MOTHIF II: PRESENTATION
THERAPEUTIC MANAGEMENT AND USE OF CLOTTING FACTORS IN HEMOPHILIA A IN FRANCE (SHL FVIII vs rFVIII-Fc)

Clinical studies results of FVIII with Extended Half-Life , including efmoroctocog alfa (rFVIII-Fc):
⇔ Impact on the global prescriptions of FVIII: difference in term of FVIII consumptions (IU/kg/week or year)
⇔ Impact on the management of prophylaxis: reduction in injection frequency
⇔ Identical clinical efficacy (ABR)

What about real-life?   The *MOTHIF II* study

Retrospective study involving the French research database BERHLINGO & consumptions and treatment regimen analysis following launch on the market of new extended half-life clotting factors to assess budget impact

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This study is part of the **French network of University Hospitals HUGO** ("Hôpitaux Universitaires du Grand Ouest").
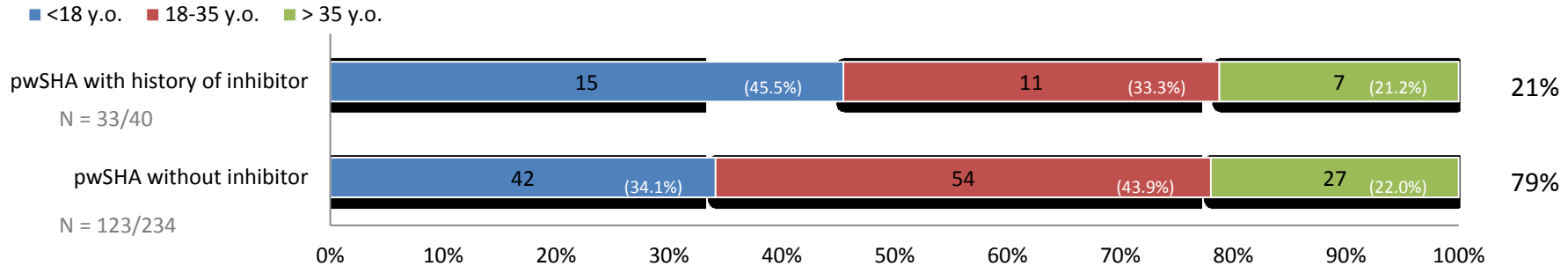
MOTHIF II: real-life, non-interventional, retrospective, before/after, uncontrolled, open label study	
Who?	Patients with severe Haemophilia A without current inhibitor, on *prophylaxis* (*pwSHA*)
Where?	7 Hemophilia Treatment Centers of the *BERHLINGO Group (Western France*) = Angers, Brest, Caen, Le Mans, Nantes, Rennes and Tours
When?	*2X12 months, before/after rFVIII-Fc supply* (**T1** = July 2015 – June 2016 **versus** **T2** = July 2017 – June 2018)
What?	Data from the *BERHLINGO database* = prescriptions of standard half-life (SHL) FVIII and rFVIII-Fc & Data from the French Nationwide Claims Database (SNDS)

MOTHIF II: POPULATION of pwSHA
THERAPEUTIC MANAGEMENT AND USE OF CLOTTING FACTORS IN HEMOPHILIA A IN FRANCE (SHL FVIII vs rFVIII-Fc)

274 severe patients with Hemophilia A without current inhibitor in the BERHLINGO cohort
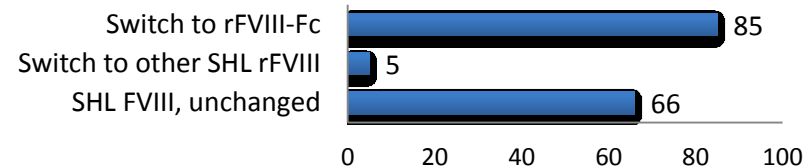➔ **156 pwSHA with complete prophylaxis prescriptions during T1 and T2**

■ <18 y.o. ■ 18-35 y.o. ■ > 35 y.o.

pwSHA with history of inhibitor — N = 33/40 — 15 (45.5%) | 11 (33.3%) | 7 (21.2%) — 21%

pwSHA without inhibitor — N = 123/234 — 42 (34.1%) | 54 (43.9%) | 27 (22.0%) — 79%

Switch to rFVIII-Fc in the same proportion, for patients with a history of inhibitor or without inhibitor

	pwSHA without inhibitor (n = 123)	pwSHA with history of inhibitor (n = 33)
No switch to rFVIII-Fc	55 (44.72%)	16 (48.48%)
Switch to rFVIII-Fc	68 (55.28%)	17 (51.52%)

