Letter by Govindarajan and Salgado Regarding Article, “Risk of Bleeding With 2 Doses of Dabigatran Compared With Warfarin in Older and Younger Patients With Atrial Fibrillation: An Analysis of the Randomized Evaluation of Long-Term Anticoagulant Therapy (RE-LY) Trial”

To the Editor:

We read with interest the article by Eikelboom et al1 on the subgroup analysis of bleeding complications with the 2 doses of dabigatran and coumadin in the RE-LY trial. It is interesting to note that the bleeding risk was the same for both doses. This was irrespective of whether patients were taking aspirin alone or a combination of aspirin and clopidogrel, whether they had renal failure, and even their age, although the higher dose (D150) had an increased trend toward major bleeding compared with the lower dose (D110).1

Atrial fibrillation is a disease of the old (>75 years), and older patients are more likely to be taking aspirin and/or clopidogrel for cardiac stent patency (more so with drug-eluting types of stents), particularly patients taking dabigatran, who have a significantly higher risk of myocardial infarction than those taking warfarin.2 It is also not uncommon to have older patients with mild to moderate renal failure who are taking both aspirin and clopidogrel. Physicians are fearful of causing harm in recommending the use of anticoagulation in these frail elderly patients, especially if they are perceived to be at risk for falls, in spite of the evidence not supporting this practice.3 Indeed, it is this patient population that has the most to gain because of the high incidence of stroke. But given the numerous risk factors for bleeding that are prevalent in the elderly (eg, a 76-year-old with renal failure and taking both aspirin and clopidogrel), physicians are left wondering whether dabigatran (especially D150) is safe at all, especially with regard to gastrointestinal bleeding. Lack of a reliable laboratory marker has not helped the cause. A broader treatment option in terms of D110 would have given us greater ammunition in prescribing anticoagulation.

As neurologists, we often face the dilemma of prescribing anticoagulation in patients after recombinant tissue-type plasminogen activator therapy. Of course, as studies have shown, dabigatran is safer than coumadin in terms of intracranial bleeding, although D110 has shown a lower trend than D150.1 But again, there are no data on the safety of dabigatran after recombinant tissue-type plasminogen activator therapy, and D110 could have been a safer alternative given its lower trend for intracranial bleeding. In our own experience here at the Cleveland Clinic Florida, we have preferred to use coumadin rather than dabigatran in patients after recombinant tissue-type plasminogen activator therapy.

The Food and Drug Administration for its part has criticized the “play-it-safe approach” and thus has reiterated its nonapproval of D110,4 but given our current lack of experience and limited knowledge, with dabigatran, the “all-or-none” approach might be self-defeating. Furthermore, the RE-LY trial was a noninferiority trial and was not designed to conclude that D150 was superior to D110, which is one of the reasons against nonapproval of D110.2,4

We conclude by emphasizing that anticoagulation is a clinical decision best left to the treating physicians and their patients and cannot be dictated by the iron hand of the Food and Drug Administration. As suggested by the authors of the RE-LY trial themselves, each dose is suitable for a unique set of patients, and thus, both doses have an independent clinical role.2 We hope the Food and Drug Administration recognizes this.

Disclosures

None.

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Circulation. 2012;125:e290
doi: 10.1161/CIRCULATIONAHA.111.053710

The online version of this article, along with updated information and services, is located on the World Wide Web at:

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