Treating VWD: what are the options?

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Conflicts of interest

Disclosure of conflict of interest for Sophie Susen

Research Support/P.I.	Biomarin, Bioverativ, CSL Behring, CorWave, Roche-Chugai, Sanofi, Shire/Takeda, Siemens Healthineers, Sobi, and Stago LFB
Employee	No relevant conflicts of interest to declare
Consultant	No relevant conflicts of interest to declare
Major Stockholder	No relevant conflicts of interest to declare
Speakers Bureau	No relevant conflicts of interest to declare
Honoraria	No relevant conflicts of interest to declare
Scientific Advisory Board	Biomarin, CSL Behring, LFB, Roche, Novo Nordisk, Sanofi, Sobi, and Takeda

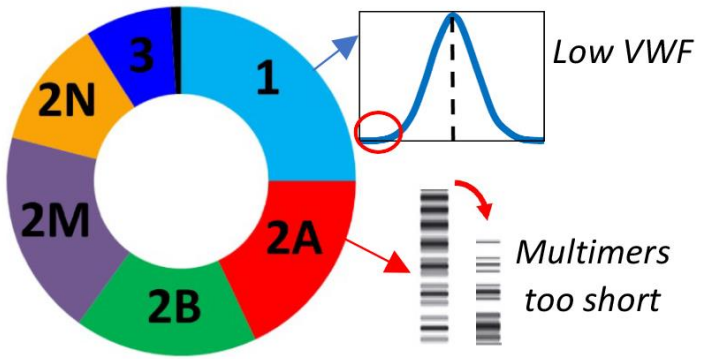
Fees go to Lille University, Lille University Hospital, association for research in cardiovascular pathology in Lille

Patients learning objectives

1. **Prophylaxis and access to home treatment**
2. **Desmopressin doesn't work for everyone**
3. **Hormone treatment options for women**
4. **Different types, different treatments**

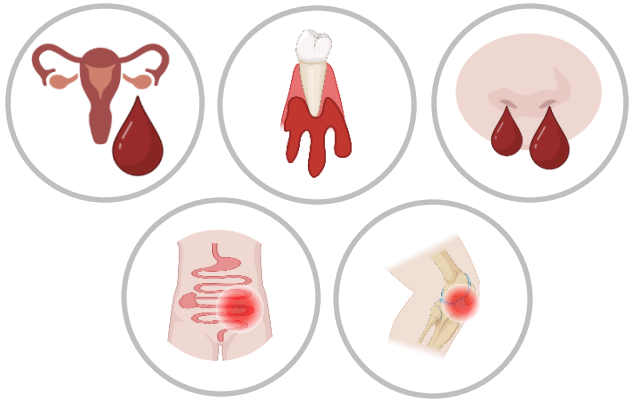
Von Willebrand disease: a heterogenous disease

A kaleidoscope of VWD types/sub-types



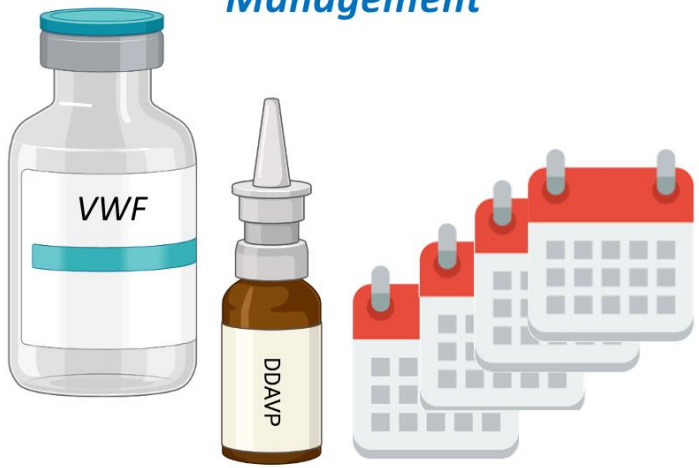
VWD is a heterogeneous disease affecting 1 per 10,0000 persons

A complex relationship between VWF and bleeding events



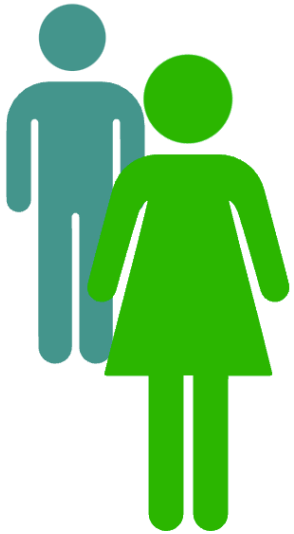
+ Heterogeneous bleeding symptoms

Management



unchanged over 30 years

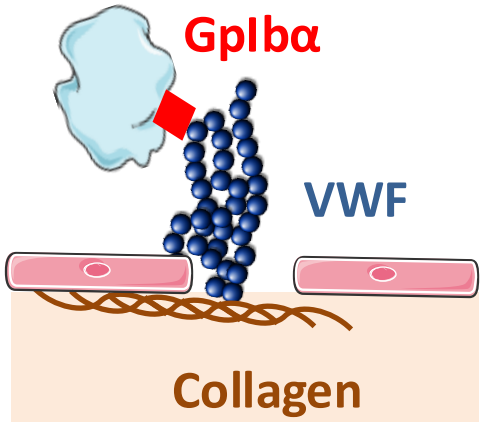
Wide variability in clinical practice, lack of high level of evidence

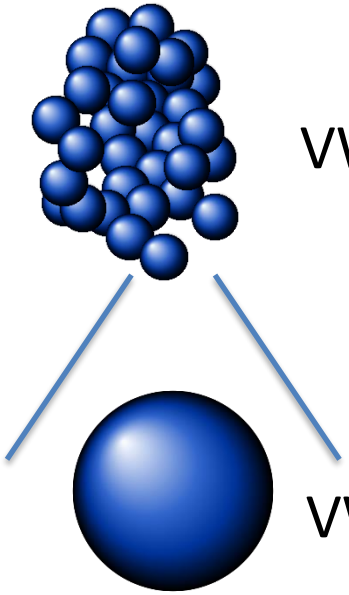


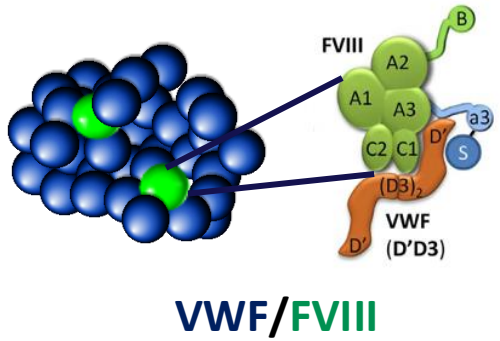
Sadler E et al. Thromb Haemost. 2000
Denis C et al. Blood. 2021
Casari C et al. Blood Adv 2023

von WILLEBRAND disease

VWF: multimeric and domain structure

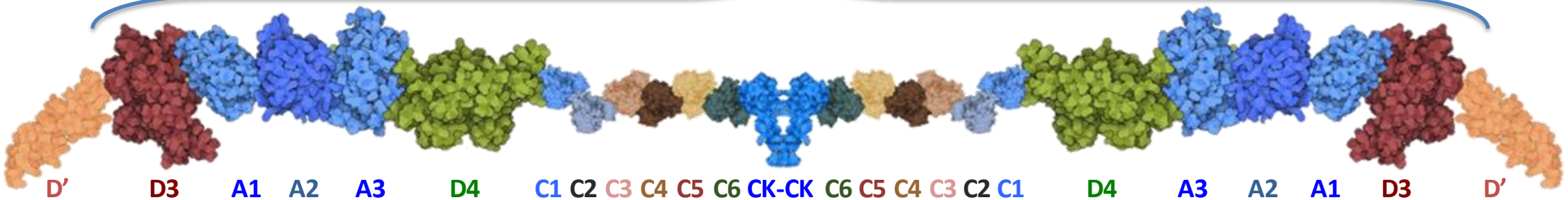






VWF/FVIII

VWF domain structure



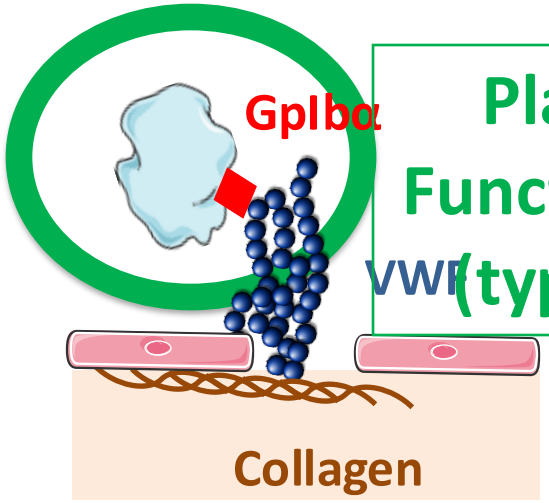
multimerization

dimerization

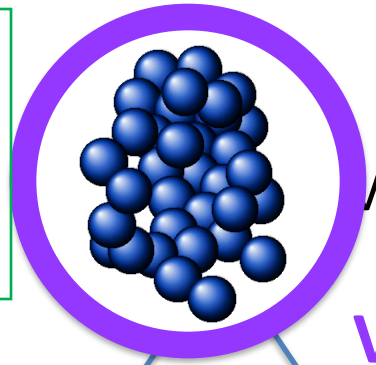
multimerization

Zhou YF et al. 2012

VWF: multimeric and domain structure

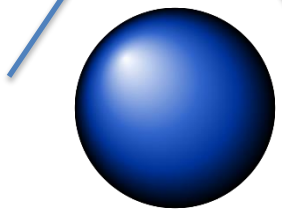


Platelet Function/nb?
VWF (type 2B)

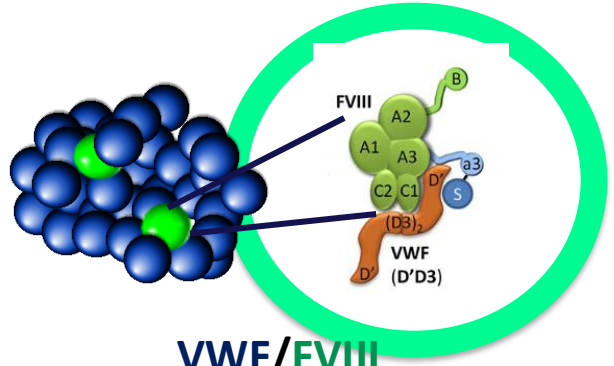


VWF multimer

VWF:Act ?



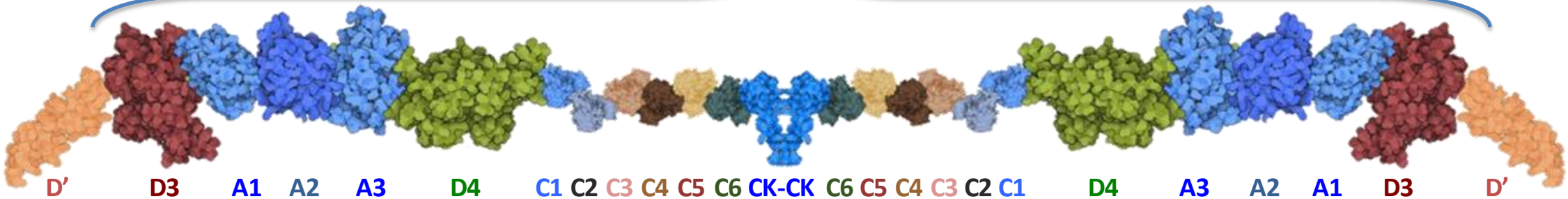
VWF dimer



VWF/FVIII

FVIII:C ?

