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Cost-effectiveness of recombinant factor VIII Fc versus emicizumab for prophylaxis in adults and adolescents with haemophilia A without inhibitors in the UK

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Abstract

Introduction: The economic and clinical burden of haemophilia A is high. Primary prophylaxis with factor VIII replacement therapy is the recognised standard of care, but the emergence of non-factor therapies, such as emicizumab, is extending treatment options for people with haemophilia A.

Aim: There are currently no direct comparisons of efficacy or cost between recombinant factor FVIII Fc-fusion protein efmoroctocog alfa (a recombinant factor FVIII Fc-fusion protein referred to herein as rFVIIIFc) and emicizumab; therefore, a cost-effectiveness model was developed to compare prophylactic treatment with rFVIIIFc versus emicizumab in patients with haemophilia A without inhibitors in the UK.

Methods: The cost-effectiveness model was based on a matching-adjusted indirect comparison and included male patients, aged ≥12 years, with haemophilia A without inhibitors. The model was designed as a Markov process with a flexible lifelong time horizon, and cost-effectiveness was presented as an incremental cost-effectiveness ratio. Base-case analysis and sensitivity analyses (including scenario analyses, one-way deterministic sensitivity analysis [DSA] and probability sensitivity analysis [PSA]) were performed using the following treatment strategies: individualised prophylaxis with rFVIIIFc and prophylaxis with emicizumab administered once weekly (scenario analyses used regimens of once every 2 weeks or once every 4 weeks).

Results: Base-case analysis, DSA and PSA indicated that, compared with emicizumab administered once weekly, rFVIIIFc individualised prophylaxis was the dominant treatment strategy, with lower costs, a greater number of quality-adjusted life years, and a lower number of bleeds.

Conclusions: rFVIIIFc has proven efficacy and is cost-effective compared with emicizumab, providing clinicians with a viable treatment option to improve the health outcomes for adults and adolescents with haemophilia A in the UK.

KEYWORDS
cost-effectiveness analysis, emicizumab, haemophilia A, prophylaxis, recombinant factor VIII Fc

Novelty statement

What is the new aspect of your work?

Currently, direct comparisons of efficacy or cost between rFVIIIFc and emicizumab are not available; therefore, a cost-effectiveness model was developed to compare prophylactic treatment with rFVIIIFc versus emicizumab in patients with haemophilia A without inhibitors in the UK.

What is the central finding of your work?

Individualised prophylaxis with rFVIIIFc compared with emicizumab administered once weekly is associated with lower costs, a greater number of quality-adjusted life years and a lower number of bleeds.

What is (or could be) the specific clinical relevance of your work?

Since rFVIIIFc is associated with improved health outcomes and lower costs, increased access to rFVIIIFc will provide clinicians with a viable treatment option to improve the outcomes for adults and adolescents with haemophilia A.

1 | INTRODUCTION

The burden of disease for haemophilia A is high; it was reported in the World Federation of Haemophilia (WFH) annual global survey that an estimated 165 379 people were living with the disease worldwide in 2020.[1] In severe forms of the disease, recurrent bleeding into joints leads to progressive joint damage and arthropathy, which are characterised by chronic joint pain, reduced mobility and impaired health-related quality of life (HRQoL).[2,3] Primary prophylaxis with factor VIII (FVIII) replacement therapy is the recognised standard of care for patients with severe haemophilia A,[4] and UK guidelines recommend that this is initiated early in life, ideally before the second joint bleed, to preserve musculoskeletal function.[5] Extended half-life (EHL) recombinant FVIII (rFVIII) replacement products are the favoured treatment option in the UK, and they can offer flexible dosing and the potential for individualised treatment to meet the needs of each patient.[6,7]

