European Reference Network
for rare or low prevalence complex diseases
Network Hematological Diseases (ERN EuroBloodNet)

CRPP Centre de Référence Pathologies Plaquettaires

MHEMO La Filière des maladies rares de l'hémostase

Session 9: Glanzmann thrombasthenia – general aspects of diagnosis and follow-up

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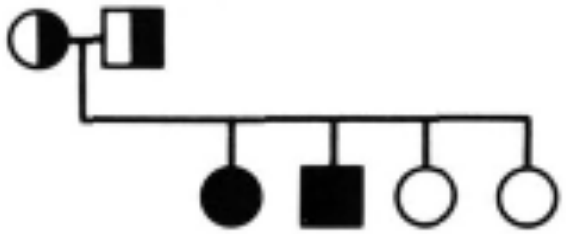
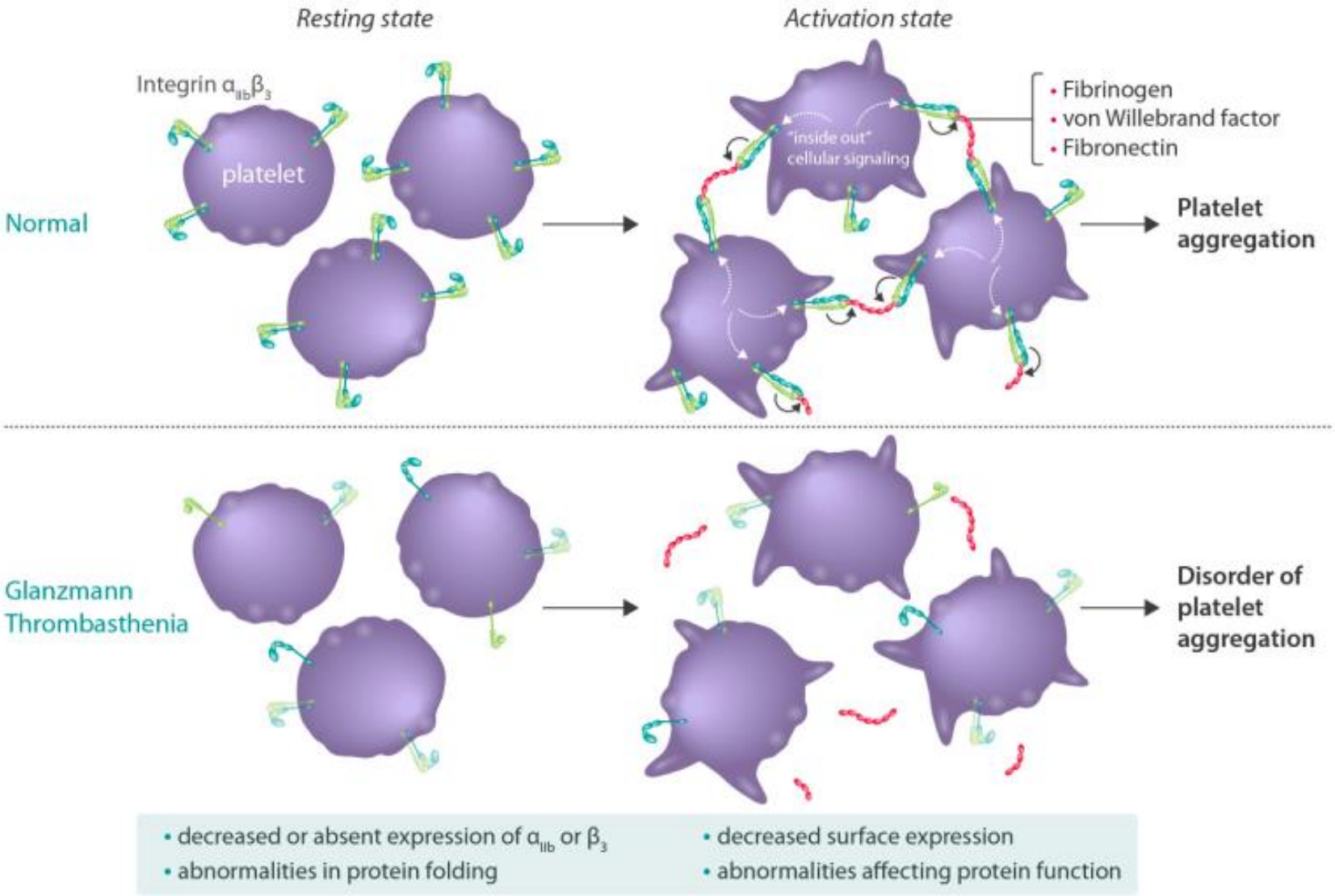
Glanzmann thrombasthenia

