Pasteurized plasma-derived VWF/FVIII concentrate (Humate P): long-term prophylaxis in von Willebrand disease

PB1446

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Introduction

- von Willebrand disease (VWD) is an inherited bleeding disorder caused by deficient/dysfunctional von Willebrand factor (VWF)[1]
- VWF replacement therapy is used in VWD management[2,3]
  - One example is pasteurized plasma-derived human VWF/factor VIII concentrate (pdVWF/FVIII), indicated for treatment of bleeding and surgical prophylaxis in VWD[4]
- While pasteurized pdVWF/FVIII is not indicated for long-term prophylaxis (LTP) in VWD in the USA,[4] it is indicated for LTP in VWD, when appropriate, in the EU[5]
  - Real-world experiences have demonstrated the safety and efficacy of its use for LTP in VWD[2]
- The ongoing ATHN 9: Severe VWD Natural History Study (NCT03853486), sponsored by the American Thrombosis & Hemostasis Network (ATHN), is investigating VWF treatment regimens in severe VWD in the USA[6]

Objective

- **To report the use of LTP with pasteurized pdVWF/FVIII in severe VWD**

Table 1: Characteristics of participants who received LTP with pasteurized pdVWF/FVIII at any point during follow-up

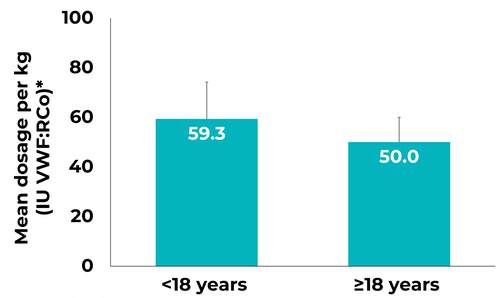
Characteristic	N=21
Age, years	
Mean (SD)	36.3 (26.7)
Median (range)	33 (4–88)
Child/adolescent, n (%)*	8 (38.1)
Adult, n (%)	13 (61.9)
Female sex, n (%)	14 (66.7)
Race, n (%)	
White	19 (90.5)
Black or African American	2 (9.5)
VWD type, n (%)	
1	1 (4.8)
2A	7 (33.3)
2B	2 (9.5)
2M	0 (0)
2N	0 (0)
3	6 (28.6)
Not available	5† (23.8)
Mean (SD) duration of LTP with pasteurized pdVWF/FVIII, months	18.9 (7.0)

*Child/adolescent was <18 years of age. †Includes one participant with VWD, type 2, type unknown.
LTP, long-term prophylaxis; pdVWF/FVIII, plasma-derived human von Willebrand factor/factor VIII concentrate; SD, standard deviation; VWD, von Willebrand disease; VWF, von Willebrand factor.

Methods

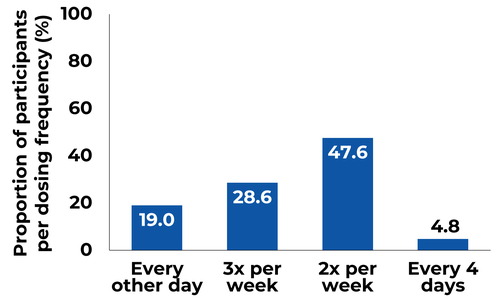
- ATHN 9 is a longitudinal, observational and prospective study to characterize the safety and effectiveness of factor replacement in participants with clinically severe congenital VWD[6]
- Exclusion criteria for the ATHN 9 study were diagnosis of platelet-type VWD or acquired VWD[6]
- Inclusion criterion for this analysis was any participant who received LTP with pasteurized pdVWF/FVIII prior to April 30, 2024
- Baseline characteristics, consumption and infusion frequency, and bleeding events were collected
- The participants' age as of their birthday in 2023 was used for this analysis

Figure 1: Mean consumption of pasteurized pdVWF/FVIII during most recent LTP regimen



*For dosage per kg, n=4 for <18 years of age and n=7 for ≥18 years of age.
†For dosage per infusion, n=4 for <18 years of age and n=6 for ≥18 years of age.
IU, international units; LTP, long-term prophylaxis; pdVWF/FVIII, plasma-derived human von Willebrand factor/factor VIII concentrate; RCo, ristocetin cofactor; SD, standard deviation; VWD, von Willebrand disease; VWF, von Willebrand factor.

Figure 2: Dosing frequency during most recent LTP regimen with pasteurized pdVWF/FVIII (N=21)



LTP, long-term prophylaxis; pdVWF/FVIII, plasma-derived human von Willebrand factor/factor VIII concentrate.