One such EHL product, efmoroctocog alfa (a recombinant FVIII Fc fusion protein referred to herein as rFVIIIFc), has been shown to be well-tolerated and demonstrated low annualised bleeding rates (ABRs) among patients with severe haemophilia A receiving individualised prophylaxis in the open-label, multicentre trials, A-LONG and Kids A-LONG, and the long-term extension study, ASPIRE.[8–10] With the availability of the non-factor therapy, emicizumab, a recombinant humanised, bispecific, monoclonal antibody that mimics the function of activated FVIII, new options for patients with haemophilia A are now available. The HAVEN clinical trial programme investigated the use of emicizumab for prophylaxis in patients with haemophilia A (most of these being patients with severe haemophilia A) with and without inhibitors and demonstrated that prophylaxis administered once weekly (Q1W), once every 2 weeks (Q2W) or once every 4 weeks (Q4W) resulted in consistently low bleed rates.[11–14] Efficacy outcomes for treatment with emicizumab were reported at a steady-state plasma level of approximately 45–55 μg/ml regardless of dosing regimen[12–14]; therefore, it is reasonable to consider dose alterations to achieve these plasma levels. Such dose alterations, particularly when reduced, may have cost implications for this treatment.

The economic burden of haemophilia A is high, particularly for patients with the severe form of the disease.[15–17] Using data from five European countries (France, Germany, Italy, Spain and the UK), the Cost of Haemophilia in Europe: a Socioeconomic Survey (CHESS) study estimated that in 2014, the total annual cost of severe haemophilia was approximately €200 000 per patient.[18] Similar costs were published in a prospective study from the US, where it was found that the annual cost for patients with severe haemophilia receiving prophylaxis was $301 392 per patient in 2011.[19] In both studies, clotting factor replacement therapy was responsible for the greatest proportion of all direct treatment costs (up to 99% in the CHESS study and 94% in the US study).[18,19] These direct costs also include visits to the emergency department, outpatient procedures, physical therapy and hospitalisation.[18,19] Whilst FVIII replacement therapy can be used for all clinical situations, including acute bleeding and surgery,[20] emicizumab is not suitable for the treatment of breakthrough bleeds or for perioperative bleed management.[4] FVIII replacement therapy is required in these situations, which has the potential to add to the treatment costs of emicizumab. Furthermore, in some emicizumab-treated patients, additional doses of FVIII replacement therapy may also be required ahead of strenuous exercise as a preventative measure,[14] potentially increasing treatment costs. For example, in an analysis of 41 emicizumab-treated patients, 61% received at least one concomitant haemophilia A medication (FVIII concentrates or bypassing agents) during the study.[14] The treatment was administered as a preventive dose

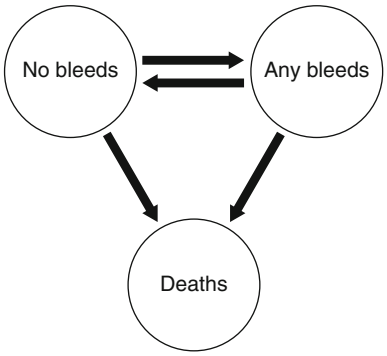

FIGURE 1 Model structure

before activity for 39% of patients and as a treatment for a bleed for 44% of patients.[14] Direct treatment costs are also influenced by differences in drug costs between rFVIIIFc and emicizumab and by factors such as wastage. In addition, high indirect treatment costs further increase the overall disease burden. Patients and caregivers, especially those caring for children with severe haemophilia A,[21] may experience loss of wages related to haemophilia.[18,19]

There are currently no direct comparisons, in terms of efficacy or cost, between rFVIIIFc and emicizumab. A matching-adjusted indirect comparison (MAIC) demonstrated similar efficacy for the mean ABR with rFVIIIFc individualised prophylaxis compared with emicizumab administered Q1W, Q2W and Q4W, with trends in favour of rFVIIIFc.[22] The objective of this analysis was to evaluate the cost-effectiveness of prophylaxis with rFVIIIFc versus emicizumab in patients with haemophilia A without inhibitors in the UK.

