Persistence and discontinuation of apixaban among patients with atrial fibrillation: a retrospective analysis in five Italian districts

Verdecchia P[1], Lanati EP[2], Verdini V[2], Corrao G[3], Scotti L[3], Airoldi C[3], Iorio A[2]

1. Department of Medicine, Hospital of Assisi, Italy
2. MA Provider, Milan, Italy
3. Department of Statistics and Quantitative Methods, University of Milan-Bicocca

INTRODUCTION

Novel oral anticoagulants (NOACs), including apixaban, have demonstrated at least similar efficacy and safety in stroke prevention compared with warfarin. However the lack of monitoring, may affect treatment persistence, which is important in ensuring optimal stroke prevention. The ARISTOTLE study for apixaban showed a discontinuity rate of 25.3% compared to the 27.5% found in the group treated with warfarin. (1)
Despite this, little is known about the rate and reasons for apixaban discontinuations in daily care.

OBJECTIVE

The aim of this study is to evaluate i) the characteristics of patients with non-valvular atrial fibrillation (NVAF) in treatment with apixaban and ii) the treatment persistence of these patients in the real world setting exploiting the data collected in five Italian hospitals.

METHODS

In this multi-centre, retrospective, observational study we collected data from clinical database on consecutive patients with a diagnosis of NVAF, aged 18 years or older who were newly prescribed with in the period from 1st of January 2014 till 31st of March 2016. The follow-up began at the first visit of the patients at one of the study centres and underwent up to 3 follow-up visits. Each patient had to attend at least one follow-up visit during the observation period, the maximum length of follow-up was 3 years.Patients were excluded if they had been treated with apixaban in the 12 months before the beginning of the study or if they were diagnosed with valvular AF (with a prosthetic heart valve or with mild/severe mitral stenosis). The study protocol and CRF developed specificaclly for this study were approved by the Ethics Committee of each study centre. Several patients' characteristics were collected including apixaban dosage, previous comorbidities and co-treatments. Treatment persistence, defined as proportion of patients still on initial drug therapy after a fixed time, was calculated by: i) no temporary or permanent discontinuation; and ii) no permanent discontinuation. Permanent interruption was defined as a treatment discontinuation > 30 days. Number and percentage of patients continuing the therapy during the period of exposure to the drug were analysed, both in case of no discontinuation or permanent discontinuation. Descriptive statistics of patients' characteristics were carried-out; in particular frequency and percentage were reported for the categorical variables, and the Kaplan Meier method was also used to calculate the cumulative probability of treatment persistence during follow-up

RESULTS

The analysed sample consisted of 766 patients affected by NVAF from five Italian Centres. Overall, 53.3% of the patients were female; mean age was 74.2 years (SD 11.1). Median $CHADS_2$ and CHA_2DS_2-VASc scores were 2.0 and 4.0, respectively, and median HAS-BLED score was 2.0 (SD 1.1).
The follow up duration was up to 3 years with different timespan: 750 patients completed the first follow up visit (V_1), at median time from the baseline 339.5 days, 253 completed the second follow up visit (V_2) at median time from V_1 of 110.9 days and only for 84 patients the third visit was recorded (V_3) at median time from V_2 of 241.5 days.

Figure 1. Co-morbidities affecting patients at baseline.
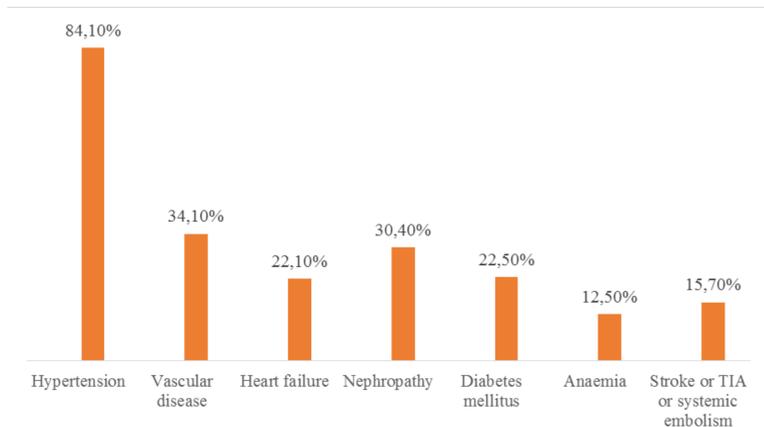
The most frequent comorbidities were cardiovascular diseases (hypertension – affecting 84.1% of patients; previous vascular disease [34.1%]; heart failure [22.1%]), renal impairment (30.4%), diabetes mellitus (22.5%) and anaemia (12.5%).

