

THE MAGELLAN STUDY METHODOLOGY: RIVAROXABAN COMPARED WITH ENOXAPARIN FOR THE PREVENTION OF VENOUS THROMBOEMBOLISM IN HOSPITALIZED MEDICALLY ILL PATIENTS

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31. Thrombosis and vascular biology

Venous thromboembolism, Medical patients, Oral anticoagulant, Clinical trial

On behalf of: The MAGELLAN Investigators

Background:

Results of recently completed trials comparing low molecular weight heparins (LMWH) or pentasacharride with placebo controls in medically ill patients have provided convincing evidence for venous thromboembolism (VTE) prevention. The efficacy and safety of VTE prevention with oral rivaroxaban 10 mg od for 35 days has been demonstrated in elective hip replacement patients.

Aims:

To compare treatment with oral rivaroxaban once daily for up to 39 days to shorter term treatment with subcutaneous enoxaparin 40 mg once daily for up to 14 days and to compare short term rivaroxaban with short term enoxaparin both administered for up to 14 days for VTE prevention and safety in hospitalized medically ill patients.

Methods:

Study design: A multinational, multicenter, randomized, double-blind, double-dummy, active comparator controlled study in patients with current and likely ongoing reduced mobility. All enrolled patients receive study medication, undergo mandatory bilateral lower limb venous ultrasonography on Day 10±4 and on Day 35±4, and are followed for an additional 60 days. Symptomatic VTE is investigated at anytime. Inclusion criteria: Age ≥40 hospitalized with: heart failure, active cancer; or acute ischemic stroke with leg paresis. Or acute infection, acute inflammatory or rheumatic disorders or acute respiratory insufficiency, immobilized, and with at least one risk factor e.g: age >75

years, previous venous thromboembolism, previous cancer or heart failure, severe venous disease, thrombophilia, recent major surgery or serious trauma, hormone replacement therapy, morbid obesity (body mass index ≥ 35 kg/m²). Exclusion criteria: Include an increased risk of bleeding; prohibited drugs or procedures: e.g anticoagulant therapy; concomitant conditions or diseases such as: allergies, severe renal or liver disease. Outcomes: The primary efficacy outcome is the composite of asymptomatic proximal DVT detected by mandatory compression ultrasonography, symptomatic proximal and distal DVT, symptomatic PE and fatal VTE reported during the treatment phase of the study: The primary safety outcome is the composite of major bleeding events and non-major clinically relevant bleeding events. All subjects have rivaroxaban levels measured at various time points. In selected centers, a full PK/PD profile is performed. Pharmacogenetics and health economic outcomes are also being assessed. Statistical methods: Primary efficacy analysis: There are two efficacy analysis populations, pertaining to the two primary efficacy endpoints. The study is powered at the 90% level to show non-inferiority at Day 10 \pm 4 days and superiority at Day 35 \pm 4 days. ~8000 patients will be randomized from ~530 sites in 52 countries. The first patient was enrolled in December 2007.

Results:

Current status: 01 March 2010, ~7300 subjects have been enrolled into the study from ~530 actively recruiting centers in 52 countries. Mean age is ~70 years, ~46% are female, ~34% have heart failure, ~9% have active cancer. ~15% have acute ischemic stroke, ~37% have acute infectious and inflammatory diseases including acute rheumatic diseases and ~22% have acute respiratory insufficiency.

Summary/conclusions:

The MAGELLAN study will determine the efficacy and safety of an extended duration of treatment with rivaroxaban compared to current standard of care.

Abstract internet id : 2189

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