2 | MATERIALS AND METHODS

2.1 | Model overview

A model was developed to evaluate the cost-effectiveness of prophylaxis in patients with haemophilia A using rFVIIIFc in comparison with emicizumab.

The patient population included male adolescents and adults (≥12 years of age) with haemophilia A without inhibitors, as evaluated in the A-LONG study.[8] The treatment strategies included in the base-case analysis were individualised prophylaxis (median dosing interval of 3.5 days) with rFVIIIFc and prophylaxis with emicizumab Q1W. Emicizumab Q2W and emicizumab Q4W treatment schedules were included in the scenario analysis. The cost-effectiveness model was developed as a Markov process consisting of a series of transitions between three pre-defined health states: 'No bleeds', 'Any bleeds' and 'Deaths' (Figure 1). This structure was based on the unpublished findings of a post hoc analysis of the A-LONG study, which showed that an absence of bleeds was associated with a higher quality of life at the end of the study follow-up.

2.2 | Cycle length and timeframe

A flexible time horizon from 1 year to a lifetime (71 years) was implemented to capture all differences between treatment arms. The cycle length was set to 6 months, and within the structure of the model, a patient may change state after each cycle.

2.3 | Model assumptions

The model was based on the assumption that the probability of moving between health states, calculated for rFVIIIFc based on patient-level data from the A-LONG and ASPIRE studies,[8,10] is stable over time. The odds ratio (OR) for the proportion of patients with no bleeding events between rFVIIIFc and emicizumab was also assumed to be stable over time; the OR was used in each cycle to estimate the proportion of patients without any bleeds. It was additionally assumed that people with haemophilia A, who receive these prophylactic treatments, have the same mortality as the general population. The ABR in the first cycle was estimated based on a previously performed MAIC analysis for each treatment option.[22] Data from the MAIC included the total study population, that is, both patients with and without bleeding events, for the calculation of ABR and the proportion of patients with no bleeding events. Using these data, the ABR for the patient population with at least one bleeding event was calculated with the following formula:

$$ABR_{bleed} = \frac{ABR}{1 - P_{no\ bleed}}$$

where

ABR_{bleed} = ABR for population with at least one bleeding event.

ABR = ABR for population including patients with and without bleeding events.

$P_{no\ bleed}$ = proportion of patients with no bleeding events.

In the model, the ABR_{bleed} was used in the first cycle. For rFVIIIFc, the values for subsequent cycles were estimated based on patient-level data from the A-LONG and ASPIRE trials[8,10]; it was assumed that the ratio between the ABRs for rFVIIIFc and emicizumab is stable over time, and based on that, the ABRs for subsequent cycles for emicizumab were calculated. Finally, it was assumed for the base-case analysis that for bleeding events, only the cost of the drug occurs and not the cost of hospitalisation or other administrative costs.

2.4 | Model inputs

A summary of base-case inputs and the data sources used to quantify them can be found in Table 1. Data relating to patient characteristics were sourced from those receiving individualised prophylaxis in the A-LONG study.[8] Clinical inputs included the

TABLE 1 Summary of base case inputs, and the lower and upper bounds tested in the deterministic sensitivity analysis

