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BRIEF COMMUNICATION

Comparative Effectiveness and Safety of Apixaban and Vitamin K Antagonist Therapy in Patients with Nonvalvular Atrial Fibrillation Treated in Routine German Practice

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Background Scarce data comparing real-world outcomes between apixaban and vitamin K antagonist (VKA) users with nonvalvular atrial fibrillation (NVAF) are available. We sought to assess the effectiveness and safety of newly-initiated apixaban vs. VKA in German NVAF patients.

Materials and Methods We performed a retrospective analysis in German outpatients using IMS Disease Analyzer data. Adults newly-initiated on apixaban or a VKA from January 2013 to March 2015 with a diagnosis of NVAF on the day of the first qualifying oral anticoagulant (OAC) prescription (index date) or any time during one year prior, and at least one year of follow-up were included. Patients experiencing a prior event in the composite endpoint, receiving an OAC before the index date, >1 OAC on the index date or switched to another OAC during follow-up were excluded. Apixaban and VKA users were 1:1 propensity-score matched. We evaluated the composite of ischaemic stroke, transient ischaemic attack (TIA), myocardial infarction (MI) or intracranial haemorrhage (ICH) in the year after OAC initiation. Cox regression was used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs).

Results In total, 835 apixaban and 835 VKA users were matched. Forty-one composite events were identified. Hazard of the composite endpoint did not differ between apixaban and VKA users (HR = 0.87, 95% CI = 0.47–1.60). Ischaemic stroke and MI occurred at dissimilar (albeit not statistically significant) rates between apixaban and VKA therapy (HR = 1.51, 95%CI = 0.54–4.24) and (HR = 0.33, 95%CI = 0.11–1.03). Only two patients (both in the apixaban cohort) experienced an ICH.

Conclusions Apixaban and VKA therapy were associated with a similar impact on the composite endpoint in real-world German practice. Additional investigation is needed to evaluate the numeric trends of ischaemic stroke and decreased number of MIs observed with apixaban, as well as the high rate of reduced dose apixaban use found in this analysis.

Keywords Anticoagulant • Vitamin k antagonist • Apixaban • Non-valvular atrial fibrillation • Stroke

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Introduction

Apixaban has been shown to be effective in reducing the risk of stroke in patients with nonvalvular atrial fibrillation (NVAF) in the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE) trial [1]; however, oral anticoagulants (OACs) are often used at different doses and in different populations than in their supporting trials [2]. To date, no evaluation of apixaban in German NVAF patients has been published. We sought to assess the real-world effectiveness and safety of newly-initiated apixaban versus VKA (predominantly phenprocoumon) therapy among German outpatients with NVAF.

Material and Methods

A retrospective analysis was performed in the outpatient setting in Germany using data from the Primary Care Physician panel of a longitudinal electronic medical record database (IMS Disease Analyzer). Adult patients newly-initiated on apixaban or a VKA from January 2013 to March 2015 with a diagnosis of atrial fibrillation on the day of the first qualifying anticoagulant prescription (index date) or any time during one year prior, and at least one year of follow-up after the index date were eligible for inclusion. A one-year pre-index period was used to identify patient co-morbidities and prior medication use. Patients with valvular AF, experiencing a prior event defined in the composite endpoint, receiving an OAC before the index date or prescribed >1 OAC on the index date or during follow-up were excluded.

Potentially eligible apixaban and VKA patients were 1:1 propensity score-matched using age, gender, CHA2DS2-VASc score and number of co-morbidities to generate an analysis cohort with minimal differences in baseline characteristics. Residual differences in matched characteristics between cohorts were assessed via standardised differences (<10% considered well-balanced) [3].

Our primary endpoint was the composite of ischaemic stroke, transient ischaemic attack (TIA), myocardial infarction (MI), intracerebral or other non-traumatic intracranial haemorrhage (ICH) during the subsequent one year of follow-up. Hazards regression was performed to calculate the hazard ratio (HR) with 95% confidence intervals (CIs) for developing the composite endpoint between the matched cohorts within the first-year after treatment initiation. Statistical analyses were performed using SAS version 9.3 (SAS Inc., Cary, NC, USA). Since analysis of only anonymised data was performed, this study was exempted from institutional review board oversight.

Results

Following matching, 835 apixaban (35.2% of which received the 2.5 mg twice-daily dose) and 835 VKA users were included (Table 1). No matched characteristic exhibited a standardised difference > 10%. In total, 41 composite endpoint events were identified during one year of follow-up (Table 2). The hazard of developing a composite endpoint event did not differ between apixaban and VKA users (HR = 0.87, 95%CI = 0.47–1.60). Ischaemic stroke and MI occurred at dissimilar (albeit not statistically significant) rates between apixaban and VKA therapy (HR = 1.51, 95% CI = 0.54–4.24) and (HR = 0.33, 95%CI = 0.11–1.03), respectively. Only two patients (both in the apixaban cohort) experienced an ICH.

Table 1 Characteristics of included patients.

Characteristic	Apixaban N = 835 n (%)	VKA N = 835 n (%)
Age, years (mean ± SD)	75.3 ± 10.6	74.8 ± 9.2
<65 years	117 (14.0)	110 (13.2)
65–74 years	245 (29.3)	248 (29.7)
≥75 years	473 (56.6)	477 (57.1)
Male gender	418 (50.1)	440 (52.7)
$CHADS_2$ score (mean ± SD)	2.0 ± 1.1	2.1 ± 1.1
CHA_2DS_2-VASc score (mean ± SD)	3.5 ± 1.5	3.6 ± 1.5
ATRIA score (mean ± SD)	2.9 ± 2.1	2.9 ± 2.0
≥1 relevant co-morbidities	619 (74.1)	653 (78.2)
Hypertension	529 (63.4)	566 (67.8)
Diabetes mellitus	163 (19.5)	207 (24.8)
Renal failure	89 (10.7)	59 (7.1)
Deep vein thrombosis	18 (2.2)	38 (4.6)
Unstable angina	16 (1.9)	25 (3.0)
Hyperthyroidism	21 (2.5)	16 (1.9)
Pulmonary embolism	3 (0.4)	14 (1.7)
Heart failure	129 (15.4)	113 (13.5)
Functional dyspepsia	5 (0.6)	3 (0.4)
≥1 Cardiovascular medication	778 (93.2)	786 (94.1)
Anti-arrhythmic	86 (10.3)	74 (8.9)
Beta blocker	619 (74.1)	622 (74.5)
ACE inhibitor	364 (43.6)	393 (47.1)
Angiotensin receptor blocker	272 (32.6)	227 (27.2)
Calcium channel blocker	262 (31.4)	288 (34.5)
Diuretic	349 (41.8)	357 (42.8)
Anti-platelet	251 (30.1)	225 (26.9)

Abbreviations: ACE = angiotensin-converting enzyme; SD = standard deviation; VKA = vitamin K antagonist.

Discussion

This study used real-world German claims data to compare the effectiveness and safety of newly-initiated apixaban and VKA therapy in NVAF patients. Apixaban and VKA use were associated with similar incidences of developing the

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