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# Switch to the extended half-life Factor rFVIII-Fc for patients with severe Haemophilia A on prophylaxis in Western France: a real-life study

***A protocol from the BERHLINGO Group, conducted with the French Nationwide Claims Database SNDS***

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## INTRODUCTION

The MOTHIF study explored **prophylaxis** with Factor VIII (FVIII) in **severe patients with Haemophilia A without inhibitor** (pwSHA) in Western France, following the arrival of an extended half-life FVIII **efmoroctocog alfa** (rFVIII-Fc) supposed to reduce intravenous injections, while maintaining good clinical efficacy on the occurrence of hemorrhagic events.

## METHOD

We investigated pwSHA followed in **7 centres of the BERHLINGO Group** (Angers, Brest, Caen, Le Mans, Nantes, Rennes and Tours), **before and after the rFVIII-Fc supply** (2x12 months: T1 = 07-2015/06-2016 versus T2 = 06-2017/07-2018). Data were extracted from both the **research database BERHLINGO** and the French Nationwide Claims Database **SNDS** (Système National des Données de Santé), and matched via the Social Insurance Number. We compared the **prescriptions / SNDS dispensations** of standard FVIII versus rFVIII-Fc & the impact on the annual bleeding rate (**ABR**).

## RESULTS

A total of 274 pwSHA were identified, whom ¾ were on prophylaxis. The **prescriptions of 156 patients on prophylaxis over both periods** were analyzed; 54% of patients have switched to rFVIII-Fc (n=85). A significant difference in the dosing frequency was observed, with an **increase in the number of patients treated twice a week parallel with a decrease in those treated three times a week** (See Figure 1, Fischer's exact test, independent samples, $\alpha$ = 5%, p =0.0127 and 0.0158). However, the **global prescribed quantities did not vary from period to period**, whatever FVIII was prescribed (230,296 IU vs 226,604 IU/patient/year, Wilcoxon signed-rank test, $\alpha$ = 5%). The SNDS data is currently being explored.

With respect to the analysis of treated bleeding events, a total of 88 patients had a complete traceability logbook for both study periods and 697 events were recorded, especially hemarthrosis (See Figure 2). As described in Table 1, no significative difference was globally observed in the ABR. Nevertheless, **for switched patients** (rFVIII-Fc only on T2), a **significant decrease of the ABR and of the amount of FVIII injected** to treat bleeding events was noted (ABR from 6.6 to 4.0 and 40% drop in FVIII required <> Wilcoxon signed-rank test, $\alpha$=5%, p=0.003 for ABR & p=0.028 for FVIII). Over T2, the ABR of switched patients became comparable to that of patients on standard FVIII (4.0 versus 3.3). For switched patients, the hemorrhagic profile was also different, with **a higher ABR at baseline and a significantly bigger proportion of hemarthroses** (48% of total treated events versus 29% for non-switched people). Their Annual Bleeding Joint Rate (**ABJR**) was also three times higher at the outset, with the **switch to rFVIII-Fc leading to its significant decrease** from 3.2 to 1.9 (See Table 2 – Wilcoxon signed-rank test, $\alpha$=5%, p=0.033 for ABJRs).

## CONCLUSIONS

The real-life study MOTHIF shows **similar results to the pivotal clinical trials** regarding the **reduction of dosing frequency** and demonstrates a **significant improvement in the hemorrhagic phenotype in patients treated with rFVIII-Fc.** More data are needed to provide a real in-depth analyse, especially with a comparative with real FVIII dispensations from SNDS. Only **real-life studies** are likely to show such results.

## ACKNOWLEDGEMENTS

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## CONTACT INFORMATION

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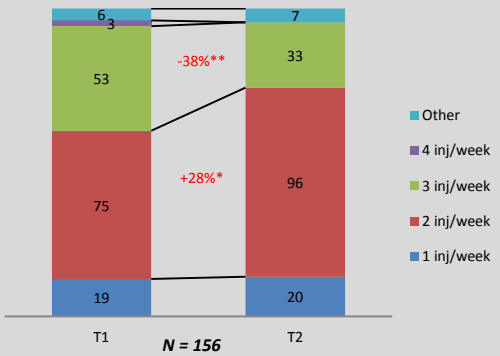
### Figure 1: dosing frequencies

over T1 = 07-2015/06-2016 & T2 = 07-2017/06-2018




***Following the availibility of rFVIII-Fc in Western France: significant increase of "twice a week" frequency parallel with a significant decrease in "three times a week" frequency***

*Fischer's exact test, independent samples, significant $\alpha$ = 5%:*
**p =0.0127 for the 2/w frequency and*
***p = 0.0158 for the 3/w frequency*

