AN ITALIAN PHARMACOUTILIZATION ANALYSIS IN PATIENTS WITH HEMOPHILIA A WITH AND WITHOUT INHIBITORS AFTER SWITCHING TO EMICIZUMAB

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BACKGROUND

- Congenital Haemophilia A (HA) is an inherited X-linked bleeding disorder caused by a deficiency of coagulation factor VIII (FVIII), characterized by spontaneous bleeding episodes, particularly in joints and muscles.
- The burden of a lifelong prophylaxis treatment to prevent bleeding events and preserve joint health for patients with haemophilia A is relevant, affecting patients, caregivers and the healthcare system.
- The arrival of emicizumab, the first non-factor replacement therapy subcutaneously administered for the treatment of haemophilia A, represented a disruptive innovation in bleeding prevention and patient management.
- In Italy there are very limited real-world publications at the moment related to pharmacoutilization and costs of the different prophylactic treatments in haemophilia A, so this could an interisting opportunity to characterize also these dimensions.

OBJECTIVES

The aim of this real-world pharmacoutilization analysis was to assess the prophylactic treatment costs in patients with severe haemophilia A, with and without FVIII inhibitors, before and after switching to emicizumab.

METHODS

- The retrospective analysis was performed using administrative databases of Local Health Units (~ 9 million subjects), including male patients with HA, who started treatment with emicizumab between January 2018 and September 2023.
- The patients were analyzed in the year before the index date, in terms of characteristics and pharmacological treatments. rFVIII and bypassing agents' costs were assessed over 12 months before the first prescription of emicizumab.
- The prophylaxis regimen was identified using an algorithm developed by Vekeman et al., which allowed to distinguish the prophylactic treatment from the on-demand one on the basis of the total units of FVIII dispensed in a year by age group[1].
- The consumption of rFVIII was evaluated only in patients on prophylaxis, with or without FVIII inhibitors. Patients with rFVIII high dosages, suggesting a possible immune tolerance induction, were excluded from the analysis.
- Considering the renegotiations processes during the years, the price per mg of emicizumab was actualized[2]. rFVIII didn't have any price modification throughout the same period[3].

RESULTS

From the database extraction we obtain 91 patients with severe HA and at least one prescription of emicizumab. Among these, the ones with at least 12 months of treatment with emicizumab are:

- 24 patients without FVIII inhibitor (mean age 26.3±21.2 years) previously on prophylaxis with rFVIII (standard half-life or extended half-life);
- 10 patients with FVIII inhibitor (mean age 23.0±23.7 years) previously treated with bypassing agents.

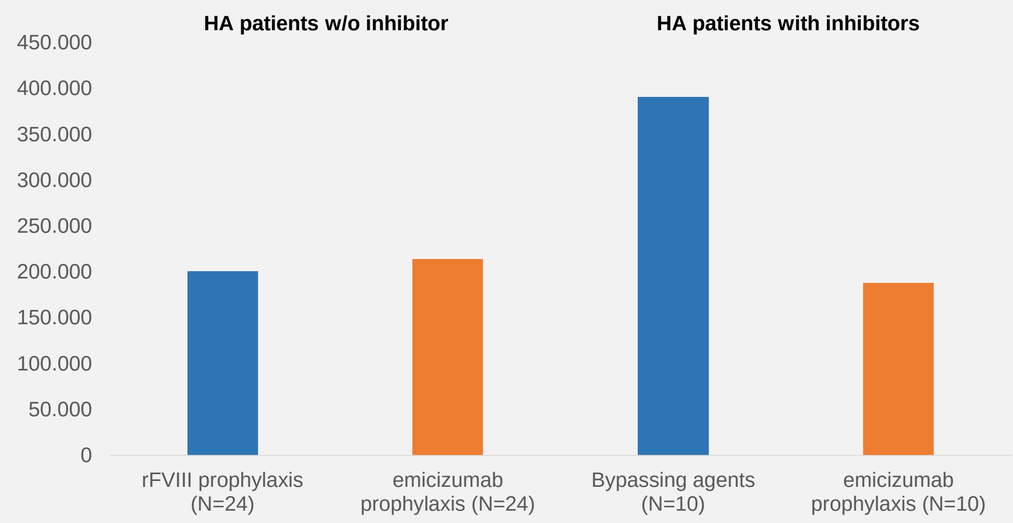
Table 1. *Patients characteristics before switiching to emicizumab*