Glanzmann thrombasthenia: autosomal recessive disorder of platelet aggregation caused by quantitative or qualitative defects in integrins $\alpha_{IIb}\beta_3$

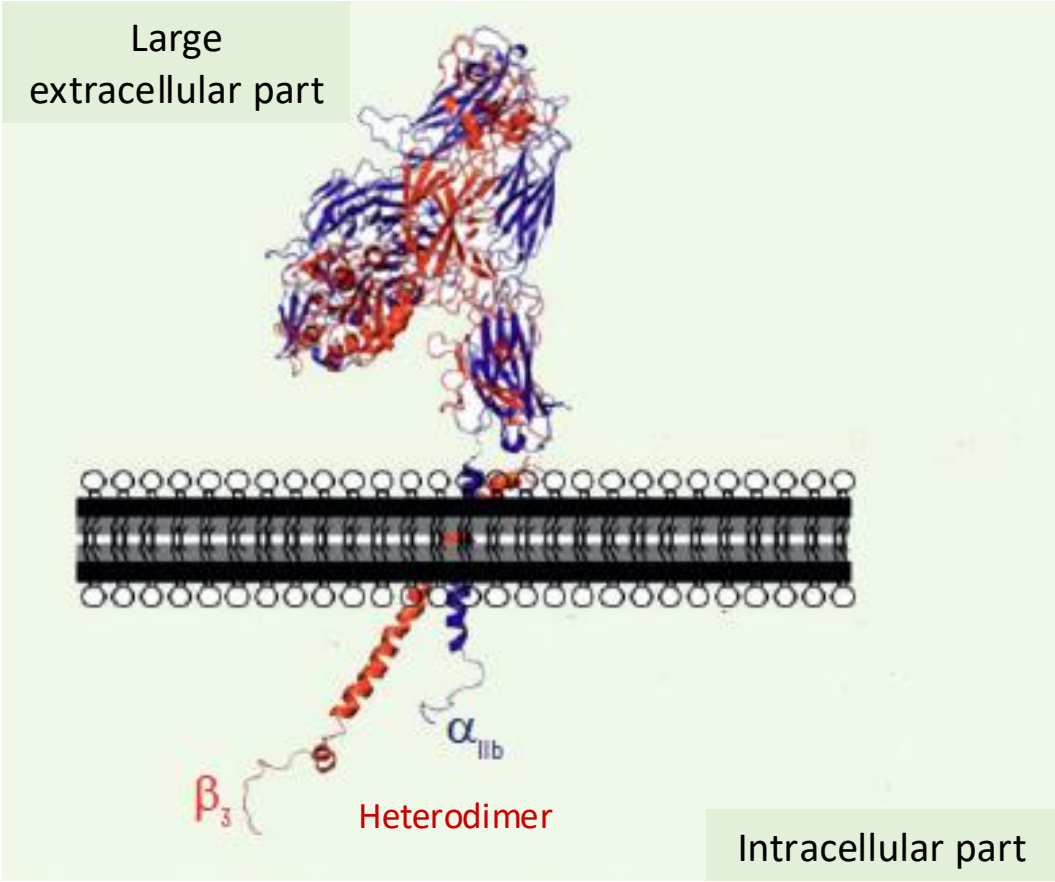




Botero et al., Haematologica, 2020

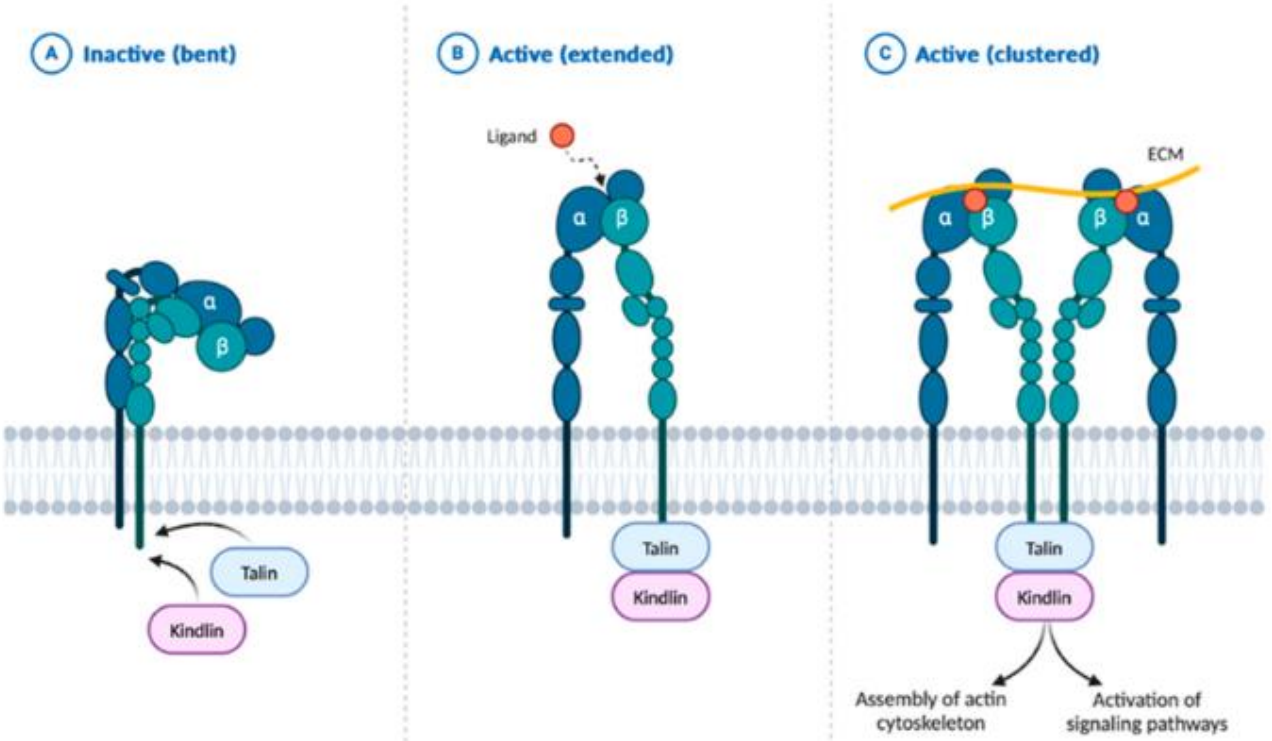
$\alpha_{IIb}\beta_3$ INTEGRIN

Major platelet integrin (50 000 à 100 000 sites)
Major role in **platelet aggregation**



Modified from Lebreton, m/s, 2016

$\alpha_{IIb}\beta_3$ Activation States and Functional Roles



Stage	Bent	Extended	Clustered
Conformation	Folded, compact	Upright, extended	Multimeric aggregation
Affinity	Low	High	High
Ligand Accessibility	Occluded	Exposed	Fully engaged
Activation Trigger	Stabilized by filamin/ SHARPIN	Inside-out signaling (talin, kindlin)	Ligand binding, FAK/Src signaling
Functional Role	Prevents adhesion, maintains quiescence	Leukocyte adhesion, platelet aggregation	Stable adhesion, mechanotransduction

Ławkowska, K.; Bonowicz, K.; Jerka, D.; Bai, Y.; Gagat, M. Integrins in Cardiovascular Health and Disease: Molecular Mechanisms and Therapeutic Opportunities. Biomolecules 2025, 15, 233.

BLEEDING SCORE

Validation of the ISTH/SSC bleeding assessment tool for inherited platelet disorders: A communication from the Platelet Physiology SSC

