Università degli Studi di Genova
DISC
Dipartimento di Scienze Chirurgiche e Diagnostiche Integrate

Title	**SSD:**	**Project Manager**: **Chairman of the Steering Committee**: Prof. Charles Marc Samama **Chief investigator**: Prof. Patrick Mismetti. Manager for S. Martino hospital center of experimentation: Prof. Lamberto Felli
A multicentre, randomised, double-blind, controlled, phase IIIb study to assess the efficacy and safety of Rivaroxaban 10mg od versus Enoxaparin 4000 IU for VTE PROphylaxis in NOn Major Orthopaedic Surgery. The PRONOMOS study		
Financing (NO PROFIT - Company)	CHU de Saint Etienne	
Summary	Epidemiological data Major orthopaedic surgery (hip, knee replacements and hip fracture) represents only a small part of all orthopaedic surgery procedures. Surgery procedures for trauma and orthopaedic surgery of the lower limbs without trauma are far more frequent (tibia osteotomy, arthrodesis, ligament repair, etc.) The incidence of trauma patients requiring surgery and prolonged immobilisation is rising, mainly because of the increasing popularity of recreational sports. However, the epidemiology and prevention of these venous thromboembolic events (VTE) after such injuries have been poorly studied. The combination of limb surgery with or without trauma in orthopaedic surgery is responsible for an increased VTE risk. Current recommendations and practices With limited and sometimes contradictory data, prior to 2012 and the completion of the Fondacast study, the American College of Chest Physicians guidelines suggested that clinicians should not use pharmacological thromboprophylaxis in these patients. In contrast, several national guidelines or expert recommendations published in some Western European countries do recommend thromboprophylaxis, at least in certain patients presenting with other VTE risk factors. In practice, the use of thromboprophylaxis in immobilised patients with isolated lower limb injuries varies greatly. Although no treatment has yet been approved for this indication, LMWH treatments are widely used in at-risk patients. There is however no consensus on the type, dose and duration of thromboprophylaxis. In addition, daily injections of LMWH, while effective, represent a heavy burden on the patients, particularly in cases of prolonged immobilisation. New prophylactic strategies Rivaroxaban is a direct oral anticoagulant which develops a potent anti-Xa action. In major orthopaedic surgery, it has proven to be more effective and as	

	innocuous as LMWH treatments (enoxaparin 4000 IU once-daily) in patients due to undergo total hip or knee arthroplasty (RECORD programme). Up until now, it has been approved in VTE prevention after total hip and knee arthroplasties. These indicated uses only represent 20 % of all orthopaedic surgical procedures. Patients in elective non major lower limb surgery and in traumatology are younger than those patients in prosthetic orthopaedic surgery. Therefore fewer VTEs and cardiovascular events are feared. These patients often receive thromboprophylaxis by injectable route for a total duration of about 6 weeks to 3 months. On the one hand, the risk of major bleeding is lower within this young population; and the other hand, convenience and cost should weigh in favour of rivaroxaban as no injections or platelet count monitoring are required. We have decided to conduct a randomised double blind study to demonstrate the non- inferiority of oral rivaroxaban at 10 mg once-daily versus sub-cutaneous enoxaparin at 4000 IU once-daily on the occurrence of major VTEs (composite endpoint combining proximal DVTs (asymptomatic and symptomatic), symptomatic events (distal and proximal DVT, pulmonary embolisms) and VTE-related deaths) up until the end of the treatment, which depends on mobilisation (for example cast or splint removal). Primary objective of the study The primary main objective is to demonstrate the non-inferiority of rivaroxaban 10 mg versus enoxaparin 4000 IU relevant to the occurrence of major VTEs up until the end of the treatment (for example, cast or splint removal). The power of the study should reveal the superiority of rivaroxaban 10 mg once-daily relevant to the occurrence of the primary endpoint. This superiority analysis will only be performed if the primary non-inferiority objective has been met.
Link to the protocol	https://clinicaltrials.gov/ct2/show/NCT02401594