REAL-WORLD EXPERIENCE IN HEMOPHILLIA B PATIENTS AFTER SWITCHING TO FIX EXTENDED HALF LIFE USING PHARMACOKINETIC POBLACIONAL SOFTWARE AND MONOCOMPARTIMENTAL MODEL

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Background and Importance

Extended half-life recombinant Factor IX concentrates (rFIX-EHL) have improved the feasibility of the prophylaxis program and the quality of life of the treated Hemophillia B (HB) patients, since they **dramatically increase the dosing interval and reduce the number of rFIX injections**

Aim and objectives

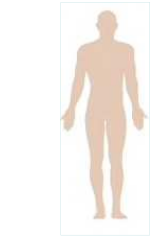
The efficiency of a pharmacokinetic-based tailored prophylaxis-dosing schedule versus standard dosing (DS) is compared, in HB, treated with two rFIX-EHL. Pharmacokinetics parameters were calculated.

Materials and methods

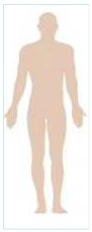
- ✓ Observational, analytical, prospective**, multicentre study**, involving HB patients, from **three different hospitals**, being treated with rFIX-EHL linked to albumin (rFIX-FP) or to fragment crystallizable (rFIX-Fc).
- ✓ Demographic and clinical data, and DS and dosing interval (DI) and actual FIX trough levels were recorded.
- ✓ Pharmacokinetic characterization was performed following both a population (WAPPS-HEMO) and a linear one-compartment (monocompartimental) approach. For each approach and rFIX preparation, **an estimation of the time to the target trough (5 IU FIX/dL)** was made. Statistical analysis was performed by means of the Student-Fischer t-test.

Results

Population
- 3 Samples / patient
- Concentrations according to first coagulative stage



6 patients rFIX-Fc (Mean age= 49 years, mean weight= 86 kg)



9 patients rFIX-FP (Mean age, 33 years, Mean weight 60 kg)

			One-compartment model		Population model WAPPS-HEMO	
Factor IX	**N**	**Standard dosing (DS)**	**Individual Tailored DI; Days with Cmin>5%**	**UI/day for T5**	**Individual Tailored DI; Days with Cmin>5%**	**UI/day for T5**
rFIX-FP	9	3222 UI (1716) / 11,9 days (4,4)	13,6 (5,1)*	240 (136)	15,0 (5,7)⁺	217 (115)
rFIXFc	6	4333 UI (606) / 14 days (0,0)	8,6 (1,2)**	508 (66)	10,2 (2,5)⁺⁺	450 (129)
Total patients	15	3667 UI (1460) / 12,7 days (3,5)	11,6 (4,7)	348 (175)	13,1 (4,8)	310 (165)

Table 1. Results how means (±∂) T: time , T5: Time with Cmin > 5% *11,9 days vs 13,6 days; p=0,40** 14 days vs 8,6 days; p<0,001. ⁺ 11,9 days vs 15,0; p=0,12 ⁺⁺ 14 days vs 10,2 days; p=0,012.

	Kel (h-1)	C0 (UI/dL)	Vd (mL/kg)	Cl (mL/h/kg)	$T_{1/2}$ (h)
X Mono (±∂)	0,0080 (0,0016)	54,01 (24,27)	117,29 (51,09)	0,906 (0,405)	**91,4** (19,0)
XWAPPS (±∂)	0,0054 (0,0012)	71,27 (21,24)	108,81 (26,82)	0,229 (0,267)	**135,7** (32,8)
P	0,002	0,001	0,442	**0,001**	**0,002**

Table 2 . One-compartment model vs WAPPS-HEMO for **rFIX-FP**. Results how means (X) and standard deviation (±∂)

	Kel (h-1)	C0 (UI/dL)	Vd (mL/kg)	Cl (mL/h/kg)	$T_{1/2}$ (h)
X Mono (±∂)	0,0278 (0,0452)	35,46 (11,12)	161,63 (50,88)	1,59 (0,52)	**71,9** (13,5)
XWAPPS (±∂)	0,0051 (0,0009)	125,60 (19,72)	217,41 (22,53)	0,12 (0,03)	**148,6** (24,4)
P	> 0,001	0,267	0,041	**0,001**	**0,001**

Tabla 3: One-compartment model vs WAPPS-HEMO for **FIXFc**. Results how means (X) and standard deviation (±∂)

Conclusion and relevance

*The efficiency of rFIX-EHL treatment following a pharmacokinetic-based tailored prophylaxis-dosing schedule versus DS, in HB patients, is significantly higher. Depending on the commercial preparation, rFIX-FP or rFIX-Fc, the daily-adjusted dose, for a 5 IU FIX/dL trough target, ranges between 217 – 240 IU/day for rFIX-FP, or 450 – 508 IU/day for rFIXFc, according to the two pharmacokinetic approaches (individually and population based).

*There are differences between Cl and t ½ parameters when there were evaluated using the one-compartment model. rFIX-FP half life was longer (91h) versus rFIXFc half life (71.9h). No differences between rFIX-FP and rFIXFc was reported using the pharmacokinetic population software (WAPPS-HEMO)