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

Media Contact
Charlotte Shyllon
CShyllon@tri-london.ac.uk
+44 (0) 7415 858 411

THROMBOSIS RESEARCH INSTITUTE (TRI) SHARES NEW GARFIELD-AF REAL-WORLD DATA ANAYSES AND UNVEILS TOOL PREDICTING RISK OF STROKE, DEATH AND BLEEDING AT ESC CONGRESS 2019

- *Major Satellite Symposium explores in depth the long term impact of atrial fibrillation and advancements in treatment that can be made from the results of the GARFIELD-AF real-world study*
- *Symposium presentation and moderated e-poster showcase the integrated GARFIELD-AF risk tool that* outperformed CHA_2DS_2-VASc at predicting mortality over 2 years and is *designed to calculate risk of death, stroke/SE and major bleed in a single tool to support treatment decision making*

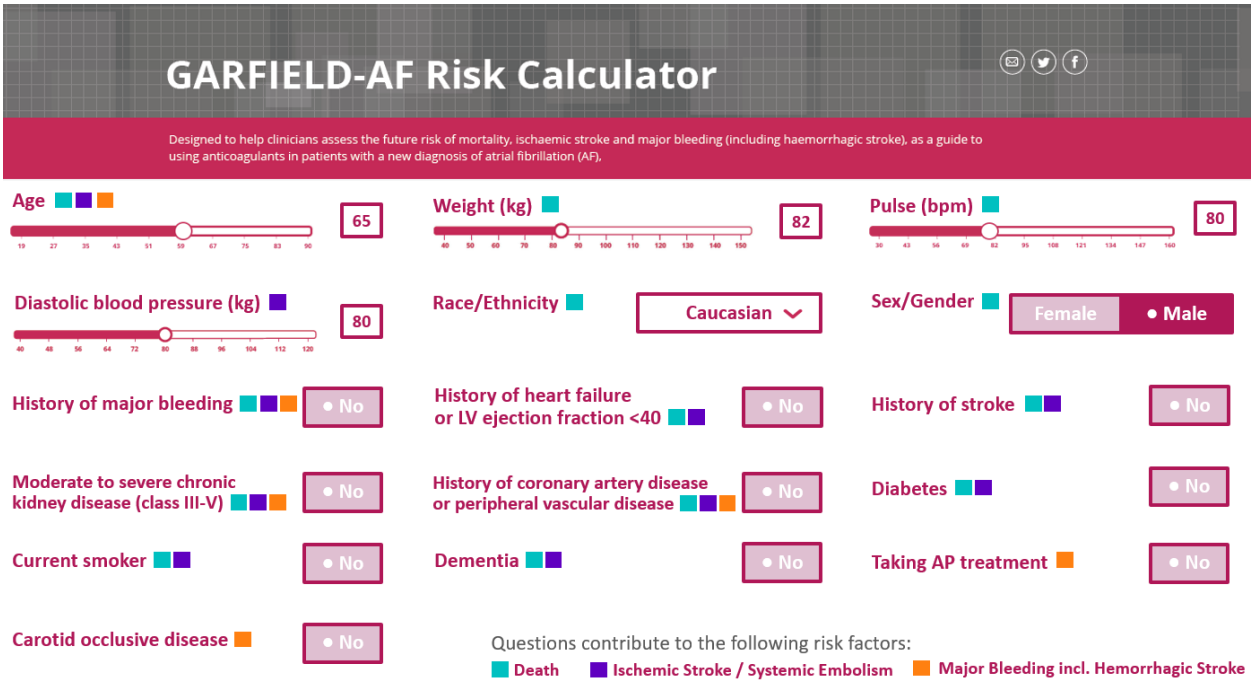
Paris, France, 3rd September 2019 – The latest results from the Global Anticoagulant Registry in the Field – Atrial Fibrillation (GARFIELD-AF) study were unveiled at ESC Congress 2019 in Paris from TRI's major Satellite Symposium entitled 'Long term impact of atrial fibrillation' as well as from participating in two late breaking sessions and two poster presentations over four days at the congress.

