Comparison of Adherence to Rivaroxaban Versus Apixaban Among Patients With Atrial Fibrillation

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ABSTRACT

Purpose: Non-vitamin K antagonist oral anticoagulant medications are increasingly used for stroke prophylaxis in patients with nonvalvular atrial fibrillation (NVAF). This study aimed to compare adherence with rivaroxaban and apixaban among patients with NVAF in routine clinical practice.

Methods: Using pharmacy and medical claims from Truven Health Analytics MarketScan databases, we identified NVAF patients aged ≥18 years treated with rivaroxaban or apixaban. Baseline demographic and clinical features were balanced using 1:1 propensity score matching. Adherence to therapy was measured at 90 and 180 days post-index date and was defined by the proportion of days covered (PDC) ≥0.80 and PDC ≥0.90. "Gaps in care," defined as those with 10 or more day gaps in supply, were also evaluated.

Findings: Between June 2012 and April 2014, 11,477 rivaroxaban and 2992 apixaban users were identified. Baseline characteristics for rivaroxaban and apixaban users were well matched. Relative to apixaban users, rivaroxaban users were more likely to have a PDC ≥0.80 at both 90 days (85.3% vs 79.9%; $P < 0.001$) and 180 days (75.8% vs 72.2%; $P = 0.001$). Similar results were observed with PDC ≥0.90. The proportion of patients with at least one 5+ and 10+ day gap in prescriptions was significantly lower in the rivaroxaban versus apixaban cohorts: 54.2% versus 62.4% ($P < 0.001$) and 40.0% versus 49.2% ($P < 0.001$), respectively.

Implications: Adherence to non-vitamin K antagonist oral anticoagulants among NVAF patients is less than ideal, and gaps in treatment are common. Those on once-a-day rivaroxaban had significantly higher adherence and fewer gaps in treatment compared with twice-a-day apixaban. Future studies are needed to explore whether these treatment differences affect comparative patient outcomes. (*Clin Ther.* 2016;▮:▮▮▮–▮▮▮)

Key words: adherence, anticoagulant, apixaban, atrial fibrillation, rivaroxaban.

INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia, with an estimated US prevalence of 5.2 million in 2010 and expected to rise to 12.1 by 2030.[1] Patients diagnosed with AF have a 2- to 5-fold increased risk of developing strokes compared with non-AF patients.[2,3] However, treatment with an oral anticoagulant can reduce this risk by up to 61%.[4] For decades, the vitamin K anticoagulant warfarin has been the standard of care for stroke prevention in AF patients.[5–7] Yet, medication nonadherence is common among those on vitamin K anticoagulant agents and has been estimated to range from 22% to 58%.[8] Furthermore, nonadherence to vitamin K anticoagulant agents has been associated with worse patient outcomes.[9,10]

In recent years, non-vitamin K antagonist oral anticoagulant (NOAC) agents have been developed for stroke prophylaxis in nonvalvular AF (NVAF) patients. These drugs do not require recurrent monitoring and have more predictable pharmacokinetic

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properties and less drug interactions compared with warfarin.[11–15] However, to date, there have been limited data on medication adherence to NOAC agents.

The two most commonly used NOACs include once-a-day rivaroxaban[16] and twice-a-day apixaban.[17] Prior work has found that dosing frequency may affect medication adherence.[18–20] In view of the difference in daily dosage regimens and the potential consequences that suboptimal adherence might have, this study assesses real-world medication adherence to rivaroxaban and apixaban among patients with NVAF using health care claims data from the United States.

METHODS

Data Source

Health insurance claims from the Truven Health Analytics MarketScan databases were used to conduct the analysis.[21] These databases feature more than 196 million covered lives and more than 300 contributing employers and 25 contributing health plans.[22] Study data were extracted from the MarketScan Commercial Claims and Encounters Database (Commercial Database) and the MarketScan Medicare Supplemental and Coordination of Benefits Database (Medicare Supplemental Database) for the period from June 2012 to April 2014. Both databases include enrollment history and claims for medical (provider and institutional) and pharmacy services. All census regions are represented, predominantly the South and North Central (Midwest) regions. The Commercial Database contains data for employees, their spouses, and dependents that are covered by employer-sponsored private health insurance. The Medicare Supplemental Database contains the health care expenses of retirees with Medicare insurance paid by employers. Truven Health Analytics MarketScan databases are de-identified and fully compliant with all Health Insurance Portability and Accountability Act privacy and security requirements to protect patient anonymity and confidentiality.

Study Design

A matched-cohort design was used to assess adherence to the NOAC agents rivaroxaban and apixaban among patients with NVAF. To be included in the study sample, patients had to be newly initiated on rivaroxaban or apixaban after February 2013 (patients newly initiated on therapy from early 2013 were analyzed because apixaban was approved for NVAF at the end of 2012 in the United States[17] and it may take a certain time for recently approved medication to be prescribed), had two or more dispensings of rivaroxaban or apixaban (the date of the first rivaroxaban or apixaban dispensing was termed as the index date), had a baseline period of at least 6 months of continuous health plan enrollment before the index date, and had at least two primary or secondary AF diagnoses (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM]: 427.31) during the baseline or the follow-up period.

Patients were excluded if they were younger than 18 years at the index date, diagnosed at baseline with valvular involvement (including ICD-9-CM: 394.0x, 394.2x, 396.0x, 396.1x, 746.5x, 996.02, 996.71 for mitral stenosis diagnosis; ICD-9-Procedure: 35.20, 35.22, 35.23, 35.24, 35.97, *Current Procedural Terminology, 4th Edition* [CPT-4]: 33405, 33420, 33422, 33425-33427, 33430, 92987 for mechanical heart valve), or did not have an observation period of at least 6 months. Patients initiating NOACs during the last days of December 2012 and in January 2013 after the approval of apixaban (ie, December 28, 2012) were also excluded in order to have balanced follow-up periods between both cohorts. In addition, apixaban patients who switched from rivaroxaban (prior use of rivaroxaban during the baseline period) were excluded to remove potential bias due to a switch from a once-daily to a twice-daily medication.

The observation period spanned from the index date to the earliest date between end of insurance coverage, end of data availability (April 30, 2014), and a switch to another oral anticoagulant (ie, warfarin, rivaroxaban, apixaban, or dabigatran), whichever occurred first.

Study End Points

Adherence to rivaroxaban and apixaban was evaluated using 2 prospectively defined and standard metrics: the proportion of days covered (PDC) and the medication possession ratio (MPR). The PDC was calculated at 90 and 180 days and calculated as the number of days of supply divided by 90 and 180 days, respectively. The MPR was calculated as the number of days of supply between the first and the last