Results

PATIENTS

- Overall, 21 participants received LTP with pasteurized pdVWF/FVIII at any time point during follow up
- Participant characteristics are summarized in **Table 1**
- Mean (SD) age was 36.3 (26.7) years and 14 participants (66.7%) were female
- Type 2A (33.3%) and type 3 (28.6%) were the most common VWD types
- Mean (SD) duration of LTP with pasteurized pdVWF/FVIII was 18.9 (7.0) months

CONSUMPTION

- Using the most recent LTP regimen, mean (SD) dosage per kg was 59.3 (14.9) IU VWF:RCo for children/adolescents and 50 (10.0) IU VWF:RCo for adults **(Figure 1)**
  - Twice weekly was the most common dosing frequency (47.6%)
  - Dosing frequency is summarized in **Figure 2**

EFFICACY

- During LTP with pasteurized pdVWF/FVIII in the study, 12 (57.1%) participants did not have a treated bleed, of which 6 (28.6%) had zero bleeds **(Table 2)**
- Eighty-nine bleeds were recorded during the study period
  - Of these 89 bleeds, 64 were treated bleeds
- Ten (47.6%) participants experienced 35 spontaneous bleeds, constituting 39.3% of all bleeds
  - The most common bleeds were mucosal (tooth/mouth related and nosebleeds), constituting 71.4% of spontaneous bleeds, followed by gastrointestinal bleeds (20.0%)
- Eight (38.1%) participants experienced 24 traumatic bleeds, representing 27.0% of all bleeds
  - Of these, the most common site of bleeding was within 'tissue', constituting 58.3% of traumatic bleeds; joint bleeds represented 20.8% of traumatic bleeds

SAFETY

- No thrombotic events and no inhibitors were reported

Table 2: Recorded bleeds during LTP with pasteurized pdVWF/FVIII

Participants with zero bleeds, n (%)	6 (28.6)
All bleeds, n (%)	15 (71.4)
Number of events	89
Treated bleeds, n (%)	9 (42.9)
Number of events	64
Spontaneous bleeds, number affected (number of events)	10 (35)
Gastrointestinal	5 (7)
Nosebleed	4 (9)
Tissue	2 (2)
Tooth/mouth related	5 (16)
Other	1 (1)
Traumatic bleeds, number affected (number of events)	8 (24)
Nosebleed	1 (1)
Joint	3 (5)
Tissue	5 (14)
Tooth/mouth related	4 (4)
Other, number affected (number of events)	10 (30)
Activity or exercise without known trauma	1 (1)
Dental procedure	1 (1)
Menstrual bleeding	2 (9)
Other	2 (2)
Unknown	7 (17)

LTP, long-term prophylaxis; pdVWF/FVIII, plasma-derived human von Willebrand factor/factor VIII concentrate.

Conclusions

- **Pasteurized pdVWF/FVIII has been widely used in the USA for over 40 years**
- **Multiple real-world studies, across various countries, have been published on the use of pasteurized pdVWF/FVIII for LTP in VWD[2]**
- **Here, we report the use of LTP with pasteurized pdVWF/FVIII over a mean duration of 18.9 months during the ATHN 9 study**
  - **Collected data demonstrated prophylactic use of pasteurized pdVWF/FVIII prior to study enrollment in the majority of participants (data not shown)**
- **Data from the ATHN 9 study continues to support the efficacy and safety of pasteurized pdVWF/FVIII for LTP in severe VWD**

References

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Disclosures

RFS: has consulted for Takeda, Pfizer, Bayer, Novo Nordisk, Octapharma, Sanofi/Sobi, Vega, Guardian Therapeutics, LFB, Hema Biologics; received IIS from Takeda, LFB/Hema Biologics, Octapharma; DSMB: Uniqure/CSL Behring; and is Chair of ATHN. **TCS:** has consulted for Octapharma, Bayer, Novo Nordisk, CSL Behring, Genentech, Biomarin, Takeda, Hema Biologics, Kedrion, Sanofi; involved in speaker bureaus for Octapharma, Genentech, Biomarin, Novo Nordisk, CSL Behring, Takeda, Hema Biologics; received Honoria from Octapharma, Genentech, CSL Behring, Novo Nordisk, Takeda, Hema Biologics, Biomarin; research funding from Spark and Biomarin; DMSC from Pfizer. **MC, ND** and **CF** report no conflict of interest related to this study. **TD and VD:** are employees of CSL Behring. **AW:** has consulted for Takeda, Pfizer, Bayer, Novo Nordisk, Octapharma, Sanofi/Sobi, Genentech/Roche, Biomarin, Spark, Hemab, Hema Biologics; research grants from Sanofi, Novo Nordisk, Pfizer, Takeda; DSMB from Takeda.

Funding

The ATHN 9 study was sponsored by the American Thrombosis & Hemostasis Network (ATHN).

Acknowledgements

Medical writing support was provided by Bioscript Group, Macclesfield, UK, in accordance with Good Publication Practice guidelines, and funded by CSL Behring. All authors reviewed the results and approved the final version of the poster.

Presented at the 33rd Congress of the International Society on Thrombosis and Hemostasis (ISTH), Washington D.C, WA, USA, June 21–25, 2025.