### Table 1: *description of ABR and patient self-administered FVIII for bleeding events in matched patients, before/after supply of rFVIII-Fc (according to the type of FVIII prescribed over T2)*

| Matched patients on prophylaxis over T1 = 07-2015/06-2016 & T2 = 07-2017/06-2018 + complete traceability logbook | | Standard FVIII only over T2 (N = 49) | rFVIII-Fc only over T2 (N = 25) | Standard FVIII & rFVIII-Fc over T2 (N = 14) | Total (N = 88 patients) |
|---|---|---|---|---|---|
| T1 | Weight in kg (mean +/- sd) | 52.7 +/- 24.4 | 48.8 +/- 21.5 | 49.0 +/- 34.0 | 51.0 +/- 25.0 |
| | Treated events (n) | 157 | 165 | 62 | 384 |
| | ABR / patient / year (mean +/- sd) | 3.2 +/- 4,4 | **6.6 +/- 6,9[b]** | 4.4 +/- 5.0 | 4.4 +/- 5.4[a] |
| | FVIII for ABR (IU/patient/year) (mean +/- sd) | 9,201 +/- 14,057 | **22,818 +/- 26,119[b]** | 10,346 +/- 19,448 | 13,083 +/- 19,568[a] |
| T2 | Weight in kg (mean +/- sd) | 56.2 +/- 21.5 | 53.3 +/- 19.7 | 51.9 +/- 32.4 | 54.7 +/- 22.9 |
| | Treated events (n) | 164 | 100 | 49 | 313 |
| | ABR / patient / year (mean +/- sd) | 3.3 +/- 4.5 | **4.0 +/- 5.5[b]** | 3.5 +/- 3.4 | 3.6 +/- 4.6[a] |
| | FVIII for ABR (IU/patient/year) (mean +/- sd) | 10,092 +/- 13,436 | **12,957 +/- 16,552[b]** | *9,308 +/- 12,816* | 10,771 +/- 14,178[a] |

***For switched pwSHA (rFVIII-Fc only on T2), significant decrease of the ABR and of the amount of auto-injected FVIII***

*[a] Wilcoxon signed-rank test, non significant $\alpha$ = 5%*

*[b] Wilcoxon signed-rank test, significant $\alpha$ = 5% (p = 0.003 for ABR & p = 0.028 for administered FVIII)*

### Table 2: *ABR versus ABJR in matched patients (switched to rFVIII-Fc and non-switched only)*

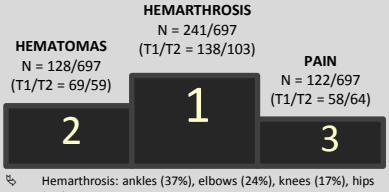
| Matched patients on prophylaxis over T1 = 07-2015/06-2016 & T2 = 07-2017/06-2018 + complete traceability logbook | Standard FVIII only over T2 (N = 49 patients) | | rFVIII-Fc only over T2 (N= 25 patients) | |
|---|---|---|---|---|
| | T1 | T2 | T1 | T2 |
| **Patients with ABR = 0 (n)** | 14 | 15 | 3 | 7 |
| **Patients with ABR ≠ 0 (n) / Total of treated bleeding events (n)** | 35 / 157 | 34 / 164 | 22 / 165 | 18 / 100 |
| **➔ ABR** | **ABR = 3.2[a]** | **ABR = 3.3[a]** | **ABR = 6.6[b]** | **ABR = 4.0[b]** |
| Whom patients treated for hemarthrosis / total of treated hemarthrosis | 17 /46 | 19 / 45 | 12 / 79 | 10 / 47 |
| **➔ ABJR** | **ABJR = 0.9[a]** | **ABJR = 0.9[a]** | **ABJR = 3.2[b]** | **ABJR = 1.9[b]** |

***For switched pwSHA (rFVIII-Fc only on T2), significant decrease of both the ABR and ABJR***

*[a] Wilcoxon signed-rank test, non significant $\alpha$ = 5% (ABR vs ABR & ABJR vs ABJR)*

*[b] Wilcoxon signed-rank test, significant $\alpha$ = 5% ( p =0.003 for ABRs and p = 0.033 for ABJRs)*

### Figure 2: self-treated bleeding events




- Hemarthrosis: ankles (37%), elbows (24%), knees (17%), hips (2%)…
- Hematomas: biceps (13%), forearms (8%), quadriceps (7%) , knees (6%)…
- Pain: ankles (19%), knees (17%), elbows (11%), wrists (6%)…