Cost-Effectiveness Analysis of Apixaban versus Edoxaban for Stroke Prevention in Non-Valvular Atrial Fibrillation Portuguese Patients

PCV49

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Background

- The most frequent cause of cardiac arrhythmia and the main responsible for stroke and thromboembolic events is **non-valvular atrial fibrillation (NVAF).**
- The **anticoagulation therapy** was recommended as a prevention of stroke in patients with NVAF in the latest guidelines of European Society of Cardiology[1].
- Considering the different options available, there is a need of evidence about the **efficiency** of the anti-coagulant treatment in these patients.
  - **Apixaban is a cost-effective option** compared to other NOAC[2]: dabigatran and rivaroxaban.
  - **Edoxaban** have been approved for stroke prevention in NVAF patients.

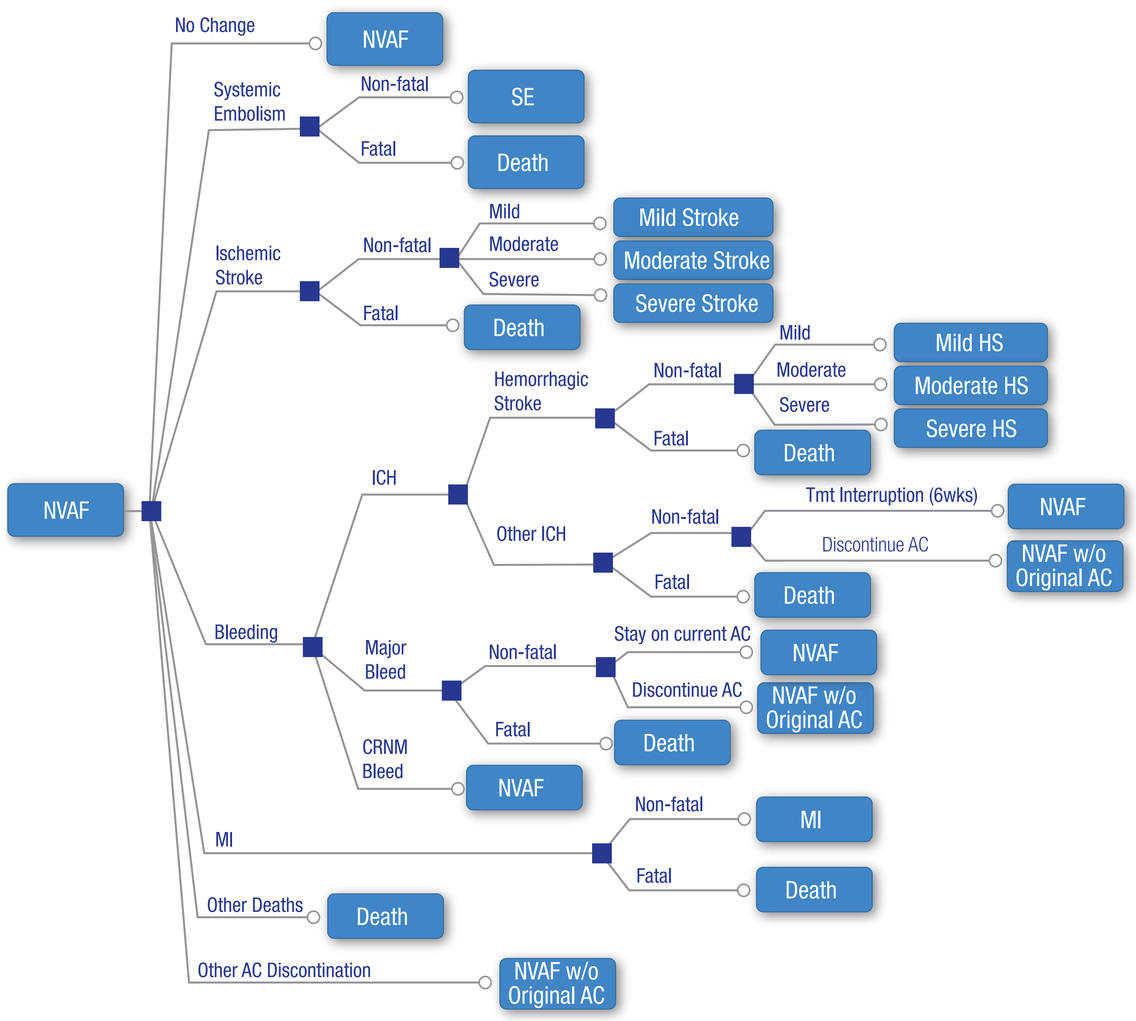
Objective

- To assess the **cost-effectiveness** of **apixaban 5 mg b.i.d** (twice a day) versus **edoxaban (60 mg daily)** and **edoxaban (30 mg daily)** for stroke prevention in NVAF patients in Portugal.