Overall, the Satellite Symposium and presentations were an excellent showcase of the breadth and value of data accrued by GARFIELD registries through their latest real-world studies, with immediate and practical implications for improved treatment of thrombosis worldwide.

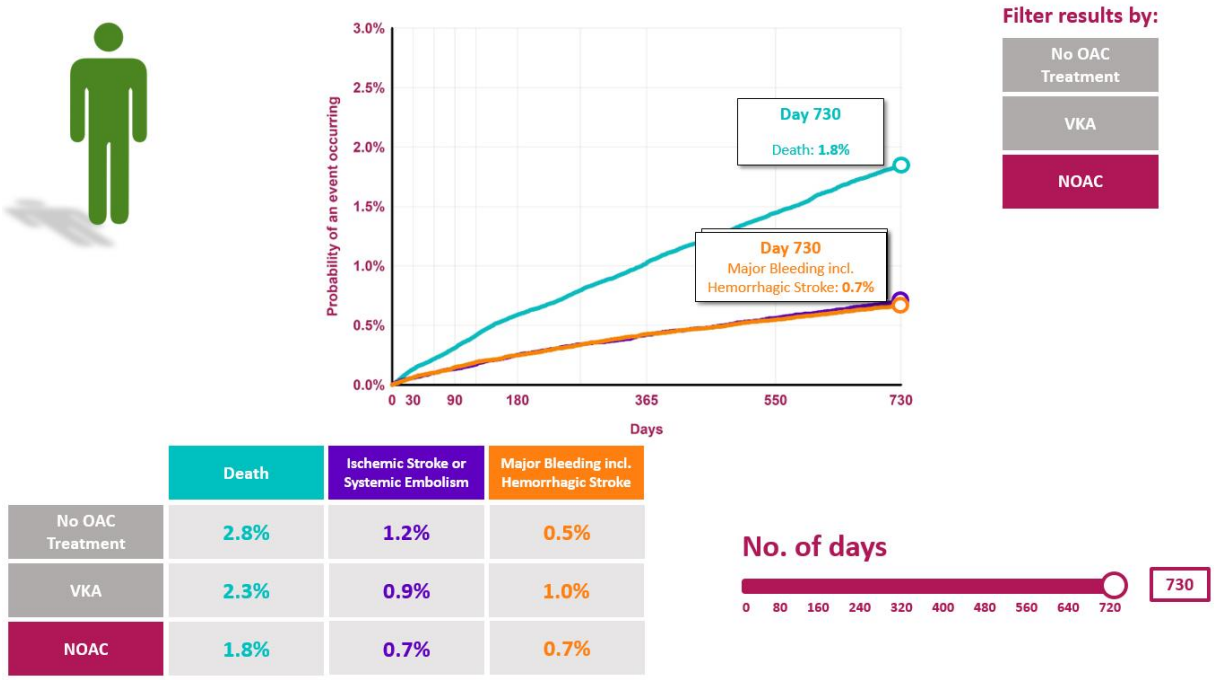
Rt Hon Professor the Lord Ajay K. Kakkar, Director of the Thrombosis Research Institute, UK, said: "Our analysis of the real-world evidence collected in the GARFIELD registries enables us to show physicians how the treatment decisions made during everyday practice around the world are impacting patient outcomes. The scale of our registries and the methodological rigour we apply mean that these data can be trusted to help inform and enhance understanding and influence treatment guidance across the globe."

The enhanced integrated GARFIELD-AF risk tool

Speaking during the Satellite Symposium and at a moderated ePoster on 'Balancing risk and benefit in patients with AF', Professor Keith A A Fox (UK) told delegates that the integrated GARFIELD-AF risk tool was designed to calculate risk of death, stroke/systemic embolism (SE), and major bleed in a single readout. The new, improved risk tool was developed using data from the last three GARFIELD-AF cohorts with 2 years' follow-up. In a validation cohort, it outperformed CHA_2DS_2-VASc at predicting mortality over 2 years.



