Poster 1301

A retrospective analysis of the safety and effectiveness of recombinant von Willebrand factor in children with von Willebrand disease undergoing surgery

Tammuella Chrisentery-Singleton, MD[1,2], Robert F. Sidonio, MD[3], Angela Weyand, MD[4], Priscilla Driscoll Shempp, MBA[5], Christine M. Gerber, BS[1], Jianzhong Hu, PhD[1], Michelle Kirby, MS[5], Caitlin Montcrieff, MSN[5], and Jorge Caicedo, MD[5]

[1]American Thrombosis & Hemostasis Network, Hickory, NC, USA; [2]Ochsner Clinic Foundation, New Orleans, LA, USA; [3]Department of Pediatrics, Emory University School of Medicine, Atlanta, GA, USA; [4]Department of Pediatrics, University of Michigan Medical School, Ann Arbor, MI, USA; [5]Takeda Pharmaceuticals U.S.A., Inc., Lexington, MA, USA

Introduction

- Von Willebrand disease (VWD), caused by deficiencies or abnormalities in von Willebrand factor (VWF), is the most common inherited bleeding disorder[1]
  - Type 1 and Type 3 phenotypes are caused by partial and complete deficiencies of VWF, respectively
  - Type 2 is caused by qualitative defects in VWD and includes four subtypes (Type 2A, Type 2B, Type 2M, Type 2N)
- Individuals with VWD may experience excessive bleeding during surgical procedures, necessitating perioperative management with available treatments[2]
- Recommendations on perioperative management are included in current management guidelines, which include suggestions to tailor therapy to the procedure's bleeding risk and to use VWF concentrates for individuals requiring a significant increase in VWF activity levels[3]
- In September 2025, recombinant VWF (rVWF) was approved for the perioperative management of bleeding in pediatric patients with VWD[4]
- This retrospective study describes the safety and effectiveness of perioperative rVWF in pediatric individuals with VWD in a real-world setting

Methods

- This study is a retrospective, observational analysis of pediatric patients (aged <18 years) diagnosed with VWD with at least one surgical procedure managed with rVWF[a] from the ATHNdataset[b]
  - Participants with severe VWD[c] were included in a subgroup analysis
- Study inclusion/exclusion criteria are shown in **Table 1**
- Study design and outcomes are shown in **Figure 1**

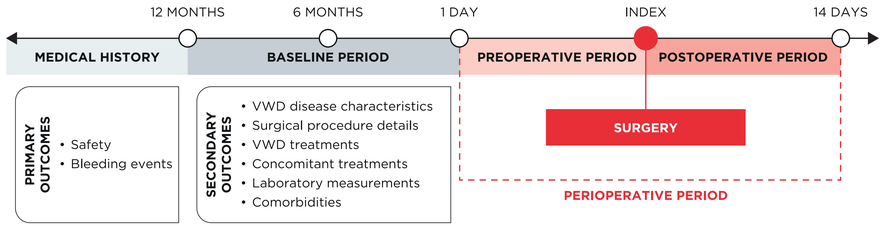
[a]rVWF treatment either recorded within 48 hours of surgical procedure or indicated as pre-procedure dose. [b]The American Thrombosis & Hemostasis Network (ATHN) is the steward of the ATHNdataset, a Health Insurance Portability and Accountability Act-compliant, de-identified patient health dataset containing data from individuals with bleeding disorders receiving care through ATHN affiliates who opt in to contribute. [c]von Willebrand factor ristocetin cofactor activity assay (VWF:RCo) <20 IU/dL.

Table 1. Inclusion and exclusion criteria

INCLUSION	EXCLUSION
Diagnosis of hereditary VWD	Neutralizing antibodies to VWF
≥1 surgical procedure managed with rVWF occurring while aged <18 years	Diagnosis of any other bleeding disorder or factor deficiency
Enrollment in the ATHNdataset	
6 months of clinical data before surgery	
14 days of clinical data after surgery	

ATHN, American Thrombosis & Hemostasis Network; rVWF, recombinant von Willebrand factor; VWD, von Willebrand disease; VWF, von Willebrand factor.

Figure 1. Study design



VWD, von Willebrand disease.

