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AS GARFIELD-AF REGISTRY EXCEEDS ITS 57,000 ENROLMENT TARGET, NEW RESULTS SHOW SUPERIOR PERFORMANCE OF THE GARFIELD-AF SCORE, A NOVEL MACHINE LEARNING TOOL, IN PREDICTING ISCHAEMIC STROKE IN LOW-RISK PATIENTS

- *New global data from GARFIELD-AF presented at ESC Congress 2016 provide real world insights on managing atrial fibrillation (AF) in everyday practice*
- *GARFIELD-AF is the largest ongoing prospective AF registry and enrolment is now complete, with 57,262 patients recruited across five cohorts*

Rome, Italy, 29th August 2016 – New analyses from the Global Anticoagulant Registry in the FIELD – Atrial Fibrillation (GARFIELD-AF) show that a novel computer-generated machine learning risk model – the GARFIELD-AF Score – is superior to CHA_2DS_2-VASc in predicting all-cause mortality, ischaemic stroke/systemic embolism (SE) and major bleeding in low-risk patients. A simplified GARFIELD-AF Score, potentially suitable for web applications, has been developed and its performance assessed using an independent contemporary registry from the USA, ORBIT-AF.

The GARFIELD-AF Score was developed after contemporary data from the GARFIELD-AF Registry revealed that approximately half of low-risk patients are receiving anticoagulation treatment[1]. "These data show that factors beyond those in current risk scores appear to be influencing prescribing decisions on anticoagulation and improved risk stratification tools are needed to better identify truly low-risk AF patients," said Professor Keith A. A. Fox, Duke of Edinburgh Professor of Cardiology at the University of Edinburgh, UK.

"The more comprehensive GARFIELD-AF Score includes multiple variables, beyond that of CHA_2DS_2-VASc, and this increased granularity will help to optimise the management of low-risk patients. The GARFIELD-AF Score has the potential to be incorporated into routine electronic record systems via web-based or mobile device applications, thereby enabling users to base treatment decisions on more precise and tailored values, as well as more complete estimates of risk based on multiple outcomes," said Professor Fox.

The GARFIELD-AF Score is based on the analyses of data from 38,984 patients, enrolled in GARFIELD-AF between March 2010 and July 2015. In low-risk patients, the GARFIELD-AF Score offered superior discriminatory value in predicting all-cause mortality, ischaemic stroke/SE or haemorrhagic stroke/major bleed with C statistics* of: 0.72, 0.62 and 0.72, respectively, compared with CHA_2DS_2-VASc which had C statistics of: 0.56, 0.56 and 0.57, respectively for each endpoint.

Global shift in AF management

Further insights from GARFIELD-AF showed a shift in how AF is being managed across the globe. The number of patients receiving anticoagulant treatment for stroke prevention has increased substantially from 57% to 71% between March 2010 and August 2015. This shift in anticoagulant management of patients with AF is largely due to the marked increase in non-vitamin K antagonist oral anticoagulants (NOACs) with or without an antiplatelet prescribing

*A higher C statistic demonstrates higher accuracy at predicting outcomes

from 4.1% to 37.0%, with a corresponding fall in vitamin K antagonists (VKAs) and antiplatelet (combined or alone) use from 83.4% to 50.6%.[1]

“The change in treatment patterns over the past 5 years suggests a greater clinical emphasis on stroke prevention,” said Professor Ajay Kakkar, Professor of Surgery at University College London and Director of the Thrombosis Research Institute, UK. “The challenge remains ensuring the appropriate patient receives the most effective and safe intervention to secure the best clinical outcome.”

Comorbidities and integrated care

New data, showcased during the GARFIELD-AF Satellite Symposium at ESC Congress 2016, revealed that mortality rates are higher during the first month after diagnosis of AF than at any other time over the subsequent 2-year follow-up. The risk of early death is greater in patients with prior history of myocardial infarction/unstable angina, moderate-to-severe chronic kidney disease, or stroke than in those without these comorbidities.

“These data from the GARFIELD-AF registry indicate the importance of comorbidities in predicting the risk of early mortality in patients with AF,” said Professor Samuel Goldhaber of Harvard Medical School and the Brigham and Women’s Hospital, USA. “The results suggest the importance of an integrated care approach for managing these patients.”

GARFIELD-AF insights still to come at ESC Congress 2016

Professor Keith A. A. Fox will present on *Monday 29th August, at 15:35–16:25 CEST* in the poster area an analysis of wide geographical variability in all-cause mortality, stroke/SE and major bleeding observed in patients with newly diagnosed nonvalvular AF. Additionally, on *Tuesday 30th August, at 10:05–10:55 CEST* in the poster area, Professor Shinya Goto from Tokai University, Isehara, Japan will present an analysis of the association between international normalised ratios, used to measure the intensity of anticoagulation, and the rates of stroke/SE, major bleeding and all-cause mortality in patients from Eastern and Southeastern Asia.

