Efficacy of Dabigatran Etexilate in a Cancer-Associated Thrombosis Murine Model

Yusra K Al Mosuli[1], Catherine A. Lemarie [1,2], Joanne Vanryn[3] & Mark D. Blostein[1,2]

[1]Lady Davis Institute for Medical Research, [2]Department of Medicine, McGill University, Montreal, Quebec, Canada and [3]Boehringer-Ingelheim, Ingelheim, Germany.

catherine.lemarie@mcgill.ca

Background

Venous thromboembolism (VTE) is a common complication of cancer. Bleeding is particularly problematic due to the use of anticoagulants and the frequent need for surgical interventions. The treatment of cancer-associated thrombosis consists primarily of low molecular weight heparin (LMWH) given parentally. Recently, direct oral anticoagulants (DOACs) have become available. DOACs require less dose adjustment and are given orally. A recent metanalysis of cancer patients treated with DOACs for VTE demonstrate that DOACs were as effective and safe as warfarin for use in cancer patients. However, no studies have directly studied DOACs in cancer patients with VTE nor compared DOACs with LMWH with selective inclusion of cancer patients only.

Objective

In a murine cancer-associated venous thromboembolism model, Dabigatran is as effective as Dalteparin.

Methods

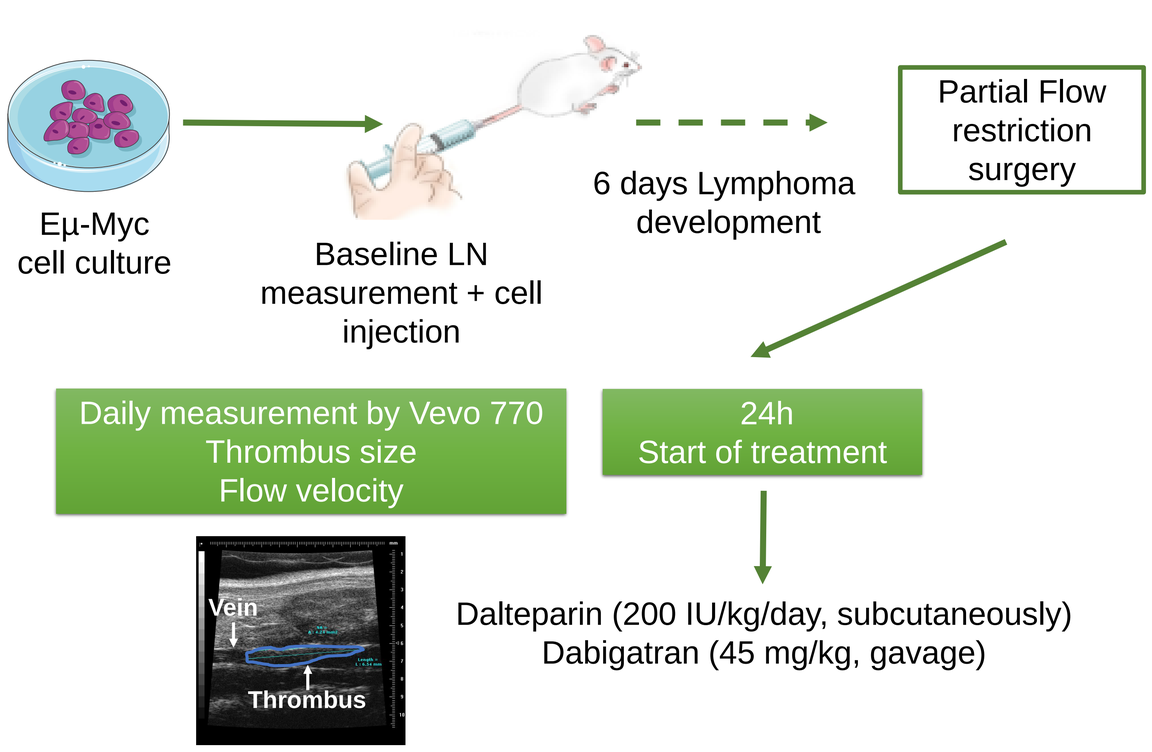

Fig 1. Cancer-associated venous thrombosis animal model: Schematic representation of the experimental procedure used for the development of cancer-associated venous thrombosis model.