VWF domain structure



multimerization

dimerization

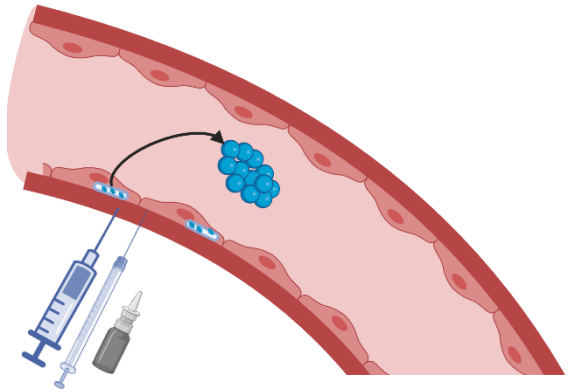
multimerization

Zhou YF et al. 2012

Current treatments for VWD

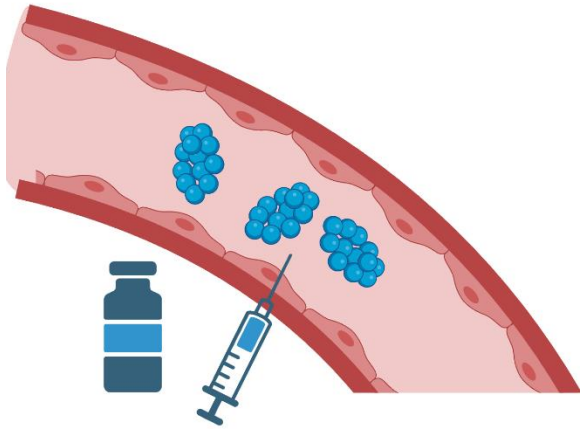
Increasing VWF and FVIII levels

DDAVP



SC or IV or intranasal

VWF products



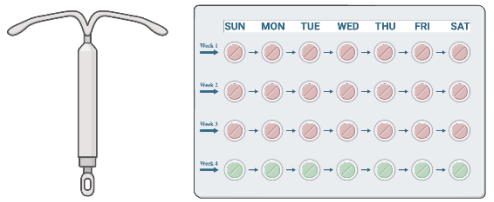
- pdVWF-FVIII, pdVWF
- rVWF

Adjunctive therapies

Antifibrinolytics

Tranexamic acid

Hormonal treatments



Estrogens+progestin
Progestin
Intrauterine device
(Levonorgestrel)

SC: subcutaneous
IV: intravenous

pdVWF: plasma derived VWF
rVWF: recombinant VWF

General principles of treatment in VWD

Table 1. Treatment of von Willebrand's Disease.*

Disease Type	Treatment	Alternative or Additional Treatment
Low VWF†	Desmopressin, administered intravenously (0.3 μg per kilogram of body weight), intranasally (total dose, 300 μg [150 μg per nostril]; in patients with body weight <50 kg, only one dose of 150 μg), or subcutaneously (0.3 μg per kilogram)	Alternative or additional treatment: tranexamic acid (1 g, 3 or 4 times daily)
Type 1	Desmopressin, at same doses as above	Additional treatment: tranexamic acid, at same dose as above
Type 2	Desmopressin, at same doses as above, or VWF–factor VIII or VWF concentrate‡	Additional treatment: tranexamic acid, at same dose as above
Type 3	VWF–factor VIII or VWF concentrate	Additional treatment: tranexamic acid, at same dose as above

Leebeek and Eikenboom , NEJM 2016

Who needs a general treatment plan?

Patients with VWD and ”low VWF”

- VWF:Act <30% and/or VWF antigen <30%
- VWF:Act between 30 – 50% and bleeding phenotype

The treatment plan should indicate if there is a need to correct FVIII/ access to home treatment

Minor bleeding
Major/life threatening bleeding

Minor surgery
Major surgery

Thresholds=>Treatment option

Treatment of VWD based on bleeding severity or intervention: threshold and duration

Indication or treatment	Target levels for VWF-ristocetin cofactor activity and FVIII activity‡ (IU/dL)	Duration of treatment (days)
Bleeding		
Mild to moderate	Peak, >50–80 on day 1; trough, >30 after day 1	1–3
Severe	Peak, >100 on day 1; trough, >50 after day 1	7–10
Intervention		
Dental extraction	Peak, >50 on day 1	1
Minor surgery	Peak, >50–80 on day 1; trough, >30 after day 1	1–5
Major surgery	Peak, >100 on day 1; trough >50 after day 1	7–10
Delivery	Peak >100 on day 1; trough, >50 after day 1	3–4

Leebeek F & Eikenboom J. N Engl J Med. 2016; 375:2067-80.

ASH/ISTH/WFH Guidelines

Major surgery

Recommendation 4a: Suggest target both FVIII and VWF:Ac of >0.50 IU/ml for at least 3 days

Recommendation 4b: Suggest against using only FVIII of >0.50 IU/ml for 3 days after surgery

=> never DDAVP

Minor surgery

Recommendation 5a: Suggest raising VWF:Ac with desmopressin or concentrate and use tranexamic acid

Recommendation 5b: Suggest giving tranexamic acid for patients with type 1 VWD with baseline VWF activity levels of 0.30 IU/mL and a mild bleeding phenotype undergoing minor mucosal procedures

Connell N et al, Blood Advances 2021

National Emergency Card for all rare diseases adapted for VWD

Information on treatment

Personnes à prévenir en priorité

Mme/M. _____ Tél : _____

Mme/M. _____ Tél : _____

Contacts médicaux

Médecin _____ Tél : _____

Suivi(e) par le centre de : _____

Tél : _____ (Jour ouvrable) Tél. : _____ (Nuit/fériés)

Téléphone médical en cas d'urgence: _____

Plus d'informations sur le site www.mhemo.fr (situation d'urgence) et www.orpha.net (Maladie de Willebrand/urgence)

CRMW orphanet MHEMO Association française des hémophiles

Ne pas utiliser

maladies rares

Photo

CARTE D'URGENCE

Emergency card

Maladie de Willebrand

Nom : _____

Prénom : _____

Date de naissance : _____

Risque hémorragique, prise en charge prioritaire : administrer un traitement spécifique en cas d'hémorragie ou d'intervention chirurgicale

Ne pas utiliser

Informations individuelles sur la maladie

Type de maladie de Willebrand :

☐ Type 1 (déficit quantitatif partiel) : ☐ Forme sévère ☐ Forme modérée

☐ Type 2 (déficit qualitatif) : ☐Type 2A ☐Type 2B ☐Type 2M ☐Type 2N

☐ Type 3 (déficit quantitatif total) ☐ Type indéterminé

Caractéristique biologique : VWF : Act (Activité fonctionnelle) : _____ %

VWF Ag (Antigène) : _____ % FVIII : _____ %

Plaquettes : _____ giga/L

Pour le type 3 inhibiteur anti-VWF : ☐ OUI ☐NON

Test à la desmopressine : Bon répondeur ☐ OUI ☐ NON

Médicament habituel de la maladie (traitement substitutif et posologie en UI/kg de poids corporel)

_____

Autres informations médicales utiles

_____

Ne pas utiliser

RECOMMANDATIONS EN CAS D'URGENCE

1. Le risque de survenue d'hémorragie grave, en particulier d'hémorragies cérébrales ou des muqueuses, dépend de l'importance du déficit

2. Pour toute question relative à la prise en charge, contacter le centre de suivi habituel du porteur de cette carte (voir la page des coordonnées)

3. Corriger la coagulation en urgence en cas d'hémorragie ou de traumatisme important et avant toute intervention chirurgicale ou geste invasif (ponctions, suture...) par injection de concentré de facteur Willebrand ou par Desmopressine si bon répondeur.

5. La prise d'aspirine ou d'anti-inflammatoire non-stéroïdien (AINS) est contre-indiquée.

6. Ecouter le patient : il connait sa maladie, son traitement et son centre de suivi

Ne pas utiliser

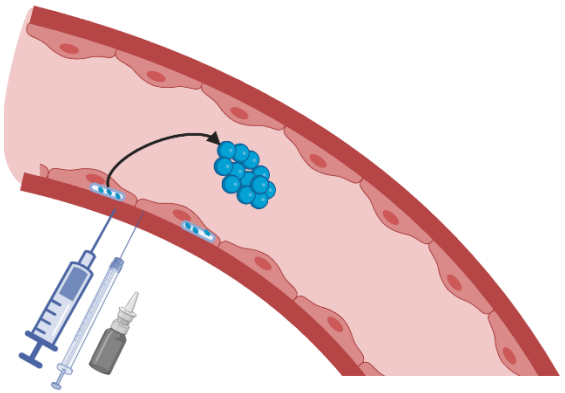
maladies rares

Liberté · Égalité · Fraternité
RÉPUBLIQUE FRANÇAISE
MINISTÈRE DES AFFAIRES SOCIALES ET DE LA SANTÉ

