Cost-effectiveness of Apixaban vs Aspirin for the Reduction of Thrombo-Embolism in High-Risk Patients with Device-Detected Atrial Fibrillation: Insights from the ARTESiA trial

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Abstract

Background and Aims: Apixaban was superior to aspirin for the prevention of stroke or systemic embolism in participants with subclinical atrial fibrillation (SCAF) in the Apixaban for the Reduction of Thrombo-Embolism in Patients with Subclinical Atrial Fibrillation (ARTESiA) trial. This was especially true for those with CHA_2DS_2-VASc score >4. Understanding the cost-effectiveness of treating SCAF is important for decision makers.

Methods: Canadian, UK, German and US direct healthcare costs (in 2023 USD) were applied to hospitalized events (including strokes and bleeds) and study drugs for all participants with a CHA_2DS_2-VASc score >4 to determine the mean cost per participant during the trial (mean follow-up 3.5 years). A daily cost of $0.63, $0.11, $2.26, and $6.06 for apixaban in Canada, UK, Germany and the US was used. If in-trial results were not cost-saving (below $0), the prospective plan was to perform a lifetime cost-effectiveness analysis using a Markov model and a willingness-to-pay of 50,000 USD per Quality Adjust Life-Year (QALY).

Results: After considering the cost of study medication and clinical events over 3.5 years, apixaban was dominant (cost-saving and more effective) in Canada (-$2,301) and the UK (-$902) but cost more in Germany and the US ($600 and $1,990 respectively). Over a lifetime, treatment with apixaban produced a net gain of 0.107 QALYs, but with costs in both Germany ($2,623 more) and the US ($9,110 more); yielding an incremental cost effectiveness ratio of $24,514 per QALY for Germany and $85,140 for the US.

Conclusion: In patients with SCAF and a CHA_2DS_2-VASc score >4, apixaban is cost-saving in Canada and the UK and cost-effective in Germany. Apixaban was not cost-effective in the US under the base cost assumption but would be cost-effective at a daily cost of $4.35, and cost saving at $3.59.

Keywords: apixaban; cost-effectiveness; subclinical atrial fibrillation; stroke prevention

What's New

- Apixaban in the ARTESiA trial has been shown to reduce the risk of stroke in patients with subclinical atrial fibrillation especially those with CHA_2DS_2-VASc >4, but the cost-effectiveness of this has not been evaluated in Canada, the UK, Germany and the US.
- Apixaban was cost-saving in Canada and the UK during the trial period.
- At a cost-effectiveness threshold of $50,000 USD per QALY, apixaban was cost-effective over a lifetime in Germany, but not cost-effective in the US.

Introduction

Atrial fibrillation (AF) is the most common form of cardiac arrhythmia and significantly increases the risk of ischemic stroke and systemic embolism, especially among the elderly[1,2]. Due to the risk of stroke, patients are routinely anticoagulated with warfarin or a direct oral anti-coagulant (DOAC). Subclinical atrial fibrillation (SCAF), also known as device-detected AF (DDAF), is a common form of AF that is asymptomatic and detectible with long-term, continuous cardiac rhythm monitoring by an implanted cardiac pacemaker or defibrillator [3]. Given the increased risk of bleeding associated with oral anticoagulation management of SCAF with oral anticoagulation is contentious.

The Apixaban for the Reduction of Thromboembolism in Patients With Device-Detected Subclinical Atrial Fibrillation (ARTESiA) trial demonstrated that apixaban was superior to aspirin in preventing stroke or systemic embolism among patients with device-detected AF, with the most pronounced benefit observed in those with a CHA_2DS_2-VASc score greater than 4[4,5]. Given the cost of apixaban and the potential savings from fewer strokes, an evaluation of the cost-effectiveness is important to inform policy makers. We hypothesize that apixaban in patients with a CHA_2DS_2-VASc score >4 will be cost-effective due to cost savings from stroke prevention.

Methods

Clinical Trial

The details and results of the ARTESiA trial and the related subgroup analysis by CHA_2DS_2-VASc tertiles have been published previous [4,5]. The overall clinical trial randomized 4012 participants from 16 countries between May 2015 and July 2021 to receive either apixaban 5mg BID or ASA 81mg OD. Participants were eligible if they were at least 55 years with subclinical atrial fibrillation (SCAF) and a CHA_2DS_2-VASc score of at least 3. Participants 75 or older were also eligible if they had a history of stroke with no other risk factors. The trial found that apixaban 5mg BID reduced the occurrence of the primary outcome of stroke or systemic embolism by 37% compared to ASA (HR 0.63; 95% CI: 0.45 to 0.88 p=0.007). To identify groups within the trial that may benefit more from apixaban, the ARTESiA trial analyzed prespecified subgroups. A subgroup analysis by CHA_2DS_2-VASc tertile (<4, =4 and >4) found that the largest risk reduction for stroke or systemic embolism was in participants with CHA_2DS_2-VAS >4 (Absolute Risk Reduction: -3.95; 95% CI: -6.72 to -1.19) [5]. In addition, a smaller subgroup of participants with subclinical AF and a previous history of stroke

or transient ischemic attack (TIA) had a lower risk of stroke or systemic embolism compared to those with no history but these results were not adjusted for multiplicity[6]. Therefore, our base case analysis is limited to participants with a CHA_2DS_2-VASc score >4 but an exploratory analysis for participants with a previous history of stroke or TIA was also performed.

