

Apixaban as an alternative to aspirin in patients with AF

Overview: Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and if left untreated is a significant risk factor for stroke and other morbidities. Therefore patients with paroxysmal, persistent or permanent AF are assessed using a tool such as [CHADS2 score](#) to determine their risk of stroke or thromboembolism and offered anticoagulation (usually warfarin) or an antiplatelet agent (usually aspirin) according to that degree of risk.

Warfarin is more effective than aspirin for the prevention of stroke in patients with AF but has a narrower benefit to risk ratio and requires lifelong coagulation monitoring. Therefore it is usually reserved for suitably motivated patients deemed to be at higher risk of stroke.

Apixaban is a Factor Xa inhibitor which is still in clinical development and not yet licensed in the UK.



Current treatment: [NICE recommends](#) that aspirin (75mg- 300mg/day) is considered in the following patient groups:

- ▶ All patients deemed to be at high risk of a stroke/ thromboembolism (previous history stroke/transient ischaemic attack or aged 75 or older with hypertension or vascular disease or clinical evidence of valve disease, heart failure or impaired left ventricular function) and who have contraindications to warfarin.
- ▶ Patients deemed to be at moderate risk of a stroke/thromboembolism (aged 65 or older with no high risk factors or aged less than 75 with hypertension, diabetes, or vascular disease) depending on their perceived risk/benefit of warfarin.
- ▶ All patients deemed to be at low risk of a stroke/thromboembolism (aged less than 65 with no moderate or high risk factors).

New evidence: Connolly et al ([N. Engl. J. Med 2011; 364:806-17](#)) conducted a trial in 5599 patients with AF for whom anticoagulation with a vitamin K antagonist was considered unsuitable. Patients were randomised to receive either apixaban (usually 5mg twice daily) or aspirin (81 to 324mg daily - dose selected at the discretion of the investigator). The primary outcome was occurrence of stroke or systemic embolism. The trial was stopped early on the advice of the data and safety monitoring board when it was shown that there was a treatment benefit in favour of apixaban at the first interim analysis after a mean follow up period of 1.1 years. The results suggest that for every 48 patients treated with apixaban instead of aspirin for one year, one less might be expected to have a stroke or systemic embolism. This reduction was consistent in terms of relative impact on rates of ischaemic stroke, hemorrhagic stroke, death and hospitalisation and across all patient subgroups assessed. Apixaban was however associated with a slightly increased rate of major bleeding events than aspirin but this difference was not statistically significant and this trend was also reflected in minor bleeding events.

Commentary: "Warfarin, with all its drawbacks in terms of interactions and monitoring requirements, has remained the 'gold-standard' treatment for AF patients for decades. However, the Stroke Improvement programme has shown that approximately a third of patients who should be on warfarin for AF (based on risk stratification) are not on warfarin. These patients are often prescribed aspirin and in the future may be treated by one of the newer oral anticoagulants.

"Apixaban is one of several new agents that aim to provide an alternative to warfarin for stroke prevention in patients with atrial fibrillation. Interestingly, this agent was studied in patients unsuitable for warfarin and demonstrated superiority whereas the other agents have gone head to head with warfarin and were either superior or non inferior to warfarin.

"Further studies are planned against warfarin, with the choice of agent based on safety, efficacy and tolerability as well as cost noting the likely premium against warfarin." - *Sotiris Antoniou, Consultant Pharmacist - Cardiovascular Medicine, North East London Cardiovascular and Stroke Network, Barts and The London NHS Trust.*