
To the Editor:

We agree with the recommendation by Alberts and colleagues\(^1\) that dabigatran etexilate should not be routinely used in patients with mechanical heart valves but we are concerned with the suggestion that dabigatran might be a reasonable alternative in cases in which standard warfarin therapy is not possible. The currently approved doses of dabigatran for stroke prevention in atrial fibrillation are 110 and 150 mg twice a day (and 75 mg twice a day in the United States) and off-label use of these doses in patients with mechanical heart valves could lead to thromboembolic complications because drug levels are inadequate.

The Randomized Evaluation of Long-Term Therapy (RE-LY) trial demonstrated that the 110-and 150-mg twice-a-day doses of dabigatran were effective for stroke prevention in patients with atrial fibrillation.\(^2\) Dabigatran is 80% renally cleared and blood levels of the drug and thus its anticoagulant effect are influenced by renal function.\(^3\) The average creatinine clearance of patients enrolled in the RE-LY trial was 68.3 mL/min (median), which is substantially lower than might be expected in patients with mechanical heart valves who are generally younger and thus have better renal function. Pharmacokinetic modeling suggests that many valve patients will require higher doses of dabigatran than those used in RE-LY to achieve the same anticoagulant effect.\(^4\)

The primary of objective of the recently launched Phase II REALIGN trial (Randomised, phase II study to Evaluate the sAfety and pharmacokinetics of oral dbIGatran etexilate in patients after heart valve replacement) is to identify doses of dabigatran etexilate that are expected to be safe and effective for the prevention of thromboembolic complications in patients with mechanical heart valves. The doses of dabigatran being tested in REALIGN range from 150 to 300 mg twice a day adjusted according to renal function and drug levels to exceed a critical threshold blood level based on experience from the RE-LY trial.

No reliable data are as yet available regarding the efficacy and safety of dabigatran in patients with a mechanical valve, which is a clinical situation distinct from left atrial thrombus formation in atrial fibrillation. Until such data are available, we do not recommend using dabigatran for the prevention of thromboembolic complications in patients with mechanical heart valves outside of the setting of a randomized trial.

Disclosures

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