In-Trial Analysis Design

An in-trial analysis from healthcare perspectives specific to Canada, the UK, Germany and the US was performed utilizing individual patient-level data collected from the trial. We hypothesized that apixaban in patients with a CHA_2DS_2-VASc score >4 would be cost-saving due to cost savings from stroke prevention. Costs for cardiovascular events, gastrointestinal (GI)/ genitourinary (GU) bleeds and study medications were included in this analysis. Each country's unit costs were applied to all participants with a CHA_2DS_2-VASc >4, giving a country-specific perspective using all participants in this subgroup. All hospitalized systemic emboli, strokes, myocardial infarctions (MIs), TIAs, heart failure (HF) and GI/GU bleeds were included with the frequency of these events derived from data pulled from the study CRFs (Table 1; Table S1). Progression to clinical AF/SCAF >24 hours occurred in almost 33% (32.5%) of participants with a CHA_2DS_2VASc >4[7]. Event and study drug data after the date of this occurrence were not included in our analysis. Other events and bleeding sites were captured in the study CRFs but were not included in our analysis due to similar/low frequency between both groups, or their occurrence was not related to the study medication. If in-trial results were not cost-saving, the prospective plan was to perform a lifetime cost-effectiveness analysis using a Markov model and assume a willingness to pay of 50,000 USD per Quality Adjust Life-Year (QALY).

Canadian non-stroke event unit costs were obtained from internal Hamilton Health Sciences data and have been used in previous publications [8,9]. These costs were inflated to 2023 CAD and converted to US dollars (Table 2). The daily cost of apixaban was obtained from the Ontario Drug Benefit formulary ($0.82 CAD = 0.63 USD). The cost of apixaban in the UK was based on the NHS daily tariff cost of apixaban (0.08 GBP = 0.11 USD) (Table S1) obtained from the British National Formulary [10]. Non-stroke event costs were based on weighted averages of relevant Healthcare Resource Group (HRG) codes for each event [11].

In Germany the daily cost of apixaban was obtained from personal communications (2.59 Eur = 2.26 USD) (Table S1) [12]. Non-stroke event costs were from our previous work on the cost-

effectiveness of rivaroxaban in the Cardiovascular Outcomes for People Using Anticoagulation Strategies (COMPASS) trial [9]. For the US perspective analysis, the price of apixaban was assumed to be $6.06 per day. This was based on the price of rivaroxaban 2.5mg BID as reported by the Institute for Clinical and Economic Review [13]. We used this cost as a pragmatic cost of apixaban that included rebates and coupons was not readily available. The cost of events was based on 2021 Medicare data from MEDPAR and inflated to 2023 USD [14](Table S1).

The cost of strokes for all countries were obtained from different sources than those described above[15–18]. Unlike the other events where costs are concentrated to the index hospitalization, the economic impact of strokes often last much longer. To reflect this reality, we use a 1-year cost of stroke obtained from literature for the in-trial analysis.

In this analysis categorical data are reported as frequencies and continuous data as means. Totals are presented as mean costs per participant with 95% confidence intervals (CIs). To account for the fact that cost data are not normally distributed, the bias corrected and accelerated method was used to bootstrap 5,000 samples to determine 95% CIs. Analyses were performed with Stata 17 (StataCorp. 2017. Stata Statistical Software Release 17. College Station, Tx: Statacorp LLC).

Lifetime Cost-Effectiveness

A deterministic Markov model was created to simulate the total costs and quality-adjusted life years (QALYs) if the ARTESIA trial had run for 23 years (Figure 1a, 1b). This time horizon was chosen to ensure all estimated costs and effects were captured[19]. The model consisted of 5 states: alive, dead, discontinued, Rankin 0-2 post-stroke and Rankin 3-5 post-stroke. It was assumed everyone began in the alive state with a mean age of 77 years and remained in the model for a maximum of 23 years. If discontinuation did not occur, one of seven events (MI, GI/GU bleed, Fatal/Non-Fatal ischemic stroke, Fatal/Non-Fatal hemorrhagic stroke and death), or no event, could be experienced. Patients who experience an MI or GI/GU bleed would begin the next cycle in the alive state.

Transition to one of the post-stroke states happens if a stroke was experienced during the alive state. Post-stroke severity was based on the distribution seen for the CHA_2DS_2-VASc > 4 subgroup. Once in a post-stroke state, participants had similar options as stroke naïve participants but with added long-term stroke costs and lower utility scores commensurate with the severity of the stroke.

If a subsequent stroke were to occur, the severity would be limited to the severity of the first with the same associated costs and utilities.

Non-cardiac death probabilities were based on data from published US lifetables [20]. One cycle in this model was equivalent to three-months and included a half-cycle correction.

Daily drug costs in the Markov model were the same as the in-trial analysis. Costs for fatal and non-fatal MIs, GI/GU bleeds and the index hospitalization for strokes were also the same as the in-trial analysis (Table S2). Post-stroke costs were derived from published literature[16,17]. Additional details can be found in the supplementary appendix.

Transition probabilities were derived from event rates calculated using participant time to event data from the ARTESIA trial. Event data that occurred after the date of progression to clinical AF/SCAF > 24 hours was not included. Annual event rates were converted to quarterly event rates and then converted to quarterly probabilities for use in the model (Table S3).

As utilities were not collected as part of the ARTESIA trial, we used a utility of 0.87 based on data collected in the COMPASS trial. This utility value was used for event-free, GI/GU bleed and non-fatal MIs (Table S3). This utility value was also adjusted for stroke severity using published quality of life data for stroke patients. [21,22]. Additional details regarding this approach can be found in the supplementary appendix. Utility values were assumed to be the same for both treatment groups. Although our utility scores use a US value set and are not unique to the countries in our analysis. We do not expect this to influence our conclusions for Germany since it has been shown there is a very strong positive correlation (ρ=0.97) between German and US value sets. [23].

