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Cost-Effectiveness of a Novel Treatment for Stroke Prevention in Patients with Atrial Fibrillation: Results from an Early Economic Analysis

Jennifer Benner[1], *Daniel Bloomfield*[2], *Nikhil Mehta*[2], *Alex Yi*[2]

[1]Stratevi, LLC, One Lincoln Street, 29th Floor, Boston, MA 02111 [2]Anthos Therapeutics, Inc., 55 Cambridge Parkway, Suite 103, Cambridge, MA 02142

ANTHOS THERAPEUTICS

OBJECTIVE

This early economic analysis explored the potential cost-effectiveness of a hypothetical new therapy that reduces the risk of stroke in patients with AF who are unsuitable for treatment with currently available anticoagulants.

INTRODUCTION

- Atrial fibrillation (AF) is a potentially preventable cause of stroke, a leading cause of long-term disability and mortality.[1,2]
- Clinical practice guidelines globally recommend the use of direct oral anticoagulants (DOACs) in patients with AF at elevated risk of stroke.[1-3]
- For many patients with AF at moderate-to-high risk of stroke, clinically significant bleeding from anticoagulants remains a concern, leading to withholding or discontinuation of anticoagulation. There remains a significant proportion of patients with AF who are either treated with an inappropriately low-dose of anticoagulant or not treated at all.[4,5]
- Patients who are unsuitable for or inadequately treated with currently available anticoagulants remain at higher risk for stroke and systemic embolism.

METHODS

Overview

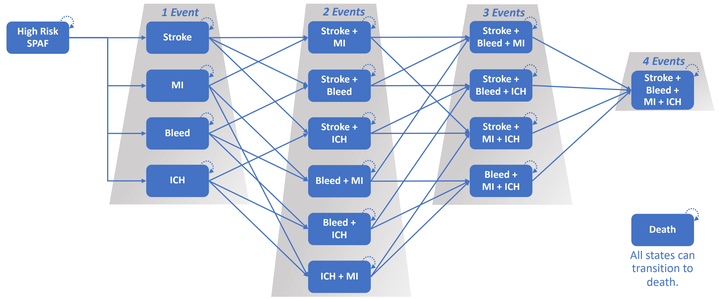
- Following National Institute for Health and Care Excellence (NICE) guidance, a Markov state-transition cohort model was developed to reflect the clinical pathways typical of patients with AF at moderate-to-high risk of stroke who are unsuitable for treatment with currently available anticoagulants.[6]
- The model used a three-month cycle length and a lifetime horizon.
- Use of a hypothetical new treatment was compared with usual care from the United Kingdom (UK) National Health Services (NHS) perspective. A plausible range of stroke risk for the new treatment was assessed.
- Clinical efficacy for the usual care arm, costs, and health state utilities were derived from the NICE guidance documentation for stroke prevention in atrial fibrillation.[6]
- All cost-related input values were inflated to 2021 British pound sterling (GBP); costs and outcomes in the model were discounted annually at 3.5%.
- Key model outcomes included clinical events, life years (LYs) and quality-adjusted LYs (QALYs), total costs, incremental outcomes (eg, clinical events, LYs, QALYs, costs), and incremental cost per QALY gained.

METHODS

Model Structure & Patient Flow

- A hypothetical cohort of adult patients with AF who are at elevated risk of stroke and not adequately treated with currently available anticoagulants received either a hypothetical new therapy or usual management. Each of the treatment strategies had the same model structure but with different event probabilities.
- In total our model had 17 states, including high risk AF and death.
- The model structure and patient flow is illustrated in **Figure 1.** Key modeling assumptions are summarized in **Table 1.**

Figure 1: Model Structure



ICH: intracranial hemorrhage; MI: myocardial infarction; SPAF: stroke prevention in atrial fibrillation.

Table 1. Key Assumptions

Assumption	Rationale
The model did not distinguish between minor and major ischemic stroke.	Per the NICE guidance document, there is limited evidence from prior RCTs to estimate the relative rates of those events.[6]
The costs and disutilities associated with SE and TIA were included in each health state; however, presence of an SE or TIA was not assumed to result in an increased risk of experiencing a stroke, MI, ICH, or bleed.	Per the NICE guidance document, SE and TIA are assumed to only have short-term effects on future risks, costs and utilities.[6]
The model did not distinguish between locations of clinically relevant bleeds (eg, gastrointestinal, non-gastrointestinal).	Based on expert clinical advice, the NICE guidance document states that "the greatest impact on risks, costs and effects is captured by the broad definition of 'clinically relevant bleeds'", which also aligns with prior RCTs reporting of bleeding events.[6]
The model assumed that patients could discontinue treatment if they experienced certain events.	Discontinuation rules were informed by the NICE guidance document.[6]
The model assumed that treatment effects were independent of age and event history.	There is no available evidence to suggest treatment effects change with age or that they depend on event history.

SE: systemic embolism; TIA: transient ischemic attack.

