COST-EFFECTIVENESS ANALYSIS OF EMICIZUMAB FOR THE TREATMENT OF PATIENTS WITH HAEMOPHILIA A WITH INHIBITORS IN PORTUGAL

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Introduction

- Haemophilia A is a rare inherited bleeding disorder due to the missing or defective clotting factor VIII (FVIII) with high impact on patients quality of life (QoL). [1] Routine infusion with FVIII concentrate is the current standard of care. Still, approximately 30% of patients develop FVIII-specific inhibitors, which results in a total or partial loss of treatment efficacy.[2–6]
- Bypassing agents (BPAs) are the only therapeutic option for patients who develop FVIII inhibitors and can be used on-demand or as prophylaxis. Activated prothrombin complex concentrate (aPCC), Feiba NF®, is the only medicine approved for prophylaxis in Portugal.[7] Nevertheless, the limited efficacy and short half-lives of BPAs requires frequent intravenous administrations, resulting in high costs and discomfort to patients.[3-6]
- Emicizumab emerges as a promising alternative by restoring FVIII function, irrespective of the presence of FVIII inhibitors. Additionally, its weekly subcutaneous administration reduces burden of administration compared to current treatment options.[8]

Objectives: To compare the costs and clinical consequences of emicizumab vs. Feiba NF®, used in prophylaxis in adult and pediatric patients, from the National Health Service (NHS) and societal perspectives in Portugal.

Methods

- A Markov model, annually-cycled, was developed to project expected annual bleeding rates (ABR), patients QoL and overall costs through a lifetime horizon. A discount rate of 5% was applied to both costs and consequences. Uncertainty was tested by deterministic sensitivity analysis (DSA) and probabilistic sensitivity analysis (PSA) .[9]
- A cohort of male patients aged 1 year and older enters the model in the "Hemophilia A with inhibitors" health state. By the end of each cycle, patients were expected to either stay alive, experience a reversible bleeding episode or evolve to death (Figure 1). Both prophylaxis treatments were assumed to be continued life-long and equally effective on the reduction of disease-related mortality.[10,11]

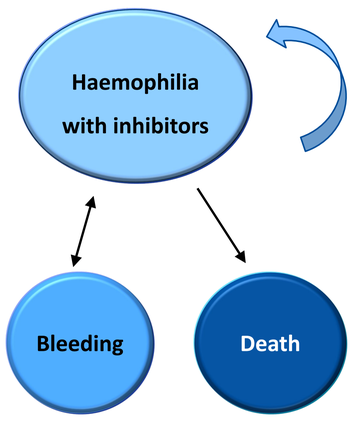

Figure 1. Model Diagram

- ABR, hospitalizations, adverse events (AE) and utilities associated with emicizumab were obtained from the trials HAVEN 1 (patients ≥12 years old) and HAVEN 2 (<12 years old).[12,13]
- Since HAVEN 1 evaluated Feiba NF® as episodic therapy, an indirect comparison HAVEN 1 data and Feiba NF® prophylactic profile from literature was performed in order to provide Feiba NF® prophylaxis clinical data.[14-16]
- Portuguese experts validated population characteristics and local resource consumption. Direct costs were obtained from official public data and included medication acquisition, hospitalizations, AEs and transportation.[17-21] Indirect costs due to patient and caregiver absenteeism were included in the societal perspective considering mean time of work absence and population average salary in Portugal.[22,23]

Model parameters

Table 1 describes the parameters considered for the base case analysis and the variation assumed for sensitivity analysis.

Table 1. Base case and sensitivity analysis parameters

Parameter	Base case	Sensitivity Analysis (SA)	
		Lower bound	Upper bound
Time Horizon	Life-time (99 years)	30 years	
		50 years	
Perspective	Societal	National Health Service	
Discount rate	5%	0%	3,50%
Cohort initial age	1 year	2 years	
		18 years	
ABR	Indirect comparison	Intra-patient comparison (HAVEN 1 & 2 trial data)	
Body weight (adults >18 yo)	70 kg	75 kg	
Relative mortality*	1.19	1.0	1.40
Utilities	0.810	0.760	0.860
Hospitalization cost (per day)	996.14 €	846.72 €	1 145.56 €
Adverse Event cost	Included	Excluded	
Transportation cost	Included	Excluded	
FEIBA NF® price	0.745€/IU	0.707€/IU	
NovoSeven® price	0.552€/ug	0.525€/ug	
Emicizumab price	Confidential	-5%	5%
Treatment adherence	100%	81%	

*Mortality risk due to Hemophilia A mild and moderate (all ages) comparatively to healthy population

Results

The base case analysis estimated an overall survival of 20.25 life years (LY) with both therapies and an increment of 3,85 quality adjusted life-years (QALY) with the use of emicizumab compared to Feiba NF® (Table 2). Considering the life-time horizon, emicizumab use resulted in an estimated reduction of 6 615 022 € and 6 611 324€ per patient considering the societal and NHS perspective, respectively. The main cost reduction driver is medication acquisition.

