

About the ROCKET AF Study

What is the ROCKET AF Study?

- ◆ ROCKET AF (**R**ivaroxaban **O**nce-daily oral direct Factor Xa inhibition **C**ompared with vitamin **K** antagonism for prevention of stroke and **E**mbolism **T**rial in **A**trial **F**ibrillation) was a prospective, randomised, double-blind, double-dummy parallel group outcomes study. It compared once-daily Xarelto® (rivaroxaban) (20 mg, or 15 mg for patients with moderate renal impairment) with dose-adjusted warfarin in 14,264 patients with non-valvular atrial fibrillation who were at risk for stroke or non-CNS systemic embolism
- ◆ ROCKET AF was an event-driven trial, which ended when the pre-specified number of events were accumulated. The primary objective of ROCKET AF was to demonstrate the efficacy of once-daily 'Xarelto' as non-inferior to dose-adjusted warfarin in the prevention of stroke and non-CNS systemic embolism in patients with non-valvular AF. The principal safety measure of ROCKET AF was the composite of major plus non-major clinically relevant bleeding events
- ◆ ROCKET AF studied a population of patients at moderate to high risk of stroke with multiple comorbidities. Patients with multiple comorbidities are typically more difficult to protect from stroke¹
- ◆ ROCKET AF was presented at the American Heart Association Congress in 2010 and published in the New England Journal of Medicine (NEJM) in September 2011²

ROCKET AF Results Summary

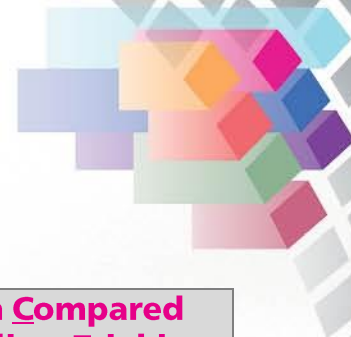
- ◆ In the study, once-daily 'Xarelto' met the primary efficacy outcome – the prevention of stroke and non-CNS systemic embolism in patients with non-valvular AF, and was shown to be non-inferior to warfarin. This was achieved with a mean time in therapeutic range (TTR) of 55% (INR values within the therapeutic range 2.0 to 3.0) among patients receiving warfarin²





- ◆ The principal safety outcome – the composite of major and non-major clinically relevant bleeding events – was similar in both treatment arms. Individually, major bleeding was also similar to warfarin. While major bleeding associated with haemoglobin loss and blood transfusion occurred more often in the rivaroxaban group, patients on ‘Xarelto’ suffered significantly fewer bleeding events of most concern to clinicians, including bleeding into a critical organ or fatal bleeding. Importantly, patients on ‘Xarelto’ showed significantly fewer intracranial haemorrhages (ICH) compared with warfarin²
- ◆ In ROCKET AF, ‘Xarelto’ was shown to have a reassuring cardiovascular profile with no increase in myocardial infarctions²
- ◆ In the study, ‘Xarelto’ was also shown to be well tolerated by patients, with no significant increase in dyspepsia³
- ◆ These results were achieved with a simple fixed one-tablet, once daily dosing regimen unique to ‘Xarelto’ (including a reduced fixed 15mg dose in patients with moderate renal impairment), in patients at risk of stroke, including those with multiple comorbidities, who are considered more difficult to protect