	Base case	Low value	High value	Source Base case	Source Low/high value
Settings and population					
Time horizon, years	71			Assumption	
Discount rate for health outcomes	0.035	0	0.05	Assumption	**Assumption**
Discount rate for costs	0.035	0	0.05	Assumption	**Assumption**
Age, years	29	23.2	34.8	A-LONG[a8]	**±20%**
Weight, kg	71.65	57.32	85.98	A-LONG[a8]	**±20%**
Cohort size	1000			Assumption	
Probability events					
Percentage of patients without bleed in the first cycle in the rFVIIIFc arm					
No bleeds	53%	47%	58%	A-LONG + ASPIRE[8,10] (the presence of bleeds in first 6 months, 62 of 149 pts)	**±10%**
Transition probabilities, subsequent cycles in the rFVIIIFc arm					
No bleeds−>No bleeds	72%	65%	79%	A-LONG + ASPIRE[8,10] transition probabilities based on the logistic mixed effects model	**±10%**
Any bleeds−>No bleeds	64%	57%	70%		**±10%**
Proportion of patients with no bleeding events, OR					
rFVIIIFc individualised prophylaxis versus emicizumab Q1W	1.05	0.60	1.82	MAIC[22]	**MAIC**[22]
rFVIIIFc individualised prophylaxis versus emicizumab Q2W	1.78	0.62	5.11	MAIC[22]	**MAIC**[22]
rFVIIIFc individualised prophylaxis versus emicizumab Q4W	2.53	1.09	5.89	MAIC[22]	**MAIC**[22]
rFVIIIFc versus emicizumab ABR_{bleed}					
rFVIIIFc in the first cycle	5.63	4.08	8.01	MAIC[22]	**MAIC**[22]
Emicizumab in the first cycle	6.36	4.38	9.33	MAIC[22]	**MAIC**[22]
Average ABR_{bleed} for rFVIIIFc in subsequent years	1.78	1.42	2.13	A-LONG + ASPIRE studies[8,10]	**±20%**
ABR decrease in second cycles					
Cycle 2	58%	46%	69%	A-LONG + ASPIRE[8,10]	**±20%**
Dosage					
Prophylaxis treatment					
Mean weekly dose—rFVIIIFc[a]	79.50	73.70	100.90	**ASPIRE**[10]	
Mean weekly dose—emicizumab	1.50	1.20	1.80	HAVEN 3 + 4[13,14]	**±20%**
Bleeding management					
Dose, per kg—rFVIIIFc	50.40	40.32	60.48	ASPIRE[10]	**±20%**
Number of administrations—rFVIIIFc	1.00	0.80	1.20	ASPIRE[10]	**±20%**
Proportion in use in the rFVIIIFc arm—rFVIIIFc[b]	100%	80%	100%	Assumption	**±20%**

(Continues)

TABLE 1 (Continued)

	Base case	Low value	High value	Source Base case	Source Low/high value
Proportion in use in the emicizumab arm—rFVIIIFc[c]	50%	40%	60%	Assumption	±20%
ER visits—no bleeds, rFVIIIFc	0	0%	0%	Assumption	±20%
ER visits—no bleeds, emicizumab	0	0%	0%	Assumption	±20%
Specialist visits—no bleeds, rFVIIIFc	0	0%	0%	Assumption	±20%
Specialist visits—no bleeds, emicizumab	0	0%	0%	Assumption	±20%
Nurse time—no bleeds, rFVIIIFc	0	0%	0%	Assumption	±20%
Nurse time—no bleeds, emicizumab	0	0%	0%	Assumption	±20%
Utility					
Health state utility—no bleeds	0.834	0.782	0.885	**A-LONG + ASPIRE**[8,10]	
Health state utility—any bleeds	0.786	0.63	0.94	A-LONG + ASPIRE[8,10]	±20%
Disutility, lasting for 7 days	0.059	0.011	0.108	**A-LONG + ASPIRE**[8,10]	
Change in utility with 1 year of age or more	−0.008	−0.01	−0.004	**A-LONG + ASPIRE**[8,10]	
Mortality					
Include increased mortality for haemophilia patients	TRUE				
Increased mortality for haemophilia patients—HR	1.00	0.8	1.00	Assumption	±20%

Abbreviations: ABR, annualised bleed rate; ABR_{bleed}, ABR for any bleeding in patients with at least one bleeding event; ER, emergency room; HR, hazard ratio; OR, odds ratio; Q1W, once weekly; Q2W, once every 2 weeks; Q4W, once every 4 weeks; rFVIIIFc, recombinant factor VIII Fc.

[a]Data from the individualised prophylactic arm of the study.

[b]Assumption that in 100% cases rFVIIIFc is used in the rFVIIIFc arm.

