INDEPENDENTLY FUNDED BY NHLBI
RETROSPECTIVE, OBSERVATIONAL, REAL-WORLD DATABASE ANALYSIS[1,2]

DAWWAS NVAF 2025

ELIQUIS VS XARELTO® (rivaroxaban) IN COMMERCIALLY INSURED PATIENTS WITH NVAF AGED ≥65 YEARS (N=63,792)[1]

Comparative effectiveness and safety of rivaroxaban with other oral anticoagulants in older adults with nonvalvular atrial fibrillation: population-based analysis in response to updated Beers Criteria®

Published in *Journal of Thrombosis and Haemostasis*

INDICATION

ELIQUIS is indicated to reduce the risk of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation (NVAF).

This study was supported by NHLBI. The funder had no influence on the study's design, conduct, or interpretation of results.

Authors affiliated with Department of Medicine, Division of Epidemiology, Vanderbilt University School of Medicine, Nashville, Tennessee, USA; Department of Medicine and Department of Pathology & Laboratory Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA.

NHLBI=National Heart, Lung, and Blood Institute; NVAF=nonvalvular atrial fibrillation; RCT=randomized clinical trial; RWD=real-world data.

ARISTOTLE RCT SUMMARY
Please see **page 2**.

RCT VS RWD
Please see **page 4**.

SELECTED 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.

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ARISTOTLE: A PIVOTAL, PHASE III, RANDOMIZED CLINICAL TRIAL OF >18,000 PATIENTS WITH NVAF[3-5]*

The primary objective of ARISTOTLE was to determine whether ELIQUIS® (apixaban) was effective (noninferior to warfarin) in reducing the risk of stroke (ischemic or hemorrhagic) or SE. The superiority of ELIQUIS to warfarin was also examined for stroke/SE (primary efficacy endpoint) and major bleeding (primary safety endpoint).

ARISTOTLE Study Design: ARISTOTLE was a double-blind study that randomized patients with NVAF (N=18,201) into 2 groups: those who received ELIQUIS 5 mg or 2.5 mg† twice daily (n=9120) or warfarin with a target INR range of 2.0–3.0 (n=9081). The median duration of follow-up was ≈1.7 years.[3,4]

*__Key inclusion criteria:__ NVAF and ≥1 risk factors for stroke: prior stroke, TIA, or SE; ≥75 years of age; arterial hypertension requiring treatment; diabetes mellitus; heart failure ≥NYHA Class 2; and decreased LVEF ≤40%.

Major bleeding was defined as clinically overt bleeding accompanied by ≥1 of the following: A decrease in hemoglobin of ≥2 g/dL; a transfusion of ≥2 units of packed red blood cells; bleeding at a critical site: intracranial‡, intraspinal, intraocular, pericardial, intra-articular, intramuscular with compartment syndrome, retroperitoneal; and fatal bleeding.

ELIQUIS demonstrated superiority in BOTH stroke/systemic embolism AND major bleeding vs warfarin.

Stroke/SE: 1.27%/yr [n=212/9120] vs 1.60%/yr [n=265/9081]

HR=0.79 (95% CI: 0.66–0.95); ***P***=0.01

RRR§= 21%; ARR§=0.33%/yr

Major bleeding‖: 2.13%/yr [n=327/9088] vs 3.09%/yr [n=462/9052]

HR=0.69 (95% CI: 0.60–0.80); ***P***<0.0001

RRR§=31%; ARR§=0.96%/yr

Superiority to warfarin was primarily attributable to a reduction in hemorrhagic stroke (0.24%/yr [n=40/9120] ELIQUIS vs 0.47%/yr [n=78/9081] warfarin, HR=0.51 [95% CI: 0.35–0.75]) and ischemic strokes with hemorrhagic conversion (0.07%/yr [n=12/9120] ELIQUIS vs 0.12%/yr [n=20/9081] warfarin, HR=0.60 [95% CI: 0.29–1.23]) compared to warfarin. Purely ischemic strokes (0.83%/yr [n=140/9120] ELIQUIS vs 0.82%/yr [n=136/9081] warfarin, HR=1.02 [95% CI: 0.81–1.29]) occurred with similar rates on both drugs.