Country data showcases for Germany, Italy, Japan and the USA are also scheduled throughout ESC Congress 2016 at the Thrombosis Research Institute (TRI) exhibition stand (E2-F675).

About the GARFIELD-AF registry

2016 marks the end of the enrolment phase for GARFIELD-AF, with 57,262 patients now enrolled. GARFIELD-AF is the largest ongoing prospective registry of patients with AF. The real world insights that continue to be gathered from the GARFIELD-AF registry are being converted into real-world evidence that helps inform and identify areas where the medical community can continue to improve patient outcomes.

GARFIELD-AF is a pioneering, independent academic research initiative led by an international steering committee under the auspices of the TRI, London, UK.

It is an international, observational, multicentre study of stroke prevention in patients with newly diagnosed AF. Patients were enrolled from over 1,000 centres in 35 countries worldwide, including from the Americas, Europe, Africa and Asia-Pacific.

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; these are:

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

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer Pharma AG, Berlin, Germany.

For more information, visit our new website: www.garfieldregistry.org

The burden of AF

Up to 2% of the global population has AF,[2] including around 8.8 million people in Europe[3] and 5–6.1 million in the United States.[4] It is estimated that its prevalence will at least double by 2050 as the global population ages.[4] AF is associated with a five-fold increase in stroke risk, and one out of five strokes is attributed to this arrhythmia.[2] Ischaemic strokes related to AF are often fatal, and those patients who survive are left more frequently and more severely disabled and have a greater risk of recurrence than patients with other causes of stroke.[2] Hence, the risk of mortality from AF-associated stroke is doubled and the cost of care is 50% higher.[2]

AF occurs when parts of the atria emit uncoordinated electrical signals. This causes the chambers to pump too quickly and irregularly, not allowing blood to be pumped out completely.[5] As a result, blood may pool, clot and lead to thrombosis, which is the number one cardiovascular killer in the world.[6] If a blood clot leaves the left atrium, it could potentially lodge in an artery in other parts of the body, including the brain. A blood clot in an artery in the brain leads to a stroke. 92% of fatal strokes are caused by thrombosis.[6] Stroke is a major cause of death and long-term disability worldwide – each year, 6.7 million people die[7] and 5 million are

left permanently disabled.[8] People with AF also are at high risk for heart failure, chronic fatigue and other heart rhythm problems.[9]

About the TRI

The TRI is a charitable foundation and multidisciplinary 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 enhance quality of care, improve clinical outcomes and reduce healthcare costs. The TRI is a member of University College London Partners' Academic Health Science Network. For more information, visit www.tri-london.ac.uk.

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1. Camm A J, Accetta G, Ambrosio G, *et al*. Evolving antithrombotic treatment patterns for patients with newly diagnosed atrial fibrillation. *Heart* 2016; doi: 10.1136/heartjnl-2016-309832.
2. Camm A J, Kirchhof P, *et al*. Guidelines for the management of atrial fibrillation: The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J* 2010; 31(19):2369-429.
3. Krijthe B P, Kunst A, *et al*. Projections on the number of individuals with atrial fibrillation in the European Union, from 2000 to 2060. *Eur Heart J* 2013; 34:2746-51.
4. Colilla S, Crow A, Petkun W, *et al*. Estimates of current and future incidence and prevalence of atrial fibrillation in the U.S. adult population. *Am J Cardiol* 2013; 112(8):1142-7.
5. National Heart, Lung, and Blood Institute. What is Atrial Fibrillation? Available at: http://www.nhlbi.nih.gov/health/health-topics/topics/af/. [Last accessed: 4 August 2016].
6. International Society on Thrombosis and Haemostasis. About World Thrombosis Day. Available at: http://www.worldthrombosisday.org/about/. [Last accessed: 4 August 2016].
7. World Health Organization. The top 10 causes of death. Fact sheet N°310. Available at: http://www.who.int/mediacentre/factsheets/fs310/en/. [Last accessed: 4 August 2016].
8. World Heart Federation. The global burden of stroke. Available at: http://www.world-heart-federation.org/cardiovascular-health/stroke/. [Last accessed: 4 August 2016].
9. American Heart Association. Why Atrial Fibrillation (AF or AFib) Matters. Available at: http://www.heart.org/HEARTORG/Conditions/Arrhythmia/AboutArrhythmia/Why-Atrial-Fibrillation-AF-or-AFib-Matters_UCM_423776_Article.jsp. [Last accessed: 4 August 2016].