A matching-adjusted indirect comparison in patients with severe haemophilia A: Comparing the efficacy and consumption of rVIII-SingleChain vs two recombinant FVIII

Santiago Bonanad[1], Ramiro Núñez[2], Jose Luis Poveda[1], Karin Kurnik[3], Georg Goldmann[4], Valeska Andreozzi[5], Björn Vandewalle[5], Sandra Santos[6]
[1]Hospital Universitari i Politècnic La Fe, Valencia, Spain; [2]Hospital Virgen del Rocío, Sevilla, Spain; [3]Dr. von Haunersches Kinderspital Klinikum der Universität München, München, Germany; [4]Institute of Experimental Haematology and Transfusion Medicine, University of Bonn, Bonn, Germany; [5]Exigo Consultores, Lisbon, Portugal; [6]CSL Behring, Lisbon, Portugal

Introduction

- Comparisons between new and established drug products have an important role in healthcare decision-making
- Given the relatively small number of patients with haemophilia A, head-to-head comparisons between different recombinant factor VIII (rFVIII) products in randomised controlled trials are difficult to conduct[1-3]

Aim

- The objective of this study was to compare the efficacy and consumption of rVIII-SingleChain with rAHF-PFM and rFVIIIFc for the prophylactic treatment of bleeding episodes in previously treated adults/adolescents with severe haemophilia A, through a matching-adjusted indirect comparison (MAIC)

Methods

- A systematic literature review (SLR) was conducted using three databases (Medline, Web Of Science and Cochrane CENTRAL)
- Publications were assessed to identify studies that included:
  - previously treated patients with severe or moderately severe haemophilia A (FVIII:C <2%) and
  - treated with the interventions of interest
- A MAIC approach was used to assess the data. This is a validated population-adjustment method that ensures comparisons are conducted between more balanced patient populations than would be the case with naïve indirect comparisons[4]
- Individual patient data from the AFFINITY clinical trial programme[5] were used to match baseline patient characteristics to those from published rAHF-PFM and rFVIIIFc trials
- After matching, the trial outcomes were compared across the enrolled populations
- For prophylactic treatment, annualised bleeding rates (ABRs), proportion of patients with zero bleeds, and FVIII consumption were analysed
- Relative treatment effects are presented as risk ratios (RR), odds ratios (OR) and median differences (MD) with 95% confidence intervals (CI)

Results

Systematic literature review

- A total of 203 records were retrieved from the databases (Figure 1)
  - Following removal of duplicates, title, abstract and full-text screening, 13 records were included in the qualitative phase of the SLR
  - Four studies were included in the quantitative phase: one rVIII-SingleChain trial (Mahlangu et al., 2016; AFFINITY[5]), two rAHF-PFM trials (Tarantino et al. 2004[6] and Valentino et al. 2012[7]) and one rFVIIIFc trial (Mahlangu et al. 2014; A-LONG[8])

Author disclosures

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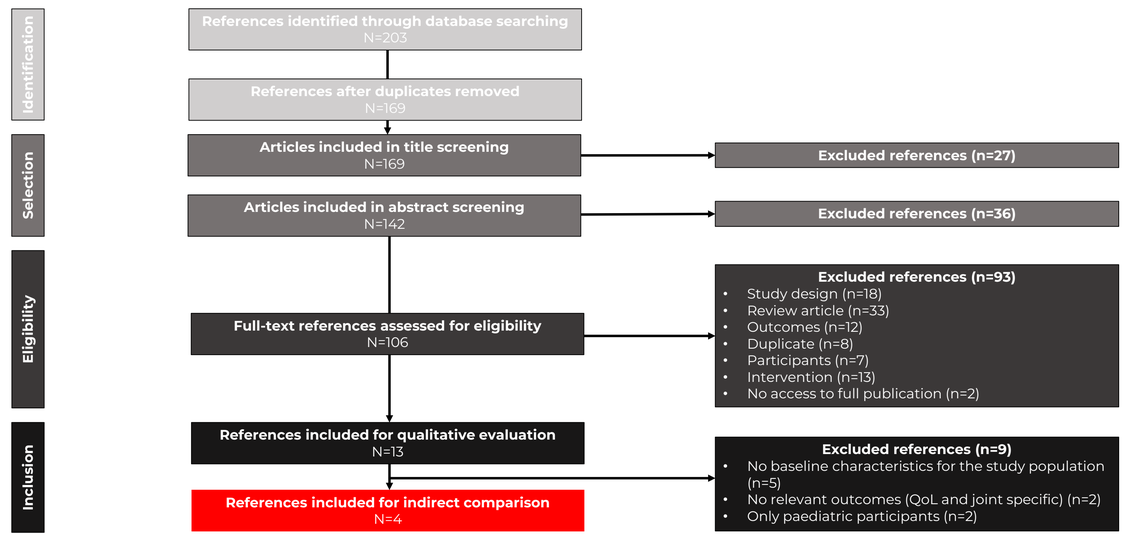
Figure 1. PRISMA flowchart for SLR



