

RE-COVER™ STUDY

KEY SUMMARY

- The first results from RE-COVER™ show that dabigatran etexilate is as effective as well-controlled warfarin in the reduction of recurrent venous thromboembolism (VTE) and deaths related to VTE¹
- Dabigatran etexilate demonstrated a significant 37% reduction in major or clinically relevant bleeding, was comparable with warfarin in major bleeds and showed a significant 29% reduction in any bleeding compared with well-controlled warfarin¹
- The benefits demonstrated in efficacy and safety with dabigatran etexilate occurred without any evidence of liver toxicity¹
- RE-COVER™ is part of the most advanced trial programme of a novel oral anticoagulant in clinical development for treatment of acute VTE¹
- Unlike warfarin, dabigatran etexilate provides predictable and consistent anticoagulant effects with a low potential for drug interactions, no food interactions, and no requirement for routine coagulation monitoring.

Study background

- Well controlled vitamin K antagonist (VKA) therapy (such as warfarin) is highly effective in the treatment of acute venous thromboembolism (VTE) following initial treatment with a fast-acting anticoagulant.² However, VKAs have several limitations which make maintaining patients within the narrow therapeutic range of INR* 2.0-3.0 difficult and inconvenient for clinicians and patients, including slow onset and offset of action, the need for routine coagulation monitoring and dose adjustment, and numerous food and drug interactions.
- Even with close monitoring in a clinical trial, patients receiving warfarin only spend half their time within this narrow therapeutic range, and INR control tends to be even lower in clinical practice.³

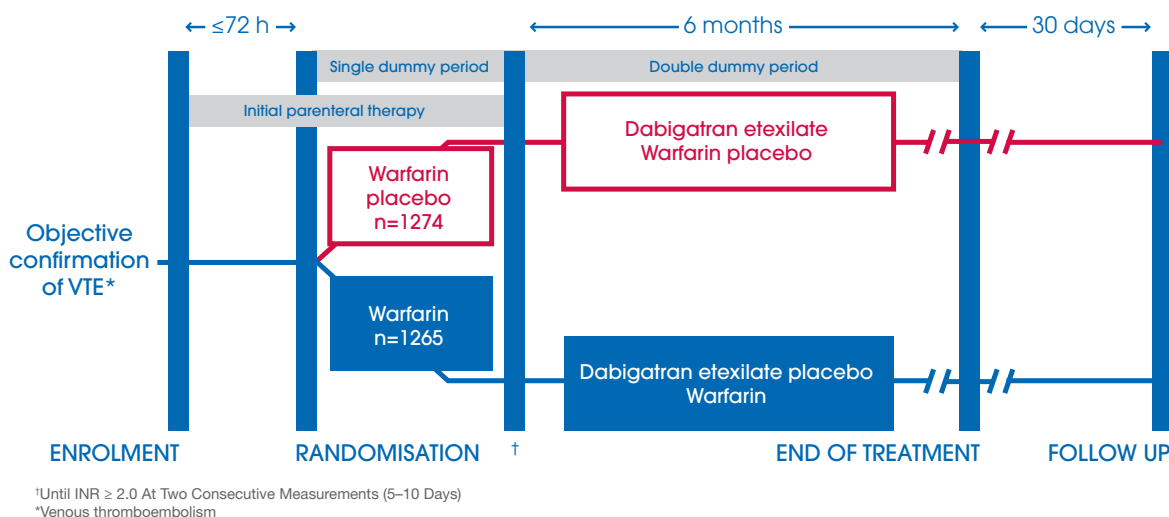
Primary objective:

- To demonstrate that the novel oral direct thrombin inhibitor dabigatran etexilate is as effective and safe as well controlled warfarin therapy for the treatment of acute VTE.¹

Study Design

RE-COVER™ is part of the most advanced trial programme of a novel oral anticoagulant in clinical development for treatment of acute VTE¹

- It is a phase III, randomised, double blind, parallel-group study¹
- It involved 2,539 patients in 228 centres, in 29 countries¹
- All patients received initial treatment (5-10 days) with a parenteral anticoagulant (low molecular weight heparin or unfractionated heparin) in line with current guidelines and well-established therapy¹
- Patients were randomised to oral dabigatran etexilate, administered at a fixed dose of 150 mg twice-daily, or dose-adjusted warfarin (to maintain an INR of 2.0-3.0)¹
- Treatment was given for six months.¹



RE-COVER™ results

RE-COVER™ demonstrated that dabigatran etexilate is as effective as warfarin in the treatment of VTE, with significantly less bleeding, no evidence of liver toxicity and with predictable and consistent anticoagulant effects. It has a low potential for drug interactions, no food interactions, and no requirement for routine anticoagulant monitoring.¹

* International normalized ratio

Results: Safety endpoints

- Dabigatran etexilate demonstrated significantly lower bleeding compared with warfarin¹
 - 37% reduction in major or clinically relevant bleeding (p=0.002)
 - 29% reduction in any bleeding (p=0.0002)
- Major bleeding was comparable between dabigatran etexilate (20 patients, 1.6%) and warfarin (24 patients, 1.9%) groups
- Death, acute coronary syndromes and liver function abnormalities were low and similar in all treatment groups.¹

Efficacy endpoints

- Dabigatran etexilate is as efficacious as warfarin in the reduction of recurrent VTE and deaths related to VTE (p<0.001 for pre-specified non-inferiority margin).¹

Implications of the RE-COVER™ results

- Dabigatran etexilate has the potential to change the standard of care for venous thromboembolism. The drug frees patients from concerns about diet and drug interactions and offers the advantage of a fixed oral dose and no need for blood monitoring, as opposed to the regular monitoring and dose adjustment needed with warfarin. This means patients can achieve the same results in a more convenient and safer manner.

Disclaimer

Dabigatran etexilate is not approved for clinical use in the treatment of acute VTE. This information is provided for medical education purposes only.

References

1. Schulman S, Kearon C, Kakkar AK, *et al.* Dabigatran etexilate versus warfarin in the treatment of acute venous thromboembolism. *N Engl J Med* 2009;361:2342-52.
2. Brandjes D, Heijboer H, Buller H, *et al.* Acenocoumarol and heparin compared with acenocoumarol alone in the initial treatment of proximal-vein thrombosis. *N Engl J Med* 1992;327:1485-9
3. Willey VJ, Bullano MF, Reynolds M *et al.* Management patterns and outcomes of patients with venous thromboembolism in the usual community practice setting. *Clin Ther* 2004;26:1149-59

For more information, contact:

Dr Reinhard Malin

Boehringer Ingelheim GmbH

Phone: +49/6132/7790815

Fax: +49/6132/77 66 01

E-mail: press@boehringer-ingelheim.com