Nature Reviews Cardiology **10**, 614 (2013); published online 17 September 2013; doi:10.1038/nrcardio.2013.145

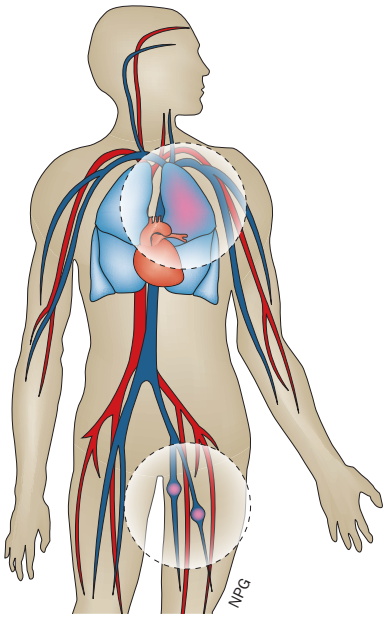
VENOUS THROMBOEMBOLISM

Edoxaban: as effective and safer than warfarin in VTE

Patients with venous thromboembolism (VTE) might benefit from treatment with the novel factor Xa inhibitor edoxaban, according to the results of the Hokusai-VTE trial, which were presented at the 2013 ESC Congress and simultaneously published in *NEJM*. VTE, manifesting as deep-vein thrombosis or pulmonary embolism (PE), can already be treated using low-molecular-weight heparin followed by a vitamin K antagonist, such as warfarin. However, recognized shortcomings of warfarin therapy, such as drug–drug interactions and the need for close therapeutic monitoring, render this treatment suboptimal. Novel, fixed-dose, fast-acting, oral anticoagulants might improve the management regimen for patients with VTE.

Dr Harry Büller and colleagues enrolled a broad spectrum of patients with VTE, including those with severe PE, in the "hope to reflect real-world practice". A total of 4,921 patients with deep-vein thrombosis and 3,319 with PE initially received heparin (according to standard clinical practice) and were then randomly assigned to either warfarin or once-daily edoxaban (60 mg, or 30 mg for those at high risk of bleeding). The study drug was given for 3–12 months, according to clinical judgement, again to simulate real-world practice.

Heparin plus warfarin is a highly effective treatment for VTE, but inconvenient for patients, so the primary efficacy outcome was noninferiority of edoxaban in terms of recurrent VTE. This end point occurred in 3.2% and 3.5% of patients taking edoxaban or warfarin, respectively (HR 0.89, 95% CI 0.70–1.13, $P<0.001$ for noninferiority). The primary safety outcome, major or clinically relevant nonmajor bleeding, occurred in 8.5% and 10.3% of patients in each group, respectively (HR 0.81, 95% CI 0.71–0.94, $P=0.004$ for superiority). The rates of death and other adverse outcomes did not differ significantly between the groups.



In those who received the half dose of edoxaban because of increased bleeding risk owing to renal impairment or low body weight ($n=1,452$), the efficacy of the drug was maintained (recurrent VTE in 3.0% taking edoxaban versus 4.2% receiving warfarin; HR 0.73, 95% CI 0.42–1.26), and the bleeding risk was reduced (7.9% vs 12.8%, respectively; HR 0.62, 95% CI 0.44–0.86).

The investigators are now testing whether "edoxaban might replace warfarin for stroke prevention in patients with atrial fibrillation. The results of this trial will be presented at the AHA Scientific Sessions in November 2013," says Dr Büller.

Gregory B. Lim

Original article The Hokusai-VTE Investigators. Edoxaban versus warfarin for the treatment of symptomatic venous thromboembolism. *N. Engl. J. Med.* doi:10.1056/NEJMoa1306638