As a result, emicizumab showed dominance over Feiba NF® (being less costly and more effective), once a reduction of approximately 1.7 million Euros per QALY gained was estimated from both perspectives (Table 2).

Table 2. Estimated costs, effectiveness, and incremental results of emicizumab over Feiba NF®– Societal and NHS perspectives

	Societal			NHS		
	Emicizumab	Feiba NF®	Incremental	Emicizumab	Feiba NF®	Incremental
Outcomes						
Life Years (LY)	20.25	20.25	0	20.25	20.25	0
QALYs	16.40	12.56	3.85	16.40	12.56	3.85
Costs						
Medication	5 569 536 €	10 725 915 €	- 5156379	5 569 536 €	10 725 915 €	- 5 156 379 €
Hemorrhage	355 609 €	1 655 467 €	- 1 299 858 €	355 609 €	1 655 467 €	- 1 299 858 €
Hospitalization	52 455 €	196 708 €	- 144 253 €	52 456 €	196 708 €	- 144 253 €
Adverse Events	2 197 €	10 422 €	- 8 225 €	2 197 €	10 422 €	- 8 225 €
Productivity lost	6 943 €	6 943 €	- €	- €	- €	- €
Transportation	3 287 €	9 594 €	-6 306 €	1 360 €	3 970 €	- 2 610 €
Total	**5 990 029€**	**12 605 050€**	**-6 615 022€**	**5 981 158 €**	**12 592 483 €**	**-6 611 324 €**
Incremental result (emicizumab vs. Feiba NF®)						
Costs	-6 615 022 €			-6 611 324 €		
QALYs	3.848			3.848		
Costs per QALY	Dominant			Dominant		

Sensitivity analysis results

The tornado diagram (Figure 2) shows the DSA based on the variation of parameters presented in Table 1. Emicizumab remained dominant in all simulations and considering both perspectives. Approximately 50% of the simulations strengthened the dominance of emicizumab and 60% showed an absolute variation of 10%, compared to the base case analysis, corroborating the robustness of the results.

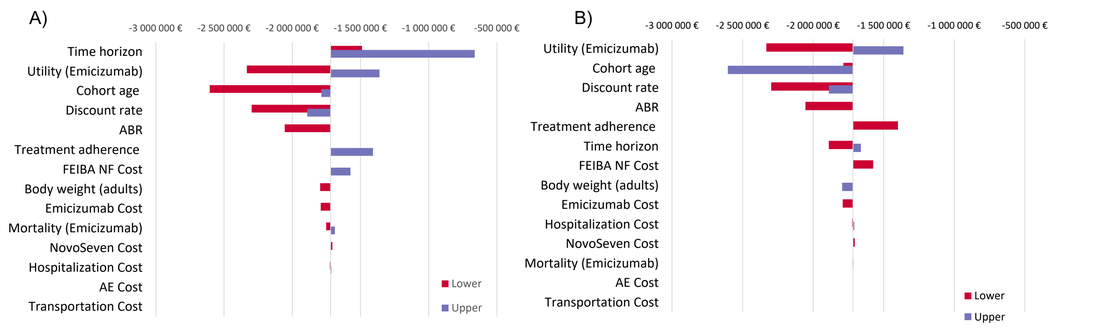

Figure 2. Tornado diagram - Societal (A) and NHS (B) perspectives.

A PSA was performed varying the key model parameters simultaneously and randomly within their probability distributions (Figure 3). There was no relevant dispersion between treatment simulations, with emicizumab cloud dislocated to the right and below Feiba NF® prophylaxis cloud, suggesting that emicizumab has consistently lower costs and more QALYs compared to Feiba NF® prophylaxis considering both perspectives.

