Rivaroxaban in Acute Coronary Syndrome (ACS)

Acute Coronary Syndrome (ACS)

Acute coronary syndrome (ACS) is a common and life-threatening condition, which occurs when a coronary artery is blocked by a blood clot, reducing blood supply to the heart. This disruption of blood flow can directly cause a heart attack, or cause severe pain in the chest (unstable angina).

Burden of ACS

Annually **2.5 million** ACS cases are diagnosed worldwide[1]

ACS patients are re-admitted to hospital on average **1.6x** for suspected secondary events[2]

The direct and indirect cost of ACS amount to **$75 billion dollars** worldwide[3]

What Triggers ACS?

The essential underlying condition for ACS is the build-up of plaque in the inner walls of coronary arteries that narrows the arteries, sometimes decreasing the amount of blood flow to the heart. This process is called atherosclerosis.

There are a variety of **risk factors** for atherosclerosis, potentially resulting in ACS, which can include[4,5]:

- Family history of heart attack or unstable angina
- High cholesterol
- High blood pressure
- Diabetes
- Smoking

Patients Require Long-Term Protection from Recurrent ACS

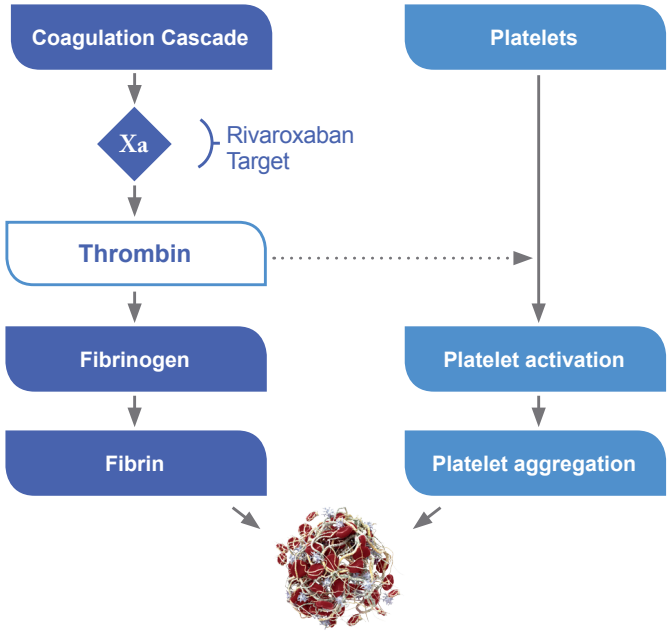
Mortality and major cardiovascular events remain as high as ~10% during the first year following an ACS, despite recent advances in antiplatelet therapy[6].

1 in 10 ACS patients will have, or are at risk of having unless appropriately treated, another major atherothrombotic event (CV death, heart attack, stroke) within the first year following the initial event[6] and 68% - 97% of deaths related to ACS occur after hospital discharge[2]

Up to 30% of patients who leave the hospital after an ACS event are re-admitted within six months[3]

Arterial clots are formed through dual pathways: Platelet Activation and Thrombin Generation

If plaque from the wall of a coronary artery ruptures, a blood clot can form at the site of the rupture. This arterial clot is formed through a dual pathway of platelet activation and thrombin generation, which is one of the most potent platelet activators[7]. If the clot is large enough to block the vessel and critically reduce blood flow, the heart muscle can be damaged[8]



ACS Treatment and Prevention

The main treatment goal for ACS patients is to prevent death, stroke or recurrent heart attack by removing an existing blood clot, and subsequently stopping the formation of new clots.

A combination of antiplatelet and anticoagulant medications that target both pathways of clot formation is commonly used in the acute treatment period after a patient first experiences a heart attack[9,10]

Unlike acute treatment, the current therapy for long-term secondary prevention of ACS does not include anticoagulant medication, but focuses on dual antiplatelet therapy of aspirin plus a drug class known as P2Y12 inhibitors*, of which clopidogrel is the most prescribed. Dual antiplatelet therapy has improved effectiveness over aspirin alone[11], however:

Antiplatelet therapy addresses only one source of clot formation - platelet activation, leaving patients exposed to continued risk after an ACS event[12].

Since thrombin levels remain elevated long after the acute phase, secondary prevention of ACS should target both pathways of clot formation[13]

COMPLEMENTARY MECHANISMS OF ACTION

Antiplatelets and anticoagulants have complementary mechanisms of action that together address the dual pathway of clot formation and have been shown to improve outcomes, continuing to provide more comprehensive long-term protection than antiplatelet therapy** alone[9,14].