There were fewer stroke events with ELIQUIS (1.19%/yr [n=199/9120]) vs warfarin (1.51%/yr [n=250/9081], HR=0.79 [95% CI: 0.65–0.95]). Similar incidence rates were observed for systemic embolism (0.09%/yr [n=15/9120] ELIQUIS vs 0.10%/yr [n=17/9081] warfarin, HR=0.87 [95% CI: 0.44–1.75]) and gastrointestinal bleeding (0.83%/yr [n=128/9088] ELIQUIS vs 0.93%/yr [n=141/9052] warfarin, HR=0.89 [95% CI: 0.70–1.14]). There were fewer intracranial hemorrhage events with ELIQUIS (0.33%/yr [n=52/9088]) vs warfarin (0.82%/yr [n=125/9052], HR=0.41 [95% CI: 0.30–0.57]).

In another clinical trial (AVERROES), ELIQUIS was associated with an increase in major bleeding compared with aspirin that was not statistically significant (1.4%/yr vs 0.92%/yr, HR=1.54 [95% CI: 0.96–2.45]; *P*=0.07).

The most common reason for treatment discontinuation in both ARISTOTLE and AVERROES was bleeding-related adverse reactions; in ARISTOTLE, this occurred in 1.7% and 2.5% of patients treated with ELIQUIS and warfarin, respectively, and in AVERROES, in 1.5% and 1.3% on ELIQUIS and aspirin, respectively.

ELIQUIS increases the risk of bleeding and can cause serious, potentially fatal, bleeding.[3]

†A dose of 2.5 mg twice daily was assigned to patients with at least 2 of the following characteristics: age ≥80 years, body weight ≤60 kg, or serum creatinine ≥1.5 mg/dL.
‡Intracranial bleeding included intracerebral, intraventricular, subdural, and subarachnoid bleeding. Any type of hemorrhagic stroke was adjudicated and counted as intracranial major bleeding.
§Statistical note: RRR was calculated as (1-HR)x100. ARR was calculated as the difference between the event rates.
‖Bleeding events were counted during treatment or within 2 days of stopping study treatment (on-treatment period). Bleeding events in each subcategory were counted once per subject, but subjects may have contributed events to multiple endpoints.

ARR=absolute risk reduction; CI=confidence interval; HR=hazard ratio; INR=International Normalized Ratio; LVEF=left ventricular ejection fraction; NYHA=New York Heart Association; RRR=relative risk reduction; SE=systemic embolism; TIA=transient ischemic attack; VKA=vitamin K antagonist.

SELECTED IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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

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AVERROES: A PHASE III, RANDOMIZED, DOUBLE-BLIND TRIAL VS ASPIRIN IN OVER 5500 PATIENTS WITH NVAF WHO WERE UNSUITABLE FOR WARFARIN[3,6,7]

AVERROES Study Design: A phase III, double-blind, randomized trial designed to compare the effects of ELIQUIS 5 mg or 2.5 mg* twice daily (n=2807) and aspirin (n=2791) (81 mg–324 mg once daily) on the risk of stroke and systemic embolism in 5598 patients with NVAF thought not to be candidates for warfarin therapy, and with ≥1 additional risk factor for stroke: prior stroke or TIA; ≥75 years of age; arterial hypertension (receiving treatment); diabetes mellitus (receiving treatment); heart failure (≥NYHA Class 2 at time of enrollment); LVEF ≤35%, or documented peripheral artery disease. Patients could not be receiving VKA therapy (e.g., warfarin), either because it had already been demonstrated or was expected to be unsuitable for them. The mean follow-up period was ≈1.1 years. The primary efficacy endpoint was stroke/SE and the primary safety endpoint was major bleeding.

*A dose of 2.5 mg twice daily was assigned to patients with at least 2 of the following characteristics: age ≥80 years, body weight ≤60 kg, or serum creatinine ≥1.5 mg/dL.

SELECTED IMPORTANT SAFETY INFORMATION

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.
  - The anticoagulant effect of apixaban can be expected to persist for at least 24 hours after the last dose (i.e., about two half-lives). An agent to reverse the anti-factor Xa activity of apixaban is available for adults. Please visit www.andexxa.com for more information on availability of a reversal agent.
- **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.

