Rivaroxaban or fondaparinux for superficial-vein thrombosis - a randomized controlled non-inferiority trial

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Objective: Superficial-vein thrombosis can lead to deep-vein thrombosis and pulmonary embolism. Rivaroxaban, an oral factor Xa inhibitor, may simplify treatment compared with fondaparinux.

Methods: In this prospective randomized open-label blinded end-point non-inferiority trial, we compared once daily oral rivaroxaban (10 mg OD) with once daily subcutaneous fondaparinux (2.5 mg OD) for 45 days in 472 patients with superficial-vein thrombosis. Only patients with symptomatic thrombosis (at least 5 cm in involving a 5-cm or longer supragenual superficial-vein segment above the knee) who had at least one additional risk factor (age over 65 years, male sex, previous venous thromboembolism, cancer, autoimmune disease, or involvement/thrombosis of non-varicose veins) were included. Main exclusion criteria were: symptoms for longer than 3 weeks, superficial venous/thrombus in a 3 cm of the sapheno-femoral junction, indication for full-dose anticoagulation therapy, significant hepatic disease or renal impairment, creatinine clearance below 30 millilitres/minute. The primary efficacy outcome was a composite of symptomatic deep-vein thrombosis or pulmonary embolism, progression or recurrence of superficial vein/thrombosis and all-cause mortality at 45 days. A. non-inferiority margin of 4.5% (absolute difference between rivaroxaban and fondaparinux) was used. The principal safety outcome was major bleeding.

Results: In the 435 patients included in the per-protocol analysis set, the primary efficacy outcome occurred in 7 of 211 patients (3.3%; 95% confidence interval [CI] 1.6 to 6.7%) in the rivaroxaban group and in 4 of 224 patients (1.8%; 95% CI, 0.7 to 4.5%) in the fondaparinux group (hazard ratio 1.9; 95% CI, 0.6 to 6.4; risk difference [rivaroxaban-fondaparinux] 1.5%; one-sided upper 95% CI 4.0%; p=0.025 for non-inferiority) at day 45. At 90 days, the rates were 7.1% and 6.7% in the rivaroxaban and fondaparinux groups, respectively (risk difference 0.4%; one-sided upper 95% CI 4.4%; p=0.047 for non-inferiority). There were no major bleeds in either group.

Conclusion: Rivaroxaban was non-inferior to fondaparinux for treatment of superficial-vein thrombosis and was not associated with more major bleeding (Supported by Bayer Vital, Germany; ClinicalTrials.gov number, NCT01499953).