Extended Thromboprophylaxis With Rivaroxaban Fails to Prevent Death, VTE

September 20, 2018 — An extended 45-day course of rivaroxaban did not reduce the risk of symptomatic venous thromboembolism (VTE) or death due to VTE in patients discharged from the hospital after an acute medical illness, according to the results of the MARINER trial.

Alex Spyropoulos, MD, professor of medicine at the Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, and MARINER investigators, reported their results in the September 20, 2018, issue of the *New England Journal of Medicine*.

Hospitalization due to acute medical illness increases the risk of VTE. Anticoagulant prophylaxis reduces the risk of VTE in the hospital; however, according to current guidelines, prophylaxis is rarely continued after discharge.

In prior studies, extended thromboprophylaxis was shown to either increase the risk of major bleeding or primarily reduce the risk of asymptomatic deep-vein thrombosis. The MARINER trial evaluated the benefit of extended prophylaxis in acutely ill patients and focused only on symptomatic or fatal events.

At hospital discharge, 12 024 medically ill patients were randomly assigned to receive either 10-mg rivaroxaban or placebo once-daily for 45 days. Among patients with moderate renal insufficiency, the dose of rivaroxaban was adjusted to 7.5 mg daily.

All participants had been hospitalized 3 to 10 days for an acute form of one of the following medical conditions: heart failure, respiratory insufficiency or exacerbation of chronic obstructive pulmonary disorder, ischemic stroke, or infectious or inflammatory disease. Additionally, all participants were at risk for VTE based on a modified IMPROVE (International Medical Prevention Registry on Venous Thromboembolism) score of at least 4 or more than 2-fold elevated levels of plasma D-dimer.

The primary composite outcome was symptomatic VTE or death due to VTE. Furthermore, each component of the primary composite endpoint was evaluated separately as a secondary efficacy outcome. The key safety endpoint was major bleeding.

In the intention-to-treat population (N = 12 019) the rate of the primary efficacy outcome did not significantly differ between the rivaroxaban group and the placebo group (0.83% vs 1.10% respectively; hazard ratio [HR], 0.76; 95% CI, 0.52-1.09; *P* = .14). However, symptomatic nonfatal VTE occurred at a lower rate among patients who received rivaroxaban compared with patients who received placebo (0.18% vs 0.42%; HR, 0.44; 95% CI, 0.22-0.89).

The authors noted that secondary efficacy analyses were exploratory, and future studies will be needed to investigate the risks and benefits.

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The risk of major bleeding was low for both groups. In the rivaroxaban group, 0.28% of patients had major bleeding events compared with 0.15% of patients in the placebo group (HR, 1.88; 95% CI, 0.84-4.23).

"Given the relatively low incidence of events despite the enrichment strategy and the lack of effect on venous thromboembolism-related death, the usefulness of extended thromboprophylaxis remains uncertain," Dr Spyropoulos concluded. "Our trial did not show a significant benefit of this rivaroxaban regimen started at hospital discharge with regard to the composite outcome of fatal or symptomatic venous thromboembolism in medically ill patients."

This study received commercial funding from Janssen Research and Development.

Spyropoulos AC, Ageno W, Albers GW, et al; MARINER Investigators. Rivaroxaban for thromboprophylaxis after hospitalization for medical illness. *N Engl J Med*. 2018;379(12):1118-1127. doi:10.1056/NEJMoa1805090

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