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SELECT CHARACTERISTICS OF RANDOMIZED CLINICAL TRIALS AND REAL-WORLD DATA

RANDOMIZED CLINICAL TRIALS[8-10]

- **Prospective design** with **prespecified,** well-defined inclusion/exclusion criteria, outcomes, and endpoints
- Patients are **randomly** assigned to treatment or comparator
- Randomized clinical trials are designed to show **causality** (ie, efficacy and safety data)

VS

REAL-WORLD OBSERVATIONAL STUDIES[9-11]

- **Observational in nature** and use data from routine clinical practice
- Patients are **not randomized**
- Can only evaluate **association** and therefore are unable to determine causality

STUDY OVERVIEW[1]

DAWWAS NVAF 2025
Real-world data analysis

OBJECTIVE: To compare stroke/SE and GI bleeding/ICH outcomes with select OACs among patients with NVAF with commercial insurance (with and without Medicare supplemental insurance) aged ≥65 years*

STUDY DESIGN: Real-world, retrospective, observational, new-user cohort analysis[1,2]

Cohort Description

Patients from the MarketScan® database covered by commercial or Medicare supplemental insurance, including:

- Treatment-naïve adults ≥65 years with a diagnosis of NVAF
- ≥12 months continuous healthcare plan enrollment prior to OAC initiation date
- Started OAC* between January 1, 2014 and December 31, 2021

Patients who met inclusion criteria were propensity score matched (1:1) to help balance baseline characteristics

ELIQUIS (n=31,896)	XARELTO (n=31,896)

Assessed Outcomes

Primary outcomes:

- Incidence of stroke/SE
- Incidence of GI bleeding/ICH

These outcomes required hospitalization and were identified based on the first listed diagnosis[1,2†]

BASELINE CHARACTERISTICS
Please see **page 6**.

*New users of ELIQUIS, XARELTO, PRADAXA® (dabigatran etexilate), or warfarin. The first recorded prescription was considered the cohort entry date. The study included 2 additional matched cohorts that are not included in this presentation: XARELTO vs warfarin and XARELTO vs PRADAXA.[1,2]

†Outcomes were defined as first hospitalization for stroke/SE or GI bleeding/ICH with ICD-9-CM and ICD-10-CM codes listed in primary position.[1,2]

GI=gastrointestinal; ICD-9-CM=International Classification of Diseases, Ninth Revision, Clinical Modification; ICD-10-CM=International Classification of Diseases, Tenth Revision, Clinical Modification; ICH=intracranial hemorrhage; OAC=oral anticoagulant.

SELECTED IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (cont'd)

- **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.
- **Increased Risk of Thrombosis in Patients with Triple Positive Antiphospholipid Syndrome (APS):** Direct-acting oral anticoagulants (DOACs), including ELIQUIS, are not recommended for use in patients with triple-positive APS. For patients with APS (especially those who are triple positive [positive for lupus anticoagulant, anticardiolipin, and anti–beta 2-glycoprotein I antibodies]), treatment with DOACs has been associated with increased rates of recurrent thrombotic events compared with vitamin K antagonist therapy.