Professor Fox said: “This risk score quantifies individual factors that contribute toward an individual patient's diagnosis or prognosis and can thereby guide and improve clinicians' assessment and treatment decisions. The tool can immediately be applied to newly diagnosed AF patients when making treatment decisions”.



	Death	Ischemic Stroke or Systemic Embolism	Major Bleeding incl. Hemorrhagic Stroke
No OAC Treatment	2.8%	1.2%	0.5%
VKA	2.3%	0.9%	1.0%
NOAC	1.8%	0.7%	0.7%

Other key insights from the Satellite Symposium

Positive outcomes from long term treatment of AF

Going out live on Twitter (@GARFIELD_reg) on Saturday afternoon, Lord Kakkar opened the Satellite Symposium with an insightful reflection on long-term outcomes of AF treatment. He noted: "GARFIELD-AF is distinguished as one of the first registries to analyse treatment patterns and outcomes in atrial fibrillation (AF) patients beyond 2 years". In a group of 20,000 patients followed for an average 3 years a clear shift in absolute risk of death was noted after 2 years. Among the approximately 93% who survived 2 years, their risk of dying during the subsequent 2 years was less than 2%.

Changes in antithrombotic therapy post diagnosis

Dr Frank Cools (Belgium) explored changes in antithrombotic therapy after AF diagnosis. The vast study underpinning his results involved nearly 24,000 GARFIELD-AF-registered AF patients. Approximately half were on VKAs and half NOACs (direct thrombin inhibitors (DTIs) or factor Xa inhibitors (FXAs)) regardless of CHA_2DS_2-VASc score <2 or ≥2. Dr Cools revealed that "approximately 90% patients starting oral anticoagulant (OAC) were still on OAC at time of last visit. In unadjusted analyses, switching occurred less with FXA compared to DTI and VKA treated patients and this difference keeps increasing over time".

Testing AF care management guidelines

Professor A John Camm (UK) spoke on management of care in AF patients when following guidelines for treatment of atrial fibrillation and comorbid conditions. The GARFIELD-AF registry was interrogated to explore how well guidelines-directed medical therapy (GDMT) was used in 44,000 at-risk AF patients (CHA_2DS_2-VASc score ≥2). Professor Camm noted that "patients who received OAC were more likely to receive all GDMTs than those who did not receive OAC. Comprehensive GDMT reduced mortality by 16% but had no effect on risk of stroke compared with inadequate or no GDMT".

Results of three-way anticoagulant comparative study

Professor Shinya Goto (Japan) detailed the effectiveness among different classes of oral anticoagulants. The study concerned at-risk AF patients treated with one of three classes of OACs: VKA, DTI, or FXA. Drawing data from the substantial GARFIELD-AF registry, a "novel statistical modelling approach" was applied to investigate outcomes (all-cause mortality, ischemic stroke, and major bleeding). The model was able to discriminate a significantly lower risk of death in FXA versus VKA and DTI groups. All other intergroup comparisons did not yield any significant differences in risk of outcome events.

Key insights from other presentations and posters

Old age as a predictor of intracranial haemorrhage

Dr Toon Wei Lim (Singapore) presented GARFIELD-AF and ORBIT-AF registry insights on predictors of intracranial haemorrhage (ICH) in patients with AF. The study analysed the combined data of 75,000 patients on anticoagulation therapy enrolled in the global GARFIELD-

AF and US-based ORBIT-AF registries. Dr Lim revealed older age was by far the most highly significant risk factor for experiencing ICH, followed by prior stroke/transient ischaemic attack (TIA). Treatment with NOAC versus VKA was associated with reduced ICH risk, whereas concurrent use of antiplatelet (AP) therapy increased ICH risk.

Haematuria in NOACs versus VKAs treatment

Dr Stefan Verstraete (Belgium) presented a poster suggesting that haematuria is more frequent in AF patients treated with NOACs versus VKAs, an insight gleaned from GARFIELD-AF registry data on over 24,000 AF patients. The poster also highlighted that haematuria may arise in approximately one in 100 AF patients on long-term OACs therapy but is usually non-serious.

