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Prescribing decisions should be made based on the approved package insert in the country of prescription.

Sponsor / Company: sanofi-aventis **Drug substance:** Enoxaparin (XRP4563)	**Study Identifier:** NCT00685958 **Study code:** SFY6771
Title of the study: Multicenter, non-comparative, open-label study to evaluate the safety and efficacy of enoxaparin sodium (RP54563) 20 mg bid for 14 days in patients with hip fracture surgery	
Study center(s): 16 centers in Japan	
Study period: Date first patient enrolled: 10 July 2006 Date last patient completed: 11 March 2007	
Phase of development: Phase 3	
Objectives: PRIMARY: To evaluate bleeding events (major bleeding and minor bleeding) of RP54563 20 mg twice a day (bid) for 14 days in patients undergoing hip fracture surgery. SECONDARY: To evaluate effects on venous thromboembolism (VTE) (deep vein thrombosis [DVT] or pulmonary thromboembolism [PTE] incidence) of RP54563 20 mg bid for 14 days in patients undergoing hip fracture surgery.	
Methodology: Multicenter, non-comparative, open-label	
Number of patients: Planned: 54 patients; Registered: 54 patients; Treated: 52 patients	
Diagnosis and criteria for inclusion: 1) Femoral neck inside or outside (trochanteric section of femur, subtrochanteric section of femur) fracture patients to be operated within 10 days 2) Male or female ≥20 years old at the time of giving informed consent	
Investigational product: enoxaparin sodium (RP54563) Dose: 20 mg bid (morning and evening). Administration: Medication was started 24 to 36 hours after surgery, and given subcutaneously in anterolateral or posterolateral abdominal wall.	
Duration of treatment: 14 days **Duration of observation:** 28 days (treatment period of 14 days and follow-up period of 14 days)	

Criteria for evaluation:

Safety: Safety was evaluated by bleeding events observed from Day 1 through Day 28 or discontinuation in follow-up period. Bleeding events were classified as major if it was associated with at least one of the following items:

- resulted in death
- was clinically overt and resulted in a transfusion of at least 2 units of packed red blood cells or whole blood
- was clinically overt and resulted in a decrease of 2 g/dL or greater in hemoglobin, compared to the baseline value
- was retroperitoneal, intracranial or intraocular bleeding
- resulted in serious or life threatening clinical events, or surgical or medical intervention to control the events.

Adverse events recording reported by the patient or noted by the investigator.

Standard hematology, blood chemistry and coagulation test were performed.

Efficacy: Efficacy was evaluated by DVT incidence using venography or by PTE incidence using lung ventilation/blood flow scintigraphy, pulmonary angiography or computed tomography (CT). DVT incidence evaluated by independent panel using venogram was used for efficacy.

Statistical methods:

Safety analyses were based on the safety population. The primary safety variable was the listing of major bleeding. The secondary analyses of bleeding were the rates of major/minor bleeding in the safety population, respectively. The 95% two-sided CI was also calculated.

Efficacy analyses were based on the intent-to-treat (ITT) population. The efficacy variable was VTE (DVT or PTE) incidence observed during the treatment period. The point estimate and 95% two-sided confidence interval (CI) of the VTE incidence based on Clopper-Pearson method were calculated. No covariates and center effects were considered.

Summary:

Safety results: Bleeding events occurred in 3 patients and the rate of bleeding events (major bleeding or minor bleeding) was 5.8% (3/52 patients) with 95% CI of 1.21 to 15.95. Major bleeding at incision site was observed in 1 patient as a serious adverse event possibly related to the study medication. The rate of major bleeding was 1.9% (1/52 patients) with 95% CI of 0.05 to 10.26.

Efficacy results: In the ITT population, the point estimate of the VTE incidence was 13.95% (6/43 patients) with 95% CI of 5.30 to 27.93. PTE was not observed in this study.

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