Abelacimab for the Treatment of Stroke Prevention in Atrial Fibrillation (SPAF): An Early Cost-Effectiveness Analysis (CEA) Versus Rivaroxaban from 5 European Country Perspectives

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OBJECTIVE

This economic model explored the potential cost-effectiveness of abelacimab versus rivaroxaban from France, Germany, Italy, Spain (EU4) and United Kingdom (UK) national health system perspectives in adults with atrial fibrillation (AF) who are high-risk for stroke and eligible for treatment with a direct oral anticoagulant (DOAC).

INTRODUCTION

- AF is a potentially preventable cause of stroke, a leading cause of long-term disability and mortality.[1,2] Affecting 60 million people worldwide, the prevalence of AF is expected to increase by 60% by 2050.[3]
- Clinical practice guidelines globally recommend the use of anticoagulants, including DOACs, in people with AF at elevated risk of stroke.[1-4]
- Despite therapeutic advances, the risk of clinically significant bleeding events remains high worldwide, leaving 40-60% of patients with a CHA_2DS_2-VASc score ≥2 either untreated or undertreated with an anticoagulant.[5-16]
- The underuse of stroke prevention in patients with AF at risk for stroke is one of the greatest public health issues facing cardiovascular patients.[17]
- Abelacimab is a novel, highly selective, investigational, fully human monoclonal antibody that binds tightly to Factor XI to block its activation and prevent the generation of the activated form (Factor XIa). In patients with AF, abelacimab 150mg is planned to be dosed subcutaneously (SC) monthly to maintain nearly complete inhibition (~99%) in a chronic setting.

ABOUT AZALEA-TIMI 71

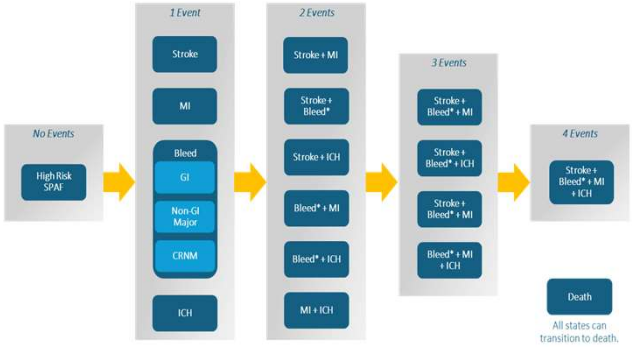
- AZALEA-TIMI 71 was an event-driven, randomized, active-controlled, blinded endpoint, parallel-group safety study evaluating the bleeding profile of two blinded doses of abelacimab relative to open-label rivaroxaban in people with AF at moderate-to-high risk of stroke.[18]
- The study enrolled 1,287 patients across 95 global study sites including the US and Canada, Europe and Asia.
- AZALEA-TIMI 71 was stopped early by the Data Monitoring Committee (DMC) due to a significant benefit favoring abelacimab across all bleeding endpoints; results at early study end were used for this analysis.

METHODS

Overview

- A previously developed Markov state-transition cohort model comparing the cost-effectiveness of abelacimab to rivaroxaban in patients with atrial fibrillation who were at high-risk of experiencing a stroke from a US perspective was adapted to include the EU4 and UK health system perspectives.[19-21] The model structure and patient flow are illustrated in **Figure 1.** Key modeling assumptions are summarized in **Table 1.**
- The model used a 3-month cycle length and a lifetime horizon.
- All costs were inflation-adjusted to 2023 Euros (€) or Great British Pounds (£). Following economic model guidelines, an annual discount rate (3.0-4.0%) was applied to both cost and utilities.[22]
- All model parameters were varied ±20% in one-way sensitivity analyses to evaluate cost-effectiveness sensitivity.

Figure 1: Model Structure



ICH: intracranial hemorrhage; MI: myocardial infarction; SPAF: stroke prevention in atrial fibrillation. **Note:** All patients remain in their current health state until they experience an event. All bleed states separate into: GI, Other Major, or CRNM bleeds.

Table 1. Key Assumptions

Assumption	Rationale
The model did not distinguish between minor and major ischemic stroke.	There is limited evidence from prior RCTs to estimate the relative rates of those events.[19] This is expected to be similar for abelacimab.
The costs and disutilities associated with SE and TIA were included in each health state; however, presence of an SE or TIA was assumed to not result in an increased risk of stroke, MI, ICH, or bleeding event.	SE and TIA are assumed to only have short-term effects on future risks, costs and utilities.[19]
The model did not include patient-relevant bleeding (PRB) events.[22]	While PRB events have a significant impact on quality of life and may lead to poor adherence, leaving patients at a high risk for experiencing a stroke, there is limited data on PRB-related costs and health state utility decrements.
The model assumed that, in any cycle, patients on abelacimab can discontinue treatment. All AEs increase the probability of discontinuation.	Clinical opinion specific to DOACs treatment discontinuation[19] and Anthos internal assumption.
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.

AE: adverse events; RCTs: randomized controlled trials; SE: systemic embolism; TIA: transient ischemic attack.