J Thromb Haemost. 2020;18:732–739

Paolo Gresele[1] | Sara Orsini[1] | Patrizia Noris[2] | Emanuela Falcinelli[1] | Marie Christine Alessi[3] | Loredana Bury[1] | Munira Borhany[4] | Cristina Santoro[5] | Ana C. Glembotsky[6,7] | Ana Rosa Cid[8] | Alberto Tosetto[9] | Erica De Candia[10,11] | Pierre Fontana[12] | Giuseppe Guglielmini[1] | Alessandro Pecci[2] | BAT-VAL study investigators*III

IPFD	N	Median ISTH-BAT (IQR)
Glanzmann thrombasthenia	79	11 (8-16)
δ-storage pool deficiency	21	6 (3.75-10.5)
Biallelic Bernard Soulier syndrome	20	8.5 (7.5-12.5)
Primary secretion defect	20	7.5 (3.5-12.5)
Familial platelet disorder associated with myeloid malignancy	8	4.5 (1-5.5)
Gray platelet syndrome	7	12 (10-14.25)
Hermansky-Pudlak syndrome	7	5 (2-13.25)
Quebec platelet disorder	7	12 (9-20.75)
Defect of the $P2Y_{12}$ Purinergic Receptor	6	10.5 (4-15)
Combined alpha-delta granule deficiency	5	8 (5.75-9)
Glanzmann Thrombasthenia Variant	5	8 (1.5-8.25)
CalDAG-GEFI defect	3	22 (13-23.5)
Defect of the TP receptor	3	4 (4-5.5)
Defects of collagen receptors	2	2.5 (2-3)
Paris-Trousseau syndrome	2	14.5 (12-17)
$cPLA_2$ deficiency	1	10 -
Platelet-type Von Willebrand Disease	1	11 -

