

BMS-Pfizer Alliance To Unveil Real-World Data Analyses - Cost, Safety and Comparative Effectiveness Findings Associated with Oral Anticoagulants in Non-Valvular Atrial Fibrillation

Friday, November 10, 2017 - 11:13am

Analyses from RWD program, ACROPOLIS, use two large U.S. databases to provide insights on Eliquis® (apixaban), warfarin, and other direct oral anticoagulants in patients with NVAf at 2017 American Heart Association (AHA) Scientific Sessions

[Bristol-Myers Squibb Company](#) (NYSE:BMJ) and [Pfizer Inc.](#) (NYSE:PFE) plan to release real-world data (RWD) analyses of outcomes associated with direct oral anticoagulants (DOAC) among non-valvular atrial fibrillation (NVAf) patients using the U.S. Medicare database – the nation’s largest insurer handling more than one billion total claims per year – as well as the Department of Defense (DoD) Military Health System (MHS) during the 2017 American Heart Association (AHA) Scientific Sessions, November 11-15 in Anaheim, California.

The RWD analysis of the DoD MHS database evaluates all-cause, stroke/systemic embolism (S/SE) and major bleeding (MB)-related medical costs associated with *Eliquis*® (apixaban), warfarin and other DOACs among NVAf patients. Two analyses of the Medicare database evaluate the risk of S/SE and rates of MB in elderly NVAf patients, with one of these analyses focusing on those patients with concomitant coronary artery disease/peripheral arterial disease (CAD/PAD). Since CAD/PAD are comorbidities that substantially increase the risk of future cardiovascular events in patients with NVAf,ii this analysis also evaluates major adverse cardiac events (MACE).

“A clearer understanding of the outcomes of comorbid NVAf populations in routine clinical practice may help inform a patient’s treatment course,” said Renato Lopes, M.D., PhD, Professor of Medicine, Duke University School of Medicine. “More information is needed around stroke and cardiovascular outcomes for NVAf patients with concomitant CAD and PAD, and further exploring DOACs and their association with outcomes such as stroke, major bleeding and MACE events in NVAf patients is an important step towards providing additional information to physicians when considering treatment decisions.”

These analyses stem from the Bristol-Myers Squibb (BMS)-Pfizer Alliance global RWD analysis program, ACROPOLIS™ (Apixaban ExperienCe Through Real-World POPuLatIon Studies), reflecting the BMS-Pfizer Alliance’s continued commitment to grow the body of evidence around the stroke risk reduction effects and other outcomes associated with *Eliquis* in highly representative patient groups and common clinical settings. *Eliquis* is a prescription medicine indicated to reduce the risk of S/SE in patients with NVAf.

It is important to note that *Eliquis* can cause bleeding that can be serious. In addition, premature discontinuation of *Eliquis* increases the risk of thrombotic events, and epidural or spinal hematomas may occur in patients treated with *Eliquis* who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Please see full indications and important safety information for *Eliquis* later in the press release.

“The ACROPOLIS analyses being presented at AHA this year exemplify the BMS-Pfizer Alliance’s focus on providing insights that can support decision-making by healthcare systems, providers and payers,” said Christoph Koenen, M.D., MBA, VP, Development Lead, *Eliquis*, Bristol-Myers Squibb. “Analyses of the potential comparative effectiveness and costs associated with *Eliquis*, warfarin and other oral anticoagulants in comorbid NVAF patients can serve as helpful insights to physicians as well as stakeholders across the healthcare delivery spectrum.”

Studies have shown that approximately 18 percent of patients with NVAF had concomitant vascular disease (CAD/PAD). The presence of PAD in patients with NVAF has been associated with higher rates of mortality, cardiovascular events and stroke. Similarly, atherosclerosis (plaque buildup that causes CAD) in patients with NVAF carries a higher risk of cardiovascular events (including cardiovascular death, myocardial infarction, stroke, and hospitalization for an atherothrombotic event).ⁱⁱⁱ

“The BMS-Pfizer Alliance is committed to investigating a wide range of NVAF patient populations, including those at higher risk for stroke such as those with concomitant CAD and PAD,” said Dr. Rory O’Connor, Chief Medical Officer, Pfizer Internal Medicine. “Using insights from routine clinical practice that are not always captured in the controlled environments inherent to clinical trials, these real-world data analyses aim to broaden the knowledge base around the safety and effectiveness of *Eliquis* and other DOACs in reducing the risk of stroke and other cardiovascular events in diverse NVAF patient populations.”

