# Pharmacokinetics of a plasma-derived von VWF/FVIII concentrate (Voncento®) in adult/adolescent and pediatric subjects with severe hemophilia A (SWIFT-HA and SWIFTLY-HA studies)

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## Introduction and Objective

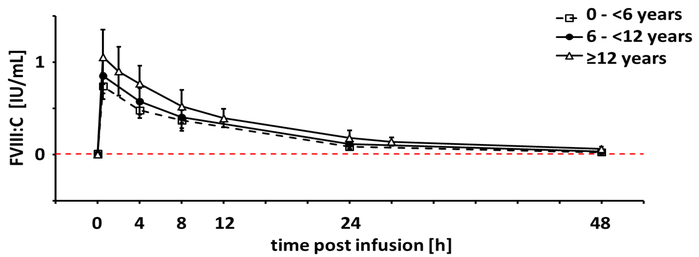
Voncento® is a plasma-derived, high-concentration, low-volume, high-purity concentrate, which contains a high level of high-molecular-weight multimers and a VWF:FVIII ratio of ~2.4:1. The SWIFT ("**S**tudies with von **Wi**llebrand factor/**F**ac**t**or VIII") program is evaluating this product in hemophilia A and VWD patients in accordance with the European clinical and pediatric guidelines. Within this program the pharmacokinetics (PK) of pretreated children <12 yrs, adolescents and adult patients with severe hemophilia A (FVIII:C <1%) was studied.

## Study Design

Subjects with severe hemophilia A received Voncento® as a single bolus infusion of 50 IU FVIII/kg body weight (n=31: children < 12 years of age; n=16: adults/adolescents). PK parameters for VWF and FVIII were derived from plasma concentration values collected prior to dosing and at 0.5, 4, 8, 24, and 48 h after infusion. PK parameters comprised Incremental recovery (IR), Half-life ($t_{1/2}$), AUC, $C_{max}$, Mean residence time (MRT), Clearance (CL), Volume of distribution at steady state ($V_{ss}$).

## PK parameters of FVIII:C

Mean (SD) concentration profiles [IU/mL] of FVIII:C




| FVIII:C | Age 0 - <6 years | | Age 6 – 12 years | | Age ≥ 12 years | |
|---|---|---|---|---|---|---|
| | N | Median (range) | N | median (range) | N | median (range) |
| **IR [(IU/mL)/(IU/kg)]** | 15 | 0.015 (0.009-0.019) | 16 | 0.016 (0.010-0.026) | 16 | 0.021 (0.011-0.032) |
| **$t_{1/2}$ [h]** | 15 | 9.62 (7.75-18.20) | 16 | 10.00 (8.89-12.50) | 16 | 13.74 (8.78-18.51) |
| **MRT [h]** | 15 | 13.51 (7.95-17.38) | 16 | 13.89 (12.11-17.07) | 16 | 16.62 (11.29-26.31) |
| **$AUC_{0-48}$ [h*IU/mL]** | 15 | 8.23 (3.96-11.04) | 16 | 9.90 (6.16-17.62) | 16 | 13.09 (7.04-21.79) |
| **$C_{max}$ [IU/mL]** | 15 | 0.75 (0.46-0.94) | 16 | 0.84 (0.51-1.21) | 16 | 1.07 (0.57-1.57) |
| **CL [mL/(h*kg)]** | 15 | 6.22 (4.22-11.34) | 16 | 4.88 (2.54-7.74) | 16 | 3.82 (2.30-7.11) |
| **$V_{ss}$ [mL/kg]** | 15 | 75.3 (63.8-197.2) | 16 | 71.9 (42.1-109.3) | 16 | 61.2 (35.1-113.1) |

AUC = area under the curve; Cmax = maximum plasma concentration; IU = International Unit; MRT = mean residence time; N = number of subjects;; Vss = volume of distribution at steady state; FVIII:C = Factor VIII: Coagulant

## Results

Concentration-time curves showed similar profiles for the adult/adolescents PK population and subjects aged < 12 years. The results for PK parameters for Factor VIII in pediatric population (< 12 yrs) are within the range of those in patients ≥ 12 years old. As expected the median IR of FVIII in the pediatric population (0-6/6-12 yrs) was slightly lower (0.015/0.016 [IU/mL]/[IU/kg]) compared to adult/adolescents hemophilia A subjects (0.021 [IU/mL]/[IU/kg]), the median $t_{1/2}$ was shorter (9.62/10.00 h vs. 13.74 h) and the median CL was higher (6.02/4.88 vs. 3.82 mL/h/kg).

## Conclusion

The results for PK parameters for Factor VIII in pediatric population (< 12 yrs) are within the range of those in patients ≥ 12 years old, thus considered as comparable with the adolescents and adults. The small differences are not considered being clinically relevant. A contemporary comprehensive development program evaluating high concentration, low volume Voncento® across all age groups in hemophilia A is now available.

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