(NS, α = 5%, Exact value of Fischer's test = 0,6996)

54% of pwSHA have switched to rFVIII-Fc

Switch to rFVIII-Fc — 85
Switch to other SHL rFVIII — 5
SHL FVIII, unchanged — 66

85 SWITCHES to rFVIII-Fc:
* 25% of the pwSHA initially treated with pdFVIII on T1 (n = 1/4)
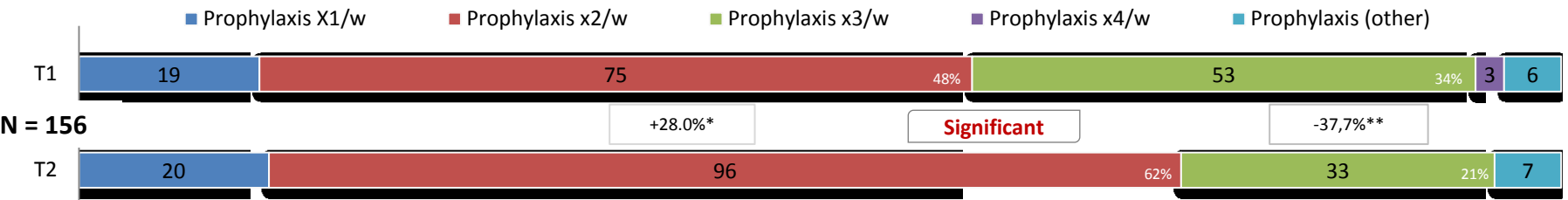** 56% of the pwSHA initially treated with rFVIII on T1 (n = 84/150)*

MOTHIF II: INJECTION FREQUENCY FOR PROPHYLAXIS
THERAPEUTIC MANAGEMENT AND USE OF CLOTTING FACTORS IN HEMOPHILIA A IN FRANCE (SHL FVIII VS RFVIII-FC)

After rFVIII-Fc supply:

Significant overall decrease in prescriptions of three FVIII injections per week (T.I.W.)
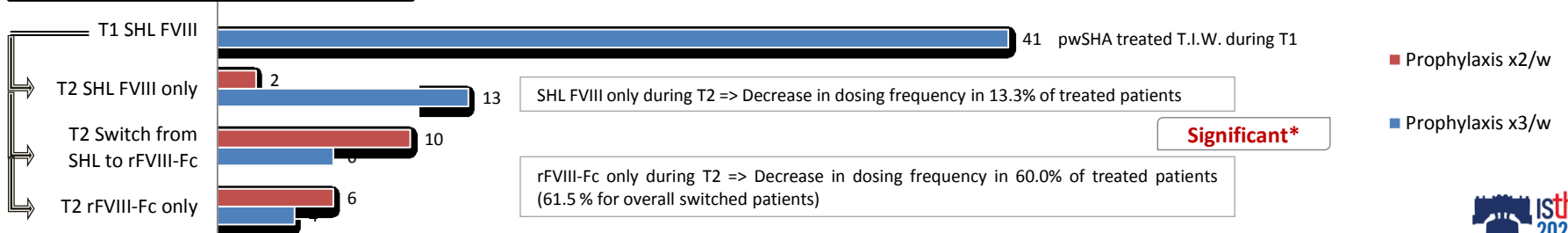
Significant overall increase in prescriptions of two FVIII injections per week (B.I.W.)

■ Prophylaxis X1/w   ■ Prophylaxis x2/w   ■ Prophylaxis x3/w   ■ Prophylaxis x4/w   ■ Prophylaxis (other)

N = 156

T1: 19 | 75 (48%) | 53 (34%) | 3 | 6

+28.0%*   Significant   -37,7%**

T2: 20 | 96 (62%) | 33 (21%) | 7

* Exact Fischer's test, independent samples, p = 0.0127. Significant, α = 5%.
** Exact Fischer's test, independent samples, p = 0.0158. Significant, α = 5%.

Patients initially on prophylaxis T.I.W.
(n = 41/53 with weight recorded)

Significant decrease in injection frequency for the patients switched to rFVIII-Fc (down to prophylaxis B.I.W.), compared to non-switched patients.