All costs and QALYs were discounted at 3% per year.

Sensitivity Analyses

Deterministic sensitivity analyses were performed for both the in-trial and modelled portion of our analysis. One-way sensitivity analyses altering the cost of strokes by ± 50% and the cost of apixaban by ±90%. The daily cost of apixaban required to achieve no difference in cost between treatment groups in Germany and the US was also determined.

For the modelled portion of our analysis multiple one-way sensitivity analyses were conducted varying event probabilities by ±50% and study drug costs by ±90%. The results of these analyses were presented in a tornado diagram.

A probabilistic sensitivity analysis was also performed to explore parameter uncertainty in our model. This plus a deterministic analysis were also done for Canada and the UK to confirm the findings of our in-trial analysis. Event probabilities were simulated using a Dirichlet distribution, costs using a gamma distribution and beta for discontinuation, utilities and stroke severity distribution.

Results

In-trial

During the trial period, cost savings from fewer events were observed in all countries in our analysis. In Canada savings attributable to events amounted to -$2,804 (95% CI: -$5,630 to $22); in the UK it was -$970 (95% CI: -$1,980 to $41) (Table 3). Event savings in Germany were -$1,259 (95% CI: -$2,455 to -$63) and -$2,874 (95 CI: -$5,945 to $197 for the US. In all countries these savings were largely a result of fewer disabling/severe ischemic strokes in the apixaban arm.

In Canada and the UK these savings were sufficient to absorb the cost of apixaban during the trial where the mean drug cost per participant was $527 for apixaban compared to $24 for ASA in Canada and $92 for apixaban compared to $24 for ASA in the UK. The net result of this was that apixaban was cost saving in both Canada (-$2,301; 95% CI: -$5,125 to $523) and the UK (-$902; 95% CI: -$1,912 to $109).

In Germany the higher daily cost of apixaban ($2.26) resulted in a mean drug cost per participant of $1,883 for apixaban compared to $24 for ASA. This exceeded cost savings from events and resulted in a mean total in Germany of $600 (95% CI: -$596 to $1,796). The highest apixaban costs in our study were from the US where at $6.06 per day the mean drug cost per participant was $4,888 for apixaban versus $24 for ASA which also exceeded cost savings from events and resulted in a mean total of $1,990 (95% CI: -$1,086 to $5,066) in the US.

In-Trial Sensitivity Analysis

In Canada and the UK our findings were not sensitive to changes to the cost of strokes and apixaban; Apixaban in ARTESiA remained cost-saving under these conditions (Table 4). In Germany and the US, the threshold cost (total mean difference in cost of $0) was $1.58 / day (versus $2.26) and $3.59 / day (versus $6.06) in the US.

Lifetime Cost-Effectiveness

As the in-trial economic results in Canada (-$2,301) and the UK (-$902) were already cost-saving and the ARTESIA trial has demonstrated the clinical benefits of apixaban, no lifetime cost-effectiveness analysis for the Canadian and UK perspective was necessary (dominant strategy). In Germany the mean total cost per participant over a lifetime was $7,560 for the apixaban group compared to $4,937 for ASA resulting in a mean difference of $2,623. The total mean cost per participant over a lifetime in the US was higher at $18,424 for the apixaban group compared to $9,314 for ASA resulting in a mean difference of $9,110 (Table 5). Over this same time horizon participants in the apixaban group accrued 4.995 QALYs compared to 4.888 for ASA. With incremental costs of $2,623 and $9,110 for Germany and the US respectively, incremental QALYs of 0.107, the ICER for Germany would be $24,514/QALY and $85,140/QALY for the US.

In a series of one-way sensitivity analyses all probabilities were varied by ±50% and all costs by ±90%. Our results were sensitive to changes in the probability of strokes in the ASA arm, as well as to the cost of apixaban similar to our in-trial sensitivity analysis (Figure 2a, 2b). In our probabilistic sensitivity analysis, apixaban was cost-effective in 48% of the samples for Germany and 38% in the US with none of the samples being cost-saving for either country (Figure 3a,3b). In Canada apixaban was 61% cost-effective with 100% of the samples being cost-saving. In the UK, apixaban was 55% cost-effective with 85% of samples being cost-saving (Supplementary Figure S1).

History of Stroke or Transient Ischemic Attack In-Trial Analysis

For ARTESiA participants with a previous history of stroke or TIA, apixaban was cost-saving in all four countries considered in our analysis (Supplementary Table S4). In Canada after adding the cost for study medication the total average difference was -$4,950 (95% CI -$10,897 to $998) in favour of apixaban. In the UK the total mean difference was -$1,854 (95% CI: -$3,912 to $204). Apixaban saved -$759 (-$3,101 to $1,584) per participant in Germany. Apixaban was also cost-saving (-$1,662; 95% CI: -$7,830 to $4,507) after factoring in the cost of study medication.

Discussion

A pre-planned sub-group analysis of ARTESIA trial demonstrated that among patients with SCAF and a CHA_2DS_2-VASc > 4, the rate of stroke or systemic embolism was 2.25%/year with aspirin compared to 0.98%/year with apixaban, the number needed to treat (NNT) to prevent stroke or systemic embolism was only 25 (95% CI:15-84) and the risk-benefit ratio was in favour of treating these patients. Our analysis found that apixaban 5mg BID was a dominant strategy (cost-saving and clinically superior) in Canada and the UK. In Germany, while apixaban was associated with higher costs, the use of apixaban would be cost-effective with an ICER of $24,514. In the US, the use of apixaban would not be cost-effective with an ICER $85,140 / QALY. While cost savings from fewer events were present in each country in our analysis the cost of apixaban was a larger influence. Our one-way sensitivity analyses confirmed this and demonstrated the robustness of our results to variations in stroke costs. Although our probabilistic sensitivity analysis results for Canada and the UK were 61% and 55% cost-effective respectively, 100% of samples in Canada and 85% in the UK were cost-saving and with the deterministic results support the findings of our in-trial analysis.