ROCKET AF: Rivaroxaban Once-Daily oral direct Factor Xa inhibition Compared with vitamin K antagonism for the prevention of stroke and Embolism Trial in Atrial Fibrillation²	
Study design	<ul style="list-style-type: none"> ◆ Randomised, double-blind, event-driven trial (more than 1,100 centres across 45 countries worldwide with a 2-year median follow-up)
Interventions	<ul style="list-style-type: none"> ◆ Oral, one-tablet, once-daily 'Xarelto' 20mg (15mg once-daily for patients with moderate renal impairment at screening) ◆ Warfarin once-daily titrated to an International Normalized Ratio of 2-3
Number of patients	◆ 14,264
Study inclusion criteria	<ul style="list-style-type: none"> ◆ Documented non-valvular AF ◆ Prior stroke, or transient ischaemic attack (TIA), or systemic embolism or at least 2 of the following: Congestive heart failure LVEF ≤35%, hypertension, age ≥75 years, diabetes mellitus
Primary efficacy endpoint	◆ Composite of stroke and non-CNS systemic embolism (blood clots occluding vessels outside the brain)
Primary safety endpoint	◆ Composite of major and non-major clinically relevant bleeding events
Safety endpoints	◆ Major bleeding/non-major clinically relevant bleeding
RESULTS	
Primary efficacy endpoint	◆ 'Xarelto' was shown to be non-inferior to warfarin*
Primary safety endpoint	<ul style="list-style-type: none"> ◆ Overall bleeding rates were comparable to warfarin ◆ 'Xarelto' demonstrated a reassuring bleeding profile: similar overall bleeding rates with a significant reduction in intracranial haemorrhages and fatal bleeds
Trial Attributes	
Patients eligible for anticoagulation according to guidelines	◆ Patients recruited were at moderate to high risk for stroke and recommended anticoagulation therapy with warfarin according to current guidelines
Primary and secondary prevention of stroke	<ul style="list-style-type: none"> ◆ Approximately half of patients included in the study had a history of stroke, transient ischaemic attack (TIA), or systemic embolism ◆ Therefore, the ROCKET AF trial population allowed for the assessment of the clinical benefit of 'Xarelto' for both primary and secondary prevention of stroke in AF patients
Age	◆ AF is more prevalent among the elderly; this age group is frequently under-treated with current therapies and often under-represented in clinical trials. The ROCKET AF study population had a higher mean age than other trials in this disease area (average 73.1 years). A quarter of patients were 78 years or older

*Among patients in the warfarin group, INR values were within the therapeutic range (2.0 to 3.0) a mean of 55% of the time (median, 58%; interquartile range, 43 to 71)





References

- 1) Gage BF, Waterman AD, Shannon W, et al. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *JAMA*. 2001;285,(22)2864-2870
- 2) Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med*. 2011;365(10):883-891
- 3) Data on file. Bayer Pharma AG, Berlin, Germany

About Rivaroxaban (Xarelto®)

Rivaroxaban is an oral anticoagulant that was discovered in Bayer HealthCare's Wuppertal laboratories in Germany, and is being jointly developed by Bayer HealthCare and Johnson & Johnson Pharmaceutical Research & Development, L.L.C. It has a rapid onset of action with a predictable dose response and high bioavailability, no requirement for routine coagulation monitoring, and a limited potential for food and drug interactions.

Rivaroxaban is marketed under the brand name Xarelto® for VTE prevention in adult patients following elective hip or knee replacement surgery, and it is the only oral anticoagulant that has consistently demonstrated superior efficacy over enoxaparin in this indication. Rivaroxaban is approved in more than 110 countries worldwide and marketed outside the U.S. by Bayer HealthCare in this indication.

In the U.S., where rivaroxaban has been available since July 2011 for VTE prevention in adult patients following elective hip or knee replacement surgery, Janssen Pharmaceuticals, Inc. (a Johnson & Johnson Company) holds marketing rights. The Bayer HealthCare sales force is supporting Janssen Pharmaceuticals, Inc. in designated hospital accounts. On November 4, Xarelto® received further marketing approval in the U.S. for the prevention of stroke in patients with Atrial Fibrillation.

The extensive clinical trial programme supporting rivaroxaban makes it the most studied and widely published oral, direct Factor Xa inhibitor. The studies, reported and ongoing, involve over 75,000 patients for the prevention and treatment of venous and arterial thromboembolic (VAT) disorders across a broad range of acute and chronic conditions, including stroke prevention in patients with Atrial Fibrillation, DVT treatment and the prevention of recurrent DVT or PE, and the secondary prevention of Acute Coronary Syndrome.

To learn more about thrombosis, please visit www.thrombosisadviser.com
To learn more about 'Xarelto' please visit www.xarelto.com

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