Bleeding score:
High
Intermediate
Low

Age at diagnosis

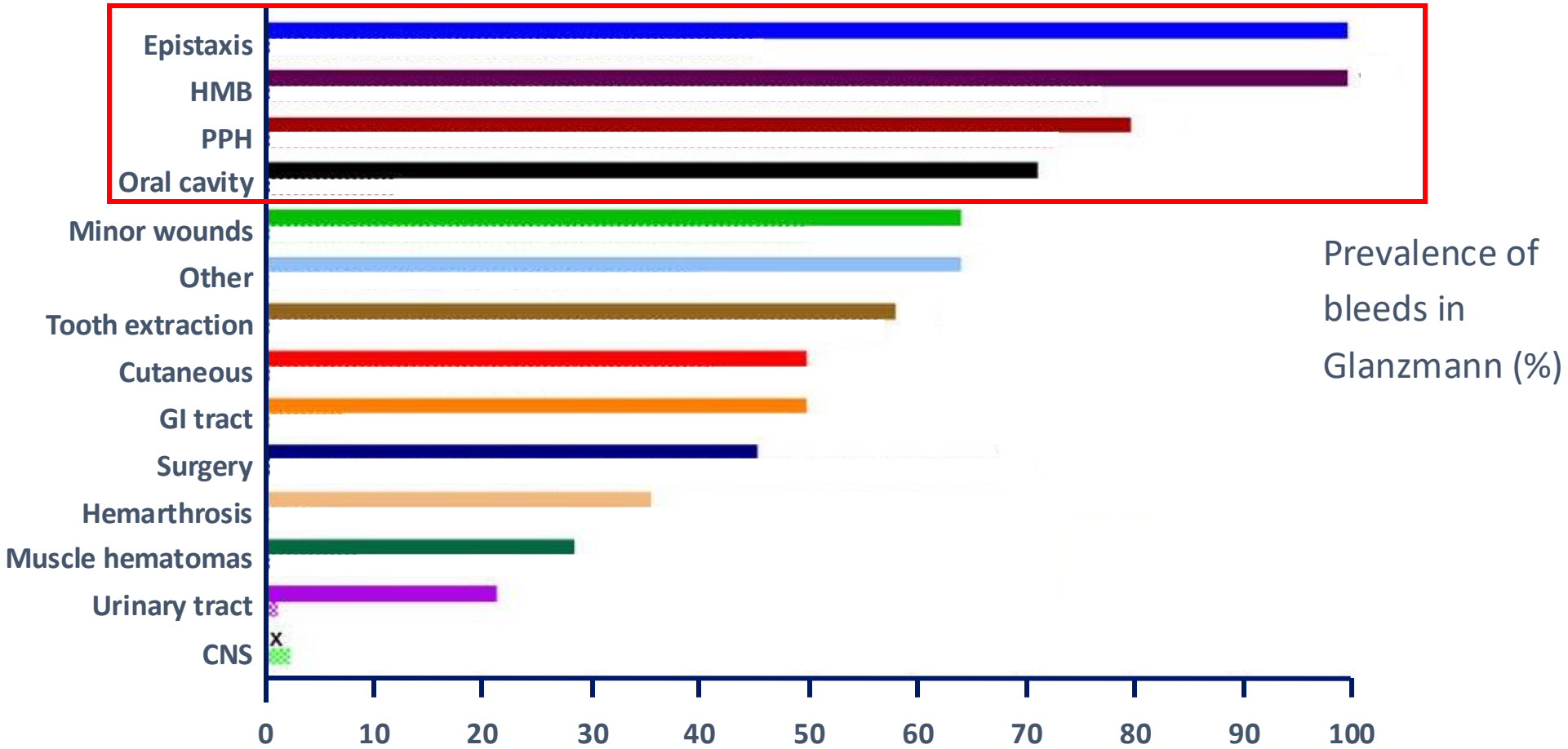
Age	Total population (N = 117)	Men/boys (n = 51)	Women/girls (n = 66)
Age at diagnosis			
<2 y	55 (47.0%)	20 (39.2%)	35 (53.0%)
2-5 y	22 (18.8%)	10 (19.6%)	12 (18.2%)
6-10 y	12 (10.3%)	7 (13.7%)	5 (7.6%)
11-19 y	13 (11.1%)	7 (13.7%)	6 (9.1%)
>20 y	15 (12.8%)	7 (13.7%)	8 (12.1%)
Age at which bleeding became apparent			
<2 y	69 (59.0%)	28 (54.9%)	41 (62.1%)
2-5 y	27 (23.1%)	17 933.3%)	10 (15.2%)
6-10 y	9 (7.7%)	1 (2.0%)	8 (12.1%)
11-19 y	6 (5.1%)	1 (2.0%)	5 (7.6%)
>20 y	6 (5.1%)	4 (6.0%)	2 (3.0%)

Data are presented as frequency (percentage).

