EINSTEIN DVT: Rivaroxaban Noninferior to Enoxaparin and Warfarin in Patients with DVT

Treatment with rivaroxaban provided a simple, safe, and effective alternative to standard anticoagulation therapy for patients with deep vein thrombosis (DVT), according to findings from the phase III Oral Direct Factor Xa Inhibitor Rivaroxaban In Patients With Acute Symptomatic Deep-Vein Thrombosis Without Symptomatic Pulmonary Embolism (Einstein-DVT; NCT 00440193). Harry R. Buller, MD, PhD, Academic Medical Center, Amsterdam, The Netherlands, presented findings from EINSTEIN DVT.

Rivaroxaban is an investigational oral factor Xa inhibitor. For patients who require anticoagulation, single-agent rivaroxaban presents an attractive alternative to standard combination therapy with low-molecular-weight heparin and warfarin, which requires subcutaneous injections, dietary restrictions, and close monitoring to confirm clotting time. One potential limitation of rivaroxaban is the lack of antidote to rapidly reverse its anticoagulation activity. By comparison, the effects of warfarin can be reversed with the administration of vitamin K.

The open-label EINSTEIN DVT trial included 3449 patients with symptomatic DVT and without symptomatic pulmonary embolism (PE). Patients were randomly assigned to treatment with rivaroxaban 15 mg twice daily for 3 weeks, followed by a 20-mg maintenance dose (n=1731), or body weight-adjusted subcutaneous enoxaparin 1 mg/kg twice daily for at least 5 days, followed by warfarin (n=1718). Anticoagulation treatment continued for 3, 6, or 12 months at the discretion of the treating physician. The primary endpoint was symptomatic venous thromboembolism (VTE), which was defined as a composite of recurrent DVT, nonfatal PE, and fatal PE.

Rivaroxaban reduced the risk of recurrent VTE compared with standard therapy (2.1% vs 2.0%), meeting the criteria for noninferiority ($p<0.0001$) and approaching statistical significance for superiority ($p=0.076$). Among individual efficacy outcomes, rivaroxaban reduced the risk of recurrent DVT by half compared with enoxaparin and warfarin (0.8% vs 1.6%). Other outcomes were comparable in the rivaroxaban and standard therapy groups, including nonfatal PE (1.2% vs 1.0%) and fatal PE (0.2% vs 0.3%).

The net clinical benefit, which accounted for symptomatic VTE plus major bleeding, also favored rivaroxaban over enoxaparin and warfarin (HR, 0.67; 95% CI, 0.47 to 0.95). An analysis of safety outcomes showed similar rates of bleeding, including major and clinically relevant nonmajor bleeding, for rivaroxaban compared with standard therapy (8.1% vs 8.1%; $p=0.77$). Rivaroxaban was not associated with liver toxicity, a safety concern with other factor Xa inhibitors.

The EISTEIN DVT trial supports the use of rivaroxaban as a simplified approach for treating DVT and preventing recurrent VTE, Prof. Buller concluded. A companion trial, EINSTEIN PE, is currently underway to compare the efficacy and safety of rivaroxaban versus enoxaparin and warfarin in patients with symptomatic PE.

UFH and Fondaparinux in ACS Patients Undergoing PCI: Results from the FUTURA/OASIS-8 Trial

The addition of a standard-dose regimen of unfractionated heparin (UFH) to fondaparinux (FONDA) during percutaneous coronary intervention (PCI) preserves the bleeding reduction benefit of fondaparinux therapy while minimizing associated catheter thrombosis risk in patients with acute coronary syndromes (ACS). However, a low-dose UFH regimen did not reduce the rate of major peri-PCI bleeding or major vascular access site complications compared with standard-dose UFH when added to FONDA treatment in this cohort. Sanjit S. Jolly, MD, McMaster University, Hamilton, Ontario, Canada, presented findings from the Fondaparinux Trial with Unfractionated Heparin During Revascularization in Acute Coronary Syndromes (FUTURA)/Organization to Assess Strategies in Acute Ischemic Syndromes (OASIS)-8 Study (NCT00790907).

FONDA was determined to reduce major bleeding and improve long-term morbidity and mortality rates compared with enoxaparin in OASIS-5. However, catheter thrombosis was more common among patients who were treated with FONDA compared with enoxaparin alone, and this risk appeared to be attenuated by adjunct UFH during PCI [OASIS-5 Investigators. *N Engl J Med* 2006; Mehta SR et al. *J Am Coll Cardiol* 2007]. FUTURA/OASIS-8 was designed to compare the safety of 2 UFH regimens in patients who were undergoing PCI (within 72 hours) who had non-ST-segment elevation ACS and had been treated with FONDA.

Patients were randomized to receive either intravenous low-dose (50 U/kg; n=1024) or standard-dose (85 U/kg or 60 U/kg if taking glycoprotein IIb/IIIa inhibitors;

Continued on page 20