

# Major Ischemic or Hemorrhagic Events and Associated Costs among Anticoagulated Patients with Non-Valvular Atrial Fibrillation in Switzerland

Oniangue-Ndza César<sup>1</sup>, Tao Charles<sup>2</sup>, Dhamane Amol<sup>3</sup>

<sup>1</sup>Bristol-Myers Squibb SA, Steinhausen, Switzerland, <sup>2</sup>Xcenda L.L.C., Palm Harbor, FL, USA. <sup>3</sup>Bristol-Myers Squibb, Lawrenceville, NJ, USA

## Introduction

- Atrial fibrillation (AF) is a globally prevalent cardiovascular condition, with 37.57 million prevalent cases and 3.05 million incident cases of AF globally in 2017. AF is associated with a substantial burden of disability, morbidity, and mortality, contributing to 287,241 deaths in 2017.<sup>1</sup>
- Across Europe, prevalent AF in 2010 was approximately 9 million among individuals older than 55 years<sup>2</sup>, and is expected to reach 14 million by 2060<sup>3</sup>. In Switzerland approximately 100'000 patients are affected by AF<sup>6</sup> and it is estimated that 10% are aged ≥65 years<sup>7</sup>
- Current clinical practice guidelines recommend anticoagulants as treatment for AF, with direct oral anticoagulants (DOACs) being the newest available treatment on the market, and with superior adverse event (AE) profiles as compared to the warfarin standard of care (SoC)<sup>4</sup>.
- A large comparative effectiveness and safety analysis of apixaban and rivaroxaban among elderly NVAf patients in the United States (US) was recently published<sup>5</sup>.
- Major ischemic or hemorrhagic events and their associated costs among anticoagulated non-valvular atrial fibrillation (NVAf) patients have not been extensively evaluated in Switzerland.

## Objective

### Model objective

- The objective of this analysis is to apply findings from the aforementioned large retrospective cohort analysis to estimate costs of major ischemic and haemorrhagic events for patients treated with apixaban and rivaroxaban from a Swiss health care system perspective.

## Methods

### Overview

- A cost model was developed to estimate the costs associated with ischemic and hemorrhagic events over a one-year time horizon in patients treated with apixaban and rivaroxaban in Switzerland, using event rates from a US retrospective cohort analysis applied to Swiss tariffs for treating these events. Clinical events were restricted to those identified in the Ray study (ischemic stroke, gastrointestinal (GI) bleeding, systemic embolism, hemorrhagic stroke, intracranial hemorrhage (ICH) and other bleeding)

### Population

- The population was restricted to patients with NVAf aged ≥65 years in Switzerland<sup>6,7</sup>. The base case analysis assumed that 9% of the population was treated with therapies other than apixaban and rivaroxaban, with the remaining 91% of the population evenly divided between patients treated with apixaban and patients treated with rivaroxaban, resulting in market shares of 45.5% for both treatments

### Clinical event rates

- Event rates from Ray were reported separately for patients treated with apixaban or rivaroxaban<sup>5</sup>. The event rates were reported per 1,000 patient-years and scaled down within the model accordingly to apply to the appropriate time horizon and population

### Costs

- Unit costs for major ischemic and hemorrhagic events (in 2022 CHF) obtained from the Swiss inpatient tariff system (Swiss DRG 2022).<sup>8</sup>

### Analyses

- Total cost per year (TCPY) and per-treated patient cost per month (PTPCM) were calculated for apixaban and rivaroxaban treated NVAf patients.
- A scenario analysis assessed the impact of market share on TCPY, adjusting market shares in increments of 20%.

### Assumptions

- Only direct costs of clinical events were included in the analysis
- Patients were assumed to be on treatment through the entire 12-month time horizon of the model with no discontinuation
- Unit costs were identical for ischemic stroke, hemorrhagic stroke, and intracranial hemorrhage as originally reported by the Swiss national tariff system

Table 1. Clinical event rates and costs

Event type	Rate for patients treated with apixaban (rate per 1,000 person-years; n=283,452 person-years) <sup>5</sup>	Rate for patients treated with rivaroxaban (rate per 1,000 person-years; n=191,153 person-years) <sup>5</sup>	Cost per event <sup>8</sup>
Ischemic stroke	7.2	8.3	CHF 8,823
GI bleeding	16.3	35.2	CHF 4,763
Systemic embolism	0.3	0.4	CHF 7,803
Hemorrhagic stroke	1.7	2.5	CHF 8,823
ICH	3.2	3.5	CHF 8,823
Other bleeding	4.4	2.5	CHF 5,365

Footnote line.