Abstract titles and presentation times of the DoD MHS analysis and the two Medicare analyses are as follows:

- *Comparisons of All-Cause, Stroke- and Major Bleeding-Related Medical Costs Among Non-Valvular Atrial Fibrillation Patients Who Initiated Oral Anticoagulation Therapies in the U.S. Department of Defense Military Health System* – November 12, from 3:15 p.m. to 4:30 p.m. PST
- *Risk of Stroke and Major Bleeding for Dabigatran, Rivaroxaban, and Warfarin Compared to Apixaban Among Non-Valvular Atrial Fibrillation Patients in the United States Medicare Population* – November 13, from 3:00 p.m. to 4:15 p.m. PST
- *Effectiveness and Safety of Apixaban versus Other Oral Anticoagulants in Older Adults With Non-Valvular Atrial Fibrillation and Concomitant Coronary Artery Disease or Peripheral Arterial Disease* – November 14, from 10:30 a.m. to 11:45 a.m. PST

As observational studies lack randomization, they can only analyze associations and not causality. In these studies, comparisons between groups of patients can be subject to potential selection bias and other limitations such as confounding. The source and type of database may also limit the ability to generalize the results and endpoints to the overall population. Therefore, real-world data should not be used as stand-alone evidence for treatment evaluation.

Below is a complete list of BMS-Pfizer Alliance presentations during the AHA Conference. Abstracts can be accessed through the [AHA Scientific Sessions 2017 Online Program Planner](#).

Clinical/Medical Data

- [Multimorbidity is Associated With Greater Risk of Thromboembolism and Bleeding in Patients With Atrial Fibrillation but a Constant Benefit of Apixaban: Results From ARISTOTLE](#)
 - Presented by Alexander KP, et al./Poster
 - *Atrial Fibrillation-Related Stroke Prevention: How To Do It Right*
 - Nov. 12, 3:15-4:30 p.m. PST
 - Clinical Science Section, Science and Technology Hall
- [Patients With Good Adherence to Study Medication Have Better Outcomes: Insights From the ARISTOTLE Trial](#)
 - Presented by Xavier D, et al./Poster
 - *Atrial Fibrillation-Related Stroke Prevention: How To Do It Right*
 - Nov. 12, 3:15-4:30 p.m. PST
 - Clinical Science Section, Science and Technology Hall
- [Variation in Patient Characteristics Does Not Explain Regional Differences in Outcomes: Findings From ARISTOTLE](#)
 - Presented by Bahit MC, et al./Poster
 - *Atrial Fibrillation-Related Stroke Prevention: How To Do It Right*
 - Nov. 12, 3:15-4:30 p.m. PST
 - Clinical Science Section, Science and Technology Hall
- [Obesity Paradox on Outcome in Atrial Fibrillation Maintained Even Considering the Prognostic Influence of Biomarkers: Insights From the ARISTOTLE Trial](#)
 - Presented by Sandhu RK, et al./Poster
 - *Obesity in CVD Risk and Prevention*
 - Nov. 14, 12:00-1:15 p.m. PST
 - Population Science Section, Science and Technology Hall

HEOR/Epi Data

- [Strokes Prevented: Biosurveillance of NValv Patient Cohorts CHA2DS2-VASc and HAS-BLED Scores Using Natural Language Processing and SNOMED CT](#)
 - Presented by Elkin PL, et al./Poster
 - *Stroke*
 - Nov. 12, 11:30-12:45 p.m.
 - Clinical Section III, Science and Technology Hall
- [Comparisons of All-cause, Stroke- and Major Bleeding-related Medical Costs Among Non-Valvular Atrial Fibrillation Patients Who Initiated Oral Anticoagulation Therapies in the US Department of Defense Military Health System](#)
 - Presented by Gupta K, et al./Poster
 - *Contemporary Investigations in Outcomes Research*
 - Nov. 12, 3:15-4:30 p.m.
 - Population Science Section, Science and Technology Hall
- [Effectiveness and Safety of Apixaban Compared to Other Oral Anticoagulants Among Non-Valvular Atrial Fibrillation Patients with Coronary Artery Disease or Peripheral Arterial Disease: A Propensity Score Matched Analysis of Four Large Databases](#)
 - Presented by Lip GY, et al./Poster
 - *Quality Assessments in Big Data*
 - Nov. 12, 3:15-4:30 p.m.
 - Population Science Section, Science and Technology Hall
- [Effectiveness and Safety of Apixaban, Dabigatran, and Rivaroxaban Among Non-Valvular Atrial Fibrillation Patients: A Propensity Score Matched Analysis of Four Large Databases](#)