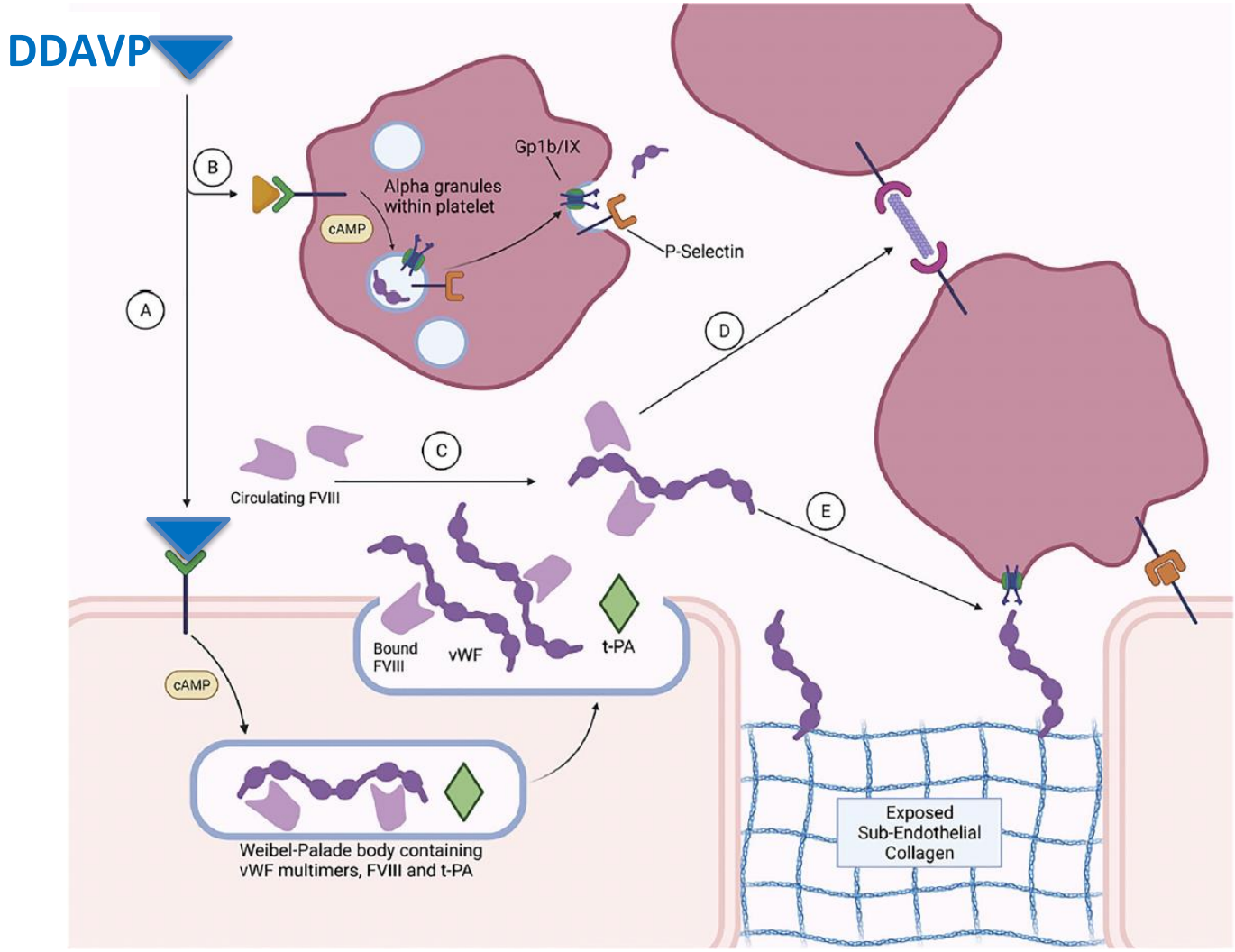
DIRECTION GÉNÉRALE DE L'OFFRE DE SOINS

Management of VWD with DDAVP

DDAVP



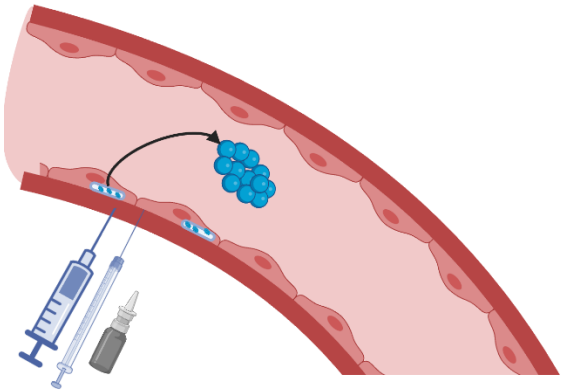
Mechanism of action



Mohinani et al. Eur J Haematol 2023

Management of VWD with DDAVP

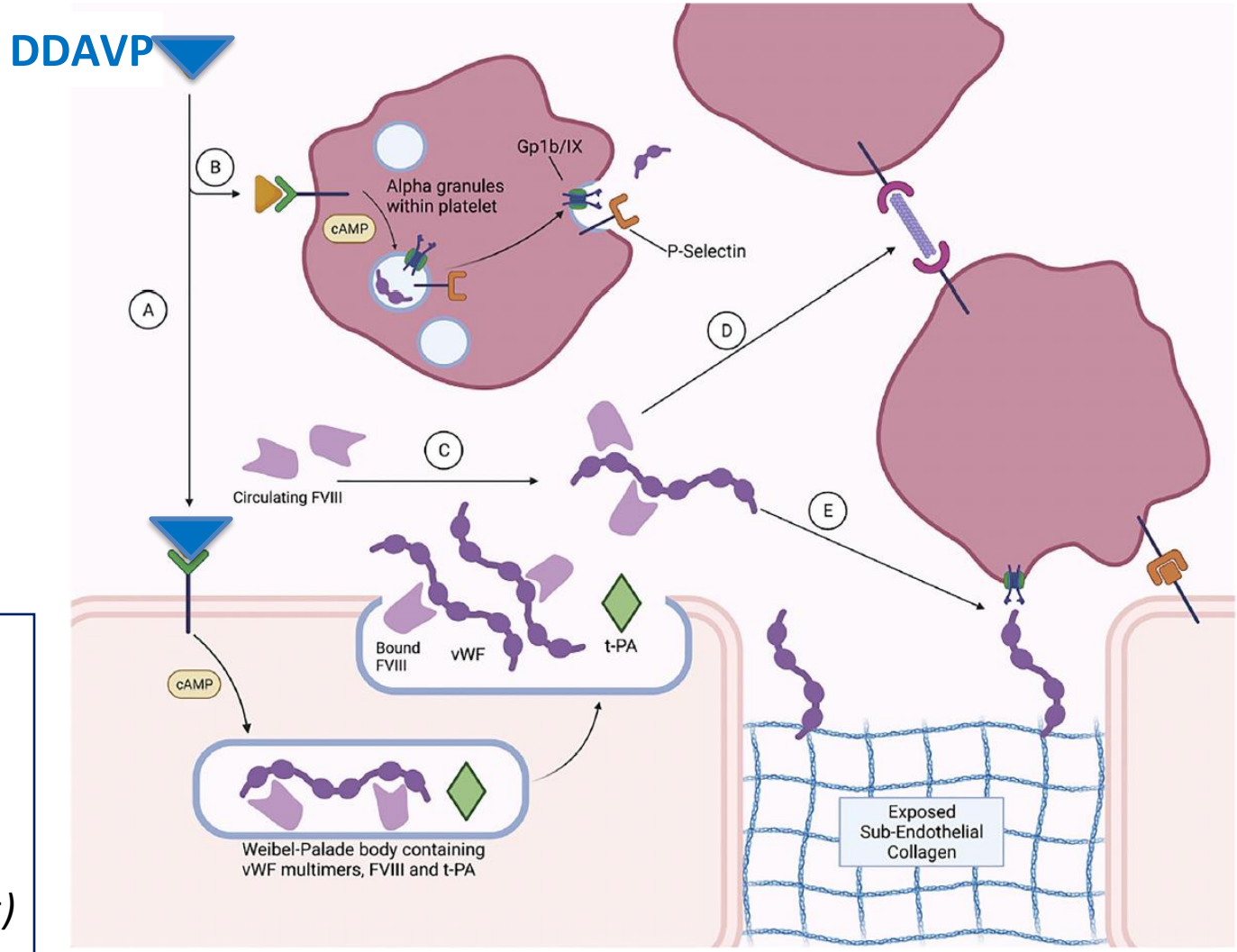
DDAVP



- ✓ **Short term effect**
- ✓ **Tachyphylaxis**
- ✓ **Variable inter-patient response**

=> *need for test dose*
VWF:Ag, VWF:Act, FVIII:C, platelets at 1h (synthesis)
And 4h (clearance) post-injection

Mechanism of action



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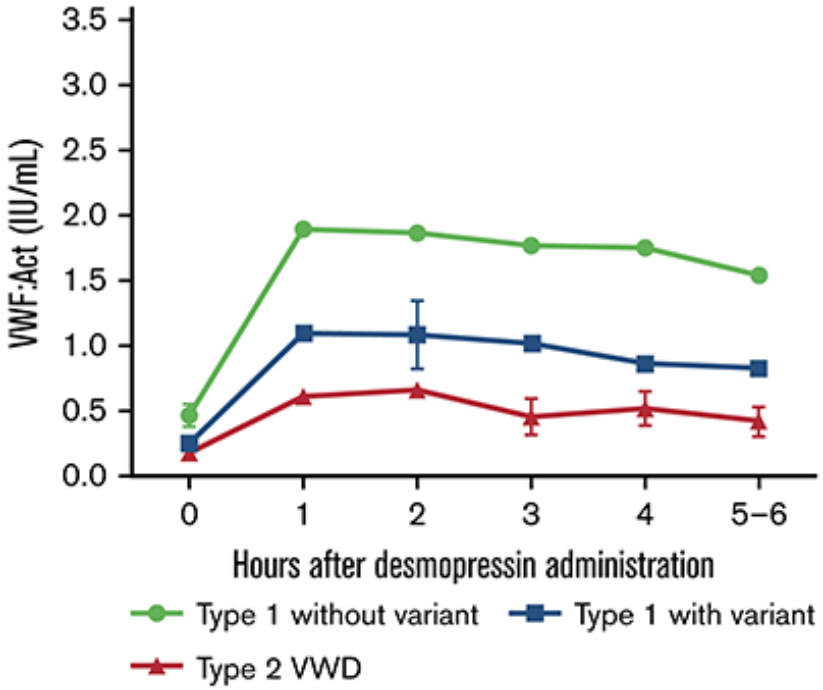
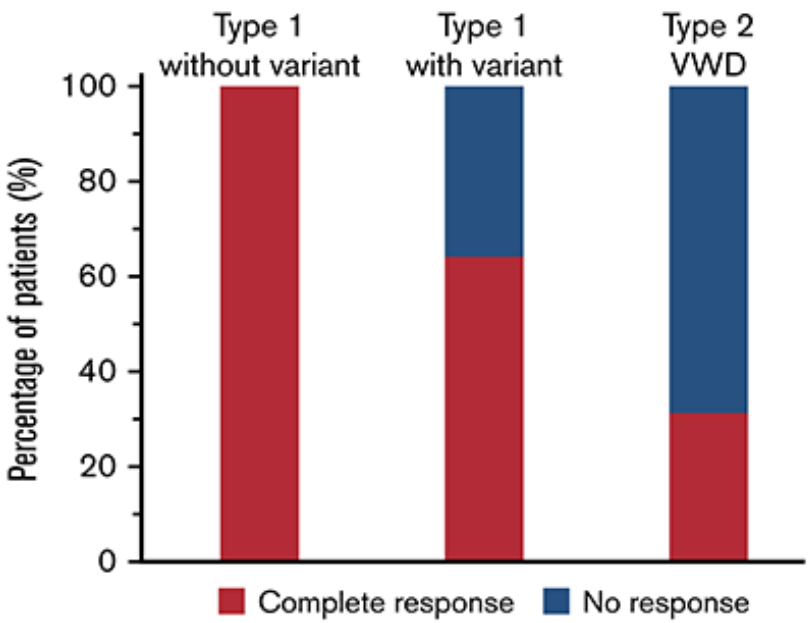
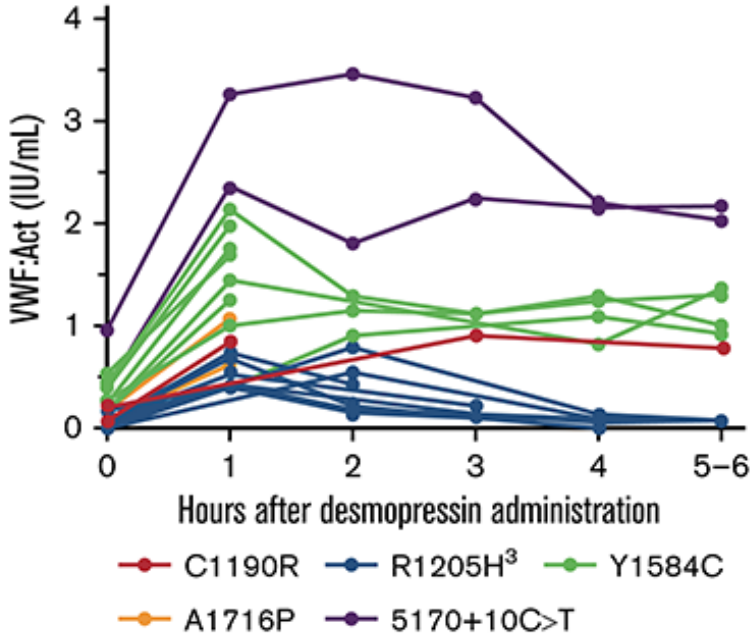
Desmopressin response depends on the presence of genetic variants



There is a clear difference in desmopressin response between patients with type 1 with and without a *VWF* gene variant and patients with type 2 VWD



Patients with type 1 VWD without a variant always have a complete response to desmopressin



The inter-individual variation in desmopressin response is explained by the genetic variant present in patients with type 1 and type 2 VWD

Atiq F et al. Blood Advances 2022

Indications for treatment with DDAVP in VWD

Type of VWD r	Indications	Utility
Type 1 vWD[a]	Surgical prophylaxis and acute bleeding episode	Evidence to support use[56–58]
Type 2A vWD[a]	Acute bleeding episodes	Generally avoided due to defective multimer formation and release[59]
Type 2B vWD	Acute bleeding episodes	Contraindicated due to bleeding and thrombocytopenia[60]
Type 2M vWD[a]	Acute bleeding episodes	Generally avoided due to defective multimer formation and release[59,61]
Type 2N vWD[a]	Acute bleeding episodes	Case report level evidence to suggest some benefit[61]

✓ *Most useful in VWD type 1*
✓ *Contraindicated in 2B,*
✓ *No use in Type 3*

Mohinani et al. Eur J Haematol 2023

Contraindications / restrictions with DDAVP

- ✓ *Active cardiovascular disease*
- ✓ *Seizure disorders*
- ✓ *Patients age < 2 years*
- ✓ *In patients with type 2B VWD is generally contraindicated*

- ✓ *Risk for hyponatremia from free water retention =>oral free water fluid intake should be restricted to prevent hyponatremia*

***Patient counseling** about desmopressin **should include strategies to mitigate risks associated with hyponatremia** (eg, free water restriction and education about signs and symptoms of hyponatremia that should lead to prompt medical evaluation) **and cardiovascular disease**.*

Connell N et al, Blood Advances 2021

What do the guidelines say about DDAVP?