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SELECT BASELINE CHARACTERISTICS (POST-MATCHING)[1]*

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Real-world data analysis

	ELIQUIS (N=31,896)	XARELTO (N=31,896)
DEMOGRAPHICS		
Age, years, mean	77.0	77.0
Male	54.0%	54.2%
Female	46.0%	45.8%
BASELINE COMORBIDITIES		
Alcohol abuse disorder	1.2%	1.2%
Anemia	8.1%	7.9%
Angina	2.3%	2.2%
Cancer	10.3%	10.3%
Chronic kidney disease	14.9%	14.5%
Chronic lung disease	18.1%	17.8%
Diabetes	24.3%	24.3%
Drug abuse	0.6%	0.5%
Heart failure	18.0%	17.4%
Hemophilia	0.3%	0.3%
HIV	0.0%	0.0%
Hyperlipidemia	35.6%	35.8%
Hypertension	63.8%	64.8%
Liver disease	1.8%	1.7%
Peripheral vascular disease	10.7%	10.3%
Renal impairment	10.1%	9.0%
Tobacco use	3.3%	3.3%
Transient ischemic attack	7.7%	7.8%
Ulcer	0.9%	0.8%
BASELINE MEDICATIONS		
Angiotensin-converting enzyme inhibitors	20.0%	19.9%
Aldosterone antagonists	3.3%	3.2%
α-Adrenergic blockers	11.5%	11.5%
Angiotensin II receptor blockers	14.1%	14.3%
Antiplatelets	8.0%	7.2%
β-Blockers	45.9%	45.8%
Calcium channel blockers	28.3%	28.5%
Direct vasodilators	2.1%	2.0%
Loop diuretics	17.0%	16.5%
Nonsteroidal anti-inflammatory drugs	9.9%	10.0%
Potassium diuretics	3.5%	3.5%
Proton pump inhibitors	19.1%	18.8%

CONTINUED ON NEXT PAGE

Coadministration of antiplatelet agents, fibrinolytics, heparin, aspirin, and chronic NSAID use with oral anticoagulants increases the risk of bleeding.[3]

*Variables used for PSM.[1,2]

PSM=propensity score matching.

SELECT BASELINE CHARACTERISTICS (POST-MATCHING)[1]* (CONTINUED)

DAWWAS NVAF 2025
Real-world data analysis

	ELIQUIS (N=31,896)	XARELTO (N=31,896)
BASELINE MEDICATIONS (cont'd)		
Selective serotonin reuptake inhibitors	8.9%	8.8%
Statins	42.8%	43.0%
Thiazide diuretics	1.9%	2.0%
INSURANCE TYPE		
Consumer-directed health plan	31.9%	35.1%
Comprehensive	0.3%	0.3%
Exclusive provider organization	14.4%	10.8%
High deductible health plan	2.6%	4.0%
Health maintenance organization	46.8%	43.8%
Others	1.8%	3.6%
Point of service	1.1%	1.3%
Point of service with capitation	0.6%	0.7%
Preferred provider organization	0.5%	0.5%
MEASURES OF HEALTHCARE USE		
Total number of inpatient procedures, mean	0.1	0..01
Total number of inpatient visits, mean	0.3	0.3
Total number of outpatient visits, mean	14.0	13.7
Total number of prescriptions, mean	17.9	17.6

Coadministration of antiplatelet agents, fibrinolytics, heparin, aspirin, and chronic NSAID use with oral anticoagulants increases the risk of bleeding.[3]

*Variables used for PSM.[1,2]

PSM=propensity score matching.

METHODS OF ANALYSIS[1]

DAWWAS NVAF 2025
Real-world data analysis

STUDY DRUG: ELIQUIS or XARELTO
STUDY DURATION: January 1, 2014 to December 31, 2021*
BASELINE PERIOD: 12 months prior to cohort entry
DATA SOURCE: MarketScan

Data source

- The MarketScan database contains medical and pharmacy data for employees, early retirees, and their dependents insured by employer-sponsored commercial or employer-sponsored commercial with Medicare Supplemental plans

Inclusion criteria†

- Treatment-naïve patients with NVAF aged ≥65 years who filled an OAC prescription between January 1, 2014, and December 31, 2021*
  - –Diagnoses were identified based on ICD-9-CM and ICD-10-CM codes (ICD-9-CM: 427.31, 427.32; ICD-10-CM: I48.x) on at least 1 inpatient or 2 outpatient claims within 12 months[1,2]
- Minimum 12 months of continuous enrollment in a healthcare plan for at least 12 months prior to cohort entry

Exclusion criteria†

- Valvular heart disease, bioprosthetic or mechanical heart valves, prior use of OACs, antiphospholipid syndrome, prior stroke/SE, or prescriptions for 2 or more different OAC medications on or before cohort entry

Outcomes†

- The primary outcomes below required hospitalization and were identified based on first listed diagnosis[1,2]:
  - –Incidence of stroke/SE
  - –Incidence of GI bleeding/ICH
- Primary effectiveness and safety outcomes were also stratified to the individual components
- Results shown are for the matched cohorts

CONTINUED ON NEXT PAGE

*The first recorded prescription was assigned as the cohort entry date. The study included 2 additional matched cohorts that are not included in this presentation: XARELTO vs warfarin and XARELTO vs PRADAXA.
†Inclusion/exclusion criteria and outcomes were defined using ICD-9-CM and ICD-10-CM codes.[1,2]

SELECTED IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

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

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.