Beyond antiplatelet therapy** alone, rivaroxaban 2.5 mg twice daily was shown to reduce mortality and CV events without increasing the risk of fatal intracranial haemorrhage (ICH) or fatal bleeds***[15,16]. However, as expected the rate of TIMI major bleeding increased with rivaroxaban 2.5 mg twice daily compared to antiplatelet therapy**[14,15,16].

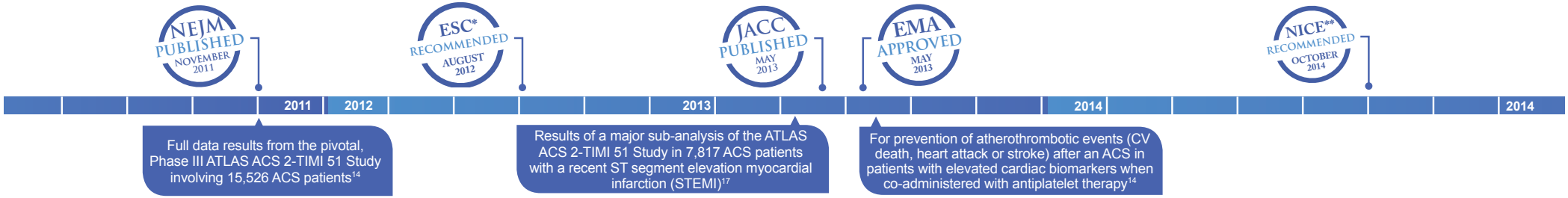
ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation (updated August 2012) recommend that treatment with rivaroxaban 2.5 mg twice daily be considered for patients with STEMI who are at low bleeding risk and receiving dual antiplatelet therapy – aspirin and clopidogrel (II B recommendation)[10]

Rivaroxaban is the only novel oral anticoagulant to provide more comprehensive protection against long-term clot formation for patients with ACS***.

* Prasugrel and Ticagrelor are also P2Y12 inhibitors
**ASA plus clopidogrel or ticlopidine or ASA alone
***Patients with elevated cardiac biomarkers without prior stroke or TIA

Rivaroxaban in Acute Coronary Syndrome (ACS) - Continued

Rivaroxaban ACS Data Publications and Regulatory Milestones



*European Society of Cardiology (ESC) issued Guidelines in August 2012 recommending low-dose rivaroxaban as a treatment option for the management of acute myocardial infarction in patients presenting with ST-segment elevation issues[10]

**UK's NICE issued draft Guidance recommending rivaroxaban as a treatment option to prevent blood clots in people who have had a heart attack as a result of a blockage or narrowing in one of the blood vessels in the heart[18]

About Rivaroxaban

Rivaroxaban is the most broadly indicated and most prescribed novel OAC[19] and is marketed under the brand name Xarelto®. Rivaroxaban is approved for five indications across seven distinct areas of use, protecting patients across more venous and arterial thromboembolic (VAT) conditions than any other novel OAC:

- The prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (AF) with one or more risk factors
- The treatment of deep vein thrombosis (DVT) in adults
- The treatment of pulmonary embolism (PE) in adults***
- The prevention of recurrent DVT and PE in adults
- The prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip replacement surgery
- The prevention of VTE in adult patients undergoing elective knee replacement surgery
- The prevention of atherothrombotic events (cardiovascular death, heart attack or stroke) after an acute coronary syndrome in adult patients with elevated cardiac biomarkers when co-administered with acetylsalicylic acid (ASA) alone or with ASA plus clopidogrel or ticlopidine

Whilst licences may differ from country to country, across all indications rivaroxaban is approved in more than 125 countries. Rivaroxaban was discovered by Bayer HealthCare, and is being jointly developed with Janssen Research & Development, LLC. Rivaroxaban is marketed outside the U.S. by Bayer HealthCare and in the U.S. by Janssen Pharmaceuticals, Inc. (a Johnson & Johnson Company).

Anticoagulant medicines are potent therapies used to prevent or treat serious illnesses and potentially life threatening conditions. Before initiating therapy with anticoagulant medicines, physicians should carefully assess the benefit and risk for the individual patient. Responsible use of rivaroxaban is a very high priority for Bayer, and the company has developed a Prescribers Guide for physicians and a 'Xarelto' Patient Card for patients to support best practice.

To learn more, please visit https://prescribe.xarelto.com
To learn more about thrombosis, please visit www.thrombosisadviser.com
To learn more about VAT, please visit www.VATspace.com
To learn more about 'Xarelto', please visit www.xarelto.com

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