In our analysis we use a cost-effectiveness threshold of $50,000 USD/QALY. However, cost-effectiveness thresholds vary from country to country and in some cases are only informally referenced. In Germany no explicit threshold exists but an "efficiency frontier analysis" is performed based on all relevant comparator treatments and an implied intervention-specific threshold is determined. Attempts at assigning a numerical value to this threshold have suggested it could be as low as $10,899 USD (€10,971 2023 Euros) to as high as $47,461 USD [24,25]. In the US, no government mandated threshold exists, however the ACC/AHA in the US suggests that an ICER below $50,000/QALY is of high value [26].

Oral anticoagulants prevent stroke but may cause major bleeding[27–29]. Secondary analyses of ARTESIA suggest that more strokes are prevented than major bleeds caused among patients with a CHA_2DS_2-VASc score > 4, those with prior cardiovascular disease and those with a prior stroke or systemic embolism[5,6,30]. However, it is overly simplistic to give strokes and major bleeds the same weight when assessing the net benefit of anticoagulation. In ARTESIA, nearly half of all strokes were fatal or disabling, while most of major bleeds were non-fatal and did not require procedural or surgical intervention[4]. It is well-accepted that strokes are significantly more likely than major bleeds to be associated with subsequent impairment in quality of life and mortality[31]. Importantly, patient preference studies also show that patients with AF place greater value on stroke reduction than

bleeding risk, while physicians are more averse to bleeding[32,33]. Additionally, current clinical risk scores, such as HAS-BLED and DOAC, demonstrate only modest predictive ability, showing area under the curve values of 0.65 (95% CI 0.55-0.70) and 0.62 (95% CI 0.59-0.71) respectively for major bleeding prediction; emphasizing the limitations in bleeding risk stratification tools used to assist with anticoagulation decisions [34]. This economic analysis provides one more method of weighing stroke prevention against bleeding risk by demonstrating cost savings for using apixaban among patients with AF and a CHA_2DS_2-VASc score > 4 in Canada and the UK and a favorably cost-effectiveness in Germany.

Limitations

There are certain limitations with the methodology used in our analysis. As a result of different stroke severity grouping between countries, stroke costs are tallied differently for each country. The lack of granularity in the groupings for Canada and the US could result in higher costs being applied to lower Rankin strokes but our one-way sensitivity analyses that varied the cost of stroke by ±50% this did not alter our in-trial conclusions for Canada and the US.

Our analysis focused on hospitalized gastrointestinal and genitourinary bleeds. This could result in a slight underestimate of the costs associated with bleeding, however these sites were the most frequent bleed sites that occurred in the ARTESiA trial. In addition, some out-of-hospital costs associated with bleeds might not be included in our analysis.

As utilities were not captured as part of the ARTESiA trial, the baseline utility in our study was based on the baseline utility in the COMPASS trial. Patients in this trial were younger but sicker compared to ARTESiA patients and on balance this makes it a reasonable proxy for ARTESiA patients with a CHA_2DS_2-VASc > 4.

While the ICER in Germany is below our willingness to pay of $50,000/QALY, our probabilistic sensitivity analysis indicates it would be cost effective in less than 50% of samples. This divergence from our deterministic model is likely due to this being an analysis of a subgroup where the lower frequency of events is a source of uncertainty in our PSA.

As the price of apixaban in the US can vary depending on rebates, coupons or direction of governance, we used the daily cost of rivaroxaban 2.5 BID obtained from a cost-effectiveness

report published by the Institute for Clinical and Economic Review group [13]. While this cost is for a different drug, both rivaroxaban and apixaban are both factor Xa inhibitors and by including discounts, rebates, concessions to wholesalers and distributors and patient assistance programs the price we use is a pragmatic proxy for the price of apixaban. Pricing for patients on Medicare is highly variable, but estimates are that the average monthly cost is currently in the range of $54, and at this price the cost effectiveness would be favorable[35]. Litigations and political processes are currently ongoing in the US and a generic version of apixaban could likely be available soon.

Conclusion

At the end of the trial apixaban 5mg BID in ARTESiA participants with subclinical atrial fibrillation and a CHA_2DS_2-VAS >4 was cost-saving in Canada and the UK compared to aspirin. In Germany apixaban was associated with higher costs during the trial but was considered cost-effective over a lifetime using a willingness to pay threshold of $50,000/QALY, however our probabilistic sensitivity analysis identified a high risk of uncertainty with these results. In the US apixaban cost more during the trial and was not cost-effective at the current estimated price of apixaban. Apixaban was not cost-effective in the US under the base cost assumption but would be cost-effective at a daily cost of $4.35, and cost saving at $3.59.

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Disclosures

AL, RKS, WT, MA, DJW, CL, JBM and CEL have no conflicts to declare.

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Data Availability

Individual patient data used for this analysis cannot be shared publicly for the privacy of individuals that participated in the study. Cost and probability data underlying this article are available in the article and in its online Supplementary material. Other data underlying this article will be shared on reasonable request to the corresponding author.

