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## **ONE-YEAR DATA FROM GLOBAL ATRIAL FIBRILLATION (AF) REGISTRY SHOW ANTITHROMBOTIC AGENTS NOT OPTIMALLY USED TO PREVENT STROKE**

*-- GARFIELD Registry presentations at ESC CONGRESS 2013 provide outcomes data on real-world treatment patterns of at-risk AF populations --*

**AMSTERDAM, 3 September 2013** – One-year outcomes data from the first cohort of the Global Anticoagulant Registry in the FIELD (GARFIELD), an innovative, independent academic research initiative, provide insights into the elevated stroke risk among subpopulations of patients with atrial fibrillation (AF). The findings, from eight abstracts presented this week at the ESC Congress 2013, collectively show that anticoagulant therapy – which is known to significantly lower stroke risk in AF patients – is consistently under-utilised among those at-risk AF patients.

GARFIELD is led by an international steering committee under the auspices of the Thrombosis Research Institute (TRI), London. It is an international, observational, multicentre, prospective study designed to understand the global burden of AF, a common condition in which the two upper chambers of the heart (the atria) quiver rather than beat rhythmically and can lead to life-threatening complications, including stroke. Up to 2% of the population has AF.<sup>1</sup> Despite the availability of highly effective preventive treatments, AF-related stroke remains a major and increasing clinical and societal burden.

“These 1-year data from GARFIELD illustrate that evidence-based stroke prevention guidelines are not always followed in everyday clinical practice,” said Professor The Lord Ajay Kakkar, Professor of Surgery at University College London and Director of the TRI, London, UK. “Taken together, these new findings re-emphasize what has been observed in clinical trials regarding stroke risk in AF patients. The research suggests there are opportunities to improve patient outcomes through more consistent application of best practice and adoption of the many innovative therapies to prevent stroke in high-risk AF patients.”

The data presented at ESC Congress 2013 are from the first of five GARFIELD cohorts. The first cohort includes a total of 10,614 patients with non-valvular AF and at least one investigator-determined additional risk factor for stroke, recruited from 540 randomly-selected sites in 19 countries. Of these patients, 5,089 were recruited retrospectively as a validation cohort and 5,525 were recruited prospectively and comprise the study populations in these abstracts. ESC Guidelines for the management of atrial fibrillation recommend that all patients at high risk of stroke be prescribed anticoagulation therapy with vitamin K antagonists (VKAs), unless contraindicated. High stroke risk is defined as a score  $\geq 2$  on the CHA<sub>2</sub>DS<sub>2</sub>-VASc risk score. Previously reported baseline data showed that in Cohort 1, 82.6% of patients had CHA<sub>2</sub>DS<sub>2</sub>-VASc  $\geq 2$  but only 62% of these patients received anticoagulant therapy.

Data for the stroke-risk stratification research presented at ESC Congress 2013 were available in 5,523 patients enrolled prospectively between December 2009 and October 2011.

The 1-year data – which are preliminary and should be interpreted with caution – were included in one oral presentation and seven poster abstracts. The oral presentation was featured at the *State of the Art: Acute coronary syndromes - current guidelines and future prospects*, a session that spotlighted the four highest-rated abstracts in this topic.

Highlights of the data, which were adjusted for relevant confounding factors, include:

### Oral Presentation

- Significantly lower use of VKAs in AF patients with acute coronary syndrome (ACS) vs. those without ACS (48.9% vs. 51.7%, respectively) despite a comparable risk of all-cause death, stroke/systemic embolism (SE), major bleeding and recurrent ACS after 1 year
  - 10.1% (n=559) of patients had a history of ACS, 44.0% (n=246) of whom had a history of stenting

### Poster Presentations

- Higher risk profile and more frequent use of antithrombotic therapy in AF patients who have had a previous stroke or transient ischaemic attack (TIA)
  - AF patients with previous stroke/TIA had a 44% increased risk of death (HR\* 1.44, p=0.037) and were more than twice as likely to suffer stroke/SE (HR 2.27, p=0.004) within the first year of diagnosis than patients who had not previously suffered stroke/TIA
  - More AF patients with previous stroke/TIA received VKAs (58.1% vs. 50.5% for no previous stroke/TIA), though these anticoagulants were markedly underutilised in both groups
- Lower risk of death in AF patients receiving rhythm control (the use of medication to restore the normal heart rhythm) vs. rate control (the use of medication to lower the heart rate closer to normal)
  - Among patients studied, 38.1% (n=2,107) were on rhythm control and 49.8% (n=2,754) were on rate control therapy
  - AF patients on rhythm control therapy had a 28% lower risk of death (HR 0.72, p=0.041) compared with patients on rate control therapy
  - Patients on rhythm control were younger and had a lower stroke risk score
  - The two groups differed in many aspects so there may be some residual confounding variables affecting the findings
- Higher overall risk profile for AF patients who have coronary artery disease (CAD)
  - 19.3% (n=1,066) of the study patients had CAD – these patients were older, more likely to be male, and more likely to receive VKA in combination with antiplatelet (AP) therapy than non-CAD patients
  - AF patients with CAD had more than twice the risk for ACS than non-CAD patients (HR 2.49, p=0.016) but a comparable risk of death, stroke/SE and major bleeds
- Lower rate of VKA usage in patients with paroxysmal AF vs. permanent AF despite a comparable level of stroke and systemic embolism risk
  - 24.4% (n=1,348) of study patients had paroxysmal AF vs. 14.2% (n=785) with permanent AF
  - VKAs, alone or in combination with AP, were used in 39.1% of paroxysmal AF patients and 61.0% of permanent AF patients
  - Risk of death was 38% lower in patients with paroxysmal vs. permanent AF (HR