Methods

- A Markov-model with **6-week cycles and 10 health states**[2] (clinical events derived from NVAF risk of embolism and anticoagulation) was adapted to assess treatment incremental costs and health outcomes over a **lifetime horizon**.

Figure 1. Markov economic model of stroke prevention in NVAF population



AC: anticoagulant; CRNM: clinically relevant non major; HS: Hemorrhagic stroke; ICH: Intracranial hemorrhage; MI: Myocardial infarction; NVAF: Non-valvular atrial fibrillation; SE: Systemic embolism; w/o: without

- **Patient population**: characteristics of the 1,000 NVAF patients included in the hypothetical cohort assessed were obtained from **ARISTOTLE apixaban trial**[5]:
  - average age (70 years)
  - 35.5% of females
  - mean CHADS2 score (2.1)
- The **efficacy** of therapies, represented in **clinical event rates per 100 patients-year**, and the safety data were derived from a **Bucher indirect treatment comparison** method of two phase III randomized, double-blind warfarin-controlled trials:
  - **ARISTOTLE** trial[5] comparing apixaban versus warfarin
  - **ENGAGE-AF** trial[6] comparing edoxaban versus warfarin
- The estimated **Hazard Ratios (HR) for edoxaban versus apixaban** were applied to event rates of ARISTOTLE trial[5].
- **Acetyl salicylic acid (ASA) administration** was considered as 2nd line for those patients who stopped or withdrew the 1st line therapy with any of the two main drugs assessed.
  - Event rates for ASA derived from a subgroup of patients with prior vitamin K antagonists exposure from the AVERROES trial[7].
- The **utilities** assigned to each health states were derived from scores of **EQ-5D** questionnaire obtained in a sample of NVAF patients in UK[8].
- Temporal **decrements of utilities** were also applied for **complications**.
- The analysis was made from the **National Health System (NHS) perspective**.
- The **total cost (€, 2019)** estimation considered:
  - **Drug acquisition costs**, which were calculated considering retail price including VAT and applying a 69% reimbursement rate, and according to SmPC authorized dosages: 10 mg/day for apixaban, 60 mg/day and 30 mg/day for edoxaban.
  - Cost of **acute and long-term complications** were obtained from several national databases[9].
  - Cost of annual **renal monitoring**[10] and monthly cost of expected dyspepsy (1.67%)[4] related to any of the anticoagulant treatments.
  - Cost of **NVAF clinical follow-up** (a routine visit every 3 months)
  - **Non-medical costs** for acute and maintenance management periods are referred to informal care and were obtained from Portuguese literature.
- **Annual discount rate (5%)**[10] was applied for both, costs and health outcomes.
- **Sensitivity analyses (SA)** were performed to assess the robustness of the model results.

Results

- In a 1,000 NVAF patient cohort, during their lifetime, **apixaban would avoid numerous complications** in comparison to edoxaban.

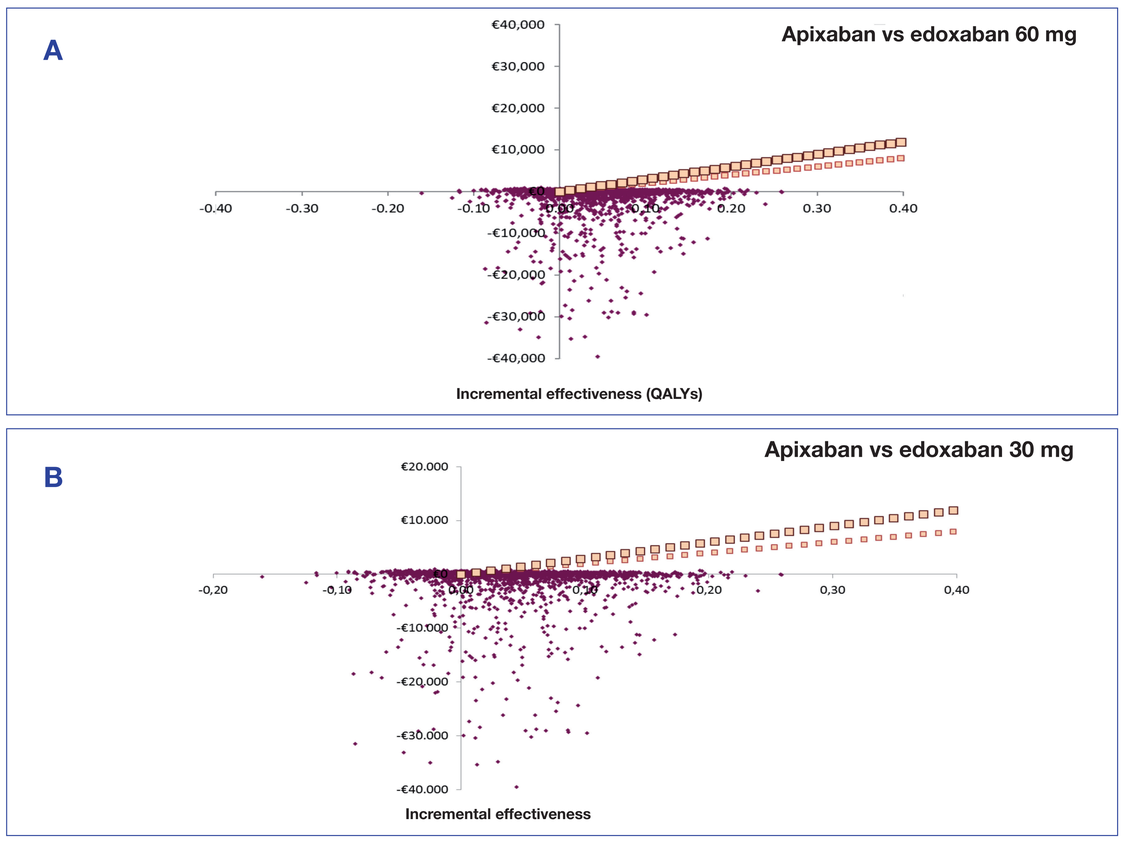
Table 1. Clinical events (base case results)