- Recommendation 2a: Suggests performing a trial of desmopressin in patients (mostly type 1 VWD) and VWF <0.30 IU/ml
- Recommendation 2b: Suggests against treating with desmopressin in the absence of a desmopressin trial

Patients with >0.30 IU/ml can be presumed to be desmopressin responsive.

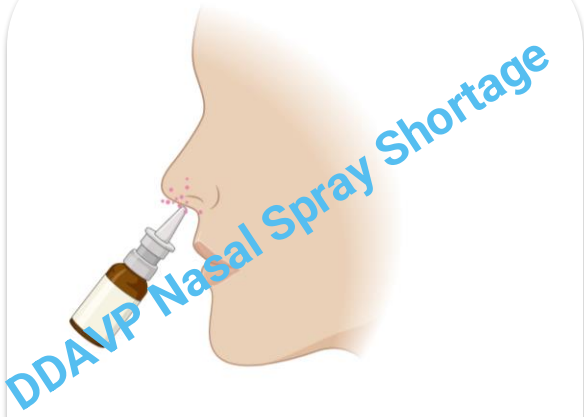
- *it is reasonable to obtain VWF levels to confirm response after administration*

Some type 2 patients respond to desmopressin=> *"a desmopressin trial may be helpful to confirm diagnosis, and desmopressin may still be useful in some instances of mild bleeding for type 2 VWD patients "*

Connell N et al. Blood advances 2021

DDAVP: route of administration

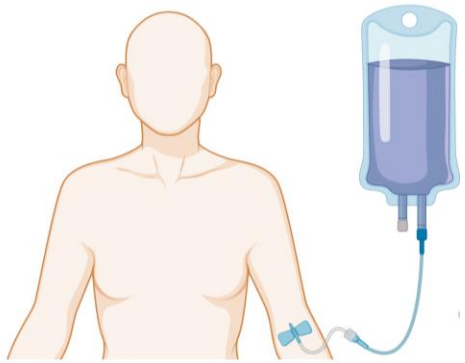
intranasal



One spray <50kgs (150 µg)
Two sprays ⩾ 50kgs (300 µg)

60kgs *Two sprays*

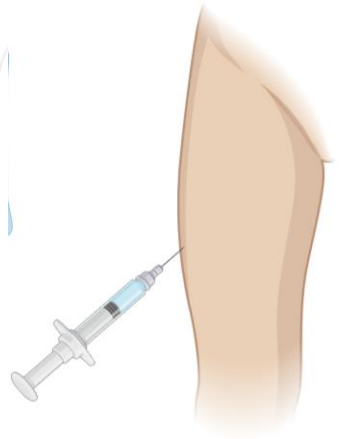
intravenous



4 µg/mL
Vials 1mL

4,5mL

subcutaneous



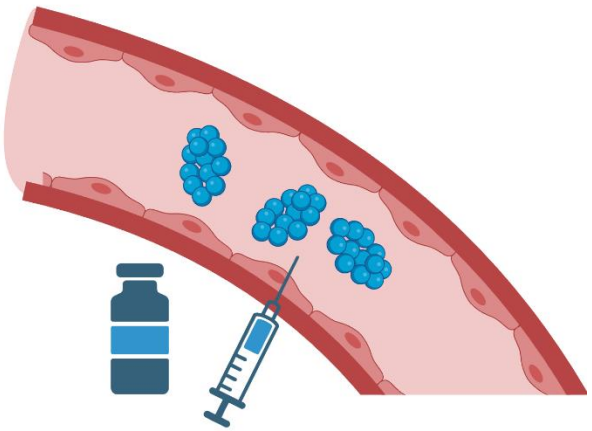
15 µg/mL
Vials 1mL

0.2-0.3 µg/kg *1,2mL*

= Free water intake <0.75 L/24H

Management of VWD with VWF products

VWF products



- pdVWF-FVIII, pdVWF
- rVWF

On demand, bleeding events

Short-term prophylaxis , surgery

Long term prophylaxis

Hemarthrosis
Gastro intestinal bleeding
Epistaxis
Menorrhagia

Factor replacement therapies for VWF

	Plasma-derived VWF						Recombinant VWF
	RCo/FVIII≤ 1	**RCo/FVIII > 1 et <10**				**RCo/FVIII ≥ 10**	**RCo/FVIII 0 FVIII**
	Wilate/ Eqwilate	Alphanate	Fanhdi	Voncento/ Biostate	HumateP/ Haemate P	Wilfactin/ Willfact	Vonvendi/ Veyvondi
$t_{1/2}$ (VWF:RCo),h	15.8	7.67	14.4	13.7	11	12.4	21.9
RCo/FVIII	0,8-1,0	0.8-1.2	1.29-1.6	2.4	2.04-2.88	>10	0 FVIII
ULM	absent	absent	absent	absent	absent	absent	present

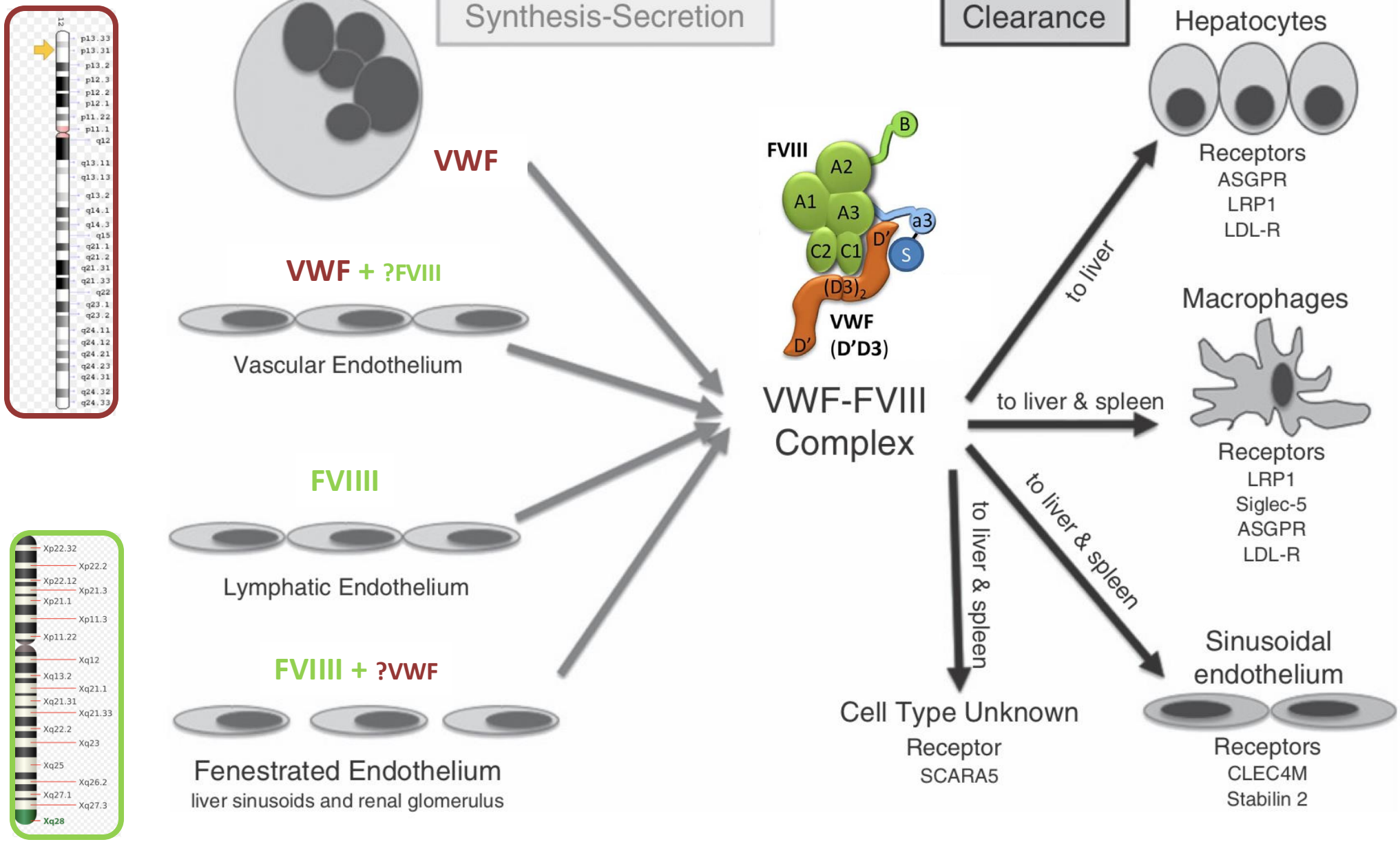
Adapted from Peyvandi F, Blood Reviews 2019

Factor replacement therapies for VWF

Products are different => do we need to personnalize treatment ?

	Plasma-derived VWF						Recombinant VWF
	RCo/FVIII≤ 1	**RCo/FVIII > 1 et <10**				**RCo/FVIII ≥ 10**	**RCo/FVIII 0 FVIII**
	Wilate/ Eqwilate	Alphanate	Fanhdi	Voncento/ Biostate	HumateP/ Haemate P	Wilfactin/ Willfact	Vonvendi/ Veyvondi
$t_{1/2}$ (VWF:RCo),h	15.8	7.67	14.4	13.7	11	12.4	21.9
RCo/FVIII	0,8-1,0	0.8-1.2	1.29-1.6	2.4	2.04-2.88	>10	0 FVIII
ULM	absent	absent	absent	absent	absent	absent	present

Adapted from Peyvandi F, Blood Reviews 2019



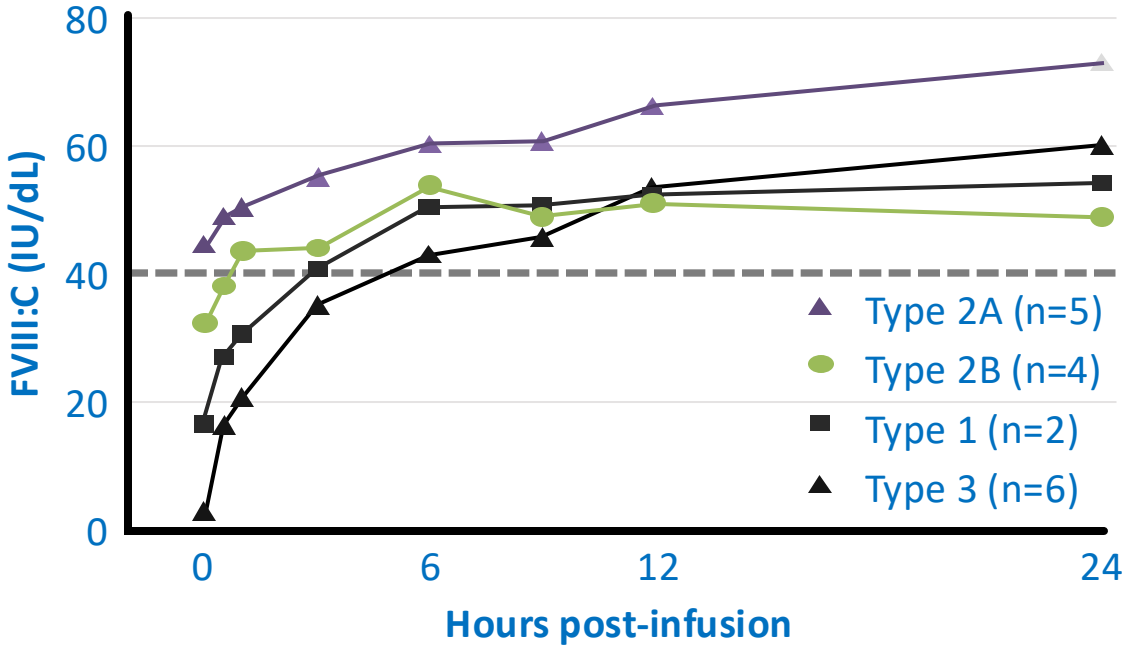
Adapted from Pipe SW, Blood 2016

Pure VWF (rVWF or pdVWF) can be used in adult patients with VWD to restore levels of FVIII