- Presented by Deitelzweig S, et al./Poster
- *Quality of Care*
- Nov. 13, 3:00-4:15 p.m.
- Population Science Section, Science and Technology Hall
- [Risk of Stroke and Major Bleeding for Dabigatran, Rivaroxaban, and Warfarin Compared to Apixaban Among Non-Valvular Atrial Fibrillation Patients in the United States Medicare Population](#)
 - Presented by Amin A, et al./Poster
 - *Quality of Care, Outcomes Research and Health Policy*
 - Nov. 13, 3:00-4:15 p.m.
 - Population Science Section, Science and Technology Hall
- [Effectiveness and Safety of Apixaban versus Other Oral Anticoagulants in Older Adults With Non-Valvular Atrial Fibrillation and Concomitant Coronary Artery Disease or Peripheral Arterial Disease](#)
 - Presented by Lopes R, et al./Poster
 - *Risk Prediction and Modification*
 - Nov. 14, 10:30-11:45 a.m.
 - Population Science Section, Science and Technology Hall
- [Routine Cardiac Implantable Electronic Device Interrogation at the Point Of Care— Implications for Stroke Prevention and Management](#)
 - Presented by Pugh M, et al./Poster
 - *Stroke Risk Stratification and Prevention in Atrial Fibrillation*
 - Nov. 14, 10:30-11:45 a.m.
 - Clinical Science Section, Science and Technology Hall
- [Eliminate Thromboembolism: Improving Anticoagulation in Non-Valvular Atrial Fibrillation Patients' \(ELITE\) Registry – Insights From the Baseline Results](#)
 - Presented by Sharma A, et al./Oral
 - *EP in a Heartbeat: Rapid Abstracts*
 - Nov. 14, 10:50-10:55 a.m.
 - Clinical Science Section, Science and Technology Hall

About *Eliquis*

Eliquis (apixaban) is an oral selective Factor Xa inhibitor. By inhibiting Factor Xa, a key blood clotting protein, *Eliquis* decreases thrombin generation and blood clot formation. *Eliquis* is approved for multiple indications in the U.S. based on efficacy and safety data from multiple Phase 3 clinical trials. *Eliquis* is a prescription medicine indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (NVAF); for the prophylaxis of deep vein thrombosis (DVT), which may lead to pulmonary embolism (PE), in patients who have undergone hip or knee replacement surgery; for the treatment of DVT and PE; and to reduce the risk of recurrent DVT and PE, following initial therapy.

ELIQUIS Important Safety Information

WARNING: (A) PREMATURE DISCONTINUATION OF ELIQUIS INCREASES THE RISK OF THROMBOTIC EVENTS, (B) SPINAL/EPIDURAL HEMATOMA

(A) Premature discontinuation of any oral anticoagulant, including ELIQUIS, increases the risk of thrombotic events. If anticoagulation with ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.

(B) Epidural or spinal hematomas may occur in patients treated with ELIQUIS who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:

- use of indwelling epidural catheters
- concomitant use of other drugs that affect hemostasis, such as nonsteroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants
- a history of traumatic or repeated epidural or spinal punctures
- a history of spinal deformity or spinal surgery
- optimal timing between the administration of ELIQUIS and neuraxial procedures is not known

Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary.

Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated.