Number of events in total population	Apixaban	Edoxaban 60 mg	Edoxaban 30 mg	Difference apixaban vs edoxaban 60 mg	Difference apixaban vs edoxaban 30 mg
Ischemic stroke	248	253	269	-5	-21
Hemorrhagic stroke	28	28	21	0	7
Systemic embolism	26	26	28	0	-2
Other ICH	13	14	13	-1	0
Other major bleeds	176	182	127	-6	49
CRNM bleeds	308	337	291	-29	17
Myocardial infarction	91	93	99	-2	-8
Other cardiovascular hospitalization	1,270	1,267	1,237	3	33
Deaths due to stroke, HS, MI, SE	334	336	355	-2	-21
Outcomes (per patient)	**Apixaban**	**Edoxaban 60 mg**	**Edoxaban 30 mg**	**Difference apixaban vs edoxaban 60 mg**	**Difference apixaban vs edoxaban 30 mg**
Life years gained	8.601	8.555	8.531	0.045	0.070
QALYs	6.105	6.071	6.041	0.034	0.064
Costs (per patient)	**Apixaban**	**Edoxaban 60 mg**	**Edoxaban 30 mg**	**Difference apixaban vs edoxaban 60 mg**	**Difference apixaban vs edoxaban 30 mg**
Total costs (payer perspective)	€9,555.68	€9,533.40	€9,354.84	€25.28	€203.84
Cost-effectiveness results				**Apixaban vs edoxaban 60 mg**	**Apixaban vs edoxaban 30 mg**
Incremental cost-effectiveness ratio (ICER) (€/LYG)				**€557.36**	**€2,905.04**
Incremental cost-utility ratio (ICUR) (€/QALY gained)				**€739.64**	**€3,167.60**

CRNM: Clinically relevant non-major; HS: Hemorrhagic stroke; ICH: Intracranial haemorrhage; MI: Myocardial infarction; SE: Systemic embolism; LYG: Life years gained; QALYs: Quality-adjusted life years

- From the NHS perspective, apixaban would yield per each patient:
  - **0.045** life-years gained (LYG) and **0.034** additional quality-adjusted life year (QALY) in comparison to **edoxaban 60 mg**
  - **0.070** LYG and **0.064** QALYs versus **edoxaban 30 mg**
- The total **incremental costs** for apixaban versus edoxaban 60 mg and 30 mg per NVAF patient would be €25.28 and €203.84, respectively.
- The **incremental cost-utility ratio (ICUR)** of apixaban versus edoxaban 60 mg and 30 mg resulted in **€739.64 and €3,167.60 per QALY gained**, respectively.
- **In probabilistic SA,** for both comparisons, **77%** and **79%** of iterations the ICUR were under a hypothetical willingness-to pay threshold of €20,000/QALY and €30,000/QALY, respectively.

Figure 2 . Probabilistic SA results



Conclusion

- **According to the shown model outcomes, apixaban could be considered a cost-effective alternative for stroke prevention in NVAF Portuguese patients, when compared with edoxaban 60 mg and 30 mg.**

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