Clinical PK trial experience with high purity plasma derived VWF concentrate in surgery

FVIII:C levels up to 24 h post infusion

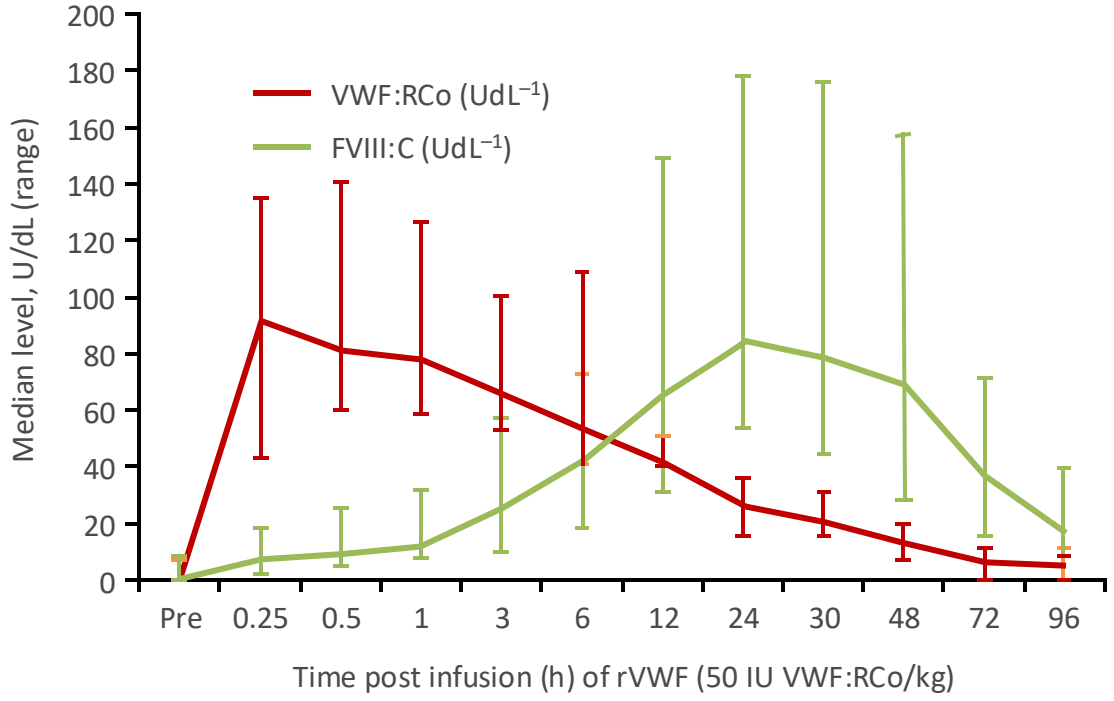
pd VWF



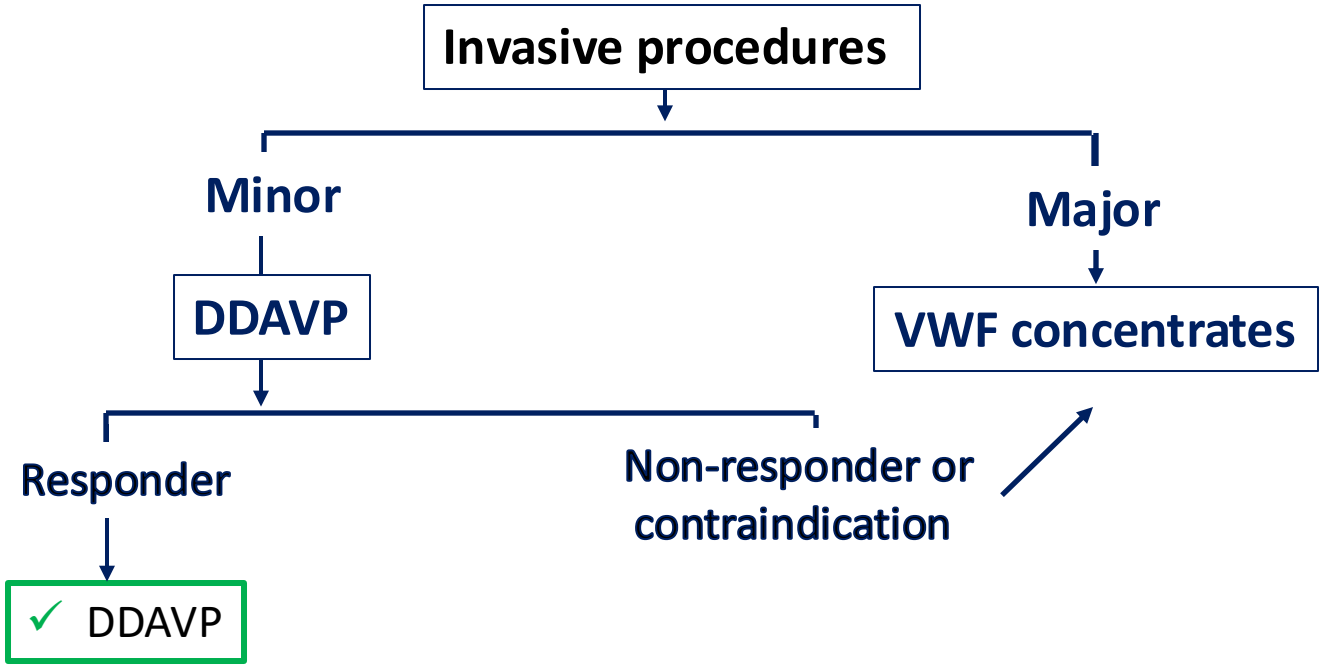
Goudemand J, et al. J Thromb Haemostas 2005;3:2219–27

Endogenous FVIII levels increased above 40% within 6 hours in the majority of VWD patients following rVWF infusion