[c]Assumption that in 50% cases rFVIIIFc is used in in the emicizumab arm.

proportion of patients without any bleeds, ABRs, mortality, HRQoL and costs. The proportion of patients treated with rFVIIIFc with no bleeds in the first cycle was based on the analysis of patient-level data from A-LONG and ASPIRE.[8,10] Using the distribution of patients in the first cycle and the transition probabilities between cycles, the proportion of patients in each state per cycle was estimated in the rFVIIIFc arm. ORs for the proportion of patients with no bleeding events for emicizumab were obtained from the previously performed MAIC analysis, which compared rFVIIIFc versus emicizumab.[22] The ABRs for both rFVIIIFc and emicizumab were obtained from the MAIC analysis,[22] and these ABRs were used to calculate the costs and quality-adjusted life years (QALYs) in the 'any bleeds' state. Transition probabilities between patients who have experienced bleeding or those without bleeding for each treatment strategy, were also used. As described earlier, the transition probabilities for rFVIIIFc were determined using patient-level data from the A-LONG and ASPIRE studies,[8,10] whereas the transition probabilities for emicizumab were estimated from the OR provided by the MAIC analysis.[22] The probability of death was applied to all patients, and the HRQoL was based on the post hoc analysis of patients from the A-LONG and ASPIRE studies.[8,10]

For rFVIIIFc, the assumed treatment strategy was based on that used in the individualised prophylaxis arm in the A-LONG study,[8] which employed a median weekly dosage of 79.5 IU/kg per week. For emicizumab, three treatment schemes were considered:

TABLE 2 Drug unit costs included in the analysis

Drug name	Unit	Unit cost, £	mg/IU in package	Price per mg/IU, £	Source
rFVIIIFc	3 ml 1000 IU	850.00	1000	0.85	Sobi
Emicizumab	30 mg/1 ml	2415.30	30.00	80.51	British National Formulary, National Institute for Health and Care Excellence[30]
	105 mg/0.7 ml (150 mg/1 ml)	8453.55	105.00	80.51	
	150 mg/1 ml (150 mg/1 ml)	12076.50	150.00	80.51	
	60 mg/0.4 ml (150 mg/1 ml)	4830.60	60.00	80.51	

Abbreviation: rFVIIIFc, recombinant factor VIII Fc.

TABLE 3 Base case results for individualised prophylaxis with rFVIIIFc versus emicizumab prophylaxis administered once weekly

	rFVIIIFc	Emicizumab	Incremental
Total costs, £	5 978 424	10 593 306	−4 614 882
Prophylaxis treatment—drug costs	5 849 077	10 453 034	−4 603 957
Bleeding management—drug costs	129 347	140 273	−10 925
Total QALYs	15.497	15.483	0.014
QALYs in no bleeds state	10.991	10.824	0.167
QALYs in any bleeds state	4.554	4.709	−0.155
QALY loss due to bleed	0.048	0.050	−0.002
Total LYs	23.23	23.23	0.00
Number of bleeds	42.14	44.34	−2.20
ICER (cost/QALYG)	Dominant		
ICER (cost/bleed avoided)	Dominant		

Abbreviations: ICER, incremental cost-effectiveness ratio; LY, life year; QALY, quality-adjusted life year; QALYG, quality-adjusted life years gained; rFVIIIFc, recombinant factor VIII Fc.

1.5 mg/kg Q1W (base-case analysis) and 3.0 mg/kg Q2W and 6.0 mg/kg Q4W (scenario analysis). The dosages for emicizumab were based on those from the HAVEN 3 and HAVEN 4 trials.[13,14] Additional administration costs were not assumed for either drug included in the analysis, as both rFVIIIFc and emicizumab can be administered by the patient at home without the supervision of a healthcare professional. In terms of bleeding management cost, 50.4 IU/kg rFVIIIFc was used per bleeding episode, as this was the median total dose per episode in the ASPIRE study.[10] As emicizumab cannot be used as on-demand treatment, the cost for breakthrough bleeding episodes and bleeding management procedures was set to 0 for emicizumab in the base-case analysis. The drug unit costs used in the model are summarised in Table 2.