## Results - base case

### A Population results

- The population evaluated was estimated to be 10,000 patients, based on the prevalence of AF in patients ≥65 years in Switzerland
- Of these patients, 9% were not treated with either apixaban or rivaroxaban, with the remaining 9,100 patients evenly divided between these two treatments for treated populations of 4,550 each.

### B Clinical event results

- In the population evaluated, there were a total of 389 clinical events experienced over a one-year time horizon, with 151 of these experienced by patients treated with apixaban, and 238 by patients treated with rivaroxaban
- Patients treated with apixaban experienced fewer events of all types except for uncategorized other bleeding events

Table 2. Clinical results, base case

Clinical results	Apixaban patients	Rivaroxaban patients	Total
<b>Clinical event counts</b>			
Ischemic stroke	33	38	71
GI bleeding	74	160	234
Systemic embolism	1	2	3
Hemorrhagic stroke	8	11	19
ICH	15	16	30
Other bleeding	20	11	31
<b>Total</b>	<b>151</b>	<b>238</b>	<b>389</b>

Results may not add up evenly due to rounding of values

### C Cost results

- Cost results generally followed the trends seen in the clinical results, with patients on apixaban seeing fewer costs for all events except other bleeding.
- Average per-patient annual event costs totaled CHF 210 for patients on apixaban compared to CHF 310 for patients on rivaroxaban, driven by the differences in event rates as well as costs of care by event type
- When scaled up to the Swiss population, and assuming equal market share for apixaban and rivaroxaban, annual event costs totaled CHF 957,057 for patients on apixaban compared to CHF 1,412,139 for patients on rivaroxaban, with a total event cost of CHF 2,369,195

Table 3. Cost results, base case

Cost results	Apixaban patients	Rivaroxaban patients	Total
<b>Per-patient costs</b>			
Ischemic stroke	CHF 64	CHF 73	
GI bleeding	CHF 78	CHF 168	
Systemic embolism	CHF 2	CHF 3	
Hemorrhagic stroke	CHF 15	CHF 22	
ICH	CHF 28	CHF 31	
Other bleeding	CHF 24	CHF 13	
<b>Total</b>	<b>CHF 210</b>	<b>CHF 310</b>	
<b>Population costs</b>			
Ischemic stroke	CHF 289,041	CHF 333,201	CHF 622,242
GI bleeding	CHF 353,248	CHF 762,842	CHF 1,116,090
Systemic embolism	CHF 10,651	CHF 14,201	CHF 24,853
Hemorrhagic stroke	CHF 68,246	CHF 100,362	CHF 168,608
ICH	CHF 128,463	CHF 140,506	CHF 268,969
Other bleeding	CHF 107,407	CHF 61,027	CHF 168,434
<b>Total</b>	<b>CHF 957,057</b>	<b>CHF 1,412,139</b>	<b>CHF 2,369,195</b>

Footnote line.

## Results - scenario

### Scenario A: increase in apixaban market share, decrease in rivaroxaban market share

- When the market share of apixaban is increased by an additional 20% from baseline, and the share of rivaroxaban is decreased accordingly, the marketplace results in 65.5% of patients on apixaban, 25.5% of patients on rivaroxaban, and the share of patients treated with other treatments remains fixed at 9%
- In this scenario (A), with no changes to clinical inputs or unit costs, the total count of clinical events falls to 350, due to the decrease in rates of clinical events driven by the additional numbers of patients treated with apixaban
- Total costs of care fell by nearly CHF 200,000 due to reductions in rates of events

Table 4. Scenario A results, increased apixaban share and decreased rivaroxaban share

	Apixaban	Rivaroxaban	Combined
<b>Clinical event counts</b>			
Ischemic stroke	47	21	68
GI bleeding	107	90	197
Systemic embolism	2	1	3
Hemorrhagic stroke	11	6	18
ICH	21	9	30
Other bleeding	29	6	35
<b>Total</b>	<b>217</b>	<b>134</b>	<b>350</b>
<b>Population costs</b>			
Ischemic stroke	CHF 416,093	CHF 186,739	CHF 602,831
GI bleeding	CHF 508,522	CHF 427,527	CHF 936,049
Systemic embolism	CHF 15,333	CHF 7,959	CHF 23,292
Hemorrhagic stroke	CHF 98,244	CHF 56,247	CHF 154,491
ICH	CHF 184,930	CHF 78,745	CHF 263,675
Other bleeding	CHF 154,619	CHF 34,202	CHF 188,821
<b>Total</b>	<b>CHF 1,377,741</b>	<b>CHF 791,419</b>	<b>CHF 2,169,159</b>

