

Novel oral anticoagulants and the 73rd anniversary of historical warfarin



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Introduction

Historical background

“The can of un-coagulated blood lying on the floor of Link’s laboratory was to change the course of history, and little did Link know what the long-term implications would be” [1]. In 1941, the Wisconsin Alumni Research Fund (WARF) scientist Karl Paul Link and his senior student Wilhelm Schoeffel could never have imagined that their research would live longer than 73 years. Link named the substance after the organization that supported his research and the name warfarin was created (Fig. 1). In the 1950s, warfarin was used as an anticoagulant for victims of heart attacks and strokes. It gained fame when it was used to treat President Dwight D. Eisenhower after his 1955 coronary event while in office [1]. The historical narrative of warfarin starts with a mysterious hemorrhagic disease (sweet clover disease) of cattle to the development of a rat poison (rodenticide), which later became one of the most commonly prescribed drugs in the history of mankind.

Warfarin is a highly effective treatment for the reduction of stroke in atrial fibrillation (AF) and its limitations are well studied. Over the last

Abbreviations

ACS	Acute Coronary Syndrome
AF	Atrial Fibrillation
ANNEXA(TM)	Andexanet Alfa a Novel Antidote to the Anticoagulant Effects of factor XA Inhibitors
APPRAISE-1	Apixaban for Prevention of Acute Ischemic and Safety Events
aPTT	activated partial thromboplastin time
ARISTOTLE	Apixaban versus Warfarin in Patients with Atrial Fibrillation
ATLAS ACS-TIMI 46	Anti-Xa therapy to lower cardiovascular events in addition to aspirin with/without thienopyridine therapy in subjects with acute coronary syndrome
AVERROES trial	Apixaban Versus Acetylsalicylic Acid to Prevent Stroke in Atrial Fibrillation Patients
CHADS ₂	Congestive Heart Failure Hypertension Age Diabetes Stroke
CHADS ₂ -VASC	Congestive Heart Failure Hypertension Age Diabetes Stroke-Vascular disease, Age, Sex
ECT	Ecarin clotting time
ENGAGE AF-TIMI 48	Effective Anticoagulation with Factor Xa Next Generation in Atrial Fibrillation-Thrombolysis in Myocardial Infarction 48
ESTEEM	Effect of Ximelagatran on Ischemic Events and Death in Patients With Atrial Fibrillation After Acute Myocardial Infarction in the Efficacy and Safety of the Oral Direct Thrombin Inhibitor Ximelagatran
EXPLORE-Xa	Phase II study of the safety, tolerability and pilot efficacy of oral factor Xa inhibitor betrixaban compared with warfarin

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