Dabigatran Etexilate Versus Enoxaparin in Preventing Venous Thromboembolism Following Total Knee Arthroplasty

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INTRODUCTION

Oral venous thromboembolic prophylaxis without monitoring or dose adjustment is an advantage for patients. Dabigatran etexilate (D), an oral direct thrombin inhibitor, is being evaluated for its prophylactic effects following orthopedic surgery in a series of clinical studies.

METHODS

This phase III, double-blind, non-inferiority study, randomized 2615 patients to 12-15 days treatment with D 150 mg qd, D 220 mg qd, or enoxaparin (E) 30 mg bid. D was given as a half dose the day of surgery (6-12 hours post-surgery) and E was started 12-24 hours post-surgery. The primary efficacy endpoint was a composite of proximal DVT, distal DVT, PE and all-cause mortality (VTE). The primary safety endpoint was major bleeding events (MBE). Patients had bilateral venography at the termination of therapy. Efficacy and safety events were adjudicated by blinded independent committees. 73% of patients were evaluable for VTE.

RESULTS

VTE rates were 33.7% (D150), 31.1% (D220) and 25.3% (E; p=0.0009, D150 mg vs E; p=0.02, D220 vs E). Rates of the composite of proximal DVT, PE and VTE-related mortality (Major VTE) were 3.0% (D150), 3.4% (D220), and 2.2% (E, p=ns). MBE rates were 0.6% (D150), 0.6% (D220) and 1.4% (E). Elevated ALT (>3 x ULN) was infrequent and similar in all groups (D150, 1.0%; D220, 0.7%; E, 0.9%).

CONCLUSION

Treatment with D220 or D150 qd was not as effective as E bid in preventing VTE, but did preserve 61% and 50%, respectively, of the putative efficacy of E compared to placebo. Differences were predominantly due to asymptomatic distal DVTs, since Major VTE occurred at similar rates in all treatment groups. Dabigatran etexilate was safe and well tolerated when given orally starting 6-12 hours following total knee arthroplasty.

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