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REAL-WORLD EVIDENCE FROM GARFIELD-AF SHOWS SUPERIOR REDUCTION IN MORTALITY WITH NON-VITAMIN K ANTAGONISTS ORAL ANTICOAGULANTS (NOACS) VS. VITAMIN K ANTAGONISTS (VKAS) IN NEWLY DIAGNOSED ATRIAL FIBRILLATION

- *High-risk patients on anticoagulants (AC) for stroke prevention also have 17% fewer deaths over 2 years of follow-up than patients who are not treated with AC*
- *Patients who receive AC plus add-on antiplatelet therapy (AP) for stroke prevention have a significantly worse prognosis than patients on AC alone*
- *More than 70% of patients on NOACs receive the recommended dose, but prescription of non-recommended doses is associated with a 51% increased risk of death*
- *A new GARFIELD-AF web-based risk tool was showcased at the European Society of Cardiology (ESC) Congress 2018 for risk assessment of patients with AF*

Munich, Germany, 28 August 2018 – A new analysis from the Global Anticoagulant Registry in the FIELD-Atrial Fibrillation (GARFIELD-AF), the largest multinational prospective registry in AF, presented today at ESC Congress 2018, confirms that NOACs are superior to VKAs in reducing 2-year mortality in higher risk patients (CHA_2DS_2-VASc score ≥2). In this study of 19,134 patients, there were 19% fewer deaths in patients initiated on NOACs than VKAs at the time of diagnosis of AF (adjusted Hazard Ratio [HR] 0.81 [95% confidence interval (CI) 0.71, 0.92]; p<0.001). During a Late-Breaking Science "Registry 2" session,[1] Professor A. John Camm, St George's, University of London, observed that these data show the results from randomised controlled trials with NOACs can be translated to the broader cross-section of patients treated in the real world. "These real-world data may reflect the impact of poor VKA control, which was found to be associated with a high risk of events according our previous research,[2]" he said.

Professor Camm also revealed that there were 17% fewer deaths (adjusted HR 0.83 [95% CI: 0.75, 0.93; p<0.001]) and 27% fewer strokes/systemic emboli (adjusted HR 0.73 [95% CI: 0.59, 0.90]; p=0.003) with ACs compared with no AC therapy in higher risk patients with a CHA_2DS_2-VASc score ≥2[1]: "This new evidence of 26,742 GARFIELD-AF patients analysed over 2 years suggests that AC therapy has a beneficial effect beyond stroke prevention."

Worse prognosis with AC+AP versus AC alone

In another Late-Breaking Science "Registry 2" presentation from GARFIELD-AF, Professor Keith Fox, University of Edinburgh, challenged the use of AC plus add-on antiplatelet (AP) therapy among those without a clear indication for AP therapy. "In this analysis of 25,815 patients with new onset AF and no prior AP or AC, those who receive AC and AP therapy at the time of diagnosis of AF have a worse prognosis than those on AC alone,[3]" said Professor Fox. Overall, treatment with AC+AP compared to AC alone was associated with increased risks of major bleeding (adjusted HR 1.45 [95% CI: 0.94, 2.23]) and all-cause

mortality (adjusted HR 1.31 [95% CI: 1.05, 1.62]) without a reduction in stroke (adjusted HR 1.60 [95% CI: 1.08, 2.35]).

The detrimental effects on non-recommended NOAC dosing

The global scope of the GARFIELD-AF registry in patients with newly diagnosed AF also provides an opportunity to evaluate whether the actual dosing of NOACs in real-life conforms to the approved dosing regimen (based on country-specific guidelines for each NOAC for stroke prevention). In a Rapid Fire session at ESC Congress 2018, Professor John Camm reported that more than 70% of the 10,417 patients received the correct dose of NOAC.[4] Dosing above the recommended dose was relatively rare (3.6%, overall), and largely confined to cases where dose-modification was not heeded for moderate-to-severe chronic kidney disease. For those patients who received non-recommended low-dose NOAC, all-cause mortality increased by 51% over the first year of follow-up (adjusted HR: 1.51% [95% CI 1.16-1.96]), compared with patients who received the recommended dose of NOAC for stroke prevention.