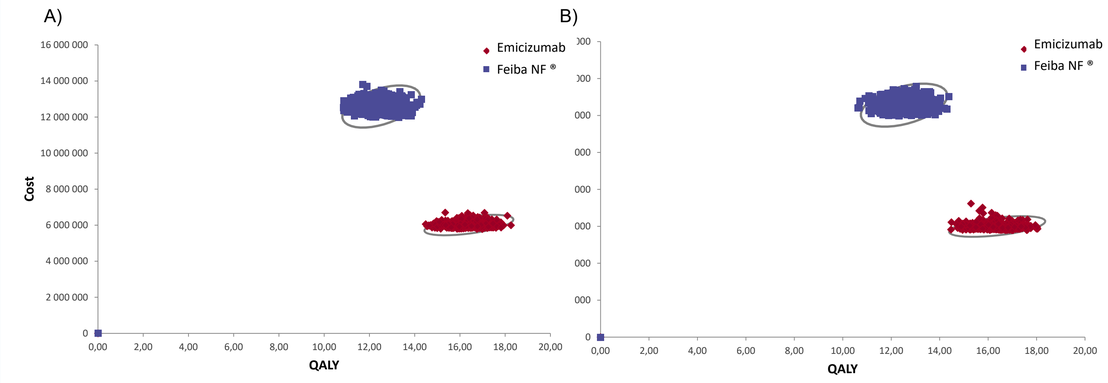

Figure 3. Total cost and QALYs of emicizumab and Feiba NF® – Societal (A) and NHS (B) perspectives

The dominant profile was confirmed in the incremental cost-effectiveness plan (Figure 4), which presents the variation in terms of incremental costs and incremental QALYs of emicizumab versus Feiba NF® in prophylaxis regimen. The resulting cloud is located exclusively in the south-east quadrant, indicating that emicizumab is consistently dominant over Feiba NF® prophylaxis.

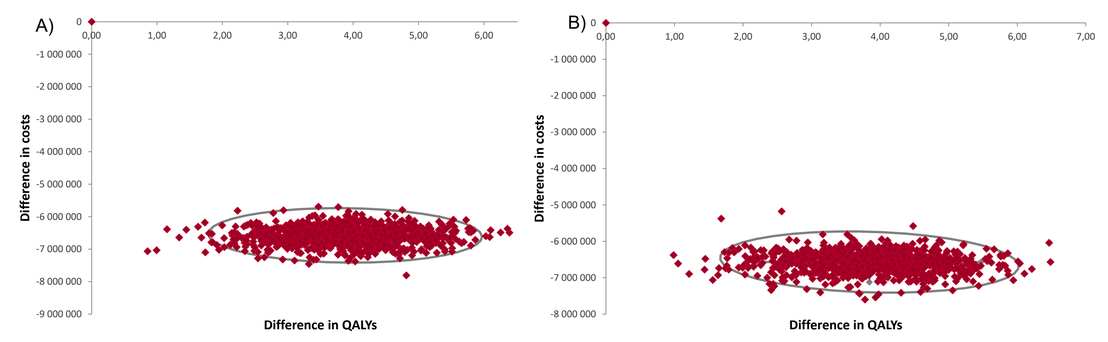

Figure 4. Cost-effectiveness plane of Emicizumab vs Feiba NF® – Societal (A) and NHS (B) perspectives

The acceptability curve (Figure 5) demonstrates that emicizumab treatment has a 100% probability of being cost-effective compared to Feiba NF® prophylaxis (from both perspectives), regardless of the willingness to pay (WTP) threshold.

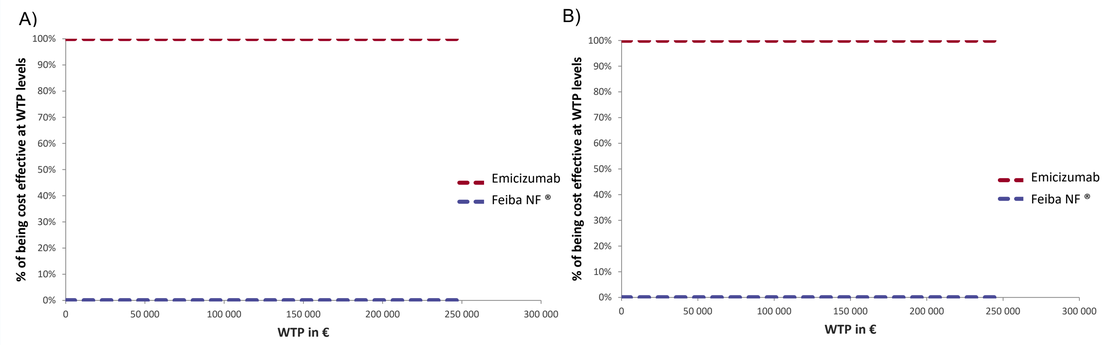

Figure 5. Cost-effectiveness acceptability curves of emicizumab vs Feiba NF® – Societal (A) and NHS (B) perspectives

Conclusions

- This analysis showed an increase of 3.85 QALYs and a reduction of more than 6.6 million Euros over lifetime with emicizumab compared to Feiba NF® prophylaxis therapy, which represents more than 50% of cost saving regardless the perspective.
- Emicizumab demonstrated to be dominant (more effective at lower cost to NHS and society) in 100% of the tested scenarios, with substantial improvement comparing to current treatment in Portugal
- Emicizumab can potentially fill the therapeutic gap as a prophylactic regimen in hemophilia A with FVIII inhibitors.

Acknowledgement

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