At baseline (V_0), 15.7% of patients had recorded at least one event among stroke, transient ischemic attack or systemic embolism (Figure 1)

Figure 2. Use of anticoagulant drugs during the year preceding study
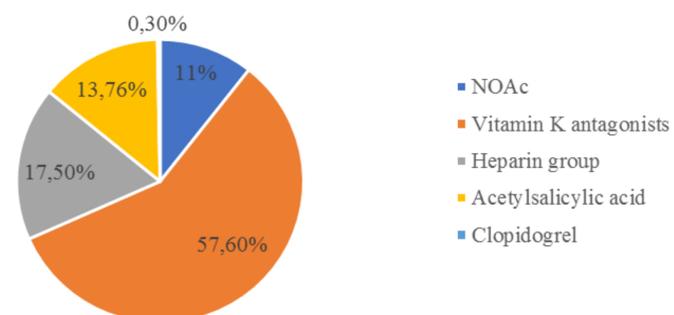
In the whole cohort, the half of patients (50.7%) were naïve to oral anticoagulants, while 219 patients had been previously treated with warfarin, heparin (66 patients), acetylsalicylic acid (52 patients), clopidogrel (1 patient) and a novel oral anticoagulant (NOAC, 40 patients) (Figure 2).

Figure 3. Patient persistency to treatment on completion of the follow-up period (1092 days) (Kaplan-Meier curves).
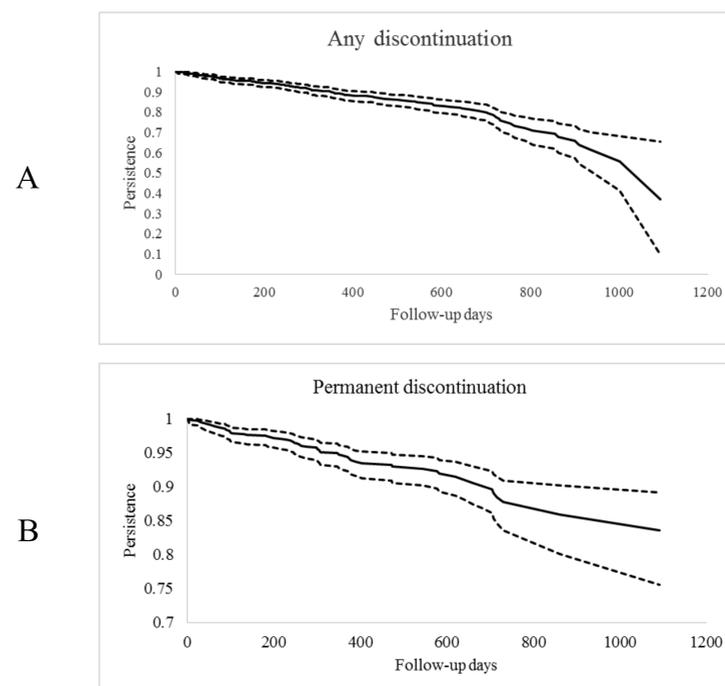
During the follow up period, 123 cases of therapy discontinuation were recorded, including also patients with more than one discontinuation. 58 were permanent discontinuations, of whom 41 occurred at V_1, 14 at V_2 and 3 at V_3. The persistence of apixaban treatment was 37.2% (10.0-65.4) (panel A) considering the absence of any type of discontinuation and 83.5% (75.5-89.2) (panel B) considering the absence of permanent discontinuation of treatment and (Figure 3). Regarding the reasons of 58 permanent discontinuations: 10 occurred for worsening of renal function, 5 for minor bleeding, 5 for itching or rush, 3 for cancer, 4 for surgery, 4 for major bleeding, 3 for stroke, 3 for patient non compliance, 3 for nausea, 2 for clinician decision, 1 for dyspepsia, 1 for valve disease, 1 for worsening of hepatic function, 1 for anaemia, 1 for heart failure, 1 for TIA, 1 for hematoma and 8 for other causes.

CONCLUSIONS

Apixaban demonstrated better persistence than warfarin data available in literature. Further studies are needed to identify the consequences of discontinuation and evaluate the impact on outcomes.

REFERENCES

1. Granger CB, Alexander HJ, McMurray JJV, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med, 2011;365:981-92.

Corresponding author
Lorenza Scotti
Laboratory of Healthcare Research & Pharmacoepidemiology, Unit of Biostatistics, Epidemiology and Public Health
Department of Statistics and Quantitative Methods
University of Milano-Bicocca, Milan, Italy
Tel.: +39. 02.64485846; E-mail: lorenza.scotti@unimib.it

Healthcare Research
Lab & Pharmacoepidemiology