Results may not add up evenly due to rounding of values

### Scenario B: decrease in apixaban market share, increase in rivaroxaban market share

- When the market share of apixaban is decreased by an additional 20% from baseline, and the share of rivaroxaban is increased accordingly, the marketplace results in 25.5% of patients on apixaban, 65.5% of patients on rivaroxaban, and the share of patients treated with other treatments remains fixed at 9%
- In this scenario(B), with no changes to clinical inputs or unit costs, the total count of clinical events rises considerably to 428, due to the increase in rates of events attributable to the additional numbers of patients treated with apixaban; only counts of other bleeding fell slightly as compared to the base case
- Combined costs of care increased by over CHF 200,000 due to reductions in rates of higher-cost events, despite the increased rate of other bleeding

Table 5. Scenario B results, decreased apixaban share and increased rivaroxaban share

	Apixaban	Rivaroxaban	Combined
<b>Clinical event counts</b>			
Ischemic stroke	18	54	73
GI bleeding	42	231	272
Systemic embolism	1	3	3
Hemorrhagic stroke	4	16	21
ICH	8	23	31
Other bleeding	11	16	28
<b>Total</b>	<b>84</b>	<b>343</b>	<b>428</b>
<b>Population costs</b>			
Ischemic stroke	CHF 161,990	CHF 479,662	CHF 641,653
GI bleeding	CHF 197,974	CHF 1,098,157	CHF 1,296,131
Systemic embolism	CHF 5,969	CHF 20,444	CHF 26,413
Hemorrhagic stroke	CHF 38,248	CHF 144,477	CHF 182,724
ICH	CHF 71,996	CHF 202,267	CHF 274,263
Other bleeding	CHF 60,195	CHF 87,852	CHF 148,047
<b>Total</b>	<b>CHF 536,372</b>	<b>CHF 2,032,859</b>	<b>CHF 2,569,232</b>

Results may not add up evenly due to rounding of values

Figure 1. Clinical event count comparison across market share scenarios

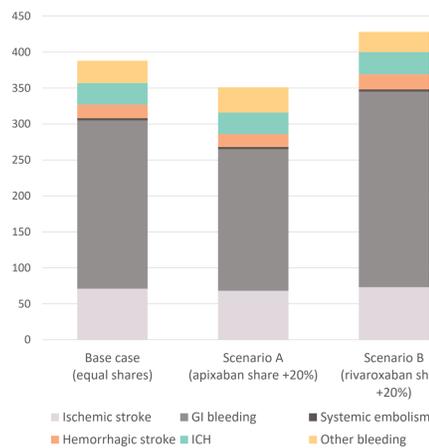
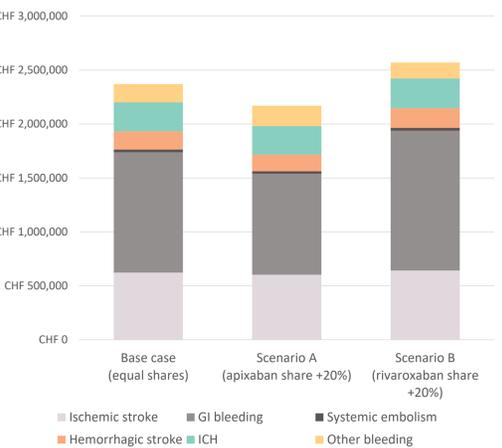


Figure 2. Clinical event cost comparison across market share scenarios



## Conclusions

- In this hypothetical cost model, the clinical benefits of apixaban as compared to rivaroxaban are noticeable when scaled up to a population level in both clinical and economic terms
- Clinical event rates were lower for patients treated with apixaban compared to patients treated with rivaroxaban
- Estimated costs of management of ischemic and hemorrhagic events among apixaban-treated NVAf patients were lower compared to rivaroxaban-treated patients in the Swiss setting.
- Scenario analyses supported these findings in both clinical and economic terms

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