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Efficacy and Safety of Dabigatran: A Comparison of Food and Drug Administration Approved Dosing Regimens

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Purpose

This study will evaluate the efficacy and safety of the two United States Food and Drug Administration (FDA) approved doses of dabigatran, 150 mg twice daily and 75 mg twice daily, utilized for the prevention of ischemic stroke in patients with non-valvular atrial fibrillation.

Background

- Non-valvular atrial fibrillation is an important cause of disabling stroke with one out of six strokes occurring in patients with atrial fibrillation.[1,2]
- Clot formation, as a result of blood stasis, in the left atrial appendage is thought to be the main source of cardioembolic ischemic strokes in patients with atrial fibrillation.[3]
- The American College of Cardiology/American Heart Association/ European Society of Cardiology guidelines recommend warfarin therapy in most patients with atrial fibrillation who have a $CHADS_2$ (Cardiac Failure, Hypertension, Age, Diabetes, Stroke [Doubled]) score of two or greater.[3]
- Dabigatran is an oral direct thrombin inhibitor currently approved in the United States for stroke and systemic embolism prevention in patients with non-valvular atrial fibrillation, based on the results of the Randomized Evaluation of Long-term Anticoagulant Therapy (RE-LY) trial.[4]
- The RE-LY trial was a randomized, noninferiority trial which evaluated the effects on stroke or systemic embolism of two fixed doses of dabigatran, 150 mg or 110 mg twice daily, and adjusted-dose warfarin.[5]
- The FDA approved doses are 150 mg twice daily or 75 mg twice daily for patients with renal dysfunction, defined as a creatinine clearance (CrCl) less than 30 mL/min.[4]
- Currently, there are no trials that assess the efficacy or safety of dabigatran 75 mg twice daily dosing for stroke prevention in patients with non-valvular atrial fibrillation.

Study Design

Retrospective chart review of thromboembolic and major bleeding event rates for the first 6 months following initiation of dabigatran 150 mg twice daily or 75 mg twice daily.

Study Population

- Inclusion Criteria
  - Patients with non-valvular atrial fibrillation initiated on dabigatran 150 mg twice daily or 75 mg twice daily for stroke prophylaxis from January 1st, 2011 to June 30th, 2011.
- Exclusion Criteria
  - Patients who discontinued dabigatran prior to discharge for reasons other than thromboembolism or major bleeding.

Methods

- The primary outcome of the study will be the occurrence rate of the composite of thromboembolic and major bleeding events.
  - A thromboembolic event will be defined as any stroke, systemic embolism, or myocardial infarction.
  - Major bleeding events will be defined as a reduction in hemoglobin level of at least 2 grams per deciliter, transfusion of at least 2 units of blood, or symptomatic bleeding in a critical area or organ.
- Patient data to be collected will include:
  - Any stroke, systemic embolism, myocardial infarction, or major bleeding
  - Age, gender, height, weight, serum creatinine, and creatinine clearance
  - History of congestive heart failure, hypertension, diabetes mellitus, or previous stroke, transient ischemic attack, or cerebrovascular accident as documented in the permanent medical record
  - Usage of concomitant anti-platelet therapy
  - Hemoglobin if bleeding suspected and any transfusions
  - Date of readmission and reason for readmission, if any
- Appropriateness of dabigatran dosing will also be assessed based on the patient's renal function in accordance with this product's FDA approved dosing recommendations.
- Following data collection, the observed rates of the composite endpoint will be reported and statistically evaluated using a 2-sided 95 percent confidence interval, computed around the difference in observed rates.

Disclosure

Authors of the presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.

- Kenneth Lupi - nothing to disclose
- Joseph Ottinger - nothing to disclose

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