

**ANTICOAGULATION THERAPY**

# Appropriate dosing of apixaban

In the ARISTOTLE trial of apixaban versus warfarin for stroke prevention in patients with atrial fibrillation, those with two or more dose-reduction criteria (aged  $\geq 80$  years, weight  $\leq 60$  kg, creatinine level  $\geq 1.5$  mg/dl) received 2.5 mg of apixaban twice daily, instead of the full dose of 5 mg of apixaban twice daily. A secondary analysis of the trial data has now been performed to determine the safety and efficacy of apixaban 5 mg twice daily in patients with only one dose-reduction criterion.

Of the 17,370 patients randomly assigned to apixaban 5 mg or warfarin in ARISTOTLE, 76.9% met no dose-reduction criteria, 22.8% met one dose-reduction criterion, and 0.3% met two dose-reduction criteria. The 3,966 patients with one dose-reduction criterion had higher rates of stroke or systolic embolism (HR 1.47) and major bleeding (HR 1.89) compared with those with no dose-reduction criteria. Compared with warfarin, the 5 mg dose of apixaban showed a similar benefit on stroke and systemic embolism in patients with one dose-reduction criterion (HR 0.94) and those with no dose-reduction

criteria (HR 0.77;  $P=0.36$  for interaction). The 5 mg dose of apixaban compared with warfarin also showed a similarly lower rate of major bleeding in patients with one dose-reduction criterion (HR 0.68) and those with no dose-reduction criteria (HR 0.72;  $P=0.71$  for interaction).

“Patients should be treated with the effective doses as studied, because using the reduced 2.5 mg twice daily dose of apixaban in this population [of patients with one dose-reduction criterion] could result in preventable strokes,” summarize the investigators. In an accompanying Editorial, Jeffrey Weitz and John Eikelboom concur: “Education is urgently needed to translate this information into practice because the inappropriate use of the lower dose of apixaban may place patients at risk for stroke.”

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**ORIGINAL ARTICLE** Alexander, J. H. *et al.* Apixaban 5 mg twice daily and clinical outcomes in patients with atrial fibrillation and advanced age, low body weight, or high creatinine: a secondary analysis of a randomized clinical trial. *JAMA Cardiol.* <http://dx.doi.org/10.1001/jamacardio.2016.1829> (2016)