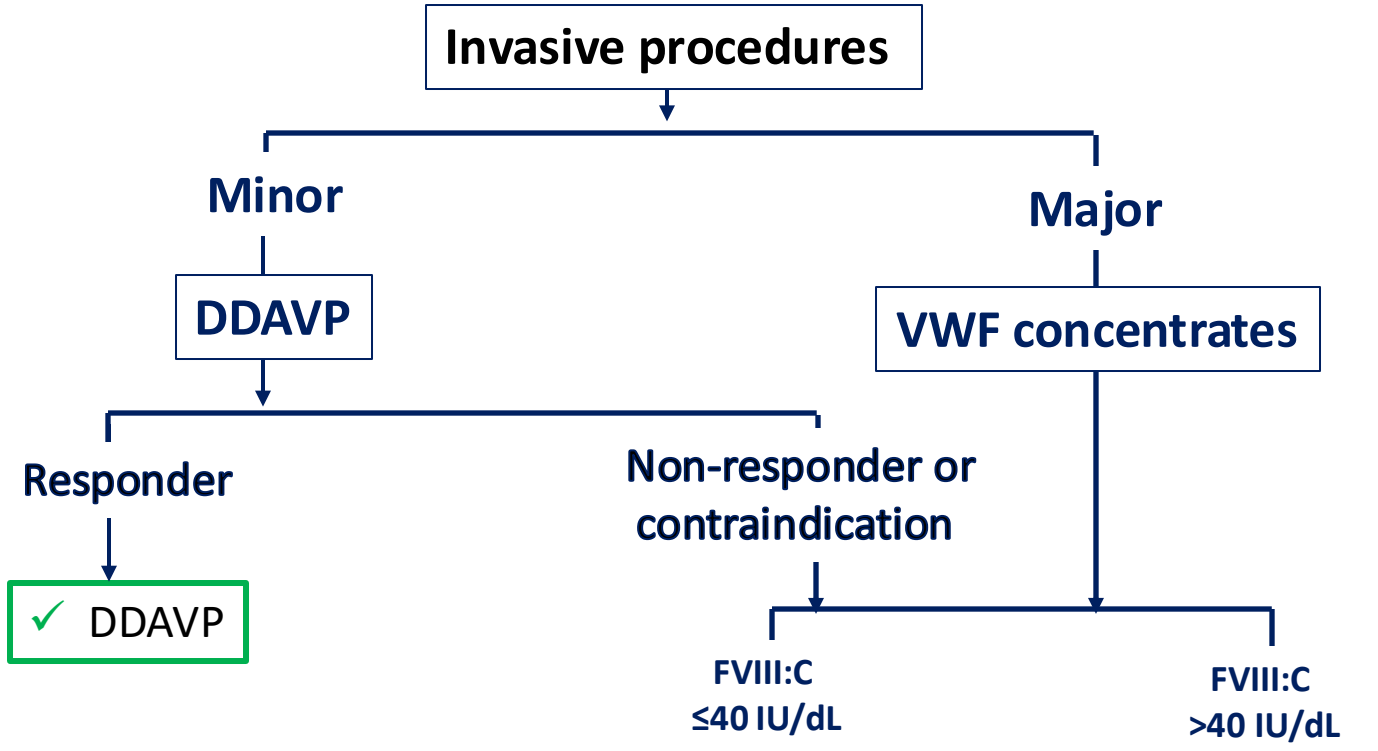
r VWF

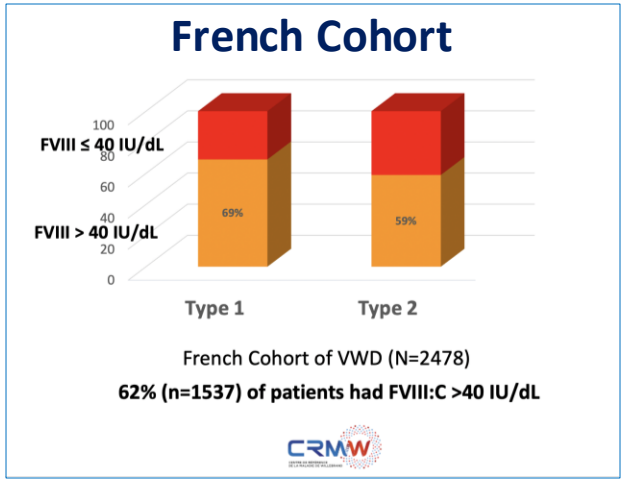


Gill JC, et al. Blood. 2015; 126(17):2038-2046

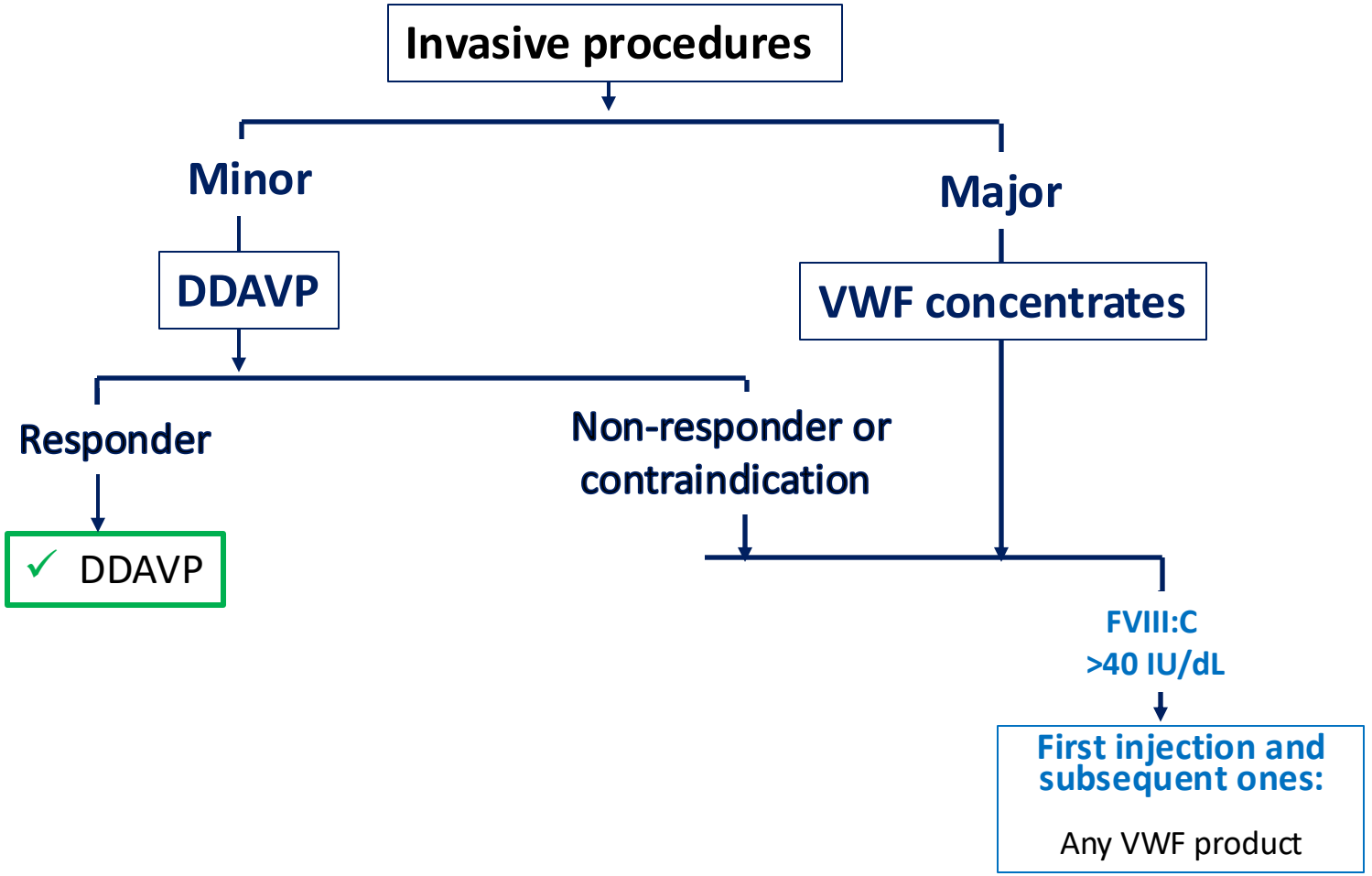


PNDS HAS 2021
Health authority national protocols for diagnosis and care

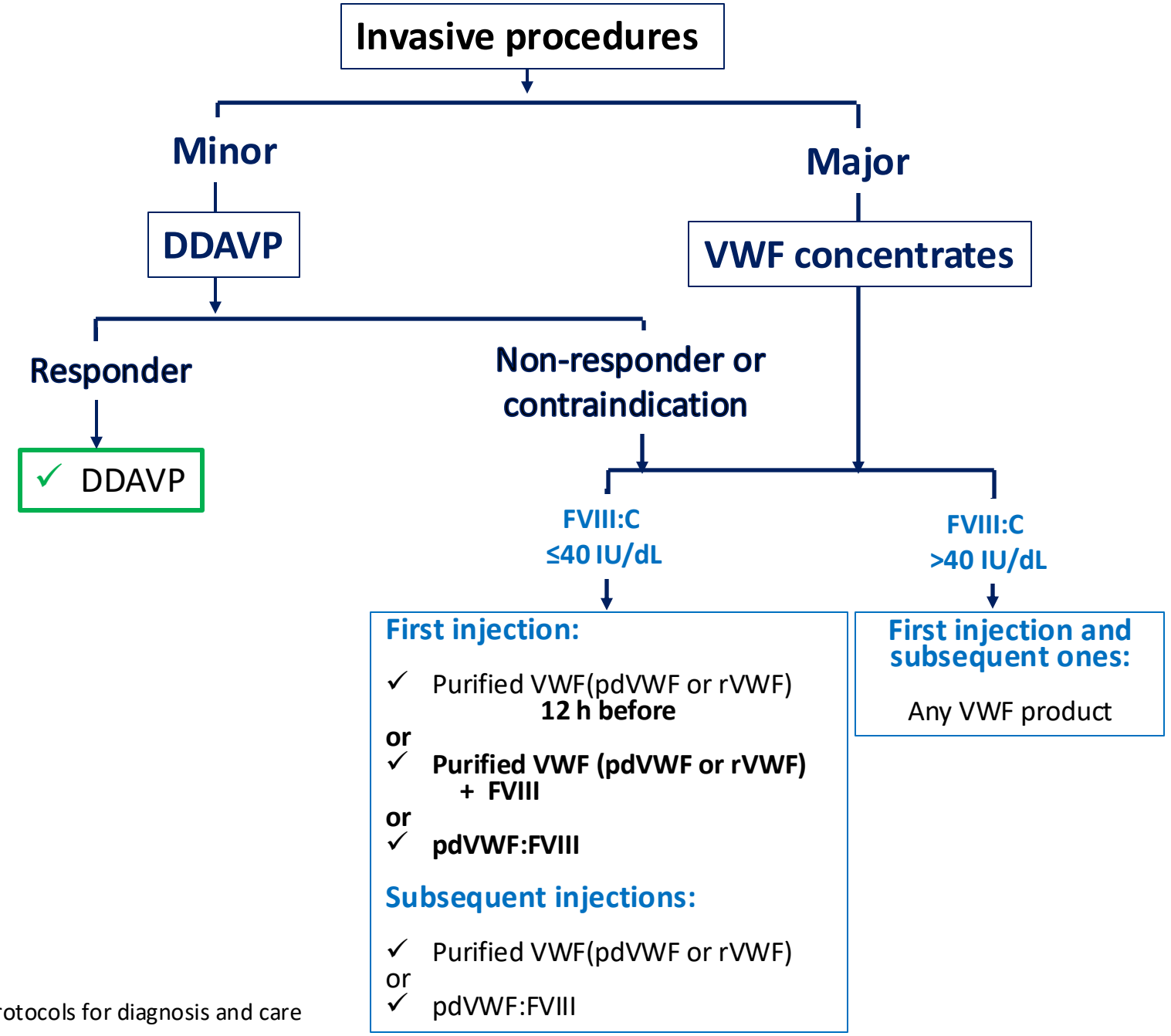




PNDS HAS 2021
Health authority national protocols for diagnosis and care



PNDS HAS 2021
Health authority national protocols for diagnosis and care

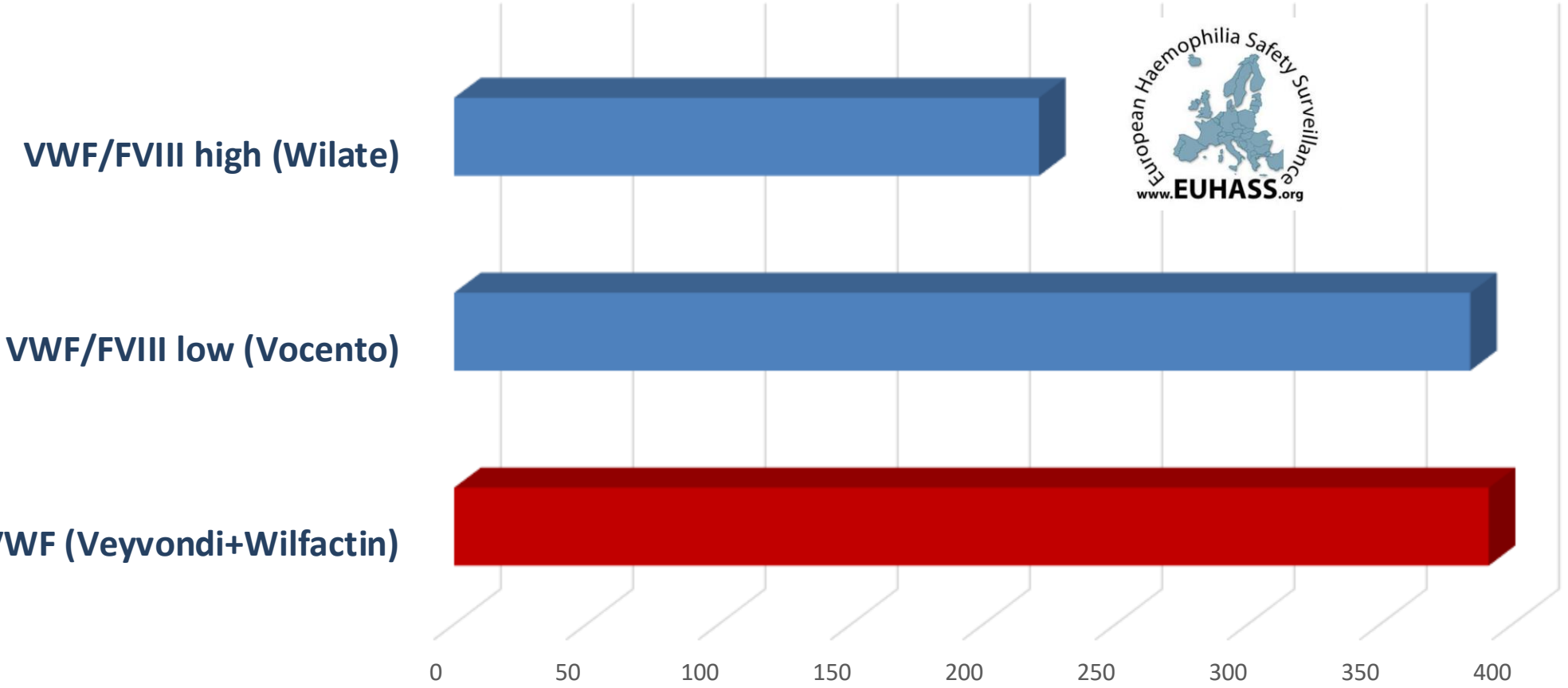


PNDS HAS 2021
Health authority national protocols for diagnosis and care

Products used: Data from EUHASS Registry

From 95 centres (reports)

1 January 2022 – 31 December 2022



EUHASS annual report 2022

Number of patients treated with each product

Long Term Prophylaxis (LTP) in VWD: definition

- Home-infusion of VWF product on a regular basis
- At least once /week
- To prevent bleeding
- 45 weeks or more/year
- Or on a regular basis during menstrual periods to reduce menorrhagia

Holm E. et al , Blood Coagul Fibrinolysis 2015

Main criteria to consider LTP in VWD

Joint Bleed

2 or more spontaneous bleeds in the same joint

3 or more in different joints

within the last 6 months

Epistaxis

3 or more bleeding episodes requiring VWF or transfusion within the last 6 months

Gastro-intestinal bleeding

2 or more severe GIB requiring VWF or transfusion or with drop in hemoglobin

Menorrhagia

PBAC>185 or requirement of VWF /transfusion within the past year

Holm E. et al , Blood Coagul Fibrinolysis 2015

Proposed definition for prophylaxis

Prophylaxis in VWD (long-term prophylaxis) is a period of *at least 3 to 6 months of treatment*

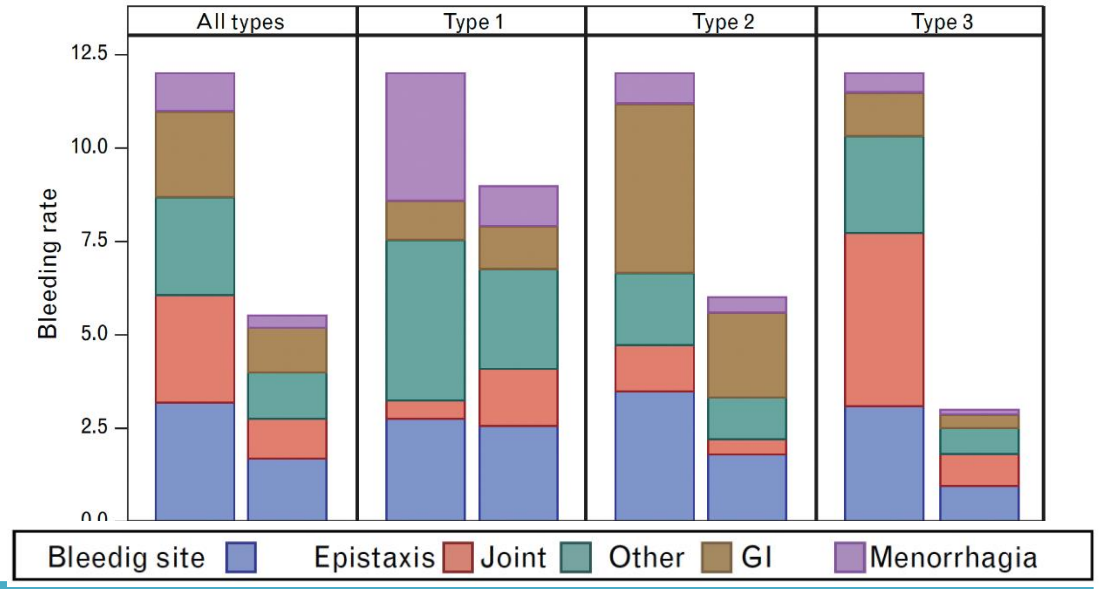
consisting of *VWF concentrate administered at least once weekly*,

or for women with HMB, use of VWF concentrate administered *at least once per menstrual cycle*

