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Pharmacoeconomic Comparison Between Rivaroxaban And Warfarin Based on Real-World Data Analysis

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INTRODUCTION

- Deep vein thrombosis (DVT) and pulmonary embolism (PE) are two manifestations of venous thromboembolism (VTE), and they are having similar predisposing factors.
- Anticoagulant therapy is the cornerstone of VTE treatment.
- Warfarin was the only available option as an oral anticoagulant (OAC) for more than 50 years for the treatment of atrial fibrillation and other thrombotic conditions.
- Novel oral anticoagulants (NOACs) or direct oral anticoagulants (DOACs) such as rivaroxaban, edoxaban and apixaban are recently approved factor Xa inhibitors that provide anticoagulation via oral route.
- The oral factor Xa inhibitors such as rivaroxaban represent a major advance in the prevention and treatment of thromboembolic disease.
- These agents have several advantages over the vitamin K antagonists such as rapid onset of action, no requirement for dose adjustment, and few drug and food interactions . Thus, these agents become widely used in the treatment and prevention of all VTE related diseases.
- Although the efficacy and safety of the factor Xa inhibitor for the prevention of VTE and stroke in patients with NVAF were shown in global clinical trials, the safety and effectiveness data from unselected patients in everyday clinical practice are yet limited.

OBJECTIVES

To investigate the safety and effectiveness of rivaroxaban and warfarin in real-world clinical practice in Saudi Arabia.

METHODS

Methods

- Retrospective cohort, real-world observational study as post-marketing surveillance.
- Patients with NVAF/venous thrombosis, arterial thrombosis, and stroke who began treatment with Rivaroxaban and Warfarin.
- Data recruited through several departments in king Khalid University Hospital , from January 2015 to December 2021, and analyzed to examine the one-year outcomes.

Baseline data

- Age, sex, body weight, height, smoking history, and any history of allergy.
- History of VTE (DVT/PE/other thrombosis, including date of onset and type (paroxysmal, distal, Lung, Hepatic, splenic, renal, IVC thrombosis and cavernous sinus thrombosis).
- History of NVAF including date of onset and type (paroxysmal, persistent, or permanent).
- Use of an anticoagulant or antiplatelet agent ≤30 days prior to rivaroxaban and warfarin administration.
- HTN, DM, hypothyroidism, kidney impairment, HF and Other medical history.
- Vital signs and laboratory tests, if performed as part of routine care.
- CrCl (mL/min) and Child-Pugh score.
- Recurrent Thrombosis / Stroke and bleeding risk profiles based on risk scores such as: D-dimer, thrombophilia, CHADS2, CHA2DS2-VASc and HAS-BLED.

Statistical analysis:

- Descriptive analysis (e.g., mean ± standard deviation or median quartile for continuous variables and frequency or percentage for categorical variables) will be conducted for baseline characteristics.
- Chi-square test (two-sided) and Fisher's Exact Test (two-sided) to compare categorical variables and Student's t-test for continuous variables. Multivariate data analysis is planned as well.
- Incidence rates will be calculated as cumulative incidence (events/100 patient-years) and will be compared using the hazard ratios and corresponding 95%confidence intervals.

RESULTS

Table 1: Demographics and clinical characteristics of study patients.
A total of 800 patients taking rivaroxaban and warfarin recruited through several departments in king Khalid University Hospital with a mean age of 58.9 and 53.8 years, respectively, were enrolled in this study. 55% of which were females. The prescriptions for NVAF were relatively higher than VTE in both groups.

Variables	Rivaroxaban (n=400)	Warfarin (n=400)	p-value
Age, years; mean ±SD	58.9 ±16.9	53.8 ±15.7	0.8
Gender; n (%)			
Male	179 (45)	176 (44)	0.7
Female	221 (55)	224 (56)	0.6
Weight, kg; mean ±SD	79.7 ± 19.3	77.2 ± 19.6	0.6
Height, m; mean ±SD	1.62 ±0.09	1.59 ± 0.16	0.9
BMI, kg/m^2; mean ±SD	30.4 ±7.3	29.7 ±7.1	0.6
Smoking Status; n (%)	24 (6)	12 (3)	0.04
VTE Hx; n (%)	114 (29)	117 (29.3)	0.6
NVAF Hx; n (%)	140 (35)	285 (71)	0.03
Antiplatelets, n (%)			
Aspirin; n (n%)	41 (10)	30 (8)	0.04
Clopidogrel; n (%)	2 (1)	2 (1)	0.9
Comorbidities; n (%)			
Hypertension	208 (52)	178 (45)	0.5
Dyslipidemia	59 (15)	84 (21)	0.4
Hypothyroidism	24 (6)	50 (13)	0.3
Renal Dysfunction	18 (5)	55 (14)	0.2
Heart Failure	58 (15)	47 (12)	0.8
Diabetes Mellitus	159 (40)	152 (38)	0.8
ALT, unit/L ; mean ±SD	38.9 (84)	35.4 ± 38	0.9
AST, unit/L ; mean ±SD	32.7 (76)	34 ± 88	0.8
ALP, unit/L ; mean ±SD	103 (77)	106 ± 94	0.8
Albumin, gm/L ; mean ±SD	31.8 (6.5)	34 ± 6.4	0.9
Bilirubin, mcmol/L; mean ±SD	13.1 (26)	9 ± 9.7	0.6
Serum Creatinine; mcmol/L ; mean ±SD	82.2 (52)	100 ± 90	0.5
Creatinine Clearance; ml/min; mean ±SD	119 (66)	109 ± 59	0.7

Table 2: Effectiveness and safety outcomes of patients
The incidence rates of recurrent thrombosis and myocardial Infarction recurrent stroke were higher in warfarin group 6.25 % comparing to zero rate in rivaroxaban group. Whereas, the incidence rate was 2.25 % for recurrent stroke in warfarin group compared to zero in rivaroxaban. On the other hand, there were no significant differences between the two groups in the rate of major and non-major bleeding.

Variables	Rivaroxaban (n=400)	Warfarin (n=400)	p-value
Effectiveness outcomes			
Recurrent Thrombosis; n (%)	0 (0)	25 (6.25)	0.001
Recurrent Stroke; n (%)	0 (0)	9 (2.25)	0.001
Myocardial Infarction; n (%)	0 (0)	25 (6.25)	0.001
Safety outcomes			
Major Bleeding; n (%)	4 (1)	3 (0.75)	0.7
Minor Bleeding; n (%)	6 (1.5)	1 (0.25)	0.01

DISCUSSION & CONCLOSIONS

In this real-life cohort study, rivaroxaban appears to be more effective for patients with VTE and NVAF compared to warfarin. Rivaroxaban was also associated with a lower risk of recurrent thrombosis, recurrent stroke, MI events. Moreover, there was no significant difference in the major bleeding events. However, non-major bleeding was significantly higher in Rivaroxaban group compared to warfarin.

REFERENCES