Treating patients with non-valvular atrial fibrillation with apixaban provides substantial consumer value and surplus compared with warfarin and rivaroxaban

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Introduction

- Atrial fibrillation (AF) is the most common form of cardiac arrhythmia,[1] affecting 3–6 million people in the US alone, with these numbers set to reach 16 million by 2050.[2]
- AF is a major risk-factor for stroke, increasing the risk of stroke five-fold when compared with patients without AF.[3] AF is also associated with greater stroke severity, resulting in higher mortality, morbidity, and greater healthcare resource utilization.[4]
- FDA approved treatments include the vitamin K antagonist (VKA) warfarin, and direct oral anticoagulants (DOACs) apixaban and rivaroxaban, which are prescribed to prevent stroke and systemic embolism in patients with non-valvular AF (NVAF).
- While meta-analyses of randomized controlled trials indicate that DOACs achieve comparable or superior efficacy to warfarin,[5,6] understanding the societal value of these interventions to both patients and healthcare providers may promote more efficient treatment decision-making in the US.
- Therefore, the aim of this analysis was to quantify the consumer value and consumer surplus of apixaban compared with warfarin and rivaroxaban. Here consumer value is defined as the savings associated with clinical events averted and the monetary value associated with fewer deaths; and consumer surplus is defined as the consumer value minus incremental treatment cost.

Objective

- The objective of this study was to estimate the consumer value and consumer surplus of apixaban compared with warfarin and rivaroxaban in patients with NVAF in the US over one year.

Methods

Consumer value

- To estimate and compare the consumer value of apixaban versus warfarin and rivaroxaban, clinical trial and retrospective cohort study data were used to derive the difference in one-year event rates for stroke, major bleeding events and all-cause mortality.
  - These events (stroke, major bleeding, and all-cause mortality) were included as they are the most clinically relevant and cost-driving events associated with AF and AF treatment.
- The efficacy (event rates) of apixaban compared with warfarin was sourced from the ARISTOTLE pivotal trial,[7] which concluded that apixaban was superior to warfarin for the prevention of stroke (hazard ratio [HR]: 0.79 [95% confidence interval [CI]: 0.65 to 0.95; P=0.01]), caused less major or clinically relevant bleeding (HR: 0.68 [95% CI: 0.61 to 0.75]), and resulted in lower all-cause mortality (HR: 0.89 [95% CI: 0.80 to 0.99]).

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Methods (continued)

- The effectiveness (event rates) of apixaban compared with rivaroxaban was sourced from a retrospective cohort study of US Medicare patients,[8] which concluded that rivaroxaban was associated with increased risk of major ischemic or hemorrhagic event (HR: 1.18 [95% CI: 1.12 to 1.24]), non-fatal extracranial bleeding (HR: 2.07 [95% CI: 1.99 to 2.15]), and total mortality (HR: 1.06 [95% CI: 1.02 to 1.09]) compared with apixaban.
- By multiplying the derived risk-reduction event rates by the respective event cost, the value of clinical events and deaths averted (per patient) was calculated in US dollars.
  - Costs for stroke and major bleeding were conservatively estimated as $80,000 and $8,000 per event, respectively, based on data from Patel et al.[9] and inflated to 2022 costs.[10]
  - To value the reduction in all-cause mortality, a value of statistical life year estimate of $12,500,000 was assumed, based on guidance from the US Department of Transportation[11,12] and the US Department of Health and Human Services.[13,14]
- Unlike warfarin, patients receiving apixaban do not require regular blood tests or frequent international normalized ratio (INR) monitoring. This benefit was captured by including inflated annual monitoring costs for warfarin (INR monitoring and general practitioner (GP) visits, estimated to be $2,493 per patient per year)[10,15-17] and apixaban and rivaroxaban (GP visits, estimated to be $177 per patient per year).[10,17]
- The value per patient was scaled to estimate the value per 100,000 patients treated with apixaban instead of warfarin or rivaroxaban.

Consumer surplus

- Consumer surplus was estimated by subtracting the incremental treatment cost from consumer value.
- The annual drug cost for apixaban was set at $6,000 per patient. The drug cost for warfarin was assumed to be $0 per patient. To provide the most conservative estimate for consumer surplus, the drug cost for rivaroxaban was also assumed to be $0 per patient.

Results

Apixaban versus warfarin

- The total consumer value of treating 100,000 patients with apixaban versus warfarin over one year exceeded $5.5 billion (Table 1).
  - $5.25 billion was attributed to the reduced all-cause mortality risk associated with apixaban treatment when compared with warfarin.
  - Approximately $232 million in savings was attributed to the reduced monitoring costs of apixaban treatment when compared with warfarin.
  - $26 million and $16 million in savings were attributed to the averted stroke and major bleed events with apixaban versus warfarin, respectively.

