ROCKET AF

About ROCKET AF

FAST FACTS

- ROCKET AF (**R**ivaroxaban **O**nce-daily oral direct Factor Xa inhibition **C**ompared with vitamin **K** antagonism for the prevention of stroke and **E**mbolism **T**rial in **A**trial **F**ibrillation) was a rigorously designed Phase 3 major outcomes study comparing rivaroxaban, an oral anticoagulant, with warfarin for the prevention of stroke in patients with atrial fibrillation (AFib)
- Results from the pivotal Phase 3 ROCKET AF trial were presented at the American Heart Association (AHA) Scientific Sessions in November 2010
- Full ROCKET AF data results were published in the *New England Journal of Medicine* in August 2011[1]
- Johnson & Johnson Pharmaceutical Research & Development, L.L.C. (J&JPRD) and Bayer HealthCare are developing XARELTO® jointly for a broad range of disorders in which blood clotting plays a major role

ROCKET AF was a randomized, double-blind, outcomes study comparing once-daily rivaroxaban 20 mg, (15 mg for patients with moderate to severe renal impairment) with dose-adjusted warfarin. The primary objective of ROCKET AF was to demonstrate the efficacy of once-daily rivaroxaban as non-inferior to dose-adjusted warfarin in the prevention of stroke and non-CNS systemic embolism in 14,264 patients with nonvalvular AFib.[1]

ROCKET AF patient demographics

- All patients enrolled in ROCKET AF were at moderate- to high-risk of stroke (risk defined by a $CHADS_2$ score greater than or equal to 2).[1] $CHADS_2$ is a clinical prediction rule for estimating the risk of stroke in patients with AFib.
- 54.8% of patients included in the ROCKET AF study had a history of stroke, transient ischemic attack (TIA), or systemic embolism which are considered the highest risk factors for stroke.[1]
- With a mean $CHADS_2$ score of 3.5, most subjects in ROCKET AF had hypertension (90.5%), the majority had a history of congestive heart failure (62.5%), and more than half had a history of prior stroke, TIA or non-CNS systemic embolism (54.8%).

The patients with AFib evaluated in ROCKET AF typify those who are treated today by physicians with an anticoagulant to help reduce the risk of stroke, and included a higher number of patients who require anticoagulation (based on current guideline recommendations) than previous trials.

Current treatment guidelines recommend oral anticoagulation in patients with AFib who are at moderate- to high-risk of stroke.[2]

- Moderate- to high-risk is defined in the recent ACC/AHA/ESC guidelines to include those subjects with a prior stroke, TIA, or non-CNS systemic embolism or those who have two or more of the following risk factors: age > 75 years, hypertension, heart failure, or diabetes mellitus.[3]

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ROCKET AF	
Study design	♦ Randomized, Phase 3, multicenter, active-controlled, double-blind, double-dummy, event-driven study ♦ Median treatment exposure was 590 days
Interventions	♦ Oral, once-daily rivaroxaban 20 mg • Patients with moderate to severe renal impairment received rivaroxaban 15 mg once daily ♦ Oral, once-daily warfarin, titrated to an International Normalized Ratio (INR) target of 2.5 (range 2.0 – 3.0)
Number of patients	14,264 patients with nonvalvular atrial fibrillation who are at risk for stroke and non-CNS systemic embolism
Study objective	Demonstrate non-inferiority of rivaroxaban compared to warfarin for the primary endpoint
Primary endpoint	Composite of stroke and non-CNS systemic embolism
Principal safety measure	Composite of major and non-major clinically relevant bleeding events

For additional information visit **www.clinicaltrials.gov**
Identifier: NCT00403767

Important Safety Information

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT XARELTO®?

For people taking XARELTO® for atrial fibrillation:

People with atrial fibrillation (an irregular heart beat) are at an increased risk of forming a blood clot in the heart, which can travel to the brain, causing a stroke, or to other parts of the body. XARELTO® lowers your chance of having a stroke by helping to prevent clots from forming. If you stop taking XARELTO®, you may have an increased risk of forming a clot in your blood.

♦ **Do not stop taking XARELTO® without talking to the doctor who prescribes it for you. Stopping XARELTO® increases your risk of having a stroke or forming blood clots in other parts of your body.**

If you have to stop taking XARELTO®, your doctor may prescribe another blood thinner medicine to prevent a blood clot from forming.

For all people taking XARELTO®:

♦ XARELTO® can cause bleeding which can be serious, and rarely may lead to death. This is because XARELTO® is a blood thinner that reduces blood clotting. While you take XARELTO® you are likely to bruise more easily and it may take longer for bleeding to stop.