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METHODS OF ANALYSIS[1] (CONTINUED)

Statistical analyses

- PSM (1:1) was conducted with each pairwise comparison controlled via 40 covariates that were potentially associated with the effectiveness or safety outcomes and choice of OACs

Follow-up period

- Patients were followed from cohort entry date until the earliest of treatment discontinuation, switch, outcome, last day of enrollment in healthcare benefits, or the end of the study period (ie, December 2021)
- The median duration of follow-up was:
  - –219 days for XARELTO patients (IQR, 82-478 days)
  - –219 days for ELIQUIS patients (IQR, 83-462 days)

IQR=interquartile range.

SELECTED IMPORTANT SAFETY INFORMATION

DRUG INTERACTIONS

- **Combined P-gp and Strong CYP3A4 Inhibitors:** Inhibitors of P-glycoprotein (P-gp) and cytochrome P450 3A4 (CYP3A4) 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 combined P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, or ritonavir). In patients already taking 2.5 mg twice daily, avoid coadministration of ELIQUIS with combined P-gp and strong CYP3A4 inhibitors.

  Clarithromycin

  Although clarithromycin is a combined P-gp and strong CYP3A4 inhibitor, pharmacokinetic data suggest that no dose adjustment is necessary with concomitant administration with ELIQUIS.
- **Combined P-gp and Strong CYP3A4 Inducers:** Avoid concomitant use of ELIQUIS with combined P-gp and strong CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin, St. John's wort) because such drugs will decrease exposure to apixaban.
- **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.

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LIMITATIONS OF ANALYSIS[1]

Study design/definitions

- Due to the nature of retrospective, observational, cohort studies, no causal relationships can be inferred, and only statistical associations were assessed
- In contrast to clinical trials, outcomes were defined by using ICD-9-CM and ICD-10-CM diagnosis codes rather than clinical outcome adjudication
- There is no guarantee that patients were dosed according to the US prescribing information for ELIQUIS and XARELTO. Medications were based on pharmacy fills and there was no way to determine if a patient took their medication as prescribed
- The primary safety outcome was a composite of GI bleeding and ICH resulting in hospitalization; other bleeding resulting in hospitalization, which is also clinically relevant, is not considered in the analysis

Bias/confounding

- In order to reduce the effect of potential selection bias, propensity score matching was conducted; however, residual confounding is possible due to unmeasured confounders or lack of adjustment for time-dependent confounders. Detailed information on potential confounders, such as health behaviors, adherence measures, and over-the-counter medications, was not available. The risk of confounding is especially important for interpreting DOAC vs DOAC comparison—which is for hypothesis generation, given the lack of head-to-head trials—and therefore results should be interpreted with caution[1,12,13]

Data collection

- Exposure misclassification is possible because there was no information about adherence
- Outcome misclassification is possible because the study outcomes were based on ICD codes
  –Study outcomes did not include ischemic or hemorrhagic events without hospitalization

Generalizability

- The study was restricted to working adults, their dependents, and early retirees with commercial or commercial and Medicare Supplemental insurance, which therefore limits the generalizability of the findings
- Median follow-up time was relatively short, and study results may not be generalizable to longer-term OAC exposure

DOAC=direct oral anticoagulant.

SELECTED IMPORTANT SAFETY INFORMATION

PREGNANCY

- The limited available data on ELIQUIS use in pregnant women are insufficient to inform drug-associated risks of major birth defects, miscarriage, or adverse developmental outcomes. Treatment may increase the risk of bleeding during pregnancy and delivery, and in the fetus and neonate.
  – *Labor or delivery*: ELIQUIS use during labor or delivery in women who are receiving neuraxial anesthesia may result in epidural or spinal hematomas. Consider use of a shorter acting anticoagulant as delivery approaches.

