Thrombosis Research Institute
Emmanuel Kaye Building
Manresa Road
London
SW3 6LR

Media Contact
Emily Chu
echu@tri-london.ac.uk
+44 (0) 207 351 8300 ext. 3383

DATA FROM GLOBAL ATRIAL FIBRILLATION REGISTRY SHOW ANTITHROMBOTIC AGENTS NOT OPTIMALLY USED TO PREVENT STROKE

-- GARFIELD-AF Registry presentations at ESC CONGRESS 2014 provide insight into treatment and outcomes of patients at risk of stroke in everyday clinical practice --

BARCELONA, 2 September 2014 – Data from nearly 12,500 patients enrolled in the Global Anticoagulant Registry in the FIELD–Atrial Fibrillation (GARFIELD-AF), an innovative, independent academic research initiative, have illustrated that stroke prevention strategies for atrial fibrillation (AF) patients remain sub-optimal despite the transition to a new era of anticoagulation featuring non-vitamin K antagonist oral anticoagulant (NOAC) therapies. The findings, presented this week at ESC Congress 2014, show that treatment patterns in everyday clinical practice are not consistent with evidence-based guidelines, and that inappropriate use and under-use of anticoagulant therapy is associated with worse outcomes for patients.

GARFIELD-AF is led by an international steering committee under the auspices of the Thrombosis Research Institute (TRI), London, UK. It is an observational study designed to clarify evolving AF treatments and outcomes for patients, clinicians and healthcare providers. Most existing data about AF have come from controlled clinical trials, whilst the burden on patients and populations in everyday clinical practice is less well understood. Up to 2% of the population has AF,[1] a common heart rhythm disorder that can lead to life-threatening complications, including stroke. Despite the availability of highly effective preventive treatments, AF-related stroke remains a major and increasing clinical and societal burden.

“The latest data from GARFIELD-AF illustrate that the introduction of innovative therapies has begun to alter the way AF patients are treated to prevent stroke,” said Professor Lord Ajay Kakkar, Professor of Surgery at University College London and Director of the TRI. “Previous research has demonstrated that patient outcomes can be improved when anticoagulant therapy is used appropriately. However, observations of everyday clinical practice in GARFIELD-AF suggest that important work remains to be done to ensure the implementation of evidence-based best practice, including the selection of suitable patients for anticoagulation and their optimal management.”

Preliminary treatment data for 31,666 GARFIELD-AF patients enrolled in 34 countries during the first three of five planned cohorts were presented in an ESC Congress 2014 satellite symposium.[2] Since the initiation of GARFIELD-AF in 2009, regulatory approval for NOACs including factor Xa inhibitors (rivaroxaban, apixaban) and a direct thrombin inhibitor (dabigatran) has altered prescribing patterns by providing an alternative to vitamin K antagonists (VKAs), the established standard of care. The proportion of AF patients receiving a NOAC has increased from 3.1% during cohort 1 (December 2009–October 2011) to 26.4% during cohort 3 (June

2013–June 2014). However, the proportion of patients receiving any anticoagulant only increased from 60.6% to 67.5% in the same period, as fewer patients received a VKA (57.5% to 41.1%).

The 12,448 prospective patients with at least one year of follow up data after AF diagnosis at the time of analysis were included in the three posters presented at ESC Congress 2014.

Only 25% of patients treated with VKAs achieve adequate anticoagulation control[3]

- The ESC guidelines suggest that patients can be considered well managed on VKA therapy if they spend at least 70% of their time in the therapeutic range, i.e. with an international normalized ratio (INR) of 2.0–3.0.[4]
- The requirement for patients on VKA to undergo routine monitoring and dose adjustment, and the difficulty of maintaining the optimal anticoagulant effect, are an important consideration when choosing between anticoagulant therapies. NOACs are given at fixed doses and exert a predictable anticoagulant effect without the need for monitoring.
- Of the 5107 GARFIELD-AF patients treated with VKAs and with INR recordings available, only 25% (n=1301) met the 70% standard for VKA control (with INR control measured as frequency in range (FIR)).
- Patients whose VKA control was sub-optimal were significantly more likely to suffer a stroke, a major bleeding event, and death.