CONTRAINDICATIONS

- Active pathological bleeding
- Severe hypersensitivity reaction to ELIQUIS (e.g., anaphylactic reactions)

WARNINGS AND PRECAUTIONS

- **Increased Risk of Thrombotic Events after Premature Discontinuation:** Premature discontinuation of any oral anticoagulant, including ELIQUIS, in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. An increased rate of stroke was observed during the transition from ELIQUIS to warfarin in clinical trials in atrial fibrillation patients. If ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.
- **Bleeding Risk:** ELIQUIS increases the risk of bleeding and can cause serious, potentially fatal, bleeding.
 - Concomitant use of drugs affecting hemostasis increases the risk of bleeding, including aspirin and other antiplatelet agents, other anticoagulants, heparin, thrombolytic agents, SSRIs, SNRIs, and

NSAIDs.

- Advise patients of signs and symptoms of blood loss and to report them immediately or go to an emergency room. Discontinue ELIQUIS in patients with active pathological hemorrhage.
- There is no established way to reverse the anticoagulant effect of apixaban, which can be expected to persist for at least 24 hours after the last dose (i.e., about two half-lives). A specific antidote for ELIQUIS is not available.

- **Spinal/Epidural Anesthesia or Puncture:** Patients treated with ELIQUIS undergoing spinal/epidural anesthesia or puncture may develop an epidural or spinal hematoma which can result in long-term or permanent paralysis.

The risk of these events may be increased by the postoperative use of indwelling epidural catheters or the concomitant use of medicinal products affecting hemostasis. Indwelling epidural or intrathecal catheters should not be removed earlier than 24 hours after the last administration of ELIQUIS. The next dose of ELIQUIS should not be administered earlier than 5 hours after the removal of the catheter. The risk may also be increased by traumatic or repeated epidural or spinal puncture. If traumatic puncture occurs, delay the administration of ELIQUIS for 48 hours.

Monitor patients frequently and if neurological compromise is noted, urgent diagnosis and treatment is necessary. Physicians should consider the potential benefit versus the risk of neuraxial intervention in ELIQUIS patients.

- **Prosthetic Heart Valves:** The safety and efficacy of ELIQUIS have not been studied in patients with prosthetic heart valves and is not recommended in these patients.
- **Acute PE in Hemodynamically Unstable Patients or Patients who Require Thrombolysis or Pulmonary Embolectomy:** Initiation of ELIQUIS is not recommended as an alternative to unfractionated heparin for the initial treatment of patients with PE who present with hemodynamic instability or who may receive thrombolysis or pulmonary embolectomy.

ADVERSE REACTIONS

- The most common and most serious adverse reactions reported with ELIQUIS were related to bleeding.

TEMPORARY INTERRUPTION FOR SURGERY AND OTHER INTERVENTIONS

- ELIQUIS should be discontinued at least 48 hours prior to elective surgery or invasive procedures with a moderate or high risk of unacceptable or clinically significant bleeding. ELIQUIS should be discontinued at least 24 hours prior to elective surgery or invasive procedures with a low risk of bleeding or where the bleeding would be noncritical in location and easily controlled. Bridging anticoagulation during the 24 to 48 hours after stopping ELIQUIS and prior to the intervention is not generally required. ELIQUIS should be restarted after the surgical or other procedures as soon as adequate hemostasis has been established.

DRUG INTERACTIONS

- **Strong Dual Inhibitors of CYP3A4 and P-gp:** Inhibitors of cytochrome P450 3A4 (CYP3A4) and P-glycoprotein (P-gp) increase exposure to apixaban and increase the risk of bleeding. For patients receiving ELIQUIS doses of 5 mg or 10 mg twice daily, reduce the dose of ELIQUIS by 50% when ELIQUIS is coadministered with drugs that are strong dual inhibitors of CYP3A4 and P-gp (e.g., ketoconazole, itraconazole, ritonavir, or clarithromycin). In patients already taking 2.5 mg twice daily, avoid coadministration of ELIQUIS with strong dual inhibitors of CYP3A4 and P-gp.

- **Strong Dual Inducers of CYP3A4 and P-gp:** Avoid concomitant use of ELIQUIS with strong dual inducers of CYP3A4 and P-gp (e.g., rifampin, carbamazepine, phenytoin, St. John's wort) because such drugs will decrease exposure to apixaban and increase the risk of stroke and other thromboembolic events.
- **Anticoagulants and Antiplatelet Agents:** Coadministration of antiplatelet agents, fibrinolytics, heparin, aspirin, and chronic NSAID use increases the risk of bleeding. APPRAISE-2, a placebo-controlled clinical trial of apixaban in high-risk post-acute coronary syndrome patients treated with aspirin or the combination of aspirin and clopidogrel, was terminated early due to a higher rate of bleeding with apixaban compared to placebo.

