# Total Hospitalizations After Peripheral Arterial Revascularization in the VOYAGER Trial

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## BACKGROUND

In the VOYAGER PAD trial, rivaroxaban reduced first and total (first and subsequent) occurrences of major adverse limb and cardiovascular events in patients with peripheral artery disease (PAD) after lower extremity revascularization (LER), but also increased incident bleeding.

Assessment of disease burden by the onset of a particular set of events does not necessarily capture all consequences of a disease process that negatively impact patients' quality of life, motivating the adoption of more patient-centered outcomes. The present analysis of VOYAGER PAD describes the total incidence and duration of hospitalizations reported during the study as a broader measure of total disease burden and net benefit of rivaroxaban therapy.

## METHODS

Patients were randomized 1:1 to rivaroxaban 2.5 mg twice daily plus aspirin (n=3286) or aspirin alone (n=3278). Investigators documented the primary reason and duration for each hospitalization occurring after randomization. Total hospitalization incidence rates (IR) were estimated by events per 100 patient-years. Treatment group comparisons on total hospitalizations as a time-to-event outcome were by marginal proportional hazards models with death as a competing terminal event, while days in hospital were compared by zero-inflated Poisson regression. All analyses were intention-to-treat.

## RESULTS

A total of 7156 hospitalizations (3265 first, 3891 subsequent) occurred during a median 2.5 years of follow-up, with 40% being hospitalizations for PAD and a small fraction (3.3%) attributed to bleeding events. The rivaroxaban IR was lower for PAD hospitalizations and higher for bleeding event hospitalizations, with more hospitalizations prevented than caused (**Figure 1**, **Table 1**). Among patients hospitalized at least once, mean days in hospital was significantly lower for rivaroxaban for PAD, for bleeding, and for any reason, so that total days in hospital were numerically lower for rivaroxaban (**Figure 1**, **Table 2**).

## CONCLUSION

Patients with PAD undergoing LER have a high rate of subsequent hospitalizations after an index procedure, driven by re-hospitalizations for PAD. Rivaroxaban decreased both the incidence and duration of PAD hospitalizations. While rivaroxaban increased incident hospitalizations due to bleeding, the mean durations of these hospitalizations were lower relative to placebo, leading to fewer total days in hospital for bleeding (1252 vs. 1531 total days). Total days in hospital was also lower for rivaroxaban. These findings may be useful for clinicians and patients weighing the risks and benefits of rivaroxaban in PAD after revascularization.

In VOYAGER, 6564 patients had 7156 total hospitalizations over a median 2.5 years follow-up, with 40% attributed to PAD and 3.3% attributed to bleeding events.

Relative to placebo, the hospitalization incidence rate in the rivaroxaban group was lower for those attributed to PAD, and although higher for those attributed to bleeding events, rivaroxaban prevented more hospitalizations than caused, with fewer total days in hospital.

These findings provide an alternative measure of total disease burden and net benefit which may be useful for clinicians and patients weighing the total risks and benefits of rivaroxaban in PAD after revascularization.

VOYAGER PAD

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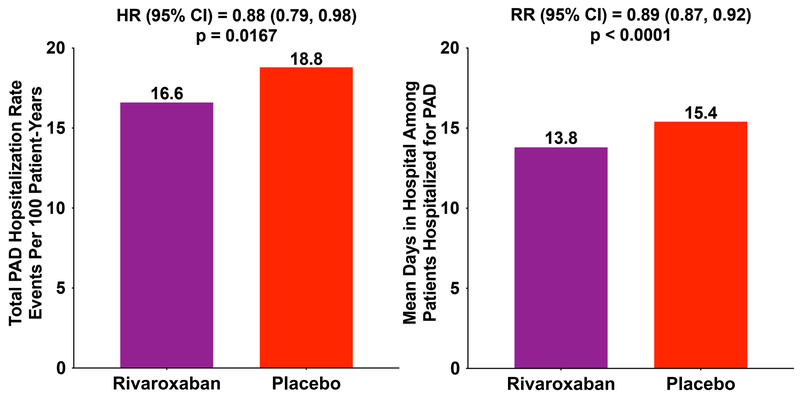
## FIGURE 1




**Treatment Effects on Total Hospitalization Rates and Mean Days Hospitalized for PAD.** HR, hazard ratio; CI, confidence interval; RR, risk ratio.

## TABLE 1

| | Total Hospitalization Rate Events Per 100 Patient-Years | | | | |
|---|---|---|---|---|---|
| **Reason for Hospitalization** | **Rivaroxaban** | **Placebo** | **Absolute Difference** | **HR (95% CI)** | **p-value** |
| PAD | 16.6 | 18.8 | -2.2 | 0.88 (0.79, 0.98) | 0.0167 |
| Bleeding event | 1.9 | 1.0 | 0.9 | 1.85 (1.36, 2.53) | 0.0001 |
| Any reason | 43.7 | 44.9 | -1.2 | 0.97 (0.90, 1.04) | 0.39 |

**Treatment Effects on Total Hospitalizations.** The hospitalization IR was lower for PAD and higher for bleeding events for rivaroxaban relative to placebo, with more hospitalizations prevented than caused. HR, hazard ratio; CI, confidence interval.

## TABLE 2

| | Days in Hospital Among Patients Hospitalized: Mean [*Total*] Days | | | |
|---|---|---|---|---|
| **Reason for Hospitalization** | **Rivaroxaban** | **Placebo** | **RR (95% CI)** | **p-value** |
| PAD | 13.8 [*11,411*] | 15.4 [*13,680*] | 0.89 (0.87, 0.92) | <0.0001 |
| Bleeding event | 9.6 [*1252*] | 21.3 [*1531*] | 0.47 (0.44, 0.51) | <0.0001 |
| Any reason | 21.6 [*35,143*] | 23.8 [*38,975*] | 0.91 (0.89, 0.92) | <0.0001 |

**Treatment Effects on Days in Hospital.** Mean days in hospital among patients hospitalized at least once was significantly lower for rivaroxaban for PAD, for bleeding, and for any reason, so that patients in the rivaroxaban group were hospitalized 3832 fewer days compared to patients in the placebo group. RR, risk ratio; CI, confidence interval.

## DISCLOSURE INFORMATION

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