Baseline patient characteristics matching

- Baseline characteristics were matched for those patients in the AFFINITY trial programme treated with rVIII-SingleChain to those of patients treated with the comparator products (Table 1)

Table 1. Baseline patient characteristics of all considered study arms and effective sample size (after matching) of the rVIII-SingleChain treated population in the AFFINITY study

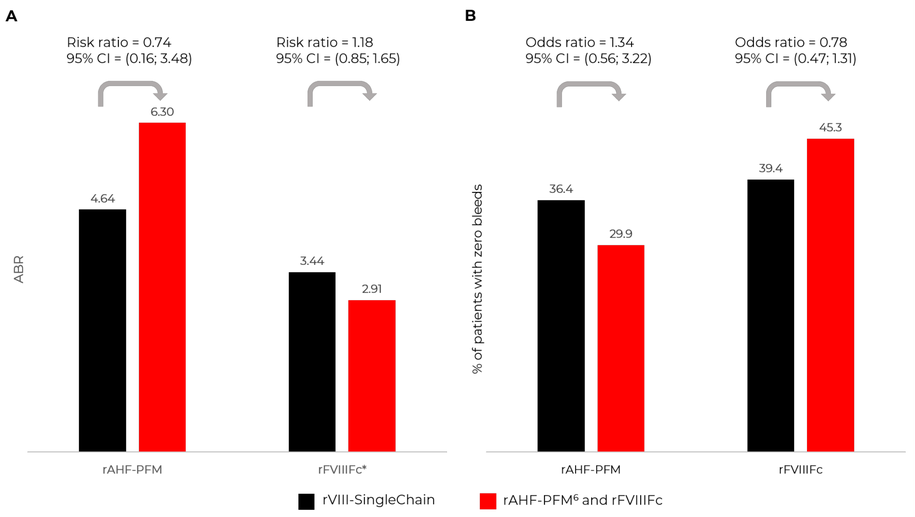
		Prophylaxis			
		rVIII-SingleChain[5]	rAHF-PFM[6]	rAHF-PFM[7]	rFVIIIFc[8]
Number of patients, n		146	111	32	118
Age	Mean	29.7	-	-	29.0*
	>18 years, %	84.2	44.1	87.5†	-
Race	White, %	69.9	92.8	93.8	66.9
Region	Europe, %	47.3	-	-	28.8
Weight	Mean	74.0	65.8	-	74.0*
Height	Mean	174.4	169.3	-	-
ESS (rVIII-SingleChain), n		-	25.1	-	123.6

*Median; †Age ≥16 years; ESS (rVIII-SingleChain): estimate of the sample size that a rVIII-SingleChain treated population in the AFFINITY trial would have required, to achieve the same sampling error as computed in the study that used weighted samples

Prophylactic treatment of bleeding episodes

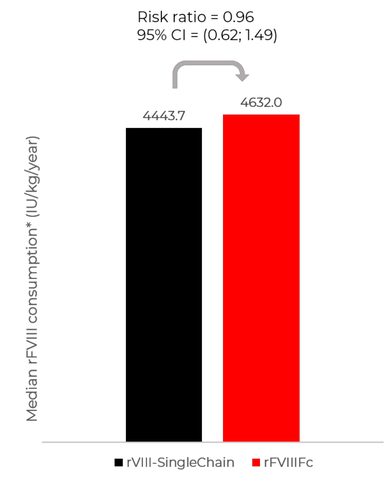
- rVIII-SingleChain demonstrated similar ABRs (RR: 0.74 [0.16; 3.48]; RR: 1.18 [0.85; 1.65]) and percentages of patients with zero bleeds (OR: 1.34 [0.56; 3.22]; OR: 0.78 [0.47; 1.31]) as rAHF-PFM[6] and rFVIIIFc, respectively (Figure 2)
- Median annualised rVIII-SingleChain consumption was significantly lower than that of rAHF-PFM[6] (MD: −1507.66 IU/kg/year [−2011.71; −1003.61]) and equivalent to that of rFVIIIFc (RR: 0.96 [0.62; 1.49]) (Figure 3)

Figure 2. Indirect comparison of rVIII-SingleChain versus rAHF-PFM[6] and rFVIIIFc for (A) mean ABR and (B) percentage of patients with zero bleeds, after matching



*Estimated by negative binomial regression model

Figure 3. Indirect comparison of rVIII-SingleChain versus rFVIIIFc for mean annualised rFVIII consumption, after matching



*(Total rFVIIIFc IU/kg received during the efficacy period / number of days in efficacy period) × 365.25

- The comparison of rVIII-SingleChain with rAHF-PFM based on the data from Valentino et al.[7], produced similar results as those presented in Figures 2 and 3 (based on the data from Tarantino et al.[6])

Conclusions

- **This study suggests that routine prophylaxis with rVIII-SingleChain in the conditions observed in the study results in consumption comparable to rFVIIIFc and significantly lower than rAHF-PFM, while maintaining a similar ABR and percentage of patients with zero bleeds, attesting to the long-acting nature of rVIII-SingleChain**

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