Connell N et al. Blood advances 2021

Improvement of bleeding with prophylaxis according to the bleeding-type indication

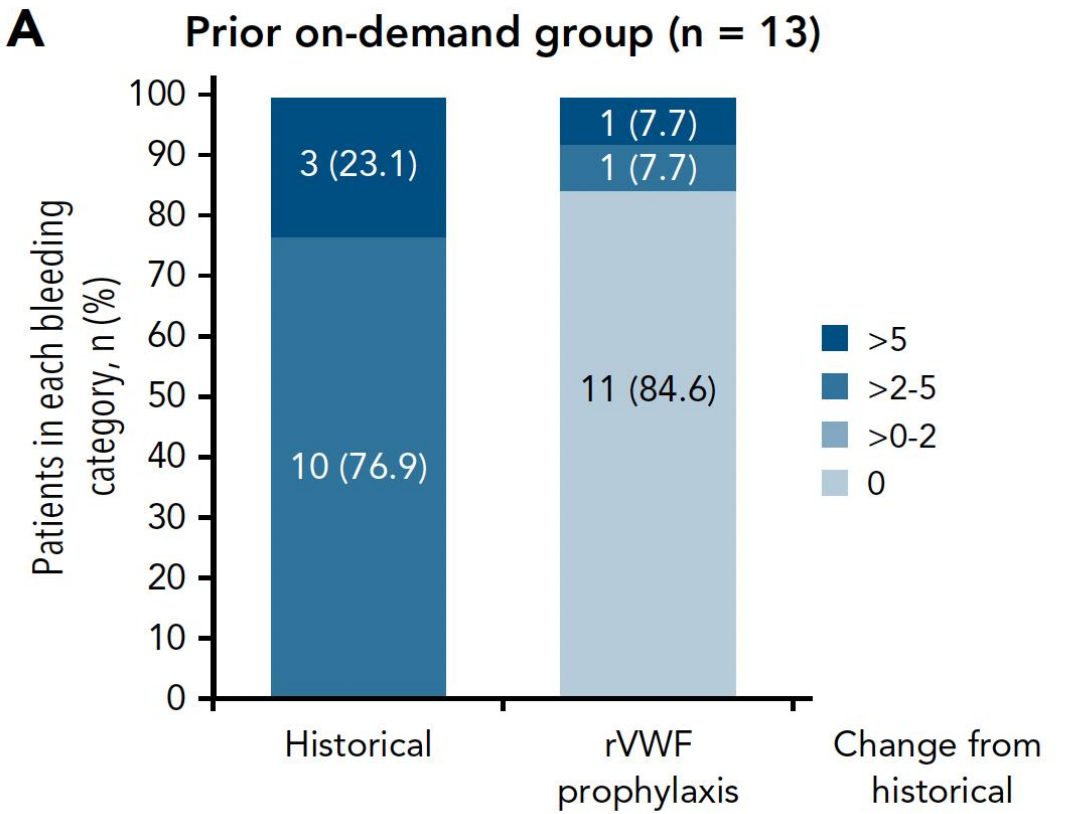
ABRs of 80 patients with VWD before and during prophylaxis (2008–2013)



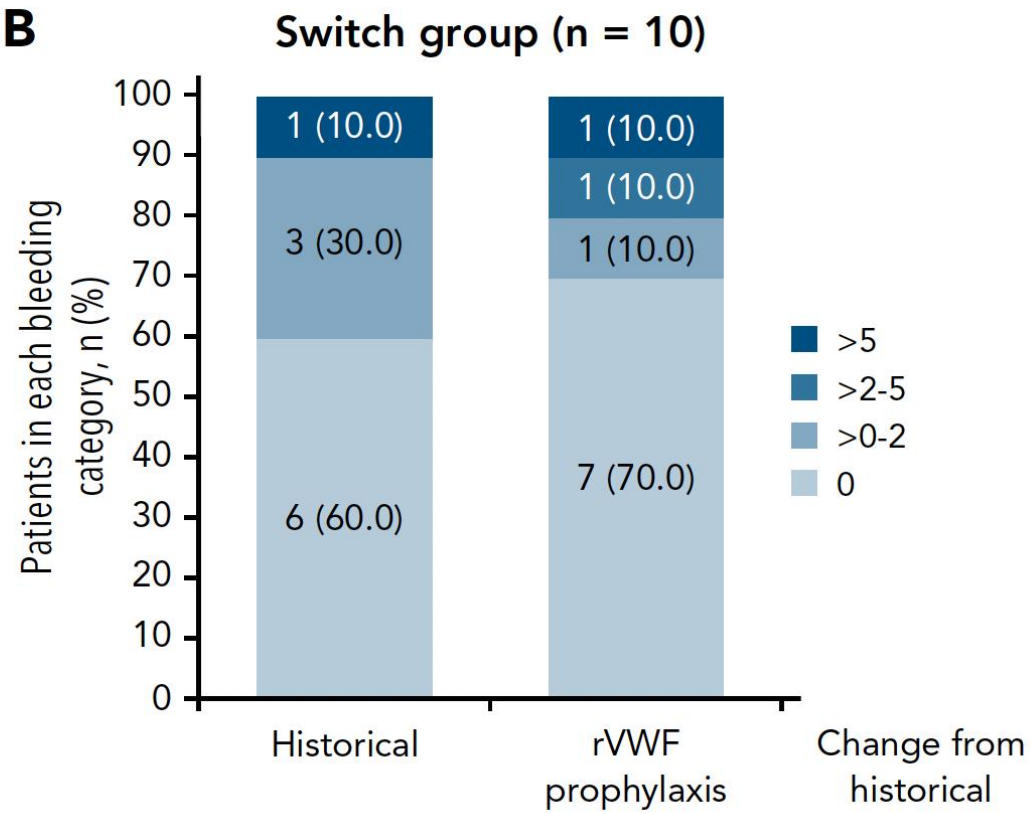
Indication	n	Prior to prophylaxis, median (IQR)	During prophylaxis, median (IQR)	Median rate change (IQR)	Median percent change (IQR)
Epistaxis	28	11.1 (6–48)	3.8 (0.21–16.8)	–6.1 (–42 to –1.5)	–86.7 (–95.5 to –49.8)
GI bleeding	18	9.3 (6–21.6)	6 (3.6–7.1)	–3.0 (–6 to 0)	–44.3 (–72.2 to 0)
Joint bleeding	25	11.9 (6–18)	0.8 (0–3.2)	–8.5 (–12 to –4.2)	–86.9 (–100 to –52.5)
Menorrhagia	9	9.6 (8.4–12)	0 (0–0.4)	–9 (–9.3 to –6)	–100 (–100 to –95.8)

Holm E et al. Blood Coagulation & Fibrinolysis 2015

Reduction of bleeding with rVWF prophylaxis



	Historical	rVWF prophylaxis	Change from historical
Mean ± SD	15.5 ± 42.0	0.7 ± 1.7	−14.8 ± 42.2
Median (range)	3.0 (3.0-155.0)	0 (0-5.8)	−3.0 (−155.0 to 2.8)



	Historical	rVWF prophylaxis	Change from historical
Mean ± SD	5.0 ± 14.4	1.7 ± 3.8	−3.3 ± 10.9
Median (range)	0 (0-46.0)	0 (0-12.1)	0 (−33.9 to 3.9)

Leebeek F et al. Blood 2022

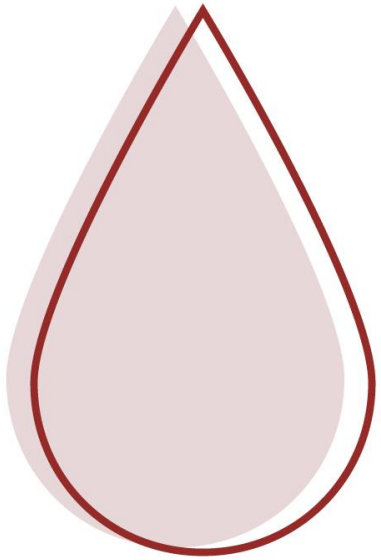
What do we know so far about LTP in VWD?

- Most common types are Type 3 (mainly) and Type 2
- Reason for initiating prophylaxis
  - Gastrointestinal bleeding and joint bleeding in adults
  - Epistaxis and joint bleeding in children
- Secondary long-term prophylaxis is efficaccious in reducing bleeding in VWD (low certainty evidence)
- Efficacy depends on bleeding symptoms (joint bleeding >>>>GI bleeding)
- All products have been used
- Few data

Abshire T et al. Haemophilia 2013
Holm E et al. Blood Coagul Fibrinolysis 2015
Abshire T et al. J Thromb Haemost 2015
Peyvandi F et al. Blood Transfus 2019
Leebeek F et al. Blood 2022

Systematic review El Alayli A et al. Haemophila 2022

ASH ISTH NHF WFH Guideline Recommendations for Management of von Willebrand Disease (VWD)



Recommendation 1

In patients with VWD with a history of severe and frequent bleeds, the guideline panel *suggests* using long-term prophylaxis rather than no prophylaxis (conditional recommendation based on low certainty in the evidence of effects ⊕⊕◯◯).

+ need for prophylaxis periodically assessed

https://doi.org/10.1182/bloodadvances.2020003264

Prevalence of Heavy Menstrual Bleeding among women with VWD

	Study Population	Prevalence of HMB
Ragni et al., 2016 [23]	1321 women with VWD from 20 US Hemophilia Treatment Centers, 18–45 years old, seen during 2012–2014.	Heavy menstrual bleeding reported by 816 (61.8%) women with VWD.
Sanders et al., 2014 [24]	664 adults with Von Willebrand disease, as compared with 500 healthy persons, in the Willebrand in the Netherlands (WiN) study.	More than 80% of women with VWD experienced menorrhagia.
de Wee et al., 2011 [25]	423 women aged ≥ 16 years old with moderate and severe VWD in the Netherlands.	Menorrhagia, defined as occurrence of ≥2 menorrhagia symptoms, was reported by 81%.
Kadir et al., 1998 [26]	150 women referred for investigation of menorrhagia whose pelvis was normal on clinical examination and who had an estimated menstrual blood loss of more than 80 mL.	13% VWD prevalence. Menorrhagia since menarche 65% of 20 women with Von Willebrand disease compared with 8,9% of 123 women without a bleeding disorder.
Woods et al., 2001 [27]	1885 patients of all ages with VWD–1142 females—from a reference center in Argentina.	47% of women more than 13 years old.

Kontogiannis et al. J Clin Med 2023

Prevalence of Heavy Menstrual Bleeding among women with VWD

	of HMB
Ragni et al., 2(	ing reported by 816 with VWD.
Sanders et al., 2	omen with VWD enorrhagia.
de Wee et al., 2	s occurrence of ≥2 was reported by 81%.
Kadir et al., 19	Menorrhagia since women with Von pared with 8,9% of bleeding disorder.
Woods et al., 2	han 13 years old.