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\* HR = Hazard Ratio, which is a measure of how often an event occurs (i.e., death) in one group vs. another

- 0.62, p=0.057)
- Stroke/systemic embolism risk was similar in both patient groups (HR=1.18, p=0.72)
- Lower stroke risk and less frequent use of anticoagulants in newly diagnosed AF patients from Asia vs. Europe
  - 28.7% (n=1,587) of patients were enrolled in Asia and 58.6% (n=3,237) were enrolled in Europe
  - Patients in Asia were, on average, more likely to be male, younger, have a lower body mass index and have fewer comorbidities than those in Europe
  - Regardless of risk level, VKA usage was significantly higher in Europe (61.4%) vs. Asia (35.8%), highlighting substantial differences in the use of available stroke-prevention therapies
- Less frequent use of VKAs among patients with new vs. permanent AF, though a similar rate of death and stroke between the two groups
  - 44.8% (n=2,477) of patients had new AF vs. 14.2% (n=785) with permanent AF
  - Use of VKAs, alone or in combination with APs, was lower in patients with new AF (52.1%) vs. permanent AF (61.0%)
  - Stroke/systemic embolism risk was 47% increased in patients with permanent vs. new AF, though this difference was not statistically significant (HR 1.47, p=0.36)
  - New AF patients were slightly younger in age
- Underutilisation of anticoagulants among a sizeable proportion of AF patients undergoing direct current conversion (DCC+) – a technique to get the heart into a normal sinus rhythm – despite guidelines recommending their use for stroke prevention
  - Few patients – 11.1% (n=614) patients – in the registry underwent DCC within four months of diagnosis, even though they were newly diagnosed with AF
  - Patients undergoing DCC were more likely to receive VKA therapy than patients not undergoing the procedure. However, 6.9% of DCC+ patients received no antithrombotic therapy and 12.5% received only AP
  - Outcomes of all-cause death, stroke/SE or major bleed at 1 year did not differ between groups

### **About GARFIELD**

The GARFIELD Registry is an observational, multicentre, international prospective study of men and women with newly diagnosed AF and one or more additional risk factors for stroke. It will prospectively follow 50,000 newly-diagnosed AF patients from at least 1,000 centres in 50 countries in the Americas, Eastern and Western Europe, Asia, Africa and Australia.

GARFIELD is the largest prospective registry of patients with AF at risk of stroke. It seeks to describe the real-life burden of this disease, and provide insights into the impact of thromboembolic and bleeding complications seen in this patient population. It will provide a better understanding of antithrombotic treatment patterns and potential opportunities for improving care and clinical outcomes amongst a representative and diverse group of patients and 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 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 six weeks and have at least one additional risk factor for stroke, and as such, are candidates for anticoagulant therapy to prevent blood clots leading to stroke. It will be left to the investigator's clinical judgment to identify patient's stroke risk factor(s). Patients will be included whether or not they receive anticoagulant therapy so current and future treatment strategies and failures can be properly understood in relation to patients' risk profiles and co-morbidities.

Data will be collected over an extended follow-up period of up to 8 years, and will include the following outcomes: thromboembolic stroke; TIA ("mini-strokes"); MI/ACS; blood clots affecting other areas of the body; bleeding events; therapy persistence; rate of discontinuation; medical consultations and hospitalizations; need for urgent and elective interventions; cardiovascular morbidity and all-cause mortality.

Among patients treated with vitamin K antagonists, additional outcomes data will include the frequency and timing of monitoring required to maintain a safe and therapeutically effective level of anticoagulation and interventions needed to manage complications due to anticoagulation therapy.

The GARFIELD Registry is made possible through an unrestricted research grant from Bayer Pharma AG.

### **The Burden of AF**

Up to 2% of the global population has AF. Over 6 million Europeans suffer from this arrhythmia, and it is estimated that its prevalence will at least double by 2050 as the population ages. Around 4.5 million people in the European Union and 2.6 million people in the United States have AF, and estimates suggest that by 2014 more than 12 million people in the Asia-Pacific region will have AF.<sup>1,2,3,4</sup> AF confers a 5-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%.<sup>5</sup> The condition 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.<sup>6</sup> 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, then 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.<sup>7</sup> People with AF also are at high risk for heart failure, chronic fatigue and other heart rhythm problems.<sup>8,9</sup> Stroke is a major cause of long-term disability worldwide – each year 5 million sufferers are left permanently disabled.<sup>10</sup>

### **About the Thrombosis Research Institute (TRI)**

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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