ETNA-AF Registry Data Provide Real-world Evidence of the Efficacy and Safety Profile of LIXIANA® (edoxaban) in Elderly Non-Valvular Atrial Fibrillation Patients

Montreal, Sept. 4, 2019 - Servier Canada announces one-year outcomes results from a study of 24,962 patients with non-valvular atrial fibrillation (NVAF) treated with LIXIANA® (Edoxaban), including elderly NVAF patients and those with and without a history of intracranial haemorrhage (ICH). One-year follow up data from the ETNA-AF (Edoxaban Treatment in routiNe clinical prActice) study were presented at ESC Congress 2019 in Paris, France, reporting the effectiveness and safety of LIXIANA in patients with NVAF.

Global ETNA-AF analyses

A new analysis, which reported the outcomes of 24,962 edoxaban-treated patients with NVAF at one year follow up supports the treatment's safety and efficacy profile in elderly and very elderly AF patients. The majority of these patients were aged 65 years or over.[1] Results showed that:[1]

- Rates of major bleeding (MB), as defined by the International Society on Thrombosis and Haemostasis (ISTH), including ICH and ischaemic stroke were generally low amongst all patient groups. Per year, ISTH-defined MB occurred in 0.6% of patients aged <65, 0.9% patients aged ≥65-<75, 1.2% patients aged ≥75-< 85 and 1.8% patients aged ≥85. ICH occurred in 0.2% patients aged <65, 0.3% patients aged ≥65-<75, 0.3% patients aged ≥75-< 85 and 0.3% patients aged ≥85. Ishaemic stroke occurred in 0.6% of patients aged <65, 0.7% patients aged ≥65-<75, 0.9% patients aged ≥75-< 85 and 1.3% patients aged ≥85.
- Whilst all-cause and CV mortality was shown to increase with age, as would be expected, CV mortality was a minor proportion of all-cause mortality in all age groups. There was also no increase in the rate of ICH with age. Per year, all-cause mortality/CV mortality occurred in 35 (1.1%)/18 (0.5%) of patients aged <65, 136 (1.8%)/62 (0.8%) of those aged ≥65-<75, 275 (3.3%)/116 (1.4%) of those aged ≥75-<85 and 196 (8.7%)/76 (3.4%) of those aged ≥85.

"These findings are important because the prevalence of NVAF and stroke risk, and therefore the need for oral anticoagulation, all increase with age," said Professor Raffaele De Caterina, Professor of Cardiology,

Institute of Cardiology at the University of Pisa, Italy. "Additionally, elderly patients are more likely to have other comorbidities and to be on various medications that may interfere with treatment. The data from this set of unselected patients support edoxaban's growing evidence of safety profile and its use as an effective treatment for elderly, and very elderly, AF patients in regular clinical care. Of particular interest is the set of data showing no apparent increase in the rate of intracranial haemorrhage in edoxaban-treated patients as a function of age, while a high rate of this occurrence and its increasing prevalence as a function of age was shown in warfarin-treated patients."

Additionally, a further 1-year follow-up analysis of the difference in outcomes between edoxaban-treated AF patients with history of ICH (i.e. those at higher risk of stroke, death and recurrent haemorrhage) and those without a history of ICH, showed that:[2]

- Incidences of ISTH-defined MB (including ICH) and clinically relevant non-major bleeding (CRNMB) were generally low in both groups.
- ICH occurred in 3 (1.2%) patients with history of ICH and 56 (0.3%) patients without history of ICH, per year. The rate of ischaemic stroke was higher in patients with history of ICH (6 [2.4%]) than in those without (165 [0.8%]), per year.

These new data suggest that edoxaban is an effective treatment option for patients with or without prior ICH, whilst also demonstrating the need for effective stroke prevention in NVAF patients with a history of ICH.[2]

"The global ETNA AF programme is the largest and most comprehensive repository of real-world data on the use of a DOAC, in this case Lixiana®. The sub-group analysis of the elderly/very elderly AF patients of this registry, which represents more than 21,000 patients, provides further evidences about the safety profile of Lixiana® in populations at high risk of bleeding. It also complements, the recently published ENTRUST-AF PCI results confirming the safety profile of Lixiana® in AF patients undergoing a successful PCI", mentioned Frederic Fasano, CEO of Servier Canada.