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Table 1 – Number of Included Events in the CHA_2DS_2-VAS >4 subgroup for Canada*

	ASA	Apixaban
Systemic Emboli	2	1
GI/GU Bleed	9	28
MI	28	24
Non disabling Ischemic Stroke	13	5
Disabling Ischemic Stroke	17	9
Fatal Ischemic Stroke	1	3
Non disabling Hem. Stroke	1	2
Disabling Hem Stroke	3	0
Fatal Hem Stroke	3	0
TIA	29	25
HF	105	124

*Data reorganized for the UK, Germany and the US available in the appendix

Table 2: Unit Costs used for the In-Trial Analysis – Canada *

	Canada
	Cost (USD)
Systemic Emboli	11,609
GI/GU Bleed	7,356
MI	10,677
Non disabling Ischemic Stroke	50,882
Disabling Ischemic Stroke	113,557
Fatal Ischemic Stroke	32,109
Non disabling Hem. Stroke	50,882
Disabling Hem Stroke	113,557
Fatal Hem Stroke	32,109
TIA	4,023
HF	10,551

*Costs for the UK, Germany and the US available in the appendix

1 Table 3: Mean in-trial costs per participant in each country (USD)

	Canada		United Kingdom		Germany		United States	
	ASA	**Apixaban**	**ASA**	**Apixaban**	**ASA**	**Apixaban**	**ASA**	**Apixaban**
Events	$8,792	$5,988	$3,154	$2,184	$3,894	$2,635	$9,517	$6,643
Study Drug	$24	$527	$24	$92	$24	$1,883	$24	$4,888
Total	$8,816	$6,515	$3,178	$2,276	$3,918	$4,518	$9,541	$11,531
Incremental Cost	-$2,301 (95% CI: -$5,125 to $523)		-$902 (95% CI: -$1,912 to $109)		$600 (95% CI: -$596 to 1,796)		$1,990 (95% CI: -$1,086 to 5,066)	
Incremental Cost (Discounted)	-$2,138		-$838		$558		$1,849	

2

3

1 Table 4: In-Trial Sensitivity Analysis

	Canada	United Kingdom	Germany	United States
Base Case	-$2,301	-$902	$600	$1,990
Stroke -50%	-$733	-$377	$1,236	$3,667
Stroke + 50%	-$3,869	-$1,427	-$36	$314
Apixaban Cost -90%	-$2,775	-$2,409	-$1,147	-$2,409
Apixaban Cost +90%	-$1,826	-$820	$2,243	$6,389

2

3

1

2 Table 5: Lifetime mean total cost difference costs per patient in USD

	Canada		United Kingdom		Germany		United States	
	ASA	Apixaban	ASA	Apixaban	ASA	Apixaban	ASA	Apixaban
Costs	$9,935	$6,829	$5,507	$3,070	$4,937	$7,560	$9,314	$18,424
Incremental Cost	-$3,106		-$2,437		$2,623		$9,110	
Incremental Cost (Discounted)	-$2,707		-$2,129		$2,319		$8,032	
QALYs	4.888	4.995	4.888	4.995	4.888	4.995	4.888	4.995
Incremental QALYs	0.107		0.107		0.107		0.107	
Incremental QALYs (Discounted)	0.086		0.086		0.086		0.086	
ICER	DOMINANT		DOMINANT		$24,514/QALY		$85,140/QALY	
ICER (Discounted)	DOMINANT		DOMINANT		$26,965/QALY		$93,395/QALY	

3

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Figure 1a: Simplified State Transition Diagram

Legend: Participants begin in the alive state. Every cycle (3 months) they chance to move to another state or remain in the same state based on their path in Figure 1b. MI = Myocardial Infarction; GI/GU = Gastrointestinal/Genitourinary

