ATLAS ACS TIMI 51

PHASE III

The Pivotal ATLAS ACS 2-TIMI 51 Study Proves 'Xarelto' 2.5 mg Twice Daily in Combination with Antiplatelet Therapy can Provide more Comprehensive Long-term Protection than Antiplatelet Therapy Alone[1]. Rivaroxaban is the only Novel Oral Anticoagulant (OAC) that has Finalised a Phase III Clinical Trial in Acute Coronary Syndrome (ACS) with a Favourable Risk Benefit Balance. It's also the only Novel OAC with Approved Indication in ACS Secondary Prevention in Europe

Low-dose 'Xarelto' Provides Additional Long-term Benefit to Antiplatelet Therapy

Specific Low-dose 'Xarelto' 2.5 mg Twice Daily for Patients after ACS

Only Novel OAC to Demonstrate Positive Benefit-risk Profile in ACS

Arterial blood clots, which may lead to primary and secondary ACS events, are formed through the dual pathways of platelet activation and thrombin generation[2].

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[3]. Unlike acute treatment, the secondary prevention of ACS is typically managed with antiplatelet therapy alone, leaving patients exposed to continued risk[4].

The study, conducted in collaboration with the Thrombolysis in Myocardial Infarction (TIMI) Study Group, examined the potential added benefit of low-dose 'Xarelto' (2.5 mg twice daily or 5 mg twice daily) in patients following an ACS event[1,5].

Risk of Recurrent ACS Events

- After hospital discharge, rates of major cardiovascular (CV) events, including death, heart attack and stroke, remain unacceptably high for ACS patients on standard antiplatelet therapy* alone
- Following an ACS, 1 in 10 patients will have another major atherothrombotic event within a year[1,6]
- The vast majority of deaths (68–97%) in patients with ACS occur after hospital discharge[7]

ATLAS ACS 2-TIMI 51 was presented at the American Heart Association (AHA) Scientific Sessions meeting and published in the New England Journal of Medicine (NEJM) in November 2011[1]. The study results were the basis of the approval of 'Xarelto' 2.5 mg twice daily for the prevention of atherothrombotic events after an ACS in adult patients with elevated cardiac biomarkers when co-administered with acetylsalicylic acid (ASA) alone or with ASA plus clopidogrel or ticlopidine. 'Xarelto' is now approved in more than 40 countries worldwide for this indication.

The extensive evaluation of rivaroxaban to protect different patient populations at risk of venous and arterial thromboembolism (VAT), makes it the most studied novel OAC in the world. Rivaroxaban (Xarelto®) is already approved for five indications in seven areas of use and its investigation - both completed and ongoing - will include more than 275,000 patients in clinical trials and real world settings.

*ASA plus clopidogrel or ticlopidine or ASA alone

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Patient Study Insights

About the Study Patient Population

- **15,526 ACS patients hospitalised with unstable angina, non-ST elevation myocardial infarction (NSTEMI) or ST segment elevation myocardial infarction (STEMI)[1]**
- **Included patients from 44 countries at 766 sites worldwide[1]**
- **93% of the patients received dual-antiplatelet therapy in addition to low-dose 'Xarelto' or placebo, and the remaining were treated with aspirin plus low-dose 'Xarelto' or placebo[1]**

Acute Coronary Syndrome (ACS)

ACS is a complication of coronary heart disease which is the single most common cause of death worldwide[8] and one of the most prevalent non-communicable diseases[9]. It occurs when a blood clot blocks a coronary artery, reducing blood supply to the heart[2]. This disruption of blood flow can be the direct cause of a heart attack, or precipitate severe pain in the chest (unstable angina), a condition indicating that a heart attack may soon occur. Elevated cardiac biomarkers are associated with heart injury, and laboratory testing of these biomarkers is routinely undertaken in clinical practice to confirm an ACS.

Efficacy Results

Both 'Xarelto' 2.5 mg and 5 mg twice daily in addition to antiplatelet therapy showed superior efficacy to antiplatelet therapy* alone, lowering the risk of recurrent major CV events (CV death, heart attack or stroke) in patients after an ACS (combined doses 8.9% vs. 10.7%, relative risk reduction (RRR) of 16%)[1]

- 'Xarelto' 2.5 mg twice daily showed a significant reduction in risk of the composite primary endpoint (9.1% vs. 10.7%), driven by a significant 34% RRR in the rate of CV death (2.7% vs. 4.1%); there was also a significant reduction in deaths from any cause (2.9% vs. 4.5%)[1]
- 'Xarelto' 5 mg twice daily also showed a reduction in the rate of the primary efficacy endpoint in the study (8.8% vs. 10.7%)[1]
- Additionally and importantly, 'Xarelto' significantly reduced stent thrombosis compared to placebo (2.3% vs. 2.9%)[1]

Safety Results

In patients receiving low-dose 'Xarelto' in addition to antiplatelet therapy, TIMI** major bleeding not associated with CABG surgery were low overall, yet statistically significantly increased compared to those treated with antiplatelet therapy* alone (2.1% vs. 0.6%)[1]

- 'Xarelto' resulted in higher rates of TIMI** major bleeding not associated with Coronary Artery Bypass Graft (CABG) surgery at both the 2.5 mg and 5 mg BID doses compared to placebo (1.8% vs. 0.6% and 2.4% vs. 0.6%, respectively)[1]

*ASA plus clopidogrel or ticlopidine or ASA alone

**The TIMI scale is one of the most well-known risk scoring methods for a patient hospitalised with a heart attack. Using a patient's current vital health information as a guide, the TIMI scale provides a numeric value for the patient's potential prognosis, including short-term risk of death

References

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