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## NEWS RELEASE

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### **ANTICOAGULANT THERAPY NOT BEING OPTIMALLY USED TO PREVENT STROKE IN PATIENTS WITH ATRIAL FIBRILLATION (AF)**

*-- GARFIELD Registry Data presented at ESC CONGRESS 2012 provides  
trends in treatment patterns that may put AF patients at risk --*

**MUNICH, 29 August 2012** – Baseline data from the first cohort of the Global Anticoagulant Registry in the Field (GARFIELD), an innovative, academic research initiative, shows that established, evidence-based guidelines for preventing stroke in patients with atrial fibrillation (AF) are not being followed in many patients and across diverse populations.

Data from the GARFIELD Registry will describe AF management 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 this week at the European Society of Cardiology (ESC) Congress assessed practice patterns based on region, gender, age, renal function, AF type and the presence of acute coronary syndrome (ACS). The findings show that anticoagulant therapy, particularly vitamin K antagonists (VKA), are under-prescribed for AF patients at high risk for stroke, while at the same time overused in patients with a very low risk for stroke.

GARFIELD is led by an international steering committee under the auspices of the Thrombosis Research Institute (TRI), London. The registry is an international, observational, multicenter, prospective study of men and women 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 two percent of the population has AF.<sup>1</sup>

AF-related stroke remains a major and increasing clinical and societal burden despite the availability of effective preventive treatment. GARFIELD will provide holistic new insights into unmet needs and challenges in AF management, identifying potential opportunities to improve patient care.

“Anticoagulant therapy is known to significantly lower the high risk for stroke associated with atrial fibrillation, yet GARFIELD data suggest that global treatment practices are not reflecting clinical trial evidence and current treatment guidelines,” said Professor the Lord Ajay Kakkar, Director of the TRI, and Professor of Surgery, University College London. “GARFIELD is the largest global disease registry that will provide the most complete view of how stroke risk is managed in AF. By understanding current treatment patterns in everyday clinical practice, we can improve disease management and highlight opportunities for the appropriate adoption of innovative strategies for stroke prevention.”

The first of five GARFIELD cohorts included 10,537 patients with non-valvular AF and with at least one additional risk factor for stroke from 19 countries in the Americas, Europe, Asia, and Asia Pacific. ESC treatment guidelines recommend that all patients at high-risk of stroke be prescribed anticoagulation therapy with VKAs, unless contraindicated with complications such as a risk of bleeding. High stroke risk is defined as a score  $\geq 2$  on the CHADS<sub>2</sub>\* or CHA<sub>2</sub>DS<sub>2</sub>-VASc\*\* risk score. In Cohort 1, 57.1% of patients had CHADS<sub>2</sub> score  $\geq 2$  and 82.6% of patients had CHA<sub>2</sub>DS<sub>2</sub>-VASc  $\geq 2$ .

Of the 6,008 Cohort 1 patients with CHADS<sub>2</sub> $\geq 2$ , only 62.2% received anticoagulant therapy, whilst only 53.1% of the 3,669 patients with CHADS<sub>2</sub>=1 were treated with anticoagulants.

“The first cohort of GARFIELD shows that more than one in three patients with atrial fibrillation who are at high risk for stroke is not being prescribed the anticoagulant therapies known to prevent a stroke,” said Sylvia Haas, MD, emeritus professor of medicine, former director of the Haemostasis and Thrombosis Research Group at the Institute for Experimental Oncology and Therapy Research, Technical University of Munich. “This year’s baseline data at ESC are showing a similar, concerning treatment pattern across a wide range of at-risk subpopulations. As we continue this prospective study, we will have a clearer picture of the patient outcomes associated with these real-world treatment practices.”

The baseline data included two oral presentations and four posters.

Steering committee member Professor Shinya Goto, Tokai University School of Medicine, Japan, presented data on the **regional differences** in antithrombotic treatment for stroke prevention.

- High-risk patients in Europe receive anticoagulants more often than patients in Asia
  - More patients in Europe had a CHADS<sub>2</sub> score  $\geq 2$  (61% vs. 45% in Asia), reflecting an AF population at higher risk for stroke
  - Among these patients that are recommended for treatment with anticoagulants according to existing guidelines, VKAs were prescribed to 69.1% in Europe and only 47.9% in Asia, highlighting the substantial differences in the use of available stroke-prevention therapies
  - VKAs were prescribed to more than half of the low-risk patients (CHADS<sub>2</sub> score =0) in Europe (54.9%) and about one-third in Asia (30.5%)

Steering committee member Professor Jean-Pierre Bassand, University Hospital of Besancon, France presented data on the impact of **gender** on antithrombotic treatment for stroke prevention.