PREGNANCY CATEGORY B

- There are no adequate and well-controlled studies of ELIQUIS in pregnant women. Treatment is likely to increase the risk of hemorrhage during pregnancy and delivery. ELIQUIS should be used during pregnancy only if the potential benefit outweighs the potential risk to the mother and fetus.

Please see full Prescribing Information, including **BOXED WARNINGS** and **Medication Guide**, available at www.bms.com.

About ACROPOLIS™

ACROPOLIS™ (Apixaban ExperienCe Through Real-WOrld POpuLatIon Studies) is the *Eliquis* (apixaban) global real-world data program designed to generate additional evidence from routine clinical practice settings to further inform healthcare decision makers, including healthcare providers and payers. The ACROPOLIS program will include retrospective, outcomes-based analyses from over 10 databases around the world, including medical records, medical and pharmacy health insurance claims data, and national health data systems.

Analyses of real-world data allow for a broader understanding of patient outcomes associated with *Eliquis* outside of the clinical trial setting, as well as insight into other measures of healthcare delivery, such as hospitalization and costs.

About ARISTOTLE

ARISTOTLE (Apixaban for Reduction In STroke and Other ThromboemboLic Events in Atrial Fibrillation) was designed to evaluate the efficacy and safety of *Eliquis* versus warfarin for the prevention of stroke or systemic embolism. In ARISTOTLE, 18,201 patients were randomized (9,120 patients to *Eliquis* and 9,081 to warfarin). ARISTOTLE was an active-controlled, randomized, double-blind, multi-national trial in patients with nonvalvular atrial fibrillation or atrial flutter, and at least one additional risk factor for stroke. Patients were randomized to treatment with *Eliquis* 5 mg orally twice daily (or 2.5 mg twice daily in selected patients, representing 4.7 percent of all patients) or warfarin (target INR range 2.0-3.0), and followed for a median of 1.8 years.

About the Bristol-Myers Squibb/Pfizer Collaboration

In 2007, Pfizer and Bristol-Myers Squibb entered into a worldwide collaboration to develop and commercialize apixaban, an oral anticoagulant discovered by Bristol-Myers Squibb. This global alliance combines Bristol-Myers Squibb's long-standing strengths in cardiovascular drug development and commercialization with Pfizer's global scale and expertise in this field.

About Bristol-Myers Squibb

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information about Bristol-Myers Squibb, visit us at BMS.com or follow us on [LinkedIn](#), [Twitter](#), [YouTube](#) and [Facebook](#).

About Pfizer Inc.: Working together for a healthier world®

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us on www.pfizer.com and follow us on Twitter at [@Pfizer](#) and [@Pfizer_News](#), [LinkedIn](#), [YouTube](#) and like us on Facebook at [Facebook.com/Pfizer](https://www.facebook.com/Pfizer).

Bristol-Myers Squibb Forward-Looking Statement

This press release contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding product development. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb's business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2016, in our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

Pfizer Disclosure Notice

The information contained in this release is as of November 10, 2017. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about Eliquis (apixaban), including its potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including, without limitation, the ability to meet anticipated clinical trial commencement and completion dates as well as the possibility of unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of Eliquis; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2016 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and

Exchange Commission and available at www.sec.gov and www.pfizer.com.

i Centers for Medicare & Medicaid Services. CMS press toolkit (webpage). Accessed on October 12, 2017.
<https://www.cms.gov/Newsroom/PressToolkit.html>

ii Bjerring Olesen, J., Gislason, G. H., Torp-Pedersen, C. and Lip, G. Y. H. (2012), Atrial Fibrillation and Vascular Disease—A Bad Combination. Clin Cardiol, 35: S15–S20. doi:10.1002/clc.20955

iii Bjerring Olesen, J., Gislason, G. H., Torp-Pedersen, C. and Lip, G. Y. H. (2012), Atrial Fibrillation and Vascular Disease—A Bad Combination. Clin Cardiol, 35: S15–S20. doi:10.1002/clc.20955

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