New GARFIELD-AF web-based risk calculator showcased

Now available as a web-based resource, the GARFIELD-AF risk calculator was showcased at the GARFIELD-AF Satellite Symposium at ESC.

"We are delighted to announce the availability of the GARFIELD-AF risk calculator which we believe has the potential to be incorporated into routine electronic systems," commented Rt Hon Professor the Lord Kakkar, Director of the Thrombosis Research Institute. The risk calculator is now available to the GARFIELD-AF research community and will be made generally available early next year.

In 2016, Professor Keith Fox and colleagues on behalf of the GARFIELD-AF investigators published results on the GARFIELD-AF risk calculator for assessing the risk of death, stroke/systemic embolism and major bleeding in patients over the first year after the diagnosis of AF.[5] This tool had superior predictive value compared to CHA_2DS_2-VASc for predicting stroke and death. It was also at least as good as HAS-BLED for predicting major bleeding in patients who received AC for stroke prevention. The value of the GARFIELD-AF risk calculator was validated using contemporary data from the ORBIT II registry from the USA.

To view the eight GARFIELD-AF data presentations at the ESC Congress 2018 and a video recording of the TRI Satellite Symposium, please visit: www.garfieldregistry.org

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 1352 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 Thrombosis Research Institute (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 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 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,[6] including around 8.8 million people in Europe[7] and 5–6.1 million in the United States.[8] It is estimated that its prevalence will at least double by 2050 as the global population ages.[8] AF is associated with a five-fold increase in stroke risk, and one out of five strokes is attributed to this arrhythmia.[6] 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.[6] Hence, the risk of mortality from AF-associated stroke is doubled and the cost of care is 50% higher.[6]

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.[9] As a result, blood may pool, clot and lead to thrombosis, which is the number one cardiovascular killer in the world.[10] 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.[10] Stroke is a major cause of death and long-term disability worldwide – each year, 6.5 million people die[11] and 5 million are left permanently disabled.[12] People with AF also are at high risk for heart failure, chronic fatigue and other heart rhythm problems.[13]

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/.

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1. Camm AJ, *et al*. Comparative effectiveness of oral anticoagulants in everyday practice. Late Breaking Registry Results 2 ESC Congress 2018. Nr 5876
2. Haas S, *et al.* Quality of vitamin K antagonist control and 1-year outcomes in patients with atrial fibrillation: a global perspective from the GARFIELD-AF registry. PLoS One 2016; 11: e0164076
3. Fox KAA, *et al.* Adverse one-year outcome for patients newly treated with oral anticoagulants plus antiplatelet therapy after a diagnosis of atrial fibrillation. Results from the GARFIELD-AF prospective registry. Late Breaking Registry Results 2 ESC Congress 2018. Nr 5878.
4. Camm AJ, *et al.* The effect of non-recommended dosing of non-vitamin K antagonist oral anticoagulants (NOACs) on 1-year mortality in patients with newly diagnosed AF. Results from the GARFIELD-AF registry. Rapid Fire Session Atrial Fibrillation – detection, treatment, outcomes. ESC Congress 2018 Nr 1354.
5. Fox KAA et al. Improved risk stratification of patients with atrial fibrillation: an integrated GARFIELD-AF tool for the prediction of mortality, stroke and bleed in patients with and without anticoagulation. BMJ Open. 2017;7: e017157.
6. Camm AJ, *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.
7. 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.
8. 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.
9. National Heart, Lung, and Blood Institute. What is Atrial Fibrillation? Available at: http://www.nhlbi.nih.gov/health/health-topics/topics/af/. [Last accessed: August 9 2018].
10. World Thrombosis Day. Know Thrombosis. Available at: http://www.worldthrombosisday.org/issue/thrombosis/. [Last accessed: 9 August 2018].
11. World Stroke Organization. World Stroke Campaign. Available at: http://www.worldstrokecampaign.org/. [Last accessed: 9 August 2018].
12. Stroke Centre. Stroke Statistics. Available at: http://www.strokecenter.org/patients/about-stroke/stroke-statistics/. [Last accessed: 9 August 2018].
13. 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: 9 August 2018].