Further new European analyses at ESC 2019

Echoing the Global registry outcomes data, additional one-year follow up analyses of 12,574 unselected elderly AF patients with comorbidities, from ten European countries, showed that the incidence of clinical events for both bleeding and stroke rates were low. Per year, MB occurred in 1.05% (n=125), ICH occurred in 0.23% (n=28) and any stroke or systemic embolic events occurred in 0.82% (n=98) of cases.[2] All-cause mortality occurred in 3.55% of patients per year, which can be rated as low in a high-risk context.[3]

This snapshot real-world analysis compared the baseline and first year outcomes data from 12,574 patients (mean age of 73.6 years) with the outcome data of the European cohort from the clinical Phase III ENGAGE AF-TIMI 48 study,[3] which investigated the safety and efficacy of edoxaban compared to warfarin, for the prevention of stroke or stroke and systemic embolic events in patients with AF.[4] In ETNA-AF, edoxaban was used in a broad range of elderly NVAF patients. Additionally, dose reduction at baseline between the ETNA-AF and ENGAGE AF-TIMI 48 was similar and overall there was a good adherence (84%) to the European label.[5]

"It is interesting to note that the higher HAS-BLED score in ETNA-AF compared to ENGAGE AF-TIMI 48 suggests that in real-world clinical settings physicians are more comfortable using edoxaban in patients with higher bleeding risk," said Raffaele De Caterina, Professor of Cardiology, Institute of Cardiology at the University of Pisa, Italy. "This new analysis reinforces the safety profile and effectiveness of edoxaban in elderly NVAF patients at high CV risk, but also suggest that the ENGAGE AF-TIMI 48 study efficacy results are being largely confirmed in general practice."

About ETNA-AF

ETNA-AF (Edoxaban Treatment in routiNe clinical prActice in patients with nonvalvular Atrial Fibrillation) is a global programme that combines data from distinct non-interventional studies in Europe, East Asia, and Japan in a single database. A total of more than 28,000 patients will be included in the ETNA-AF registries and followed for two years (patients in Europe will be followed for four years). The primary objective of ETNA-AF is to collect information on the use of edoxaban in routine clinical practice, including the safety and efficacy profile in non-preselected patients with NVAF.[6],[7],[8],[9],[10]

About Atrial Fibrillation

AF is a condition where the heart beats irregularly and rapidly. When this happens, blood can pool and thicken in the chambers of the heart causing an increased risk of blood clots. These blood clots can break off and travel through the blood stream to the brain (or sometimes to another part of the body), where they have the potential to cause a stroke.[11]

AF is the most common type of heart rhythm disorder affecting approximately 350,000 Canadians and is associated with substantial morbidity and mortality.[12],[13] Compared to those without AF, people with the arrhythmia have a 3-5 times higher risk of stroke.[14] One in five of all strokes are a result of AF.[15]

About Edoxaban

Edoxaban is an oral, once-daily, direct factor Xa (pronounced "Ten A") inhibitor. Factor Xa is one of the key components responsible for blood clotting, so inhibiting this makes the blood thin and less prone to clotting. Edoxaban was discovered and developed by Daiichi Sankyo Co., Ltd. On June 27, 2016, Daiichi Sankyo and Servier Canada entered into an agreement whereby Servier Canada would market the oral, once-daily anticoagulant edoxaban in Canada, upon approval by the Canadian health authority. Edoxaban is currently marketed in more than 30 countries and regions around the world.

About Servier Canada

Servier Canada is an affiliate of the independent French Servier Group governed by a Private Foundation. We, at Servier, are committed to therapeutic progress to serve patient needs. We work assiduously to provide the Canadian medical community and its patients with innovative therapeutic solutions. As such, Servier Canada is partnering with various players in the life science ecosystem including researchers, clinicians, entrepreneurs and innovators. In addition to these research partners, the International Center for Therapeutic Research (ICTR) located in Laval, is dedicated to preclinical and clinical development with more than 50 studies conducted throughout Canada over the last 10 years. More information is available at www.servier.ca

About the Edoxaban Clinical Research Programme
More than 10 studies, more than 100,000 patients worldwide

Daiichi Sankyo, who discovered edoxaban, is committed to expanding scientific knowledge about this DOAC, as demonstrated through research programmes evaluating its use in a broad range of cardiovascular conditions, patient types and clinical settings in atrial fibrillation (AF) and venous thromboembolism (VTE) designed to further build on the results of the pivotal ENGAGE-AF and Hokusai-VTE studies. More than 100,000 patients worldwide are expected to participate in the Edoxaban Clinical Research Programme, which is comprised of more than 10 RCTs (randomised, controlled trials), registries and non-randomised clinical studies, including completed, ongoing and future research. Our goal is to generate new edoxaban clinical and real-world-data regarding its use in AF and VTE populations, providing physicians and patients worldwide with greater treatment assurance.

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