- Women were less likely to receive anticoagulant therapy despite existing evidence for their increased stroke risk,
  - 60.5% of women had a CHADS<sub>2</sub>  $\geq 2$  vs. 51.2% of men; When using the more detailed (CHA<sub>2</sub>DS<sub>2</sub>-VASc) assessment, which accounts for female gender as a stroke risk factor, nearly all women were high risk (score  $\geq 2$ ): 95.8% vs. 70.5% of men
  - According to the CHA<sub>2</sub>DS<sub>2</sub>-VASc risk score, women at high and moderate risk for stroke are under-treated relative to their male counterparts.
  - Among high-risk patients:
    - 57% of women vs. 62% of men received anticoagulant therapy based on CHA<sub>2</sub>DS<sub>2</sub>-VASc  $\geq 2$
    - 62% of both men and women received anticoagulant therapy based on CHADS<sub>2</sub>  $\geq 2$

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\* CHADS<sub>2</sub> is a detailed assessment of stroke risk in AF patients based on five known risk factors = congestive heart failure, hypertension, age  $\geq 75$ , diabetes, stroke (doubled)

\*\* CHA<sub>2</sub>DS<sub>2</sub>-VASc is a detailed assessment of stroke risk in AF patients based on eight known risk factors = congestive heart failure, hypertension, age  $\geq 75$  (doubled), diabetes, stroke (doubled), vascular disease, age 65–74, and female gender

- Among patients with moderate risk, 40% of women vs. 52% of men received anticoagulant therapy based on CHA<sub>2</sub>DS<sub>2</sub>-VASc =1
- 50% of women vs. 56% of men received anticoagulant therapy based on CHADS<sub>2</sub>=1
- Approximately 43% in each group with low stroke risk (CHADS<sub>2</sub>=0) received anticoagulant therapy
- 40% of 'truly' low-risk men (CHA<sub>2</sub>DS<sub>2</sub>-VASc=0) received anticoagulant therapy (with or without APs); none of the women were classified as 'truly' low risk

Steering committee member Professor Gregory Lip, University of Birmingham, UK, presented data on the impact of **age** on antithrombotic treatment for stroke prevention.

- The oldest patients with high stroke risk are the least likely to receive VKAs, despite stroke risk increasing with age
  - Among patients with CHADS<sub>2</sub> score ≥2, the use of VKAs (with or without AP) was greatest in patients ages 65 to 74 years (66.5%) and lowest in those ages 75 or older (60.4%)
  - In patients with CHADS<sub>2</sub> =1, patients aged 65-74 are again more likely to receive anticoagulants than patients aged 75 or older (57.5% vs 50.4%)

Professor Shinya Goto also presented data on the impact of **renal function** on the use of antithrombotic treatment for stroke prevention.

- AF patients with worsening renal dysfunction appear more likely to receive combination therapy with VKAs and APs
  - 33.0% of Cohort 1 patients have some level of renal dysfunction (from mild dysfunction to renal failure)
  - Approximately half (48.2%) of the AF patients with any level of renal impairment were treated with VKAs alone, with 11.7% receiving combination therapy (VKA+AP)
  - As the severity of renal dysfunction increased, the use of VKAs alone decreased from 48.0% in patients with normal renal function to 34.1% in patients with renal failure. The use of VKA+AP in combination increased from 9.9% to 26.8% between these same groups.

Professor Gregory Lip also presented data on the impact of **AF type** on antithrombotic treatment for stroke prevention.

- Anticoagulant therapy is not consistently prescribed across AF categories, despite guidelines recommending it for all high-risk patients regardless of AF type
  - VKAs were prescribed less often in patients with paroxysmal AF (defined as recurrent episodes that self-terminate in less than seven days) than in patients with persistent or permanent AF (42% versus 51.2% and 56.6%, respectively).

Steering committee member Professor Freek Verheugt, Onze Lieve Vrouwe Gasthuis, Netherlands, presented data on the impact of an **ACS history** on antithrombotic treatment for stroke prevention.

