THROMBOSIS

An effective therapy for leg SVT

A report published by the CALISTO investigators in the *New England Journal of Medicine* demonstrates the first effective medical therapy for patients with superficial-vein thrombosis (SVT) of the legs. When compared with placebo, a daily subcutaneous dose of fondaparinux 2.5 mg was associated with an 85% reduction in the composite end point of all-cause death, symptomatic deep-vein thrombosis (DVT) or pulmonary embolism (PE), and symptomatic recurrence of SVT or extension of SVT to the saphenofemoral junction.

SVT is a common condition affecting the veins located just below the surface of the skin—most frequently in the lower limbs (the small and great saphenous veins). This complaint is usually benign; however, SVT is a recognized risk factor for DVT and pulmonary embolism. Predisposing factors for SVT include pregnancy, obesity, immobilization following surgery, and varicose veins. Historically, the evidence-base for the treatment of SVT has been sparse. As the CALISTO investigators write, "recommendations in various guidelines are weak and, in practice, therapeutic strategies vary". Establishing an effective treatment for this condition is, therefore, an important goal of research.

The anticoagulant Factor Xa inhibitor fondaparinux has previously been shown to effectively prevent venous thromboembolism in a variety of patient populations. The CALISTO study was conducted with the aim of determining whether this agent could also be a safe and effective prophylaxis against the complications of SVT.

This randomized, placebo-controlled trial involved 171 treatment centers in 17 countries in Europe and the Middle East. Enrolled patients ($n = 3{,}002$) had lower limb SVT of ≥5 cm in length, as determined by compression ultrasonography. Individuals with DVT, PE, or cancer, pregnant women, patients who had received an antithrombotic agent for >48 h, and those in whom ligation or stripping of the veins was deemed necessary, were excluded. Patients were randomly assigned in a 1:1 ratio to receive fondaparinux 2.5 mg per day or placebo for 48 days.

The majority of patients were female (64%) and there was a high prevalence of pre-existing varicose veins in the study population (89%). By day 47 after randomization, the incidence of the primary composite end point was significantly lower in the fondaparinux group than in the placebo group (0.9% vs 5.9%; relative risk 0.15, 95% CI 0.08–0.26, $P<0.001$). All individual components of this outcome measure were reduced to a similar extent with the use of fondaparinux. In addition, the need for surgical treatment of SVT was reduced by 82% with fondaparinux when compared with placebo. The benefits of the drug persisted to day 77 after randomization. Importantly, the incidence of bleeding was not increased in the fondaparinux group and no cases of thrombocytopenia were reported. Although the investigators speculate that "the 45-day regimen of subcutaneous injections could be questioned from a practical standpoint", they also acknowledge that the 90% patient adherence to therapy is reassuring and indicates that this strategy could be feasible in the clinical outpatient setting. Professor Alexander Turpie from McMaster University in Canada, who was not involved in the CALISTO trial, commented that this "well designed and executed study ... will change practice. The consistency of the effect across all components of the primary outcome is important."

Alexandra King

Original article Decousus, H. *et al.* Fondaparinux for the treatment of superficial-vein thrombosis in the legs. *N. Engl. J. Med.* **363**, 1222–1232 (2010)