Results

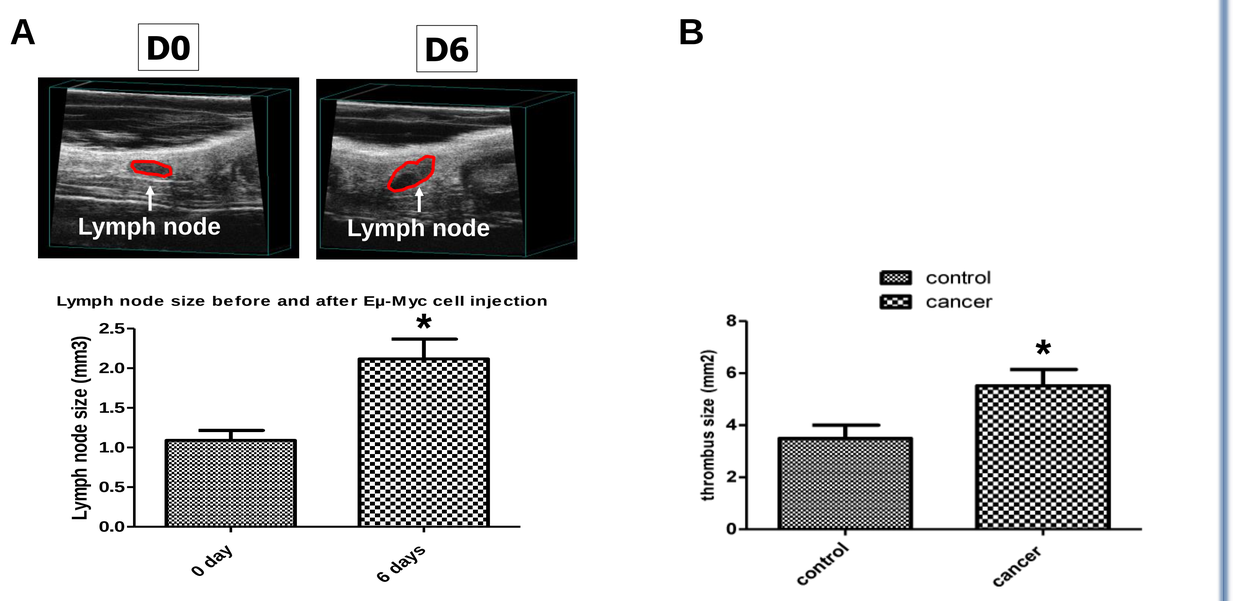

Fig 2. B cell lymphoma promotes venous thrombosis: (A) lymph node size at D0 and D6. Lymph nodes were measured before (D0) and after (D6) injection of Eμ-Myc cells using a High Frequency Ultrasound System (HFUS). (B) Quantifications of thrombus size in mice with or without cancer. Partial ligation of the vena cava was performed at D6 and 24h later monitoring for thrombus formation was done. (*P <0.05)