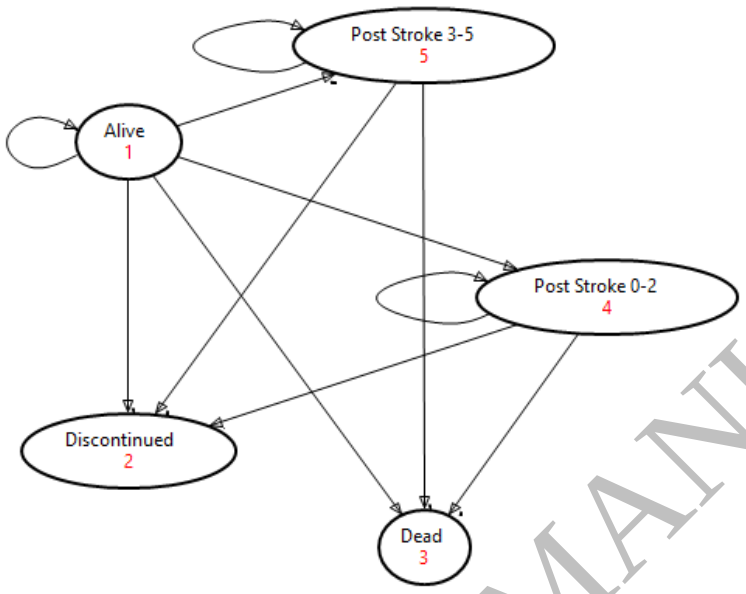


Figure 1b: Patient flow for States 1,4 and 5

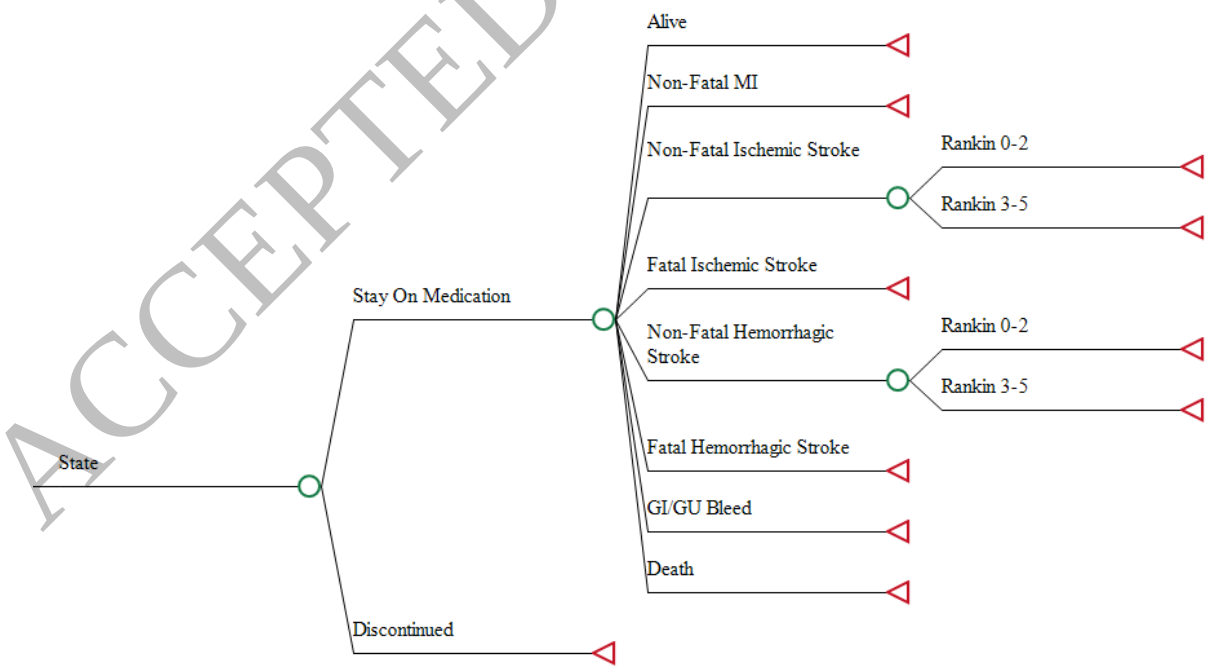
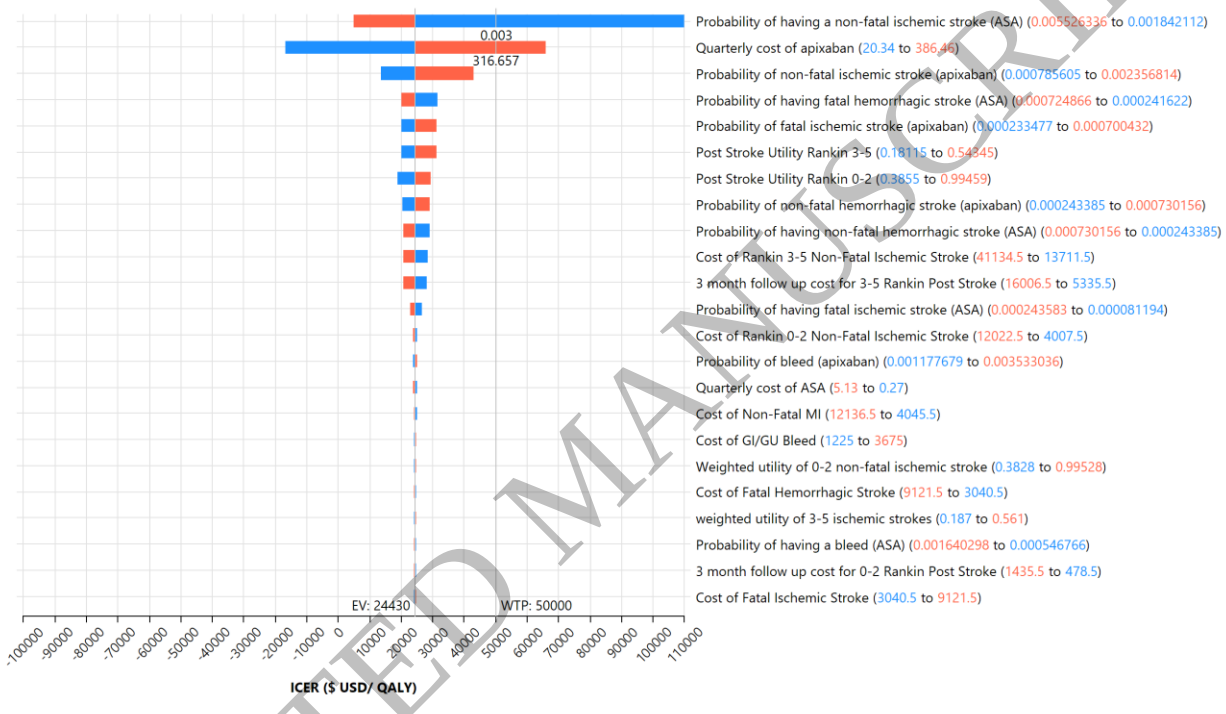


Figure 2: Tornado diagram of one-way deterministic sensitivity analyses for a) Germany and b) the US

Legend: Red bars indicate increases to the value used in the sensitivity analysis, blue are decreases. ASA = acetylsalicylic acid; MI = Myocardial Infarction; GI/GU = Gastrointestinal/Genitourinary; EV = Expected Value; ICER = Incremental Cost-Effectiveness Ratio

a)



b)

