

Title: A pilot study on Dabigatran etexilate in malignancy associated venous thromboembolism

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Dabigatran etexilate is an oral direct thrombin inhibitor. It was shown in the RE-COVER study to be effective in the treatment of venous thromboembolism and was associated with a lower bleeding risk than warfarin. [1,2] It is not metabolized by cytochrome P450 system in the liver and therefore, in contrast to other direct oral anti-coagulants, concomitant administration of CYP3A4 inducers or inhibitors would not lead to significant drug-drug interactions. We conducted a prospective single arm study to evaluate the efficacy and safety of dabigatran etexilate in the treatment of malignancy associated venous thromboembolism. Primary endpoint is first episode of objectively documented symptomatic recurrent venous thromboembolism (deep vein thrombosis, pulmonary embolism) during the 12-month study period. Safety outcomes were major, clinically relevant non-major, and any minor bleeding episodes during the oral-only treatment period.

A total of 24 patients with malignancy associated venous thromboembolism were recruited in the study. Male to female ratio was 1.18:1 and the median age was 62.5 year (range 33-81). Carcinoma of lung was the most common underlying malignancy (N=8) followed by genitourinary malignancies (N=5). Pulmonary embolism was diagnosed in 15 patients while 7 patients presented with deep vein thrombosis of lower limbs or pelvic veins. One patient had thrombus in subclavian vein and the remaining patient had internal jugular vein thrombosis. Dabigatran etexilate was given at a dose of 150mg twice daily after five days of subcutaneous Tinzaparin 175 iu/kg daily. At least 6-month treatment of dabigatran etexilate was given. After a median follow-up of 7 months (range 2-27 months), there has been no breakthrough thrombosis observed. Median duration of dabigatran treatment was 5 months (range 1-23 months). Seven patients have completed their course of anticoagulation uneventfully. Four patients stopped dabigatran because of major bleeding and two of them had underlying genitourinary malignancy. Seven patients died of their underlying malignancies during the study period.

Reference:

1. Schulman S, Kearon C, Kakkar AK, et al. Dabigatran versus warfarin in the treatment of acute venous thromboembolism. *N Engl J Med.* 2009;361(24):2342-52.
2. Schulman S, Goldhaber SZ, Kearon C, et al. Treatment with dabigatran or warfarin in patients with venous thromboembolism and cancer. *J Thromb Haemost.* 2015 Jul;114(1):150-7.