Assumptions & Inputs

- Clinical inputs were derived from the NICE Guidance and relevant clinical trials.
- More specifically, clinical event probabilities in the usual care arm of the model were sourced from the placebo arm of the ELDERCARE-AF clinical trial, which assessed the efficacy of low-dose edoxaban in very elderly patients with AF in Japan.[7] Where the ELDERCARE-AF trial did not report an event, we assumed the probability for the associated event came from the NICE Guidance.[6]
- The baseline risk of stroke was dependent on the distribution of CHA_2DS_2-VASc scores at baseline and the estimated risk of stroke for each score.[8]
- The additional risk of future events, mortality including excess mortality burden by event, and treatment discontinuation rates and rules were informed by the NICE Guidance.[6,9-11]
- Key model parameters and input values are summarized in **Table 2**.

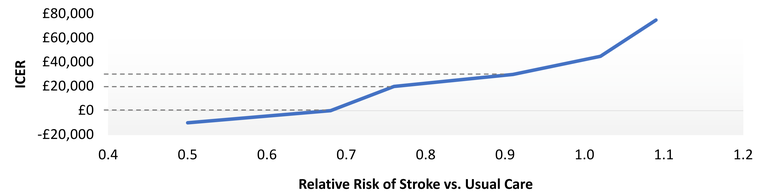
Table 2. Key Model Parameters

Characteristic	Value
Age (years)[6]	70 years
Gender (% female)[6]	40%[6]
CHA_2DS_2-VASc[8]	
2	17.3%
3	23.5%
4	23.7%
5	17.2%
≥6	18.3%
Transition Probabilities	**Rate per Cycle**
Stroke (CHA_2DS_2-VASc)[8]	
2	1.9%
3	2.9%
4	4.2%
5	5.6%
≥6	7.9%
ICH[7]	0.16%
MI[6]	0.79%
Bleed[7]	2.95%
TIA[6]	2.50%
SE[7]	0.24%
Acute Event	**Cost per Event, £**
Stroke[12]	14,586
ICH[12]	14,368
MI[13]	6,060
Bleed[13]	2,197
TIA[13]	1,335
SE[13]	2,977
Chronic Event	**Annual Cost per Event, £**
Stroke (Year 1 Onwards)[12]	4,533
ICH Management (Year 1)[14,15]	25,041
ICH Management (Year 2 Onwards)[14,15]	12,011
Event/Health State	**Utility Value**
High-Risk SPAF[16,17]	0.779
Acute Stroke (Disutility)[18]	-0.590
Post-Stroke[19]	0.690
Acute ICH (Disutility)[20]	0.600
Post-ICH[19]	0.740
Acute MI (Disutility)[21]	0.683
Post-MI[21]	0.718
Acute Bleed (Disutility)[18]	-0.030
Post-Bleed[19]	0.740
TIA (Disutility)[18]	-0.131
SE (Disutility)[18]	-0.131

RESULTS

Figure 2. Potential Stroke Risk Reduction for a Hypothetical New Treatment

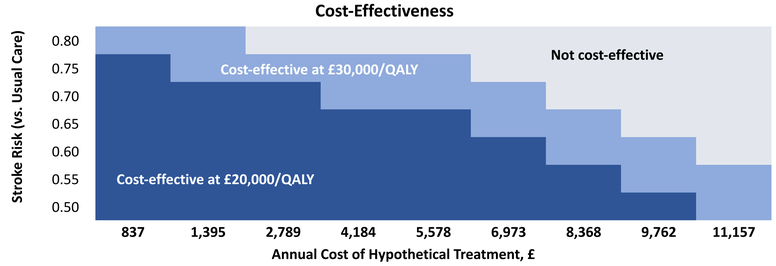
Compared to usual care, a new treatment that reduced the risk of stroke by at least 9% was cost-effective at a £30k/QALY threshold assuming a monthly cost that is 20% higher than apixaban, a commonly prescribed anticoagulant, and relative risks of 0.75, 1.3, and 1.0 for myocardial infarction, bleeds, and intracranial hemorrhage versus usual care (**Figure 2**).



Note: Dotted lines indicate £0/QALY, £20,000/QALY, and £30,000/QALY, respectively.

Figure 3. Price Threshold Analysis for a Hypothetical New Treatment

Considering a range between 0.5-0.8 for the relative risk of stroke versus usual care, the new treatment remained cost-effective up to an annual cost of £1,952-£9,762 (**Figure 3**).



SUMMARY & CONCLUSION

- There remains a significant unmet need for a safer anticoagulation option for stroke prevention in patients with AF.
- A new treatment option for patients with AF at moderate-to-high risk of stroke who are unsuitable for treatment with currently available anticoagulants is a potentially cost-effective treatment option.
- In clinical trials of novel and potentially safer anticoagulant options, special attention should be paid to gathering evidence to support their use in patient segments that are currently not being treated with existing anticoagulants.

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DISCLOSURES & CONFLICTS OF INTEREST

- This study was conducted by Stratevi, LLC with financial support provided by Anthos Therapeutics, Inc.
- JB: Stratevi, LLC (current employment)
- DB: Anthos Therapeutics (current employment)
- NM: Anthos Therapeutics (current employment)
- AY: Anthos Therapeutics (former employment)

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