2 in 5 low-risk patients receive anticoagulation against guideline recommendations[5]

- AF patients with a CHA_2DS_2-VASc risk score[6] of 0 are considered by the ESC guidelines to be at low risk of stroke and are not candidates for anticoagulant therapy with either a VKA or a NOAC.[4]
- Of the 440 GARFIELD-AF patients with a CHA_2DS_2-VASc score of 0, 40% received an anticoagulant (32.4% received a VKA and 7.6% received a NOAC).
- The data also confirmed that these low-risk patients tended to have fewer adverse clinical outcomes, including a substantially lower risk of all-cause death, compared to patients with CHA_2DS_2-VASc ≥1, supporting the guideline recommendation against treating low-risk patients with anticoagulant therapy.

Older patients are more likely to receive anticoagulant therapy[7]

- Amongst GARFIELD-AF patients, increasing age was associated with more frequent oral anticoagulant use, a greater incidence of co-morbidities and higher risks of stroke/systemic embolism, death and major bleeding events.
- In patients aged 65 or over, cardiovascular death was not the primary cause of mortality.

About GARFIELD-AF

The GARFIELD-AF Registry is an independent academic research initiative. The registry is an observational, multicentre, international prospective study of patients with newly diagnosed AF. It will prospectively follow 50,000 patients from at least 1000 centres in 35 countries in the Americas, Eastern and Western Europe, Asia, Africa and Australia.

Contemporary understanding of AF is based on data gathered in controlled clinical trials. Whilst essential for evaluating the efficacy and safety of new treatments, these trials are not representative of everyday clinical practice and hence, uncertainty persists about the real-life burden and management of this disease. GARFIELD-AF seeks to provide insights into the impact of anticoagulant therapy on thromboembolic and bleeding complications seen in this patient population. It will provide a better understanding of the potential opportunities for improving care and clinical outcomes amongst a representative and diverse group of patients

and across distinctive populations. This should help physicians and healthcare systems to appropriately adopt innovation to ensure the best outcomes for patients and populations.

The registry started in December 2009. Four key design features of the GARFIELD-AF protocol ensure a comprehensive and representative description of AF:

- Five sequential cohorts of prospective, newly-diagnosed patients, facilitating comparisons of discrete time periods and describing the evolution of treatments and outcomes.
- Investigator sites that are selected randomly within carefully assigned national AF care setting distributions, ensuring that the enrolled patient population is representative.
- Enrolment of consecutive eligible patients regardless of therapy to eliminate potential selection bias.
- Follow-up data captured for a minimum of 2 and up to 8 years after diagnosis, to create a comprehensive database of treatment decisions and outcomes in everyday clinical practice.

Included patients have been diagnosed with non-valvular AF within the past 6 weeks and have at least one additional risk factor for stroke, and as such, are potential candidates for anticoagulant therapy to prevent blood clots leading to stroke. It is left to the investigator's clinical judgment to identify a patient's stroke risk factor(s), which are not restricted to those included in established risk scores. Patients are included whether or not they receive anticoagulant therapy, so current and future treatment strategies and failures can be properly understood in relation to patients' individual risk profiles.

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The burden of AF

Up to 2% of the global population has AF.[1] Around 6 million people in Europe[8], 3–5 million people in the United States[9,10] and up to 8 million people in China have AF.[11,12] It is estimated that its prevalence will at least double by 2050 as the population ages. AF confers a five-fold increase in the risk of stroke, and one in five of all strokes is attributed to this arrhythmia. Ischaemic strokes in association with AF are often fatal, and those patients who survive are left more frequently and more severely disabled and more likely to suffer a recurrence than patients with other causes of stroke. In consequence, the risk of death from AF-related stroke is doubled and the cost of care is increased by 50%.[13]

AF occurs when parts of the atria emit uncoordinated electrical signals that cause the chambers to pump too quickly and irregularly, not allowing blood to be pumped out completely.[14] As a result, blood may pool, clot and lead to thrombosis, which is the number one killer in both the developed and developing world. If a blood clot leaves the left atrium, it could potentially lodge in an artery in other parts of the body, particularly in the brain. A blood clot in an artery in the brain leads to a stroke. Ninety-two per cent of fatal strokes are caused by thromboses.[15] People with AF also are at high risk for heart failure, chronic fatigue and other heart rhythm problems.[16] Stroke is a major cause of death and long-term disability worldwide – each year 6.7 million die[17] and 5 million sufferers are left permanently disabled.[18]

About the TRI

The TRI is a charitable foundation and multi-disciplinary research institute dedicated to the study of thrombosis and related disorders. TRI's mission is to provide excellence in thrombosis research and education, to develop new strategies to prevent and treat thrombosis and thereby improve quality of care, advance clinical outcomes and reduce healthcare costs. The TRI is a member of University College London Partners Academic Health Science System.

For more information, visit http://www.tri-london.ac.uk/garfield.

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