Cost-Effectiveness of Apixaban Versus Other New Oral Anticoagulants for Stroke Prevention in Atrial Fibrillation☆

Gregory Y.H. Lip[1]; Thitima Kongnakorn[2]; Hemant Phatak[3]; Andreas Kuznik[4]; Tereza Lanitis[5]; Larry Z. Liu[6]; Uchenna Iloeje[7]; Luis Hernandez[8]; and Paul Dorian[9]

[1]University of Birmingham Centre for Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom; [2]Evidera, Bangkok, Thailand; [3]Bristol-Myers Squibb, Princeton, New Jersey; [4]Pfizer, New York, New York; [5]Evidera, London, United Kingdom; [6]Pfizer, New York, New York, Weill Medical College of Cornell University, New York, New York; [7]Alexion Pharmaceuticals, Hartford, Connecticut; [8]Evidera, Lexington, Massachusetts; and [9]University of Toronto, St. Michael's Hospital, Toronto, Ontario, Canada

ABSTRACT

Background: Apixaban (5 mg BID), dabigatran (available as 150 mg and 110 mg BID in Europe), and rivaroxaban (20 mg once daily) are 3 novel oral anticoagulants (NOACs) currently approved for stroke prevention in patients with atrial fibrillation (AF).

Objective: The objective of this study was to evaluate the cost-effectiveness of apixaban against other NOACs from the perspective of the United Kingdom National Health Services.

Methods: A Markov model was developed to evaluate the pharmacoeconomic impact of apixaban versus other NOACs over a lifetime. Pair-wise indirect treatment comparisons were conducted against other NOACs by using ARISTOTLE (Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation), RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy), and ROCKET-AF (Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation) trial results for the following end points: ischemic stroke, hemorrhagic stroke, intracranial hemorrhage, other major bleeds, clinically relevant nonmajor bleeds, myocardial infarction, and treatment discontinuations. Outcomes were life-years, quality-adjusted life years gained, direct health care costs, and incremental cost-effectiveness ratios.

Results: Apixaban was projected to increase life expectancy versus other NOACs, including dabigatran (both doses) and rivaroxaban. A small increase in therapeutic management costs was observed with apixaban due to projected gains in life expectancy and lower discontinuation rates anticipated on apixaban versus other NOACs through lifetime. The estimated incremental cost-effectiveness ratio was £9611, £4497, and £5305 per quality-adjusted life-year gained with apixaban compared with dabigatran 150 mg BID, dabigatran 110 mg BID, and rivaroxaban 20 mg once daily, respectively. Sensitivity analyses indicated that results were robust over a wide range of inputs.

Conclusions: Although our analysis was limited by the absence of head-to-head trials, based on the indirect comparison data available, our model projects that apixaban may be a cost-effective alternative to dabigatran 150 mg BID, dabigatran 110 mg BID, and rivaroxaban 20 mg once daily for stroke prevention in AF patients from the perspective of the United Kingdom National Health Services. (*Clin Ther.* 2014;36:192–210) © 2014 The Authors. Published by Elsevier HS Journals, Inc. All rights reserved.

Key word: Stroke prevention, apixaban, cost-effectiveness, atrial fibrillation, new oral anticoagulant.

INTRODUCTION

Having atrial fibrillation (AF) increases a person's risk of experiencing stroke almost 5-fold.[1] Traditionally, prophylactic treatment in this setting has been based

Current affiliation: Bristol-Myers Squibb, Princeton, New Jersey

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on vitamin K antagonists (VKAs), drugs that have been in use for 60 years[2] for their confirmed effectiveness in preventing thromboembolic events.[3] However, the well-known challenges in managing VKA therapy, such as monitoring requirements and the risk of hemorrhages, have resulted in such therapy being underused in the treatment of AF.[4] Given this context, the development of novel oral anticoagulants (NOACs), such as dabigatran, rivaroxaban, and apixaban, and their demonstrated efficacy in clinical trials have been encouraging with regard to addressing the need for improved stroke prevention treatments for patients with nonvalvular AF (NVAF).[2,5] Dabigatran, a direct thrombin inhibitor, given at a dose of 110 mg BID, demonstrated noninferiority to warfarin in the primary end point of stroke and systemic embolism coupled with a significantly lower risk of major hemorrhage.[6] In addition, dabigatran 150 mg BID was superior to warfarin in the prevention of stroke and systemic embolism, with rates of major hemorrhage similar to warfarin. Rivaroxaban, an oral factor Xa inhibitor, was noninferior to warfarin in the prevention of stroke or systemic embolism, with no significant difference between the treatments in the risk of major bleeding.[7] Apixaban, another oral factor Xa and the third NOAC to receive European Union marketing authorization for the prevention of stroke and systemic embolism in AF,[8] is the only oral anticoagulant that has been shown to be superior to dose-adjusted warfarin in terms of reduction in the rates of stroke and systemic embolism, major bleeding, and all-cause mortality.[9]

This evidence on NOACs underpins current guidelines from the European Society of Cardiology, which recommend the use of these drugs as "broadly preferable to VKA in the vast majority of patients with NVAF."[10] These drugs also offer the potential advantage of not requiring the anticoagulant monitoring needed for VKA therapy. The choice among NOACs, however, is not clear; this choice requires consideration of several practical issues, including patient characteristics, tolerability, and health economic outcomes.[2,10,11] A key means of capturing such elements is a cost-effectiveness analysis that investigates how the differences in costs associated with therapy relate to differences in benefits. This analysis can be conducted by using modeling techniques, which are commonly accepted as valid approaches to understanding the health economic consequences of different therapeutic alternatives.[1] Of note, many such analyses have compared an individual NOAC (ie, apixaban, rivaroxaban, dabigatran) versus warfarin by using data from randomized clinical trial data,[13–19] and several studies included all of the 3 NOACs from a US or Canadian perspective.[20–22] Crucially, however, no previous study has compared health economic outcomes between the 3 NOACs by using indirect treatment comparison data from a UK perspective conforming the drugs with their European labels.

From a health care payer's point of view, the absence of such data is a major gap in the evidence to inform decisions on resource allocation for NOACs. In particular, it is important to know whether the clinical advantages in terms of the efficacy and safety profile of apixaban over warfarin, as observed in randomized clinical trials, translate into health economic benefits, especially when compared with other NOACs, without head-to-head clinical trial data. The objective of the present study, therefore, was to assess the cost-effectiveness of apixaban (5 mg BID) versus the other NOACs (including dabigatran and rivaroxaban) approved for stroke prevention in patients with NVAF. The study was conducted from the perspective of the United Kingdom National Health Service.

METHODS

This study involved construction and use of an economic model to estimate long-term clinical and economic outcomes for patients with NVAF treated with apixaban, dabigatran, or rivaroxaban.

Model Design

The model used a Markov cohort approach. In the context of this study, such a model would conceptualize the course of AF by exploring what might happen over time to a hypothetical cohort of patients with the condition over a lifetime horizon. This analysis was performed by representing the disease course in terms of mutually exclusive health (or disease) states,[12,23] such as NVAF without complications, NVAF with stroke, or NVAF with bleeding, that the patients can enter, remain in, or move ("transition") between as an approximation to potential real-life patient journeys. Time in a Markov model is represented as a recurring fixed interval, known as the model cycle.[12,23] It is assumed that during each cycle, patients may remain in