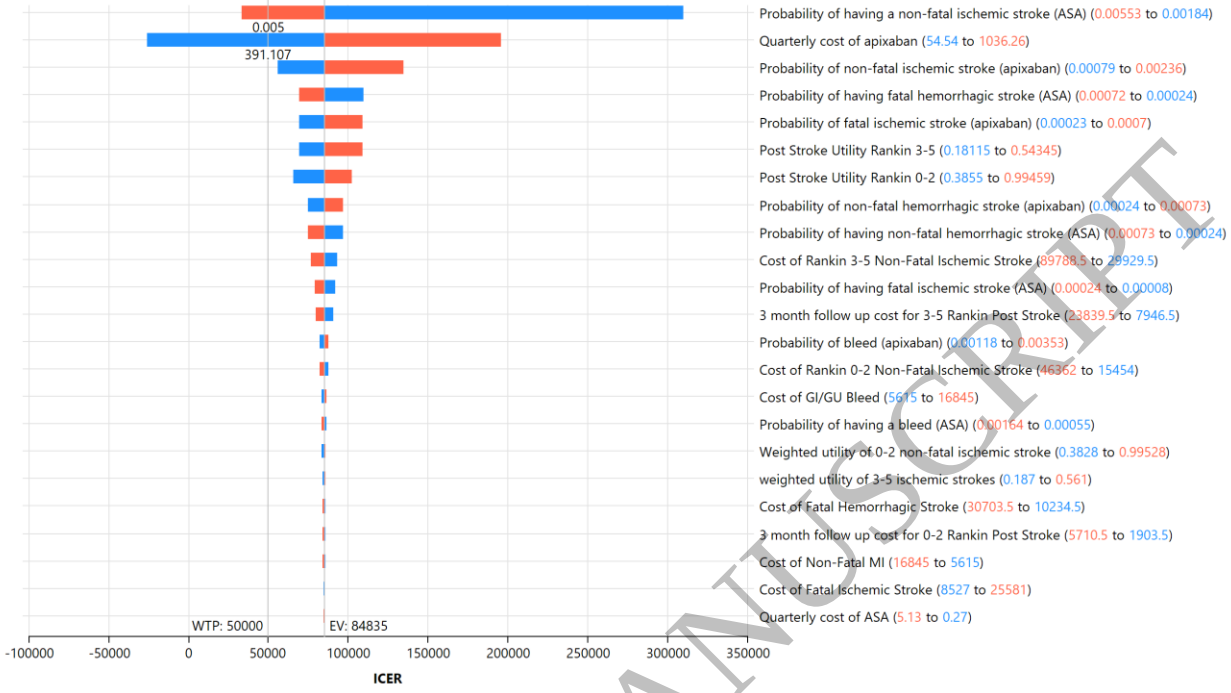
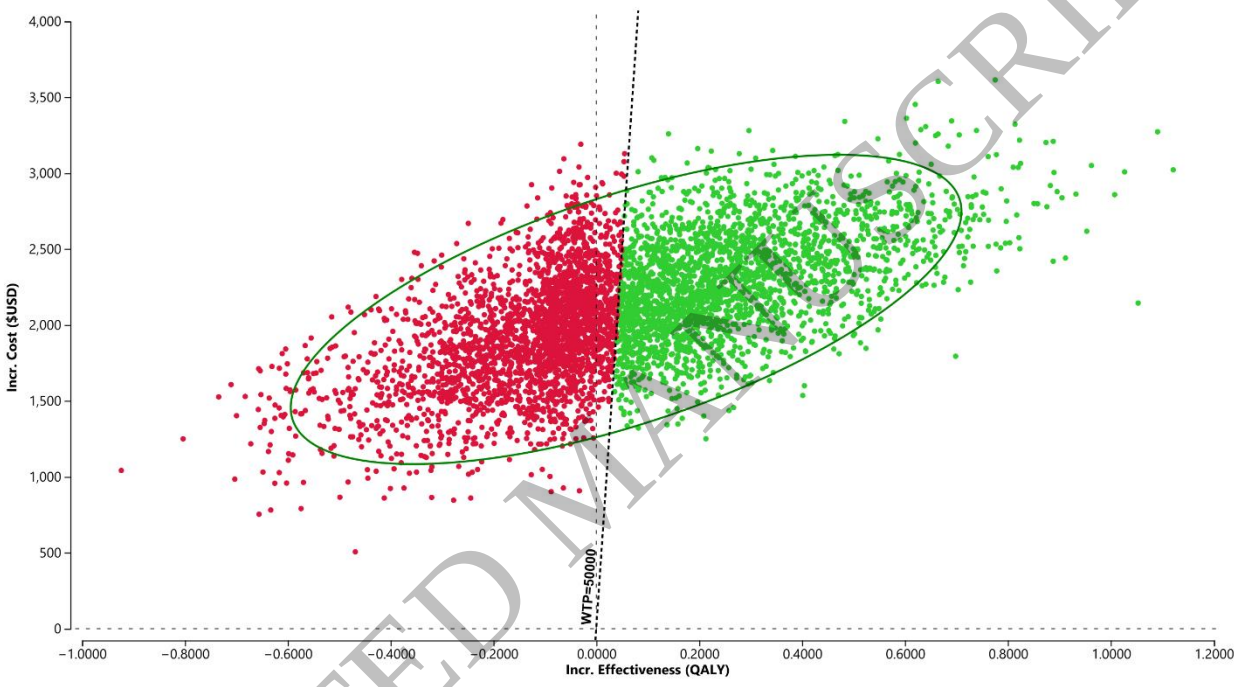