Results

- This analysis included nine participants in the full cohort and four participants with severe VWD in the subgroup
- Participant demographic and disease characteristics are listed in **Table 2**
- Baseline disease markers were available from two participants, both of whom were in the subgroup
  - Mean (SD) factor VIII (FVIII) activity was 64.8 (51.9) IU/dL, and mean (SD) VWF antigen assay and VWF:RCo measurements were 33.5 (11.8) IU/dL and 4.0 (0.0) IU/dL, respectively

Table 2. Participant demographic and disease characteristics

DEMOGRAPHIC CHARACTERISTICS	TOTAL (N=9)	SUBGROUP (n=4)
Age at time of surgical procedure, years		
Mean (SD)	12.8 (4.0)	13.3 (4.8)
Median (range)	13.0 (6.0–17.0)	14.5 (7.0–17.0)
Sex assigned at birth, n (%)		
Female	6 (66.7)	2 (50.0)
Male	3 (33.3)	2 (50.0)
Race, n (%)		
Asian	1 (11.1)	1 (25.0)
Black/African American	1 (11.1)	0
White	7 (77.8)	3 (75.0)
Ethnicity, n (%)		
Hispanic, Latino, or Spanish origin	2 (22.2)	1 (25.0)
Not Hispanic, Latino, or Spanish origin	7 (77.8)	3 (75.0)
VWD type, n (%)		
Type 1	6 (66.7)	1 (25.0)
Type 2A	3 (33.3)	3 (75.0)
Mean diagnostic markers[a], IU/dL (SD)		
VWF:Ag	39.3 (23.0)	20.8 (15.4)
VWF:RCo	28.1 (20.5)	8.5 (5.2)
Identified genetic defect[b], n (%)	2 (22.2)	2 (50.0)
Pathogenicity of identified genetic defect, n (%)		
Pathogenic	2 (22.2)	2 (50.0)
Variant of unknown significance	1 (11.1)	1 (25.0)
Comorbidities, n (%)		
Iron deficiency/anemia	2 (22.2)	0
Other[c]	2 (22.2)	0

[a]The lowest laboratory value from all historical laboratory measurements. [b]A total of four genetic defects in two participants were identified. [c]Other comorbidities include anxiety, asthma, Ehlers-Danlos syndrome, epistaxis, abdominal wall hernia, hearing loss, and ulcerative colitis.
VWD, von Willebrand disease; VWF:Ag, von Willebrand factor antigen; VWF:RCo, von Willebrand factor ristocetin cofactor.

Recombinant von Willebrand factor was effective in the management of surgical bleeding in pediatric individuals with von Willebrand disease, with no new identified safety signals

Summary and Conclusions

- **Most of the pediatric participants in the full cohort were diagnosed with Type 1 VWD; most in the subgroup with severe VWD were diagnosed with Type 2A VWD**
- **There were no adverse events or treatment-emergent side effects; two participants reported three allergic reactions to pdVWF**
- **Of the 12 surgeries in the full cohort, most were gastrointestinal or genitourinary, and minor in severity; all of the eight procedures with known outcomes were reported as successful**
- **The four surgeries in the subgroup were split between ear, nose, and throat procedures and gastrointestinal or genitourinary procedures; most of the procedures were minor in severity and both of the procedures with known outcomes were reported as successful**
- **There were no postoperative bleeds reported**
- **None of the procedures required FVIII, tranexamic acid, desmopressin, anemia treatment, or transfusion for hemostatic control**

References

1. Kalot MA, et al. *Haemophilia*. 2020;26:106–116.
2. O'Donnell JS and Lavin M. *Hematology Am Soc Hematol Educ Program*. 2019;2019:604–609.
3. Connell NT, et al. *Blood Adv*. 2021;5:301–325.
4. VONVENDI [von Willebrand factor (recombinant)]. Prescribing Information. Takeda US Inc.; September 2025.
5. Peyvandi F, et al. *J Thromb Haemost*. 2019;17:52–62.

Acknowledgments

This study was funded by Takeda Pharmaceuticals U.S.A., Inc., Cambridge, MA, USA. Medical writing support was provided by Nivedita Saxena, an employee of Parexel, and was funded by Takeda Pharmaceuticals U.S.A., Inc.

Presented at the ASH Annual Meeting & Exposition, December 6–9, 2025
E-mail contact: tsingleton@athn.org
This poster is intended for healthcare professionals

Results (continued)

Baseline Treatments

- Two participants (22.2%) had reported ever having received rVWF; both were included in the subgroup (50.0%)
  - One participant received rVWF as follow-up, and the other received rVWF as part of their routine prophylaxis regimen
- Five participants (55.6%) received plasma-derived VWF (pdVWF); four of these participants were in the subgroup (100%)
- One participant (11.1%) received antifibrinolytics; this participant was not in the subgroup

