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## **POOR CONTROL OF ANTICOAGULANT THERAPY LEADS TO INCREASED ADVERSE EVENTS FOR PATIENTS WITH ATRIAL FIBRILLATION (AF)**

*-- Global GARFIELD Registry data presented at American Heart Association Scientific Sessions provides insight into stroke, bleeding and mortality risk in everyday clinical practice --*

**LOS ANGELES, November 7, 2012** –Twelve-month data from the Global Anticoagulant Registry in the FIELD (GARFIELD) show that poor management of stroke prevention therapy is widespread in everyday clinical practice, which may lead to elevated rates of mortality, stroke and bleeding among individuals with newly diagnosed with atrial fibrillation (AF).

Data from the GARFIELD Registry describes AF management and outcomes in everyday clinical practice, highlighting unmet needs and challenges in the use of anticoagulation, which is known to significantly lower stroke risk in AF patients. The data presented today at the American Heart Association (AHA) Scientific Sessions evaluated clinical outcomes, such as stroke, major bleeding and mortality, in relation to patient risk profiles and antithrombotic treatments in a representative worldwide AF population.

Of the 9,971 patients observed, only 5,724 (57 percent) were treated with a vitamin K antagonist (VKA). Of those patients, 57 percent were not treated effectively, with a poorly controlled International Normalized Ratio, or INR, a measure of how long it takes the blood to clot.

In this analysis, only 24.5 percent of patients received well-controlled VKA therapy in clinical practice. In the first year from diagnosis with AF:

- 2.2 percent of patients died and 1.3 percent experienced a stroke or systemic embolism (SE).
- In patients not treated with a VKA, these event rates rose to 2.85 percent and 1.54 percent, respectively.
- Among patients treated with a VKA, effective versus poor anticoagulant control results were: 0.86 percent versus 1.72 percent annual mortality and 0.86 percent versus 1.34 percent annual stroke/SE.

Up to two percent of the population has 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.<sup>1</sup> AF-related stroke remains a major and increasing clinical and societal burden, despite the availability of effective preventive treatment.

“These first 12-month data from GARFIELD demonstrate a high mortality rate in patients with newly diagnosed atrial fibrillation,” said Professor Ajay Kakkar, Director of the Thrombosis Research Institute, London, Professor of Surgery, University College London and Chair of the GARFIELD Steering Committee. “We know that anticoagulation can improve patient outcomes in AF, but if it is not controlled properly, as appears often to be the case in actual practice, patients may be put at increased risk for poor clinical outcomes. Further insights into real world outcomes will be provided in the second year of follow-up.”

Of 10,537 patients enrolled in GARFIELD Cohort 1, follow-up data were available for 9,971 patients. These data, presented in the Special Reports hotline session, showed:

- Ninety seven percent of patients had a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 1 or higher, putting them at high risk for stroke and making them eligible for anticoagulation therapy, according to established clinical guidelines.
- One-year event rates for patients receiving VKA therapy (n=5,727) versus those not on VKA therapy (n=4,244) included:
  - Stroke/SE (1.07 percent versus 1.54 percent, respectively)
  - Major bleed (.75 percent versus .36 percent, respectively)
  - Death (1.74 percent versus 2.85 percent, respectively)
- Event rates based on VKA time in the therapeutic range (TTR) ≥60 percent (n=2,009) versus <60 percent TTR (n=2,657) were as follows:
  - Stroke (.86 percent versus 1.34 percent, respectively)
  - Major bleed (.55 percent versus 1.0 percent, respectively)
  - Death (.86 percent versus 1.72 percent, respectively)
- The presence of multiple risk factors increased the likelihood of an adverse event. Risk factors included heart failure, LVEF <40 percent, hypertension, age 75 years or older, diabetes, previous stroke/TIA/SE, vascular disease, age 65-74 years and/or female gender.
  - Unadjusted mortality rates increased nearly five-fold for patients with five or more risk factors versus those with two or fewer.
  - The risk of stroke/SE increased more than 100 percent for those with five or more factors versus those with two or fewer.

“The high death rate and stroke rate from AF are highlighted in this real-life cohort,” said Samuel Z. Goldhaber, MD, Professor of Medicine, Harvard Medical School, Senior Staff Cardiologist, Brigham and Women’s Hospital, and Member of the GARFIELD Steering Committee.

“GARFIELD provides us with the take home message that there remains a wide gap between anticoagulation guidelines and actual clinical practice. Our challenge is to redouble our efforts in clinician education and implementation of proven measures to prevent stroke in AF patients.”

### **About GARFIELD**

The GARFIELD Registry is an observational, multicenter study of men and women with newly diagnosed AF and one or more additional risk factors for stroke. The programme is conducted by the Thrombosis Research Institute, London. It will prospectively follow 50,000 newly-diagnosed AF patients from at least 1,000 centers in 35 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, providing insights into the impact of thromboembolic and bleeding complications, antithrombotic treatment patterns and potential opportunities for improving clinical outcomes amongst a representative and diverse group of patients. This should help physicians and healthcare systems appropriately adopt innovation to ensure the best outcomes for patients and populations.

Four key design features ensure a comprehensive and representative description of AF:

- Five sequential cohorts of 10,000 prospective 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.
- Enrollment of consecutive eligible patients to eliminate potential selection bias.

- At least two years of follow-up after diagnosis to create a database of clinical events and treatment changes.

Included patients have been diagnosed with non-valvular AF within the past six weeks, have at least one additional risk factor for stroke, and are candidates for anticoagulant therapy to prevent blood clots leading to stroke. It will be left to the investigators' clinical judgment to identify patients' 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' stroke risk profile and co-morbidities.

Data will be collected over a six-year period, and will include the following outcomes: thromboembolic stroke; transient ischemic attacks (TIA, or "mini-strokes"); blood clots affecting other areas of the body; bleeding events; therapy persistence; rate and reason for discontinuation; medical consultations and hospitalizations; need for urgent and elective interventions; cardiovascular morbidity and all-cause mortality.

Among patients treated with anticoagulant therapy, 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 two percent of the global population has AF, 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 2.2 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. Ischemic 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 percent 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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