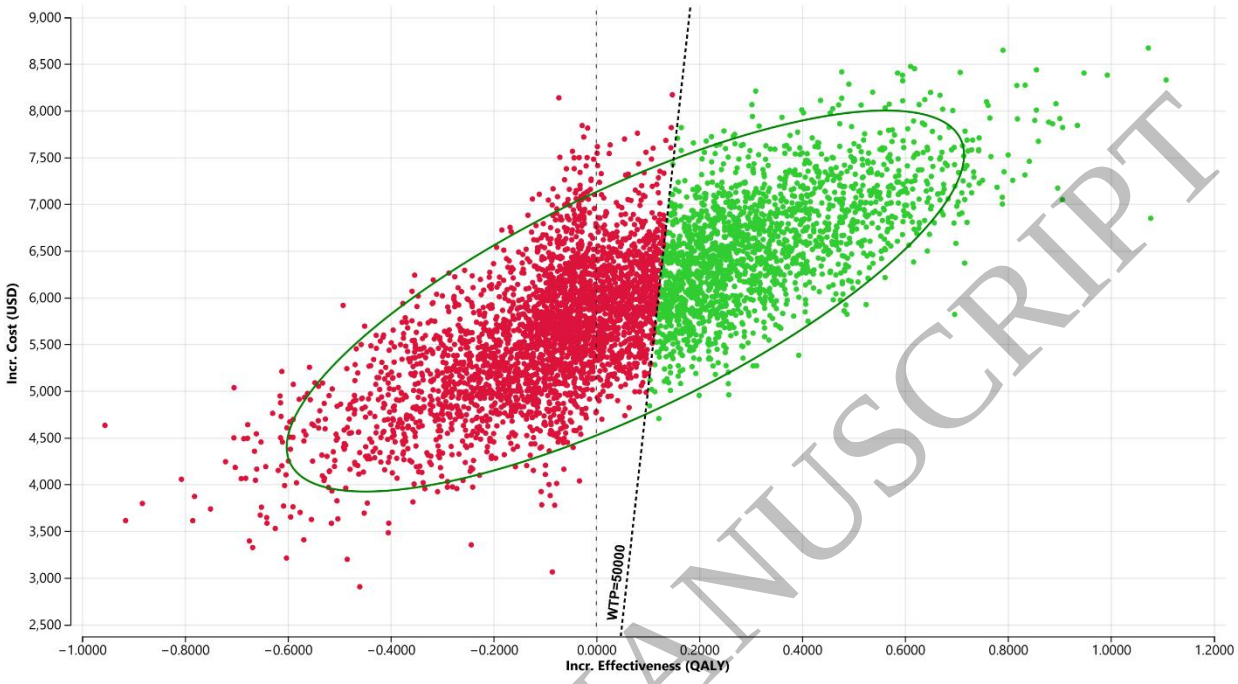
Figure 3: Probabilistic sensitivity analysis plot of 5000 samples for a) Germany and b) the US

Legend: Points in red represent samples that are above a willingness-to-pay threshold of $50,000 USD per QALY and therefore not cost-effective. Points in green are cost-effective. WTP = Willingness-to-pay; USD = US Dollars; QALY = Quality Adjusted Life Years

a)



b)



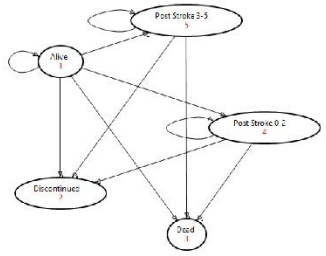
Cost-effectiveness of apixaban vs aspirin for the reduction of thrombo-embolism in high-risk patients with device-detected atrial fibrillation: insights from the ARTESiA trial

Background

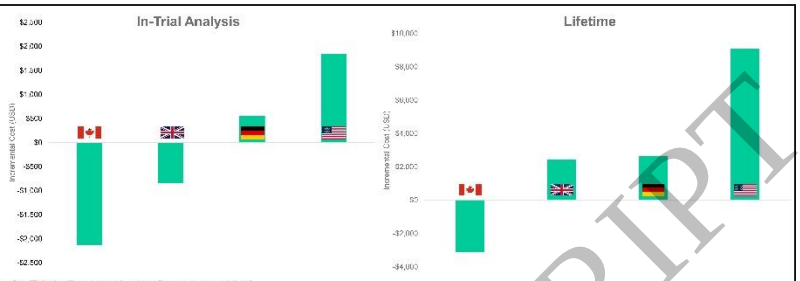
- **Primary Objective:** to evaluate the cost-effectiveness of apixaban in SCAF patients with a CHA_2DS_2-VASc score > 4.
- The ARTESiA trial showed that apixaban reduced stroke or systemic embolism and increased major bleeding vs. aspirin in patients with SCAF.

Methods

- Economic analysis from perspective of four countries
- In-trial analysis and lifetime Markov model
- Direct health care costs (in 2023 USD) were applied to hospitalized events and study drugs



Results



- **In-Trial:** Cost-saving in Canada and UK
- **Lifetime:** Cost-saving in Canada and UK, cost-effective in Germany, not cost-effective in the US under base cost assumption
  - 0.107 QALYs gained
- PSA results were 61% Cost-effective in Canada, 55% in the UK, 48% in Germany, 38% in the US
- Cost-effective in the US at $4.35/day, cost-saving at $3.59/day

Conclusions

- Apixaban in ARTESiA was cost-saving in Canada and the United Kingdom compared to aspirin
- Germany was cost-effective using a willingness to pay threshold of $50,000/QALY.
- In the United States, Apixaban was not cost-effective in the US under the base cost assumption but would be cost-effective at a daily cost of $4.35, and cost saving at $3.59.

Graphical Abstract