T1 SHL FVIII: 41   pwSHA treated T.I.W. during T1

T2 SHL FVIII only: 2 / 13

SHL FVIII only during T2 => Decrease in dosing frequency in 13.3% of treated patients

T2 Switch from SHL to rFVIII-Fc: 10 / 0

Significant*

T2 rFVIII-Fc only: 6

rFVIII-Fc only during T2 => Decrease in dosing frequency in 60.0% of treated patients (61.5 % for overall switched patients)

■ Prophylaxis x2/w
■ Prophylaxis x3/w

* Exact Fischer's test, independent samples, p = 0.028. Significant, α = 5%

Slide recording – PB0501 – author: **Valérie HORVAIS**, Nantes University Hospital, France

MOTHIF II: FVIII PRESCRIBED FOR PROPHYLAXIS in pwSHA
THERAPEUTIC MANAGEMENT AND USE OF CLOTTING FACTORS IN HEMOPHILIA A IN FRANCE (SHL FVIII vs rFVIII-Fc)

Similar amounts of FVIII prescribed/year/patient for prophylaxis during T1 and T2

↳ *regardless of the type of FVIII*

T2: significant overall decrease of the prescribed dose of FVIII/kg/week

↳ *Significant decrease in weekly dose on rFVIII-Fc*

Matched pwSHA, prophylaxis during T1 & T2. Weight information noted (n = 129/156 patients)		SHL FVIII during T1 and SHL FVIII only during T2 (N = 62)	SHL FVIII during T1 and switch from SHL to rFVIII-Fc during T2 period (N = 29)	SHL FVIII during T1 and rFVIII-Fc only during T2 (N = 38)	Total (N = 129)
T1	*Prescribed FVIII (IU/patient/year) (mean +/- sd)*	207,529 +/- 120,685	237,328 +/- 127,163	230,400 +/- 113,055	220,965 +/- 119,781
	Prescribed FVIII (IU/kg/week/patient) (mean +/- sd)	81.0 +/- 30.5	88.2 +/- 25.9	**83.1 +/- 38.7[a]**	**83.2 +/- 32.1[b]**
T2	*Prescribed FVIII (IU/patient/year) (mean +/- sd)*	211,135 +/- 106,154	232,208 +/- 98,809	220,402 +/- 91,138	218,602 +/- 99,884
	Prescribed FVIII (IU/Kg/week/patient) (mean +/- sd)	76.9 +/- 28.3	86.7 +/- 29.3	**75.2 +/- 38.0[a]**	**78.6 +/- 31.7[b]**

[a] *Wilcoxon signed-rank test, significant, α = 5% (p = 0.048) &*
[b] *Wilcoxon signed-rank test, significant, α = 5% (p = 0.006)*

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MOTHIF II: KEY POINTS
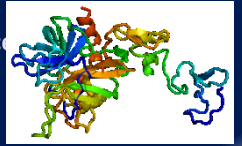## THERAPEUTIC MANAGEMENT AND USE OF CLOTTING FACTORS IN HEMOPHILIA A IN FRANCE (SHL FVIII vs rFVIII-Fc)

Does rFVIII-Fc have an impact on the injection frequency and on the FVIII prescriptions, in real-life, for pwSHA without inhibitor on prophylaxis, in comparison with SHL FVIII?

Real-life, non-interventional, retrospective, before/after, uncontrolled, open label study

| T1: SHL FVIII for all | → | rFVIII-Fc supply | → | T2: switched & non-switched pwSHA |

129 pwSHA whom*: BERHLINGO centers (France) On prophylaxis Complete prescriptions on T1/T2 (weight noted)	**Treatment unchanged SHL FVIII** N = 62 patients	**Switch to rFVIII-Fc only** N = 38 patients
Decrease of weekly injection frequency: x3/w *on T1* ➡ x2/w *on T2*	13% of treated patients *(n = 15)* ┊SIGNIFICANT┊	**60%** of treated patients *(n = 10)*
Prophylaxis dose of FVIII: T1 vs T2	81 Vs **77** IU/kg/week *T1 vs T2 = ↘ NOT SIGNIFICANT (n=62)*	83 Vs **75** IU/kg/week SIMILAR *T1 vs T2 = ↘ SIGNIFICANT (n = 38)*

*Results of 29 patients who switched to rFVIII-Fc during T2 not presented here

Similar results to the pivotal clinical trials regarding the **reduction of the weekly injection frequency**
Similar amounts of FVIII prescribed/pwSHA/year. No difference on the weekly prophylaxis dose between switched/non-switched patients at the end of the study.

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