	Pts (N=91)
Age at index-date, mean (SD)	25.7 (22.2)
Age groups	
0-12 years, n (%)	38 (41.8)
13-17 years, n (%)	6 (6.6)
18-34 years, n (%)	17 (18.7)
35-64 years, n (%)	24 (26.4)
≥ 65 years, n (%)	6 (6.6)
Estimated weight (Kg), mean (SD)	53.9 (30.3)
Charlson index, mean (SD)	0.3 (0.8)
Charlson index = 0, n (%)	72 (79.1)
Charlson index = 1-2, n (%)	18 (19.8)
Charlson index ≥ 3, n (%)	<4

A detailed analysis in the treatment costs of the 34 patients showed that:

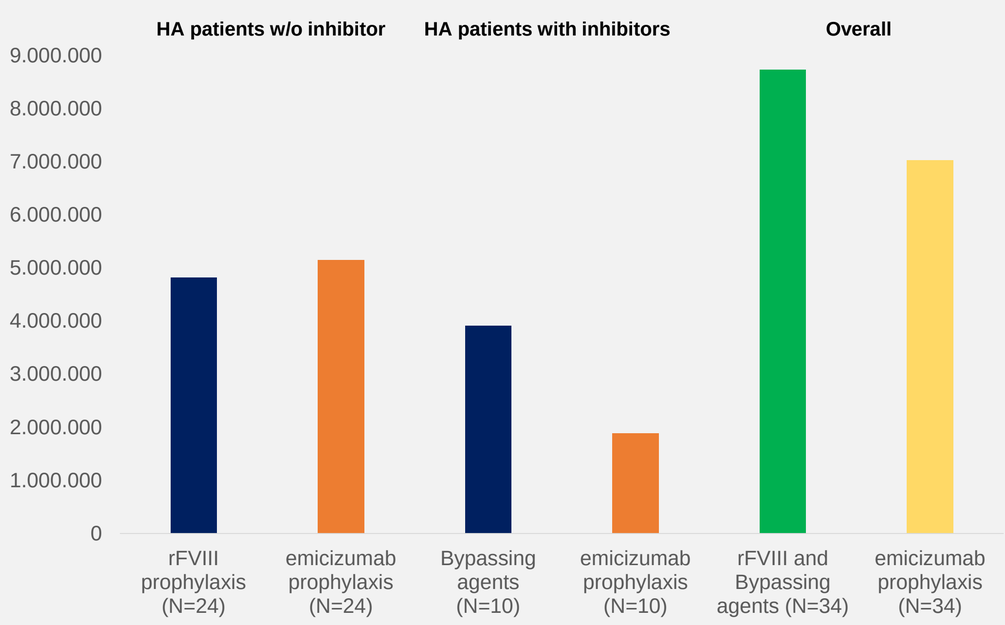
- The mean annual treatment cost in patients without inhibitor is €200.699 (VAT included) for rFVIII and €214.271 (VAT included) after switiching to emicizumab (Figure 1).
- The mean annual treatment cost in patients with FVIII inhibitor is €390.751 (VAT included) for bypassing agents and €187.943 (VAT included) after switiching to emicizumab (Figure 1).

Figure 1. *Mean annual treatment costs for patients with HA with and without inhibitors pre vs post switch to emicizumab*



- Considering the cumulative drug costs of all the 34 patients with severe HA, with and without inhibitor, we could see an overall reduction in the drug expenditure of 1,7 million € after switching to emicizumab (Figure 2).

Figure 2. *Cumulative drug costs (€) for patients with HA pre vs post switch to emicizumab (N=34)*



CONCLUSION

The data from this analysis, based on a sample of 34 patients, shows clearly that, after switching to emicizumab, there's a significative reduction (-51,9%) in the costs of treatment for patients with inhibitors, while for patients without inhibitors the treatment costs are comparable, with a slight increase of 6,8% after switching to emicizumab from rFVIII prophylaxis.
These results need also an additional consideration: since emicizumab emicizumab requires loading doses in the first year, the savings generated could be even higher from the second year (maintenance period)[4].

1. *Vekeman F, et al. Development and Validation of a Classification Algorithm for Prophylactic Versus on-Demand Factor VIII Therapy in Patients With Hemophilia A. Value in Health 15, fasc. 4 (2012): A110.*
2. *Agenzia Italiana del Farmaco. Determina 21 febbraio. 2020. Regime di rimborsabilità e prezzo a seguito di nuove indicazioni terapeutiche del medicinale per uso umano «Hemlibra». (Determina n. 206/2020). (20A01588). Roma: Gazzetta Ufficiale della Repubblica Italiana, 2020; n. 71: pp. 26-28*
3. *Anagrafica Farmaci So.re.sa [Internet]. 2018-2023.*
4. *European Medicine Agency [Internet]. Assessment report. Hemlibra. International non-proprietary name: emicizumab. Procedure No. EMEA/H/C/004406/II/0027.*

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