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You may have a higher risk of bleeding if you take XARELTO® and take other medicines that increase your risk of bleeding including:

- aspirin or aspirin containing products,
- non-steroidal anti-inflammatory drugs (NSAIDs)
- warfarin sodium (Coumadin®, Jantoven®)
- any medicine that contains heparin
- clopidogrel (Plavix®)
- prasugrel (Effient®)
- ticagrelor (Brilinta®)

Tell your doctor if you take any of these medicines. Ask your doctor or pharmacist if you are not sure if your medicine is one listed above.

Call your doctor or get medical help right away if you develop any of these signs or symptoms of bleeding:

- tingling, numbness or muscle weakness, especially in your legs. This is particularly important if you had a procedure called spinal or epidural puncture as part of your anesthesia during surgery.
- any unexpected bleeding, or bleeding that lasts a long time (such as nose bleeds that happen often, unusual bleeding from gums, or menstrual bleeding that is heavier than normal or vaginal bleeding)
- bleeding that is severe or that you cannot control
- red, pink or brown urine
- bright red or black stools (look like tar)
- cough up blood or blood clots
- vomit blood or your vomit looks like "coffee grounds"
- headaches, feeling dizzy or weak
- pain, swelling, or new drainage at wound sites

WHO SHOULD NOT TAKE XARELTO®?

Do not take XARELTO® if you:

- currently have abnormal or unusual bleeding
- are allergic to rivaroxaban or any of the ingredients of XARELTO®

WHAT SHOULD I TELL MY DOCTOR BEFORE OR WHILE TAKING XARELTO®?

Before taking XARELTO® tell your doctor if you:

- Have ever had bleeding problems
- Have liver or kidney problems
- Have any other medical condition
- Are pregnant or planning to become pregnant
- Are breastfeeding or plan to breastfeed

Tell all of your doctors and dentists that you are taking XARELTO®. They should talk to the doctor who prescribed XARELTO® for you before you have any surgery, medical or dental procedure.

Tell your doctor about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements. Some of your other medicines may affect the way XARELTO® works. Certain medicines may increase your risk of bleeding.

Especially tell your doctor if you take:

- ketoconazole (Nizoral®)
- itraconazole (Onmel™, Sporanox®)
- ritonavir (Norvir®)
- lopinavir/ritonavir (Kaletra®)
- indinavir (Crixivan®)
- carbamazepine (Carbatrol®, Equetro®, Tegretol®, Tegretol®-XR, Teril™, Epitol®)
- phenytoin (Dilantin-125®, Dilantin®, Phenobarbital, Solfoton™)
- rifampin (Rifater®, Rifamate®, Rimactane®, Rifadin®)
- St. John's wort (Hypericum perforatum)

Ask your doctor if you are not sure if your medicine is one listed above. Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

HOW SHOULD I TAKE XARELTO®?

Take XARELTO® exactly as prescribed by your doctor. **Do not change your dose or stop taking XARELTO® unless your doctor tells you to.**

For people who have:

- **atrial fibrillation:** Take XARELTO® 1 time a day **with your evening meal. Stopping XARELTO® may increase your risk of having a stroke or forming blood clots in other parts of your body.**
- **hip or knee replacement surgery:** Take XARELTO® 1 time a day **with or without food.**

Your doctor may stop XARELTO® for a short time before any surgery, medical or dental procedure. Your doctor will tell you when to start taking XARELTO® again after your surgery or procedure.

Do not run out of XARELTO®. Refill your prescription for XARELTO® before you run out. When leaving the hospital following a hip or knee replacement, be sure that you will have XARELTO® available to avoid missing any doses.

If you miss a dose of XARELTO®, take it as soon as you remember on the same day.

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If you take too much XARELTO®, go to the nearest hospital emergency room or call your doctor right away.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF XARELTO®?

XARELTO® can cause bleeding which can be serious, and rarely may lead to death. *Please see "What is the most important information I should know about XARELTO®?"*

Tell your doctor if you have any side effect that bothers you or that does not go away.

Discuss any side effects with your doctor. You are also encouraged to report side effects to the FDA: visit *http://www.fda.gov/medwatch* or call 1-800-FDA-1088. You may also report side effects to Janssen Pharmaceuticals, Inc. at 1-800-JANSSEN (526-7736).

Please see full **Product Information**, including **Medication Guide**.

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References:

1. Patel, MR, Mahaffey KD, Garg J, et al. Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation. *NEJM* 2011; 365(10):883-891
2. Fuster V, Lars ER, Cannom DS, et al. 2011 ACCF/AHA/HRS Focused Updates Incorporated Into the ACC/AHA/ESC Practice Guidelines for the Management of Patients with Atrial Fibrillation, *Circulation*. 2011, 123:e269-e367.
3. Lip G, et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor based approach: The Euro Heart Survey on Atrial Fibrillation. *Chest* 2010; 137: 263–272.

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