2.5 | Analysis outcomes

Health outcomes were estimated in terms of: QALYs divided into no bleeds state, any bleeds state or 1 week utility loss due to bleeding event; total life years (LYs); and number of bleeds. Cost outcomes were calculated as the total treatment cost, which was divided for prophylaxis treatment (drug costs) and bleeding management (drug costs and administration costs). Cost-effectiveness was presented as an incremental cost-effectiveness ratio (ICER), which is a measure of the economic value of an intervention compared with an alternative treatment[23]:

$$\text{ICER} = \frac{\Delta \text{Cost}}{\Delta \text{QALY}}$$

where

$\Delta Cost$ = the difference between the total cost of intervention (rFVIIIFc) and comparator (emicizumab)

$\Delta QALY$ = the difference between the QALYs for intervention (rFVIIIFc) and comparator (emicizumab).

2.6 | Sensitivity analysis

One-way deterministic sensitivity analyses (DSAs) were conducted for all uncertain parameters, the impact on the ICER was evaluated, and the parameters and assumptions that had the greatest impact on the results were identified. A probabilistic sensitivity analysis (PSA) was also performed, and key parameters were varied according to their statistical distributions; 10 000 simulations with different sets of input values were performed and drawn randomly from prespecified statistical distributions. A scenario analysis was conducted on

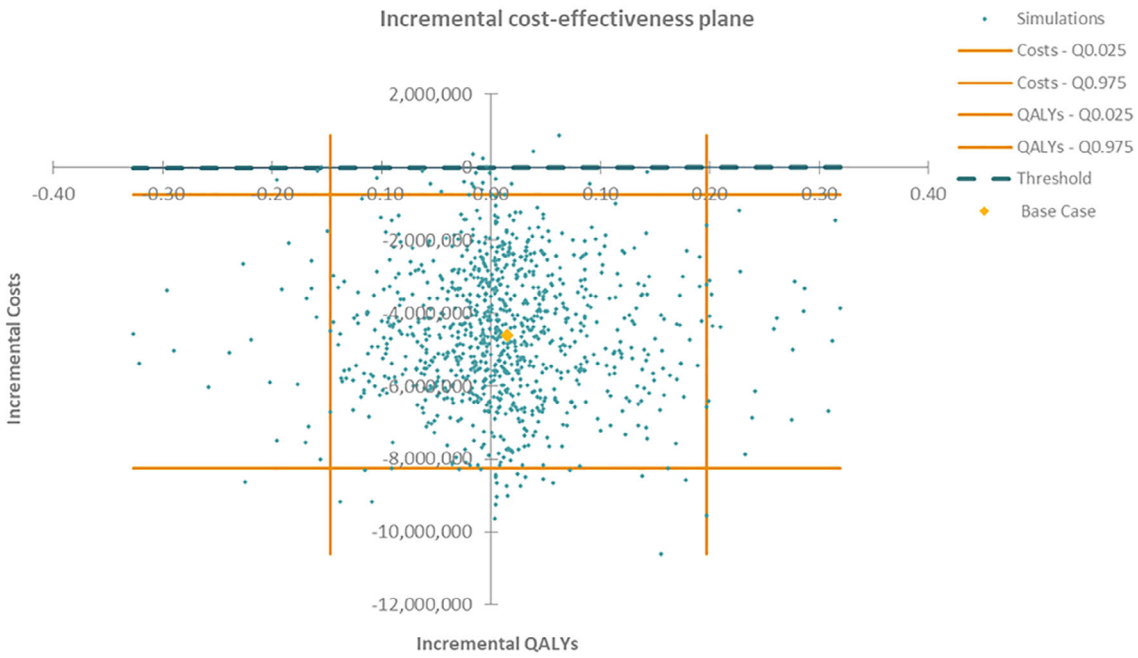

FIGURE 2 Probabilistic sensitivity analysis of individualised prophylaxis with recombinant factor VIII Fc compared with emicizumab administered once weekly. QALY, quality-adjusted life year.

emicizumab prophylaxis administered Q2W or Q4W as part of the sensitivity analyses.

