YM150, an Oral Direct Factor Xa Inhibitor, as Prophylaxis for Venous Thromboembolism in Patients with Elective Primary Hip Replacement Surgery. A Dose Escalation Study

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INTRODUCTION

Activated factor X (FXa) is a pivotal blood coagulation factor positioned at the crossroads of the extrinsic and intrinsic coagulation cascade. Inhibitors of FXa are anticoagulants that could be used in the prevention and treatment of thrombosis and venous thromboembolism (VTE).

METHODS

YM150 is a once daily, orally active FXa inhibitor. A randomized, enoxaparin-controlled, dose escalation study was performed in 174 patients undergoing elective primary hip replacement surgery to assess safety and efficacy of 7-10 days of treatment with oral doses of YM150 (3, 10, 30, or 60 mg once daily starting 6-10 h after surgery) s.c. enoxaparin (40 mg once daily starting 12 h before surgery). Safety is defined as major and/or clinically relevant non-major bleeding, and efficacy as venous thromboembolism detected by mandatory bilateral venography on the last treatment day and/or symptomatic VTE. The study was open-label with blinded evaluation of all outcomes by an independent Adjudication Committee.

RESULTS

There were no major bleeds. Three clinically relevant non-major bleeds were reported, 1 (2.9%; 95% CI: 0-16%) in the 3 mg and 2 (5.7%; 1-19%) in the 10 mg YM150 dose groups. No trend was observed in the incidence of minor bleeds with dose of YM150 in the range 10 mg to 60 mg daily. The proportion of patients with minor bleeding events in the enoxaparin group (22%; 11-41%). 147 patients (84%) were considered to have an evaluable venogram. The incidences of VTE were 52% (95% CI: 31-72%), 39% (22-57%), 23% (9-40%), and 19% (7-37%) for the respective 3, 10, 30, and 60 mg YM150 once daily dose groups in comparison with 39% (22-57%) for enoxaparin. Logistic regression analysis revealed a statistically significant dose-related trend (*P*=0.006) for patients reaching the VTE endpoint during YM150 treatment. No trend in any of the measured safety parameters was observed with study treatment (YM150 or enoxaparin) or dose of YM150.

CONCLUSION

Oral, once daily doses of YM150, 10 to 60 mg administered 6 to 10 h after primary hip replacement, were shown to be safe, well tolerated and effective in this study.

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