Assumptions & Inputs

- Clinical inputs were derived from prior models and AZALEA-TIMI 71 trial.[18-20] Cost and utility estimates were derived from literature and publicly available sources.[23-49] Key input values and model parameters are summarized in **Table 2 and Table 3**. Of note:
  - The hazard ratios reported in the primary read-out of AZALEA-TIMI 71 informed the relative risks (RR) of GI (RR= 0.07), Non-GI Major (RR=0.26) and CRNM Bleeding (RR=0.39).[18]
  - The overall risk of stroke in the rivaroxaban arm was calculated as the weighted average of stroke risks by CHA_2DS_2-VASc scores at baseline. Risks of stroke and baseline distribution of CHA_2DS_2-VASc scores were sourced from prior models and AZALEA-TIMI 71, respectively.[9,18-21] Because AZALEA-TIMI 71 was a safety study, the model assumed no difference in stroke or MI risk between abelacimab and rivaroxaban.[18]
  - The wholesale acquisition cost of rivaroxaban was sourced from national drug pricing databases in June 2024 (France: €58.05, Germany: €82.10, Italy: €105.10, Spain: €54.45, €54.75).[30-34] As a placeholder given it is not yet FDA-approved, abelacimab's price was assumed to be at parity with rivaroxaban and require a one-time up-front training cost. Event costs and utilities were derived from publicly available sources.
  - Total costs and quality-adjusted life years (QALYs) were compared over a lifetime.
  - The effects of prior bleeding events on mortality were reported as hazard ratios (HRs). Bleeding events included stroke (HR= 1.32), ICH (HR=1.32), MI (HR=1.03), and bleeding (HR=1.32) were assumed to be multiplicative.[35] Publicly available sources were used to inform discontinuation rates.[19]

Table 2. Key Clinical & Utility Input Values

Clinical Inputs: Abelacimab[18-21]		Utility Inputs: Chronic Health State Utilities[24-26]		Utility Inputs: Acute Event Disabilities[27-29]	
Health State	RR vs. Rivaroxaban	Event/Health State	Value	Event	Value
Stroke*	1.00	High-Risk SPAF	0.779	Stroke	-0.590
ICH	0.33	Post-Stroke	0.690	ICH	-0.030 (Assumption)
MI	1.00 (Assumption)	Post-ICH	0.740	MI	-0.096
GI Bleed	0.07	Post-MI	0.718	GI Bleed	-0.079 (Assumption)
Non-GI Major Bleed	0.26	Post-GI Bleed	0.700	Non-GI Major Bleed	-0.151
CRNM Bleed	0.39	Post-Non-GI Major Bleed	0.628	CRNM Bleed	-0.058
TIA	1.00	Post-CRNM Bleed	0.721	TIA	-0.131
SE	1.00			SE	-0.131

Table 3. Key Economic Inputs Values

	Cost Inputs				
Event	France, €[36-38]	Germany, €[39,40]	Italy, €[41,42]	Spain, €[33, 43-45]	UK, £[46-49]
Stroke	8,633 †	22,575 †	20,434	6,540 †	15,639
ICH	9,872	10,463 ‡	4,111	8,176	15,406
MI	4,092	6,006	13,589	5,429	6,719
GI Bleed	2,816	2,361	3,715*	3,755	1,828
Non-GI Major Bleed	3,621	1,466	3,715 *	3,890	2,863
CRNM Bleed	2,345	41	3,715 *	2,654	1,125
TIA	3,396	4,505	3,089	2,912	1,480
SE	8,264	2,508	3,089 **	3,664	3,301
Stroke (Year 1 Onwards)	1,574	673	1,198 (Assumption***)	1,198	4,861
ICH Management (Year 1)	2,273	1,271	1,271 (Assumption***)	200	23,088
ICH Management (Year 2 Onwards)	Assumed equivalent to year 1				11,075

*Costs for specific bleeding event types (e.g., GI, non-GI, CRNM) were assumed equivalent to the cost of an overall bleeding event. **Cost of SE was assumed equivalent to TIA given no estimates specific to SE were available in the literature.***Chronic event management costs were not available from the Italian perspective. †Estimated as a weighted average of minor ischemic stroke and major ischemic stroke. ‡Estimated as weighted average of minor ICH and major ICH.

RESULTS

Table 3. Base Case Findings

	Per Person Outcomes	France	Germany	Italy	Spain	UK
Abelacimab vs. Rivaroxaban	Total Costs	-€392	-€594	-€693	-€488	-£7,347
	Total LYs	0.1	0.2	0.2	0.2	0.2
	Total QALYs	1.3	1.5	1.5	1.5	1.4
	ICER (Δcost / ΔQALY)	*Abelacimab dominates*	*Abelacimab dominates*	*Abelacimab dominates*	*Abelacimab dominates*	*Abelacimab dominates*

LYs: life years; QALYs: quality-adjusted life years; USD: United States Dollar.

- Base case model results indicate that over a lifetime, on a per-person basis, treatment with once-monthly abelacimab resulted in improvements of 1.3-1.5 QALYs and cost savings of €392-693 (EU4) and £7,347 (UK) compared to daily-dosed rivaroxaban. These results indicate that abelacimab was dominant (i.e., lower costs, higher QALYs) versus rivaroxaban from five European country perspectives (**Table 3**).
- In one-way sensitivity analyses, abelacimab was found to be cost-effective across all 5 countries assuming a variance of ±20%. The RR of CRNM bleed and RR of ICH for abelacimab vs. rivaroxaban, are key drivers of model results, irrespective of country.

SUMMARY & CONCLUSION

- This is the first analysis assessing the potential cost-effectiveness of abelacimab, an investigational once-monthly, Factor XI inhibitor for people with AF at moderate-to-high risk of stroke, from the EU4 and UK national health system perspectives.
- These results indicate that abelacimab was dominant (i.e., lower costs, higher QALYs) versus rivaroxaban from five European country perspectives. These results align with an earlier analysis of the cost-effectiveness of abelacimab from the US-payer perspective, which also found abelacimab to be dominant compared to rivaroxaban.[21]
- The results from this early economic analysis indicate that abelacimab could be a cost-effective option for patients with AF at moderate-to-high risk of stroke in Europe.

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DISCLOSURES & CONFLICTS OF INTEREST

This study was conducted by Stratevi, LLC with financial support provided by Anthos Therapeutics, Inc. AE, JB, JLM are employees of Stratevi, LLC. DB if an employee of Anthos Therapeutics