2.7 | Model validation

The model was validated using face, internal and cross validation. Face validation ensured the model was appropriate for the given disease area and complied with the best modelling practices and Health Technology Appraisal requirements, and it was based on the review of published materials for haemophilia A. Internal validation ensured the model was programmed correctly and in line with the model specification, and it also involved a quality check of the model codes and formulas, the model inputs and their compliance with sources, and the model outputs. Finally, cross-validation compared the model results with the results of published analyses for similar indications.[2,24,25]

3 | RESULTS

3.1 | Base-case analysis

Individualised prophylaxis with rFVIIIFc compared with emicizumab administered once weekly was associated with lower costs, a greater number of QALYs and a lower number of bleeds (Table 3), so it was the dominant treatment. Over 23.23 LYs, total costs of rFVIIIFc treatment were £5 978 424 in comparison with £10 593 306 for emicizumab, a reflection of the lower cost of rFVIIIFc. Across the same period, total QALYs were 15.497 and 15.483, and the total discounted number of bleeds were 42.140 and 44.340, for rFVIIIFc and emicizumab, respectively.

3.2 | Sensitivity analysis

For the scenario analysis, individualised prophylaxis with rFVIIIFc (as used in the base-case analysis) was also cost-effective compared with emicizumab prophylaxis administered Q2W or Q4W.

For all tested values in the one-way DSA, individualised prophylaxis with rFVIIIFc was the dominant strategy, resulting in lower total costs and a greater number of QALYs compared with emicizumab administered Q1W.

PSA resulted in the same outcome as the base-case analysis. Using 10 000 simulations, individualised prophylaxis with rFVIIIFc was dominant when compared with emicizumab administered Q1W. Considering a cost-effectiveness threshold of £30 000 QALYs, individualised prophylaxis with rFVIIIFc was cost-effective against emicizumab in approximately 99.4% of simulations and was the dominant strategy in 55.3% of simulations (Figure 2 and Table S1).

3.3 | Model validation

Model validation demonstrated that the results presented in the literature were not comparable to the cost-effectiveness model results presented in Table S2, mainly due to factors such as differences in patient populations or dosing regimens.

4 | DISCUSSION

The objective of this analysis was to evaluate the cost-effectiveness of prophylaxis with rFVIIIFc versus emicizumab in patients with haemophilia A without inhibitors in the UK; to the best our knowledge, there are no other direct comparisons of the cost-effectiveness between the two treatments. The base-case analysis of the cost-effectiveness model demonstrated that individualised prophylaxis with rFVIIIFc was the dominant strategy compared with emicizumab administered Q1W and was associated with lower costs, a greater number of QALYs and a lower number of bleeds.

Model validation was carried out to compare the model results presented here with the results of other relevant analyses for the same indication; however, the results currently presented in the literature were not consistent with the parameters tested in this model. For instance, the Cavazza 2016 study aimed to determine the economic burden of haemophilia from a societal perspective and obtained the HRQoL of patients with haemophilia across Bulgaria, France, Germany, Hungary, Italy, Spain, Sweden and the UK.[2] Total treatment costs were higher than in our analysis; however, the results were based on data from only two UK-based patients and were published before either of the treatments in the present analysis were available. For these reasons, it is difficult to compare the results between the two studies.