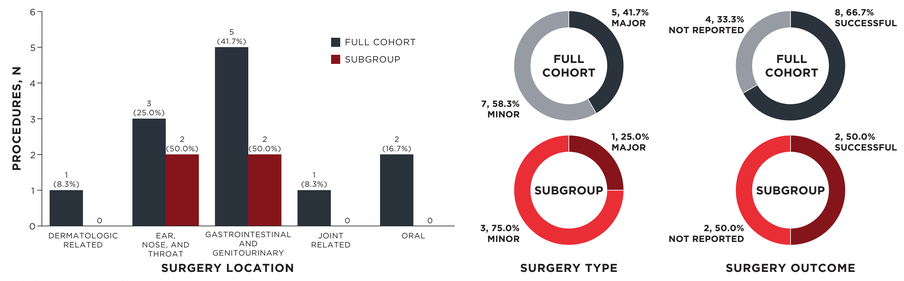
Safety

- There were no adverse events, as defined by the European Haemophilia Safety Surveillance program
- There were no treatment-emergent side effects, including hypersensitivity/allergic reactions, thrombotic events, VWF inhibitor development, transfusion-transmitted infections, malignancy, cardiovascular events, neurological events, or death
- Two participants (22.2%), of whom one was in the subgroup (25.0%), reported allergic reactions to treatment with pdVWF

Surgical Procedures

- Twelve surgical procedures in the full cohort, including four in the subgroup, were evaluated (**Figure 2**)
  - Eight surgeries in the full cohort, including two in the subgroup, were reported as successful; outcomes of the remaining four surgeries were not reported

Figure 2. Characteristics and outcomes of surgical procedures treated with rVWF



rVWF, recombinant von Willebrand factor.

- Twenty-two rVWF infusions, including ten in the subgroup, were administered for perioperative management (**Table 3**)
  - All procedures were treated with a mean (SD) of 1.0 (0) rVWF infusions in the preoperative/index period
  - Five procedures in the full cohort, including three in the subgroup, were treated with a mean (SD) of 0.8 (1.2) infusions (subgroup: 1.5 [1.3]) in the postoperative period
- No postoperative bleeds were documented
- No surgical procedures required FVIII, tranexamic acid, desmopressin, anemia treatment, or transfusion for hemostatic control
- pdVWF was postoperatively administered in one individual in the subgroup, related to the participant's routine prophylaxis regimen
- Antifibrinolytics were used in one procedure in the preoperative/index period and in a second procedure in the postoperative period

Table 3. Perioperative rVWF treatment patterns

	TOTAL (N=9)		SUBGROUP (N=4)	
	PROCEDURES (n=12)	INFUSIONS (n=22)	PROCEDURES (n=4)	INFUSIONS (n=22)
rVWF infusion by treatment time, n (%)				
Preoperative/index	12 (100)	12 (54.5)	4 (100)	4 (40.0)
Postoperative	5 (41.7)	10 (45.5)	3 (75.0)	6 (60.0)
	TOTAL DOSAGE	DOSAGE BY BODY WEIGHT[a]	TOTAL DOSAGE	DOSAGE BY BODY WEIGHT[a]
Mean dosage during the preoperative/index period, IU (SD)	2126.5 (1422.5)	43.0 (14.4)[b]	2105.0 (916.4)	43.9 (16.5)
Mean dosage during the postoperative period, IU (SD)	2139.0 (785.7)	53.1 (6.6)[c]	2616.7 (652.4)	53.1 (6.6)

[a]Only infusions administered to participants with weight measurements within the perioperative setting were included. [b]Dosage by body weight was available for 7/12 infusions. [c]Dosage by body weight was available for 6/10 infusions.
rVWF, recombinant von Willebrand factor.

Discussion

- Effectiveness results from this analysis, including surgery outcome and factor consumption, are consistent with previous reports on perioperative rVWF use in adult and pediatric phase 3 clinical trials[4,5]
- No new safety signals were identified[4]

Limitations

- This study has a small sample size, due to the rarity of pediatric individuals with VWD requiring surgery and perioperative management with rVWF in a real-world context
- Data for this analysis were extracted from the ATHNdataset[a]
  - Some data may have been unavailable during the defined study interval
  - The ATHNdataset includes clinical data from patients with bleeding disorders from across the United States, suggesting that these data may be generalizable to the broader population of children with VWD requiring perioperative management with rVWF

[a]The American Thrombosis & Hemostasis Network (ATHN) is the steward of the ATHNdataset, a Health Insurance Portability and Accountability Act-compliant, de-identified patient health dataset containing data from individuals with bleeding disorders receiving care through ATHN affiliates who opt in to contribute.