Results (continued)

- The total consumer surplus of treating 100,000 patients with apixaban versus warfarin over one year exceeded $4.9 billion, based on an incremental drug cost of apixaban versus warfarin of $6,000 per patient per year (Table 1, Figure 1).

Table 1. Event rates, consumer value and consumer surplus per 100,000 patients treated with apixaban versus warfarin based on Granger et al.[7]

	APIXABAN (N=9,120) Event rate %/year	WARFARIN (N=9,081) Event rate %/year	Event rate difference %/year	Event cost/value per event avoided (USD)	Value per 100,000 patients/year (USD)
Stroke	1.19	1.51	0.32	80,000	26,000,000
Major bleeding†	4.07	6.01	1.94	8,000	16,000,000
All-cause death	3.52	3.94	0.42	12,500,000	5,250,000,000
Incremental monitoring costs‡					231,600,000
Total consumer value					5,523,000,000
Total consumer surplus§					4,923,000,000

†Defined as "Major or clinically relevant nonmajor bleeding" in Granger et al.[7] ‡Monitoring cost of warfarin = $2,493 and apixaban = $177 per patient per year. §Based on an incremental drug cost of apixaban vs. warfarin of $6,000 per patient per year.

Apixaban versus rivaroxaban

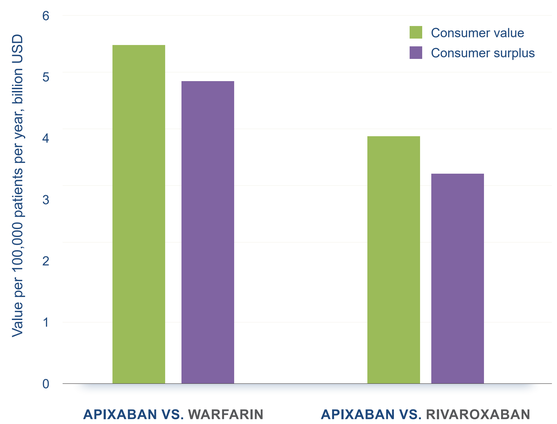
- The total consumer value of treating 100,000 patients with apixaban versus rivaroxaban over one year exceeded $4 billion (Table 2).
  - Approximately $4 billion was attributed to the reduced all-cause mortality risk associated with apixaban treatment when compared with rivaroxaban.
  - $22 million and $17 million in savings were attributed to the averted stroke and major bleed events with apixaban versus rivaroxaban, respectively.
- The total consumer surplus of treating 100,000 patients with apixaban versus rivaroxaban over one year exceeded $3.4 billion, based on an incremental drug cost of apixaban versus rivaroxaban of $6,000 per patient per year (Table 2, Figure 1).

Table 2. Event rates, consumer value and consumer surplus per 100,000 patients treated with apixaban versus rivaroxaban based on Ray et al.[8]

	APIXABAN 283,452 PY Event rate (adjusted) %/year	RIVAROXABAN 191,153 PY Event rate (adjusted) %/year	Event rate difference %/year	Event cost/value per event avoided (USD)	Value per 100,000 patients/year (USD)
Stroke†	1.34	1.61	0.27	80,000	22,000,000
Major bleeding‡	1.85	3.97	2.12	8,000	17,000,000
All-cause death	4.10	4.42	0.32	12,500,000	4,000,000,000
Total consumer value					4,039,000,000
Total consumer surplus§					3,439,000,000

†Defined as "Major ischemic or hemorrhagic event" in Ray et al.[8] ‡Defined as "Nonfatal extracranial bleeding" in Ray et al.[8] §Based on an incremental drug cost of apixaban vs. rivaroxaban of $6,000 per patient per year.
PY, person-years.

Figure 1. Incremental consumer value and consumer surplus for apixaban versus warfarin and apixaban versus rivaroxaban



Limitations

- Variations in the definitions of outcomes in the studies used to inform event rates and costs in this analysis may have led to over- or under-estimations of the consumer value.
- This analysis assumes the costs of warfarin and rivaroxaban are $0 and therefore results may underestimate the true consumer surplus of apixaban.

Conclusions

- Apixaban is a valuable treatment option for patients with NVAF, providing significant consumer value and consumer surplus compared with warfarin and rivaroxaban.
- Results indicate that the use of apixaban generates substantial savings and value for patients treated with NVAF in the US, where the reduced risk of all-cause mortality associated with apixaban treatment is the greatest driver of the estimated surplus.

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Disclosures

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