevention is essential for the management of AF, and the landscape for stroke prevention has changed with the availability of non-vitamin K antagonist oral anticoagulants (NOAC).

Several NOACs now exist, offering similar (or better) effectiveness, safety, and convenience to the vitamin K antagonists (VKAs);¹ those with evidence from large randomized trials of stroke prevention in patients with AF fall into two drug classes: the direct thrombin inhibitors (e.g. dabigatran), and the oral factor Xa inhibitors (e.g. rivaroxaban, apixaban, and, most recently, edoxaban).

In this Journal, Jonas Bjerring Olesen and colleagues² present findings from a large descriptive drug utilization study of all oral anticoagulation-naïve AF patients initiating oral anticoagulation from 22 August 2011 through 31 October 2013. The authors identified more than 18 000 patients of whom 53% initiated warfarin treatment, 38% dabigatran, 7% rivaroxaban, and 1% apixaban. One interesting finding was that patients prescribed rivaroxaban or apixaban had a higher predicted stroke and bleeding risk compared with warfarin or dabigatran initiators.

The European Society of Cardiology (ESC) Guidelines recommend oral anticoagulation for patients with a CHA²DS₂-VASc score of 2 or more (Class I recommendation) and are in favour of this therapy in patients with a CHA²DS₂-VASc score of 1 (Class IIa recommendation).³ In this Danish study, all users of NOAC had CHA²DS₂-VASc scores higher than 2. While warfarin remains a viable option, the ESC Guidelines state that NOACs may be preferred over warfarin, given their greater efficacy, safety, and convenience. Novel OACs have been increasingly used in Europe, including in patients with newly diagnosed AF. However, there are restrictions to the use of NOACs in patients with a various degree of renal impairment, and each of these agents has been issued with a set of specific rules relating to renal function.³ In this study on new users by Olesen et al., it is therefore very reassuring that users of NOAC were fewer among patients with chronic kidney disease in accordance with the ESC Guidelines, most notably for dabigatran (80% of this drug is eliminated renally). However, a substantial proportion of dabigatran initiators are patients who are switched from warfarin, so-called switchers, and they differ substantially from new users in terms of comorbidities and stroke risk.⁴ One must take this into consideration when data are interpreted. Indeed, another Danish drug utilization study recently showed that a large proportion of NOAC users switch back to VKA within a short timeframe.⁵ Reasons for this were not clear.

In observational studies of intended drug effects or safety, substantial confounding (by indication) is to be expected since the perceived risk is often closely related to the physician’s choice of treatment. Where there is confounding, there is also the possibility of residual confounding. Taken to the extreme, heterogeneity in risk factors (measured or unmeasured) between treatment groups in key risk factors might be a possible explanation for observed associations or differences. Therefore, a careful choice of methods and principles that can mitigate confounding is imperative. Post-marketing cohort studies can indeed contribute to our understanding of drug safety and effectiveness over time. As an example, prescribing information and our knowledge about NOAC drug characteristics show differences in terms of how patients received different NOACs. However, we need...
studies that actually compare outcomes as a consequence of these differences.

Novel OACs have heralded a new era in anticoagulation for patients with AF. To ensure that patients derive the maximum benefit from therapy, understanding the differences between NOACs and VKAs and the practical implications for day-to-day practice is critical. However, clinical experience of NOACs outside of trials remains limited, and further insights into appropriate use will undoubtedly become apparent as these agents are prescribed more widely.

Conflict of interest: T.B.L. has been an investigator for Janssen Scientific Affairs and Boehringer Ingelheim, and served on speaker bureaux for Bayer, Bristol-Myers Squibb/Pfizer, Janssen Pharmaceuticals, Takeda, Roche Diagnostics, and Boehringer Ingelheim.

References