Minor bleeds should not be assumed benign

Professor Jean-Pierre Bassand (France) unveiled registry evidence on short- and long-term prognostic implications of bleeding in patients with newly diagnosed atrial fibrillation. Among 52,000 newly diagnosed AF patients studied, risk of death was significantly higher in those with any type of bleeding versus no bleeding. This implies that not only major bleeds but also minor and clinically relevant non-major bleeds should not be considered benign events. Intracranial haemorrhage accounted for 40% of all fatal bleeding at 30 days and 21% at 1 year. After 30 days, most deaths in patients who bled were linked to non-cardiovascular causes. “Their comprehensive management should be advocated,” commented Professor Bassand.

Up to 2% of the global population has AF,[1] including around 8.8 million people in Europe[2] and 5–6.1 million in the United States.[3] It is estimated that its prevalence will at least double by 2050 as the global population ages. TRI’s pioneering research programme, across medical disciplines and across the world, continues to provide breakthrough solutions in thrombosis.

About the GARFIELD-AF registry

GARFIELD-AF is a worldwide observational programme that aims to enhance the breadth and depth of understanding of stroke prevention in atrial fibrillation (AF), ultimately informing strategies to improve patient outcomes, safety and utilisation of healthcare resources.

It offers a unique opportunity to obtain a comprehensive and contemporary description of the spectrum of patients with AF and their management worldwide as they evolve over time. The registry is important in bridging the gap between research and clinical practice, serving to increase awareness of the importance of thrombosis and its treatment.

GARFIELD-AF recruited patients with newly diagnosed nonvalvular AF and at least one risk factor for stroke. A total of 57,262 patients were recruited from over 1000 centres in 35 countries worldwide, including the Americas, Europe, Africa and Asia-Pacific, over five sequential cohorts. Follow-up is over a minimum of 2 years and up to 8 years after diagnosis, to create a comprehensive database of treatment decisions and outcomes in everyday clinical practice.

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

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 non-valvular 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 AG, Berlin, Germany.

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

The burden of AF

Up to 2% of the global population has AF,[1] including around 8.8 million people in Europe[2] and 5–6.1 million in the United States.[3] It is estimated that its prevalence will at least double by 2050 as the global population ages.[3] AF is associated with a five-fold increase in stroke risk, and one out of five strokes is attributed to this arrhythmia.[1] 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.[1] Hence, the risk of mortality from AF-associated stroke is doubled and the cost of care is 50% higher.[1]

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.[4] As a result, blood may pool, clot and lead to thrombosis, which is the number one cardiovascular killer in the world.[5] 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.[5] Stroke is a major cause of

death and long-term disability worldwide – each year, 6.5 million people die[6] and 5 million are left permanently disabled.[7] People with AF also are at high risk for heart failure, chronic fatigue and other heart rhythm problems.[8]

About the TRI

The TRI is dedicated to bringing new solutions to patients for the detection, prevention and treatment of blood clots. The TRI's goal is to advance the science of real-world enquiry so that the value of real-world data is realised and becomes a critical link in the chain of evidence. Our pioneering research programme, across medical disciplines and across the world, continues to provide breakthrough solutions in thrombosis.

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

###

1. 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.
2. 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.
3. 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.
4. National Heart, Lung, and Blood Institute. What is Atrial Fibrillation? Available at: http://www.nhlbi.nih.gov/health/health-topics/topics/af/. [Last accessed: 10 August
5. World Thrombosis Day. Know Thrombosis. Available at: http://www.worldthrombosisday.org/issue/thrombosis/. [Last accessed: 3rd September 2019].
6. World Stroke Organization. World Stroke Campaign. Available at: http://www.worldstrokecampaign.org/. [Last accessed: 3rd September 2019].
7. Stroke Centre. Stroke Statistics. Available at: http://www.strokecenter.org/patients/about-stroke/stroke-statistics/. [Last accessed: 3rd September 2019].
8. 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: 3rd September 2019].