About Stroke Prevention in Atrial Fibrillation

Fast facts

- **Atrial Fibrillation (AF) is the most common sustained cardiac arrhythmia**
- **AF occurs when the upper chambers of the heart (known as the atria) beat irregularly. Because the atria do not empty completely, blood does not flow properly, potentially allowing blood clots to form**
- **An ischemic stroke can result if part of a blood clot dislodges from the atria and becomes lodged in the brain**
- **AF increases the risk of stroke five fold and is estimated to be responsible for approximately 15-20% of the 15 million strokes which occur worldwide every year. Patients with AF represent a substantial population at high risk of stroke and, in particular, severe stroke**
- **Currently the most widely used therapy for the prevention of stroke in AF patients are Vitamin K antagonists (VKAs) e.g. warfarin, also classified as oral anticoagulants, and acetylsalicylic acid (aspirin)**
- **VKAs are effective if managed well, but have multiple food and drug interactions, a narrow separation between doses which are effective and doses which give unacceptably high bleeding risk, therefore frequent monitoring is required and management is challenging**

What is Atrial Fibrillation (AF)?

AF is the most common sustained disorder of heart rhythm[1] and is a major risk factor for ischemic stroke and death in the general population. Approximately six million individuals in Europe and 2.3 million individuals in the US have AF and the numbers are growing substantially.[1]

- AF occurs when the upper chambers of the heart beat irregularly[2]
- Because the atria do not empty completely when they fibrillate, blood does not flow properly, potentially allowing blood clots to form[2]

Stroke

- A stroke is the rapidly developing loss of brain function(s) due to disturbance in the blood supply to the brain, caused by a blocked or burst blood vessel[3]
- Strokes can be classified into two major categories:
  - *Ischemic strokes* occur due to an interruption of the blood supply due to a blockage
  - *Hemorrhagic strokes* occur due to rupture of a blood vessel or an abnormal vascular structure which leads to bleeding inside the brain[4]
- Stroke is among the leading causes of death or disability in developed countries[5] and is the second most common cause of death after heart disease
- In 2004, 5.7 million people died from strokes globally[6]
- More than 50 million people worldwide are currently recovering from stroke[7]
- A stroke often results in devastating and long-lasting paralysis, impaired cognitive function and significant disability, with severe impact on quality of life for the patient and their family

AF as a risk factor of stroke

Blood clots which have formed as a result of AF may dislodge from the atria and travel to the brain, where they may block the flow of blood causing an ischemic stroke[2]

- 85% of all strokes are ischemic and approximately 15-20% of those strokes are a result of AF[8]
- Strokes in patients with AF are more severe than in those without the condition and are associated with a 50% likelihood of death within one year[8]
- Furthermore, the presence of AF increases the risk of long-lasting and severe disability after a stroke by almost 50%[8]

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The economic burden of stroke in patients with AF

Despite current therapies, strokes account for 2–3% of the total healthcare expenditure in the European Union with a calculated cost of €38 billion in 2006.[9]

- The number of people with AF is expected to almost triple by 2050, potentially increasing the total healthcare expenditure to more than €60 billion over the coming years[10,11]
- The increase of patients with AF is a result of:
  - An ageing population[12]
  - Improved survival of patients with conditions which predispose AF (e.g. heart attack)[12]

Current treatments and clinical challenges

- Currently the most widely used therapy for the prevention of stroke in AF patients are Vitamin K antagonists (VKAs) e.g. warfarin, also classified as oral anticoagulants, and acetylsalicylic acid (aspirin)
- VKAs are effective if managed well, but have multiple food and drug interactions, a narrow separation between doses which are effective and doses which give unacceptably high bleeding risk, therefore frequent monitoring is required and management is challenging. This leads, in the real world, to substantial under-treatment of AF patients at risk for stroke[13]
- Registries have shown that patients that receive anticoagulation therapy only spend half of their time within the narrow therapeutic window, and as such are at risk of increased bleeding or increased risk of stroke[13]
- Aspirin is less effective than VKAs and is recommended only for patients with contraindications to VKAs or with a low risk of stroke[14]

GARFIELD registry to generate a naturalistic view on AF management

- The ongoing Global Anticoagulant Registry in the FIELD (GARFIELD) is investigating real-life treatment patterns in newly diagnosed AF patients at risk for stroke who are started on oral anticoagulant therapy and those who are at risk of stroke but do not receive preventive therapy
- This is the largest, global disease registry in AF and plans to enrol 55,000 AF patients at risk for stroke. The results will provide a naturalistic view of the clinical effectiveness and economic impact of AF management including anticoagulant treatment interventions. GARFIELD will allow identification of persisting unmet needs and quantify the real-life clinical and economic benefits of new treatment options such as rivaroxaban in stroke prevention[15]
- GARFIELD is an academic research initiative of the Thrombosis Research Institute (London, UK), conducted in collaboration with a global investigator network. It is planned to include 1,000 centers in 50 countries. The program is made possible through an unrestricted research grant from Bayer Schering Pharma

New developments for stroke prevention in AF

The limitations of current treatments have led to the development of alternative therapies and management strategies that may offer favourable benefit-risk profiles and convenience.

- Treatments targeting single components of the coagulation pathway (Factor Xa and thrombin) are the furthest advanced new therapies in development[16]
- Of these anticoagulants, three targeting Factor Xa (rivaroxaban, apixaban and edoxaban) are currently in Phase III trials for stroke prevention in patients with AF,[16] and a direct thrombin inhibitor, dabigatran, has currently completed a Phase III study in this disease area

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