~50 to 100%

- *Depression*
- *Anxiety*

Tran AD et al, J Thromb Haemost 2024
Roberts JC et al, Haemophilia 2023

Heavy menstrual bleeding

- *Recommendation 6a:*

The panel suggests in women who do not wish to conceive using either hormonal therapy (such as use combined oral contraceptive or levonorgestrel intrauterine device) or tranexamic acid rather than desmopressin

- *Recommendation 6b:*

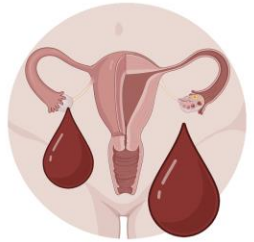
The panel suggests in women who wish to conceive using tranexamic acid over desmopressin

- *Good practice statement*

The panel encourages the development of multidisciplinary clinics in which the gynecologists and hematologists see the patients jointly

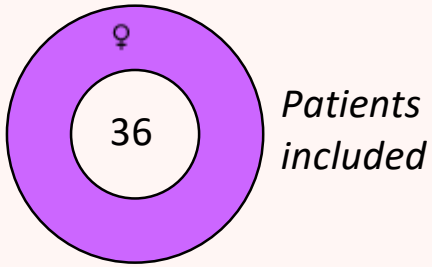
Connell N et al. Blood Advances 2021

Heavy menstrual bleeding : New data

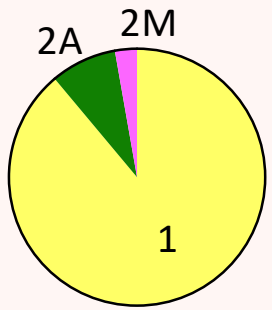


VWDMin study – patients with mild to moderate VWD and HMB

STUDY	rVWF IV D1 (D2)	&	Tranexamic acid (TXA) 1300mg D1-to-D5
Groupe 1:	*cycles 1-2*		*cycles 3-4*
Groupe 2:	*cycles 3-4*		*cycles 1-2*



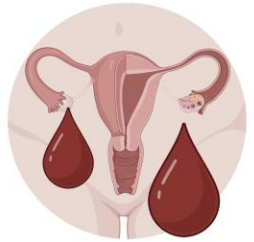
Patients included



Types of VWD

Ragni Lancet Haematol 2023

Heavy menstrual bleeding : New data



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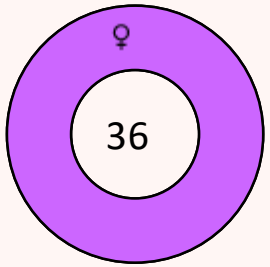
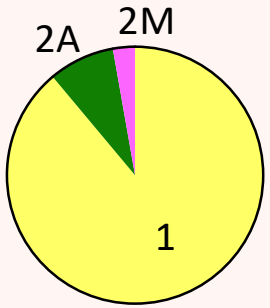


Patients included



Types of VWD

RESULTS

Paramètre évalués:

- ***Correction of PBAC to normal range 0%***
- ***Modest decrease in PBAC with TXA vs rVWF***
- ***= QOL***
- *TXA cheaper*

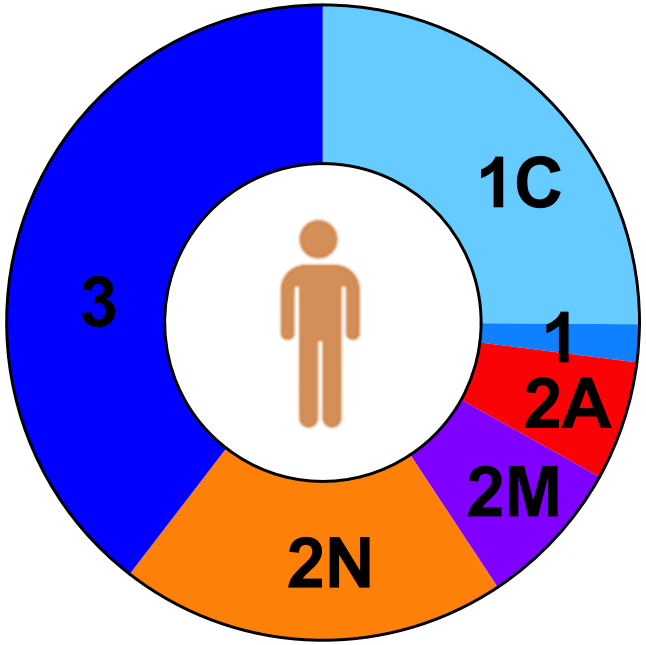
VWF is not superior to tranexamic acid in reducing heavy menstrual bleeding in patients with mild or moderate VWD

=> shared decision on the best treatment option

Ragni Lancet Haematol 2023

New therapeutic options for VWD

- **FVIII:C ≤ 15IU/dL**



≃ 8% of patients in the French cohort of VWD

- **To restore FVIII procoagulant activity**

Severe VWF defect
& secondary FVIII
deficiency

Absence of VWF →
6X shorter FVIII- half-life

VWD-type 3
VWD-type 2N
(other Severe types)

Emicizumab
SC Q1W, Q2W, Q4W

Emicizumab in VWD

Off-label use in Type 3 patients (~15 published cases)

	Age (years)	Inhibitor (y/no)	Follow-up (months)
Weyand	5	yes	9
Sigaud Abstract	48	yes	NA
Cefalo Abstract	11 months	yes	12
Barg	9	no	11
Vo Abstract	2, 6, 41, 44	no	NA
Shanmukhaiah	6 11	yes no	6 6
French cohort (Unpublished data)	6, 11 3, 20, 40, 42	yes(2) no (5)	NA

No adverse events
ZERO spontaneous bleeds
Improvement of QOL
Limited follow-up

Longer follow-up?
Surgeries? Trauma?
Other types of VWD?

Weyand et al. Blood Advances 2019; Sigaud et al. ISTHabstract 2020; Cefalo et al. Haemophilia 2020; Vo et al. ISTHabstract 2021; Barg et al. Blood Cells Molecules and Diseases 2021; Shanmukhaiah et al. Haemophilia 2022, LeMaistre et al. *Blood Coagulation & Fibrinolysis 2024, Giuffrida et al.* Semin Thromb Hemost. 2024

Emicizumab in VWD

RECRUITING

Clinical study

NCT05500807 - Sponsor Bleeding and Clotting Disorders Institute Peoria, Illinois/ IIS supported by Genetech

Emicizumab prohylaxis in severe VWD and VWD+Hemophilia A (monocentric observationnal study)

40 patients, 2-90yo
Severe type 3/VWF:Ag or VWF:act ≤ 20 IU/dL
Any VWD + hemophilia (mild/moderate/severe)
Patient on current prophylaxis

18 months of follow-up
Bleed occurrence / AE/ Thrombosis/HRQOL PRO's

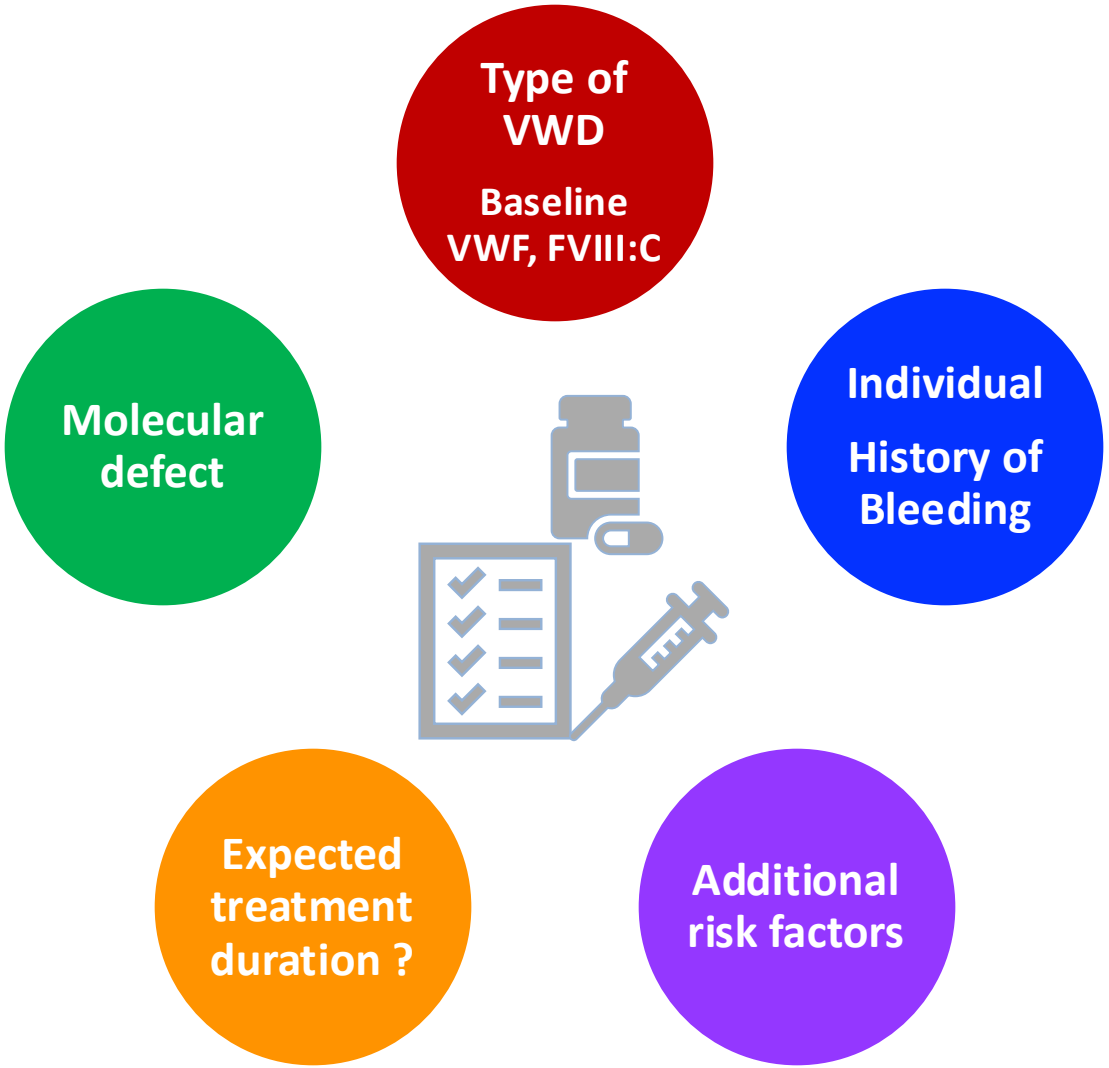
End of the study 03/2026

Clinical study

More to come in type 3?

Weyand et al. Blood Advances 2019; Sigaud et al. ISTHabstract 2020; Cefalo et al. Haemophilia 2020; Vo et al. ISTHabstract 2021; Barg et al. Blood Cells Molecules and Diseases 2021; Shanmukhaiah et al. Haemophilia 2022, LeMaistre et al. *Blood Coagulation & Fibrinolysis 2024, Giuffrida et al.* Semin Thromb Hemost. 2024

Conclusion



= **Need for personalization of treatment**

= Choose the product

= Choose the treatment regimen

and choose according to the best knowledge in high risk patients/situations

In a shared decision process

www.ehc.eu

vwd@ehc.eu

@EHC_Haemophilia

EHC - European Haemophilia Consortium

European Haemophilia Consortium

@EHCTVChannel EHC Youtube channel

www.eurobloodnet.eu

@ERNEuroBloodNet

eurobloodnet-european-reference-network-on-rare-hematological-diseases

Eurobloodnet - European Reference Network on Rare Hematological Diseases

ERN-EuroBloodNet's EDUcational Youtube channel

This project is carried out within the framework of European Reference Network on Rare Haematological Diseases (ERN-EuroBloodNet)-Project ID No 101085717. ERN-EuroBloodNet is partly co-funded by the European Union within the framework of the Fourth EU Health Programme.

Co-funded by the European Union

Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or European Health and Digital Executive Agency (HaDEA). Neither the European Union nor the granting authority can be held responsible for them.