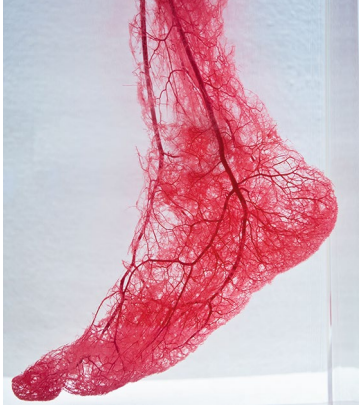
VASCULAR DISEASE

Rivaroxaban reduces ischaemic events in patients with PAD



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Rivaroxaban plus aspirin compared with aspirin alone is associated with reduced incidence of ischaemic events, including acute limb ischaemia, in patients with peripheral artery disease (PAD) who had undergone lower-extremity revascularization. This finding from the VOYAGER PAD study was presented at the virtual ACC Scientific Sessions 2020.

Patients with PAD who are treated with revascularization for limb symptoms have a 4-fold increased risk of subsequent vascular complications compared with patients who have never undergone revascularization. The previously published COMPASS trial showed that in a population of patients with chronic and stable PAD, rivaroxaban added to aspirin therapy significantly reduced the risk of ischaemic events compared with aspirin therapy alone. The VOYAGAER PAD investigators thus sought to determine the safety and efficacy of adding this anticoagulant to aspirin to lower ischaemic risk in patients with PAD after revascularization.

The investigators randomly assigned 3,286 patients to rivaroxaban (2.5 mg twice daily) plus aspirin and 3,278 patients to placebo plus aspirin. At a median follow-up of 28 months, the incidence of the primary end point (a composite of acute limb ischaemia, major amputation for vascular causes, myocardial infarction, ischaemic stroke or cardiovascular death) was 17.3% in the rivaroxaban group and 19.9% in the aspirin group (HR 0.85, 95% CI 0.76–0.96, $P=0.009$). The benefit of rivaroxaban was consistent across all subgroups, occurred early (from 3 months) and continued to accrue over time. Importantly, the principal safety outcome of TIMI major bleeding was not significantly different between the two treatment groups, but the incidence of the secondary safety outcome of ISTH major bleeding was greater in the rivaroxaban group. Overall, the investigators estimated that for every 10,000 patients treated for 1 year, the addition of rivaroxaban to aspirin therapy will prevent 181 ischaemic events at the expense of 29 TIMI major bleeding events.

> “The benefit of rivaroxaban was consistent across all subgroups, occurred early (from 3 months) and continued to accrue over time”

“Our results extend and complement the observations in the COMPASS trial, which showed reductions in ischaemic risk … in a broad population of patients with chronic [PAD],” summarize the investigators.

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ORIGINAL ARTICLE Bonaca, M. P. et al. Rivaroxaban in peripheral artery disease after revascularization. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa2000052 (2020)

ANTICOAGULATION THERAPY

Apixaban therapy is effective and safe for cancer-associated VTE

Apixaban therapy is as effective as low-molecular-weight heparin (LMWH) therapy for the prevention of recurrence of venous thromboembolism (VTE) in patients with cancer, with no increase in major bleeding events. These findings from the Caravaggio trial were presented at the virtual ACC 2020 Scientific Sessions.

VTE is a common complication and a major cause of morbidity and mortality in patients with cancer. Management of VTE in these patients is challenging because the risks of recurrent thrombosis and bleeding are higher than in individuals without cancer. Major guidelines recommend LMWH as the first-line therapy for cancer-associated VTE, but LMWH requires daily subcutaneous injections. The guidelines have recently included the non-vitamin K antagonist oral anticoagulants (NOACs) edoxaban and rivaroxaban, which are more convenient to use and have been shown to be as effective as LMWH although with a higher risk of bleeding. These shortcomings and the good efficacy–safety balance of the NOAC apixaban in the general population of patients with VTE prompted Agnelli and colleagues to test this agent in the cancer setting.

> “These findings reinforce the efficacy data and improve the safety data compared with other NOACs”

The Caravaggio trial included patients with symptomatic or incidental acute proximal deep-vein thrombosis or pulmonary embolism who were randomly assigned to receive oral apixaban or subcutaneous LMWH (dalteparin) at standard regimens.

During the 6-month treatment period, recurrent VTE (the primary efficacy end point) occurred in 5.6% of 576 patients in the apixaban group and in 7.9% of 579 patients in the LMWH group, which met the requirement for noninferiority (HR 0.63, 95% CI 0.37–1.07, $P<0.001$). The rate of major bleeding events was similar in both groups (3.8% versus 4.0%), including gastrointestinal bleeding events (1.9% versus 1.7%). Mortality was also similar in the two groups and was mostly related to cancer.

“These findings reinforce the efficacy data and improve the safety data compared with other NOACs, and expand the proportion of patients with cancer and VTE who will be eligible for treatment with this agent, including patients with gastrointestinal cancer,” highlights Agnelli. The investigators now plan to perform subanalyses of the Caravaggio trial, including assessing drug–drug interactions. In addition, the API-CAT study to assess the efficacy and safety of apixaban beyond 6 months is ongoing.

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ORIGINAL ARTICLE Agnelli, G. et al. Apixaban for the treatment of venous thromboembolism associated with cancer. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa1915103 (2020)
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