Raft of rivaroxaban good news from the USA, implications for South African clinical practice

Rivaroxaban has been approved by the US Food and Drug Administration (FDA) for the prevention of stroke and systemic embolism in non-valvular atrial fibrillation. From the American Heart Association (AHA) 2011 congress earlier this week, the results of the ATLAS ACS 2-TIMI 51 trial have shown rivaroxaban improves cardiovascular outcomes and reduces cardiovascular and all-cause mortality in acute coronary syndromes (ACS).1,2

With the added recognised use of rivaroxaban in knee and hip arthroplasty and in the prevention and treatment of venous thromboembolism, deep-vein thrombosis and pulmonary embolism,3 South African medicine regulators will need to widen their assessment of the value of this factor Xa inhibitor locally.

The ATLAS ACS 2-TIMI 51 trial results were widely welcomed at the AHA, with the lead investigator, Dr Michael Gibson of Harvard Medical School noting that rivaroxaban treatment for about two years in ACS patients resulted in a very robust reduction in the primary endpoint of cardiovascular death, myocardial infarction and stroke (RRR of 16%). The risk of all-cause death was reduced by 30% with the addition of rivaroxaban to the standard treatment of ACS.4

Importantly patients did as well on the lower dose, with less bleeding than on the higher dose. There was an increase in major bleeding rates not related to coronary bypass grafting and intracranial bleeding without a significant increase in fatal bleeding or adverse events in patients receiving rivaroxaban compared to standard therapy.

Expert opinion

Prof Sylvia Haas, Technical University, Munich, Germany, a well-known expert from Munich and frequent visitor to South Africa commented on the importance of this study for clinical practice.

The results of ATLAS ACS 2-TIMI 51 have the potential to lead into a new era in secondary prevention of thromboembolic complications after ACS. This landmark study aimed to lower cardiovascular events in patients with recent ACS compared to standard care and this has been successfully achieved for both doses of the oral factor Xa inhibitor rivaroxaban tested, and for each dose alone.

A cumulative incidence of 10.7% for the combined endpoint, consisting of cardiovascular death, myocardial infarction (MI) and stroke, was seen in patients randomised to placebo and this was reduced to 8.9% for both rivaroxaban groups combined. In patients treated with the higher dose of rivaroxaban of 5 mg bid, this endpoint was significantly reduced to 8.8%, and for patients treated with 2.5 mg bid to 9.1%, which was also statistically significant. There were also reductions in rates of death from both cardiovascular causes and any cause for the 2.5-mg dose but not for the 5-mg dose.

As expected, the bleeding rates were higher for the patients receiving the
combination of anticoagulation and anti-platelet therapy. This effect was dose related, i.e. bleeding rates were lower in the 2.5- than in the 5.0-mg group. Although the rate of intracranial bleeding was higher than with placebo, there was no increase in fatal bleeding events.

In conclusion, rivaroxaban is the first new oral anticoagulant to demonstrate a clinically relevant benefit in ACS.

1. FDA Announcement, 11 November 2011.