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STROKE/SE AND GI BLEEDING/ICH IN PATIENTS TREATED WITH ELIQUIS VS XARELTO[1]

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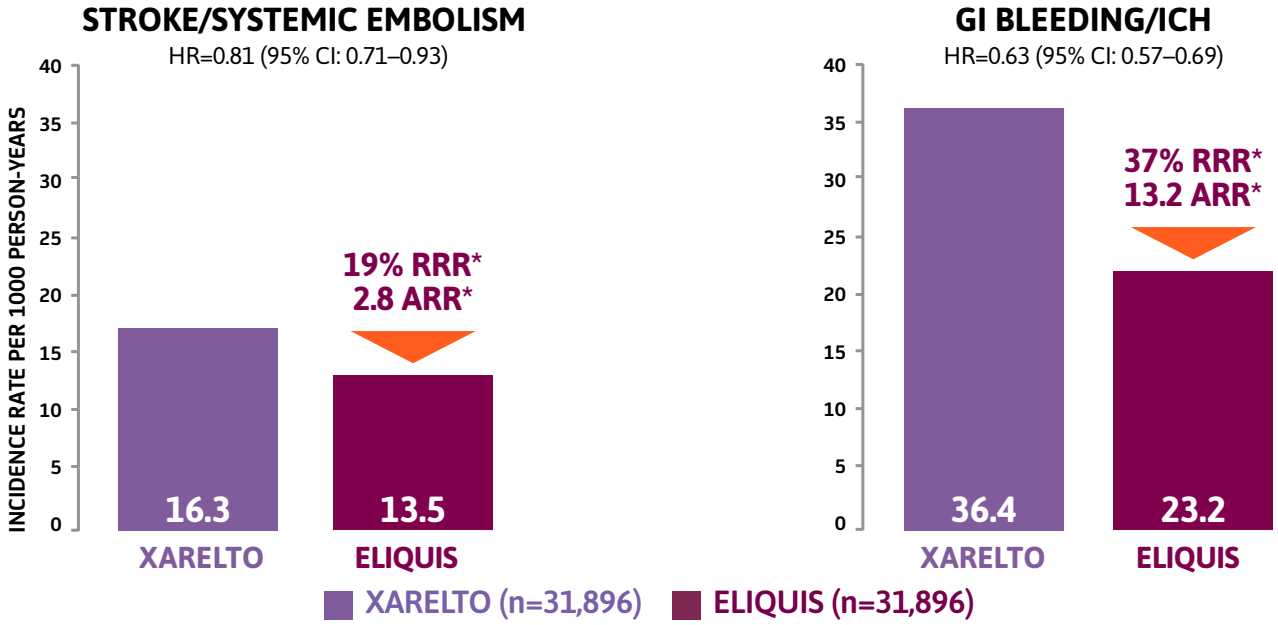
Real-world data analysis



In this real-world analysis, ELIQUIS was associated with relative risk reductions of 19% for stroke/SE and 37% for GI bleeding/ICH vs XARELTO

ELIQUIS increases the risk of bleeding and can cause serious, potentially fatal, bleeding.[3]

Retrospective, observational analyses are not intended for direct comparison with clinical trials and are designed to evaluate associations among variables; causality cannot be established in observational analyses.[14]

- Other real-world data analyses comparing ELIQUIS with other DOACs, using various data sources, time periods, study methodologies, and outcome definitions—showing different findings—have also been published[12,13,15,16]

The definitions of outcomes, follow-up period, and the patient population in ARISTOTLE were different than in this analysis.[1,3]

There are currently no results from DOAC vs DOAC head-to-head clinical trials.[12,13]

*Statistical note: HRs were represented as XARELTO vs ELIQUIS in the original publication and are inverted in the figures on the left as ELIQUIS vs XARELTO. RRR was calculated as (1-HR)x100. ARR represents the difference between the event rates and is expressed as per 1000 person-years.

ARR=absolute risk reduction; CI=confidence interval; HR=hazard ratio; RRR=relative risk reduction.