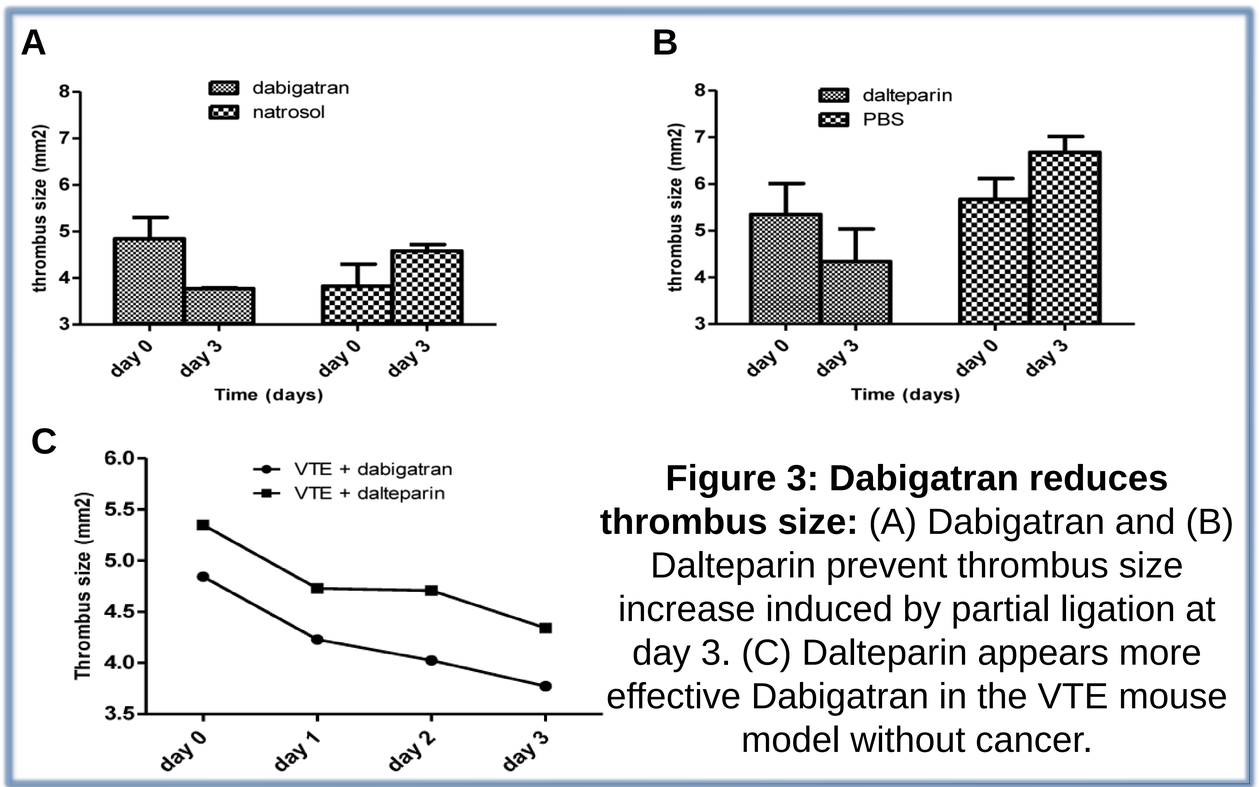

Figure 3: Dabigatran reduces thrombus size: (A) Dabigatran and (B) Dalteparin prevent thrombus size increase induced by partial ligation at day 3. (C) Dalteparin appears more effective Dabigatran in the VTE mouse model without cancer.

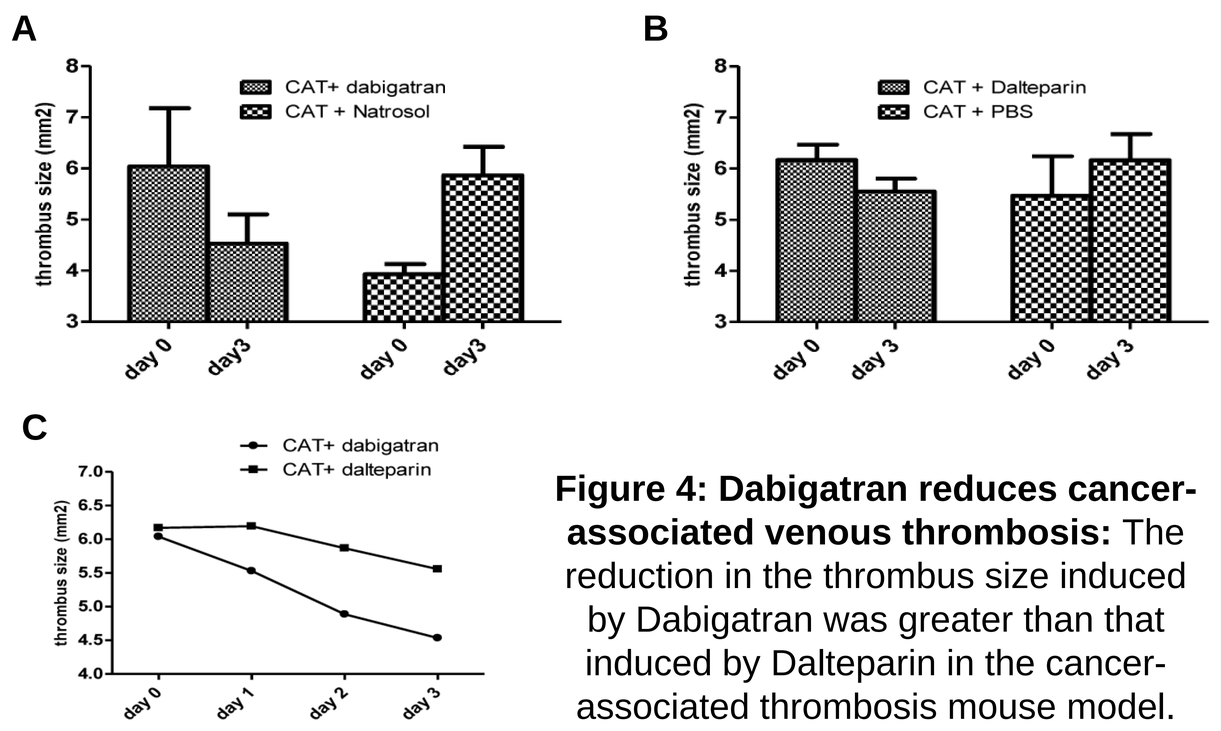

Figure 4: Dabigatran reduces cancer-associated venous thrombosis: The reduction in the thrombus size induced by Dabigatran was greater than that induced by Dalteparin in the cancer-associated thrombosis mouse model.

Conclusions

Both Dalteparin and Dabigatran are effective in reducing the size of the thrombus in our mouse model, although the efficiency differs between cancer and non-cancer associated thrombosis. Dalteparin is more efficient when compared to Dabigatran in thrombosis not associated with cancer whereas the efficiency of Dabigatran is superior in cancer-associated thrombosis. As a proof of principle, the above described models can be further employed to study the pathophysiology of VTE and cancer-associated thrombosis and provide biologic plausibility for pursuing further studies for using DOACs, specifically, Dabigatran, in cancer-associated thrombosis.

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Catherine Lemarie
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