Of note, FVIII replacement therapy can be used for all clinical situations.[20] Conversely, emicizumab is not suitable for on-demand treatment,[4] which may lead to additional treatment costs associated with emerging clinical need, such as FVIII replacement therapy for breakthrough bleeds and surgery. With regard to FVIII replacement therapy, the flexibility of treatment allows patients with haemophilia A to tailor treatment to their lifestyle and clinical profile. rFVIIIFc can be administered 3–4 times per week to maintain higher FVIII levels for patients who are physically active or those with joint damage, or it can be administered less frequently (every 3–5 days) to maintain FVIII levels similar to those of the more frequently dosed standard half-life rFVIII.[7] A minimum target plasma trough level of 3%–5% FVIII activity is recommended to prevent breakthrough bleeding in patients with haemophilia A, and the ability to measure this is crucial in order to individualise prophylaxis regimens.[26]

The results of this analysis are in line with a previous study, which compared the cost-effectiveness of rFVIII products (both SHL and EHL) with emicizumab for the treatment of patients with severe haemophilia A without inhibitors in the United States. A pooled analysis of rFVIII products (both SHL and EHL) suggested rFVIII prophylaxis was cost-effective in the long-term for this patient population compared with emicizumab.[27] Furthermore, a cost-utility analysis from Sweden, which compared the cost of rFVIIIFc prophylaxis against other rFVIII products, suggested that prophylaxis with rFVIIIFc may be a cost-effective lifelong option over other FVIII products.[28]

The validity of the current model is highlighted by the fact that statistical analysis of patient-level data was used to feed into the model and justify the structure. Other models have not had access to such data.[28] The assumptions of the model could also be considered plausible based on currently available information, as there are no data to suggest that there are changes in the clinical outcomes between rFVIIIFc and emicizumab treatment over time; however, this does indicate that there is currently a lack of data about changes in clinical outcomes, and further exploration of these changes may be required in order to inform future cost-effectiveness studies.

The model is further limited in that no direct comparisons in terms of the efficacy of rFVIIIFc and emicizumab currently exist. rFVIIIFc has been shown to be at least as effective as emicizumab in the MAIC analysis previously discussed,[22] and this methodology has been previously validated in the instance where direct comparisons are not possible.[29] Another potential limitation of the current analysis is the exclusion of costs associated with hospital visits and other clinical factors, such as joint health. For instance, a serious bleed may require additional hospitalisation or outpatient visits in clinical practice. Moreover, the costs of bleeds are approximated in the current analysis. The costs associated with hospital visits and other clinical factors, such as joint health, are excluded. Meanwhile, the cost of FVIII bleeding treatment could be overestimated as it is based on the dose used in clinical trials, which may be higher than in the real-world setting. However, this approximation has little impact on the total incremental costs as numbers of bleeds are similar between the two compared strategies used in this model. Furthermore, the impact of the severity of bleeds on costs and QALYs could not be quantified due to insufficient data. It would be reasonable to assume that severe bleeds would result in increased healthcare utilisation and a reduction in QALYs, and this warrants further investigation.

5 | CONCLUSIONS

The outcomes reported here indicate that rFVIIIFc is a dominant strategy, leading to improved health outcomes and lower costs compared to emicizumab. Providing increased access to rFVIIIFc will provide clinicians with a viable treatment option to improve the outcomes for adults and adolescents with haemophilia A in the UK.

AUTHOR CONTRIBUTIONS

The concept and design of the article was led by Nana Kragh. Anna Tytula, Michał Pochopien and Samuel Aballéa conducted the statistical analysis. All authors interpreted the data and contributed to drafting and revising the article, provided their final approval of all content and agree to be accountable for all aspects of the work.

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CONFLICTS OF INTEREST

Francis Fatoye reports grant/research support from Swedish Orphan Biovitrum AB. Anna Tytula is an employee of Putnam PHMR, a consultancy company that received funding from Sobi for this research. Michał Pochopien, Samuel Aballéa and Mondher Toumi were employees of Putnam PHMR, a consultancy company that received funding from Sobi for this research. Nana Kragh, Zalmai Hakimi, Jameel Nazir and Linda Bystrická are employees and shareholders of Swedish Orphan Biovitrum AB.

DATA AVAILABILITY STATEMENT

Qualified researchers may request access to data that support the findings of this study. Any patient level data will be anonymized and study documents will be redacted, including to protect the privacy of our trial participants.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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