SELECTED IMPORTANT SAFETY INFORMATION

LACTATION

- Breastfeeding is not recommended during treatment with ELIQUIS.

FEMALES AND MALES OF REPRODUCTIVE POTENTIAL

- Females of reproductive potential requiring anticoagulation should discuss pregnancy planning with their physician. The risk of clinically significant uterine bleeding, potentially requiring gynecological surgical interventions, identified with oral anticoagulants including ELIQUIS should be assessed in these patients and those with abnormal uterine bleeding.

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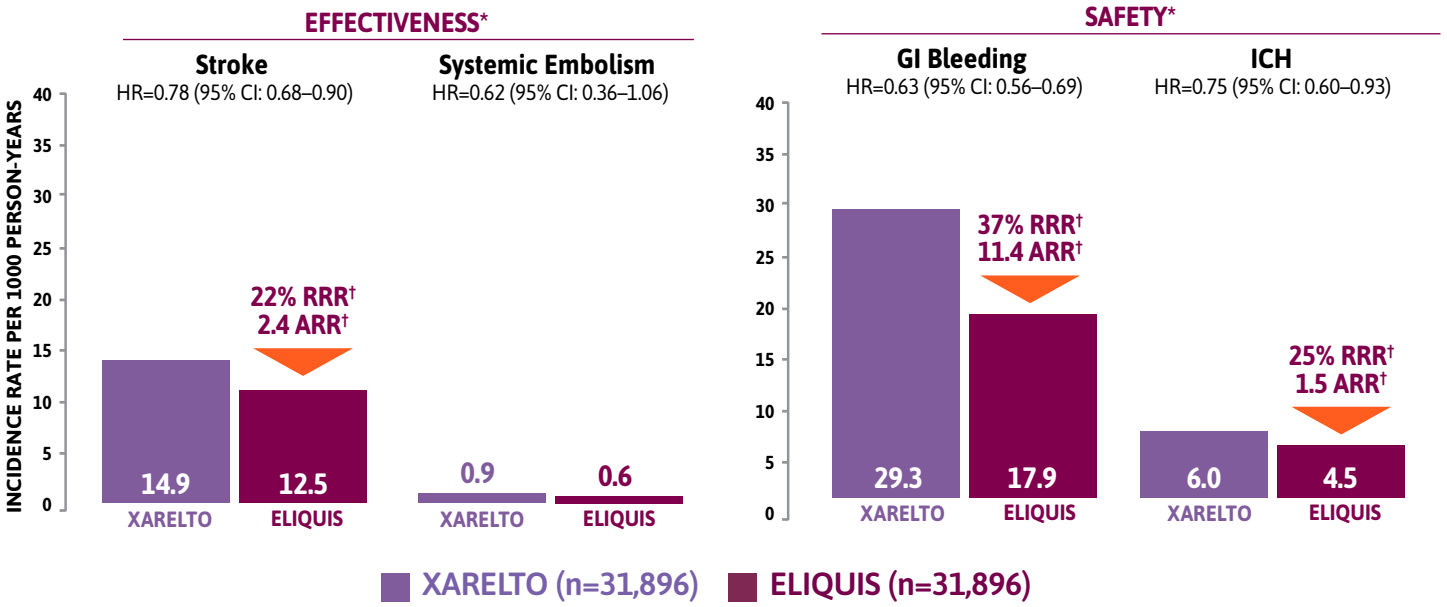
COMPONENTS OF STROKE/SE AND GI BLEEDING/ICH OUTCOMES[1]

DAWWAS NVAF 2025
Real-world data analysis



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There are currently no results from DOAC vs DOAC head-to-head clinical trials.[12,13]

*These outcomes required hospitalization and were identified based on the first listed diagnosis.[1,2]
†Statistical note: HRs were represented as XARELTO vs ELIQUIS in the original publication and are inverted in the figures above as ELIQUIS vs XARELTO. RRR was calculated as (1-HR)x100. ARR represents the difference between the event rates and is expressed as per 1000 person-years.

SELECTED IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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

Please see additional Important Safety Information throughout and click here for U.S. Full Prescribing Information, including **Boxed WARNINGS**.

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