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LATE-BREAKING REAL-WORLD RESULTS FROM GARFIELD-AF PRESENTED AT THE AHA SCIENTIFIC SESSIONS 2018 SHOW PERMANENT DISCONTINUATION OF ORAL ANTICOAGULATION PUTS PATIENTS WITH ATRIAL FIBRILLATION AT RISK

- *Among 22,810 patients with AF studied over 2 years, the discontinuation rate was 9.5%*
- *Stopping OAC for at least 7 days, resulted in significantly worse clinical outcomes including a higher chance of dying, even if OAC was restarted afterwards*
- *Reasons for discontinuation included physician (43.3%) or patient (16.8%) decisions*

Chicago, USA, 12 November 2018 – Patients with atrial fibrillation (AF) who stopped taking an oral anticoagulant (OAC) treatment for at least 7 days had a significantly worse clinical outcome, associated with a higher chance of death, stoke or myocardial infarction, whether or not OAC was restarted.

"These results imply that discontinuation of OAC treatment in the AF population should be discouraged, even if there seems to be a 'valid' reason to do so. Starting (or restarting) OAC treatment requires effective communication with patients, continuous follow-up and counselling," observed lead investigator Dr Frank Cools, AZ Klina, Brasschaat, Belgium, during the Late-Breaking 'Lessons from Large Registries' session yesterday at American Heart Association Scientific Sessions 2018.[1]

These analyses from Global Anticoagulant Registry in the FIELD-Atrial Fibrillation (GARFIELD-AF) provide a detailed picture of the rate and impact of OAC discontinuation in 22,810 AF patients who were followed prospectively over 2 years. Almost one in ten (9.5%) of these patients who started OAC for stroke prevention at the time of diagnosis of AF discontinued treatment over a 2-year follow-up, with nearly half of discontinuations (43.8%) occurring within the first 4 months of starting treatment. "Surprisingly only 23.5% of patients were restarted on an OAC at some point," noted Dr Cools.

In contrast to patients who remained on OAC, those who discontinued had a significantly increased risk for all endpoints ($p<0.001$), including the composite measures of: death/non-haemorrhagic stroke (NHS) + systemic embolism (SE)/myocardial infarction (MI); death/NHS+SE; death; NHS+SE; and MI.

Reasons for discontinuation were mainly the consequence of a physician (in 43.3% of cases) rather than a patient decision (16.8% of case). Patient characteristics associated with a higher risk of discontinuation included: history of bleeding (odds ratio (OR) 1.80, $p<0.001$), Caucasian vs. other races (OR 1.60, $p<0.001$), paroxysmal vs. persistent AF (OR 1.20, $p=0.011$), use of antiplatelet therapy (OR 1.18, $p=0.009$), and emergency room vs. office care setting (OR 1.35, $p<0.001$). A patient with any bleeding event (regardless of severity) was at least 2.5 times more likely to discontinue OAC over the 2 years of follow-up.

Factors associated with a lower discontinuation risk were increasing age (OR 0.97, $p=<0.0001$), prior stroke/transient ischaemic attack (OR 0.72, $p=0.0008$), history of hypertension (OR 0.83, $p=0.001$),

increasing body mass index (OR 0.89, p=0.012), permanent vs. persistent AF (OR 0.68, p<0.001) and inclusion by cardiologists compared to primary care physicians (0R 0.82, p=0.046).

To view the slide presentation of Dr Cools, please visit: http://af.garfieldregistry.org/publications/2018-2/aha-congress-presentation

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 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,[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, 6.5 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 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. Cools F, *et al*. The risk of permanent discontinuation of oral anticoagulation in patients with atrial fibrillation: data from the GARFIELD-AF registry. LBP.04. Lessons from Large Registries Session. American Heart Association Scientific Sessions 2018.
2. 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.
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: August 9 2018].
6. World Thrombosis Day. Know Thrombosis. Available at: http://www.worldthrombosisday.org/issue/thrombosis/. [Last accessed: 16 October 2018].
7. World Stroke Organization. World Stroke Campaign. Available at: http://www.worldstrokecampaign.org/. [Last accessed: 16 October 2018].
8. Stroke Centre. Stroke Statistics. Available at: http://www.strokecenter.org/patients/about-stroke/stroke-statistics/. [Last accessed: 16 October 2018].
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: 16 October 2018].