- Compared to the overall AF population, patients with a history of ACS were more likely to receive antiplatelet therapy with or without VKA
  - 9.9% of Cohort 1 patients have a history of ACS
  - Patients with an ACS history were most likely to receive a VKA alone (29.4%), despite guidelines recommending VKA plus one or more antiplatelet (AP) for at least 3-6 months. 23.8% of patients received VKA plus one AP; 23.7% received one AP alone.
  - Although ESC guideline recommendations do not change considering the presence of previous percutaneous coronary intervention (stenting), patients with stents were more likely to receive combination therapy (31.0% vs. 24.1% among patients without stents)
  - Treatment patterns for ACS patients without previous stenting are similar to the

overall AF population, suggesting that ESC guidelines are more frequently adopted in ACS patients with a stent than in those without

TRI will present the first 12-month follow-up outcomes data from the GARFIELD Registry at the upcoming American Heart Association's Scientific Sessions 2012 in Los Angeles, CA, United States. Recruitment for the second cohort of the GARFIELD Registry began on 5 October 2011. Baseline data from this cohort also will be available later this year.

### **About GARFIELD**

The GARFIELD Registry is an observational, multicenter, 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 centers 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 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.
- Follow-up data captured for at least two years after diagnosis, to create a comprehensive database of clinical events and treatment changes.

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' 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 also 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. 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, reaching more than 12 million. 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 by their stroke 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, thereby not allowing blood to be pumped out of the atria 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 are not only at a five times higher risk of suffering a stroke than the general population, but they are also 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 stroke 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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<sup>1</sup> Jamil-Copley S; Kanagaratnam P. (12/6/10). Stroke in atrial fibrillation-hope on the horizon? J R SOC INTERFACE. 8/16/12. Available at: [http://rsif.royalsocietypublishing.org/content/7/Suppl\\_6/S765.full](http://rsif.royalsocietypublishing.org/content/7/Suppl_6/S765.full),

<sup>2</sup> The Lancet Neurology. Stroke prevention: getting to the heart of the matter. 8/16/12. Available at: [http://www.atrialfibrillation.org.uk/files/file/Articles\\_Medical/Lancet%20Neurology-%20getting%20to%20the%20heart%20of%20the%20matter.pdf](http://www.atrialfibrillation.org.uk/files/file/Articles_Medical/Lancet%20Neurology-%20getting%20to%20the%20heart%20of%20the%20matter.pdf)

<sup>3</sup> Thrombosis Advisor. Thrombosis Facts. 8/16/12. Available at: <http://www.thrombosisadviser.com/en/resources/thrombosis-facts.php>

<sup>4</sup> Chinese Medical Journal 2004 ; 117 ( 12 ) : 1763-176. Available at: [http://dronedarone-atrial-fibrillation-pressoffice.com/sites/default/files/event-document/af\\_in\\_the\\_asia-pacific\\_region.pdf](http://dronedarone-atrial-fibrillation-pressoffice.com/sites/default/files/event-document/af_in_the_asia-pacific_region.pdf)

<sup>5</sup> European Society of Cardiology. Guidelines for the Management of Atrial Fibrillation. 8/16/12. <http://eurheartj.oxfordjournals.org/content/early/2010/09/25/eurheartj.ehq278.full>

<sup>6</sup> National Heart Lung and Blood Institute. What is Atrial Fibrillation. 8/16/12. Available at: [http://www.nhlbi.nih.gov/health/dci/Diseases/af/af\\_what.html](http://www.nhlbi.nih.gov/health/dci/Diseases/af/af_what.html)

<sup>7</sup> Thrombosis Research Institute. About Thrombosis.8/16/12. Available at: <http://www.tri-london.ac.uk/about.asp>

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<sup>8</sup> Rockson SG, Albers GW. Comparing the guidelines: anticoagulation therapy to optimize stroke prevention in patients with atrial fibrillation. *J Am Coll Cardiol* 2004;43(6):929-35.

<sup>9</sup> American Heart Association. Why is AF a Problem?. 8/16/12. Available at: [http://www.heart.org/HEARTORG/Conditions/Arrhythmia/AboutArrhythmia/Why-is-AF-a-Problem\\_UCM\\_423776\\_Article.jsp](http://www.heart.org/HEARTORG/Conditions/Arrhythmia/AboutArrhythmia/Why-is-AF-a-Problem_UCM_423776_Article.jsp).

<sup>10</sup> World Heart Foundation. The Global Burden of Stroke. 8/16/12. Available at: <http://www.world-heart-federation.org/cardiovascular-health/stroke/>