Res Pract Thromb Haemost. 2024;8:e102586

BLEEDING MANIFESTATIONS

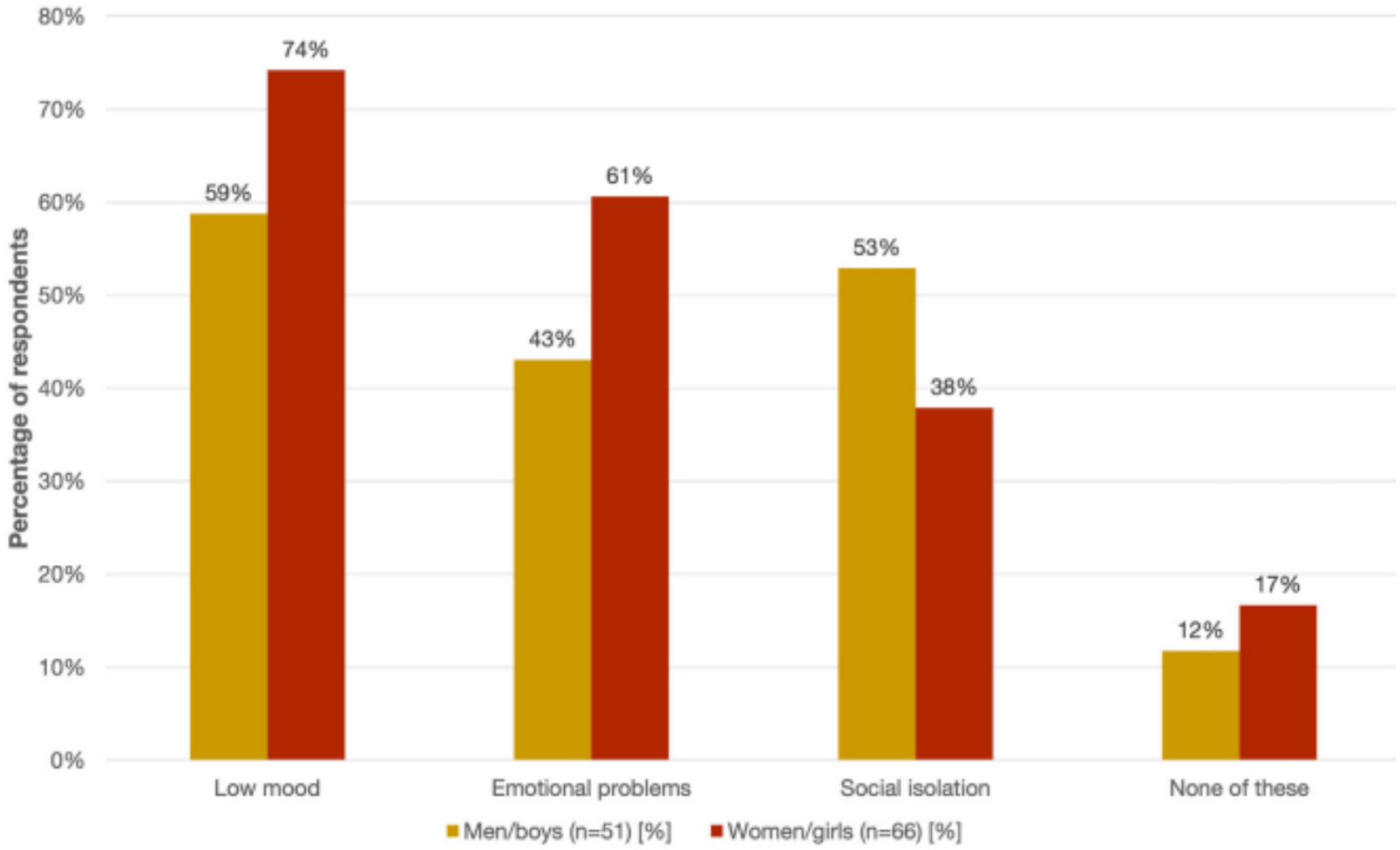
- Mainly characterized by mucocutaneous symptoms
- Variable severity from minor to life-threatening hemorrhage



Modified from Blaauwgeers MW, AJH, 2020

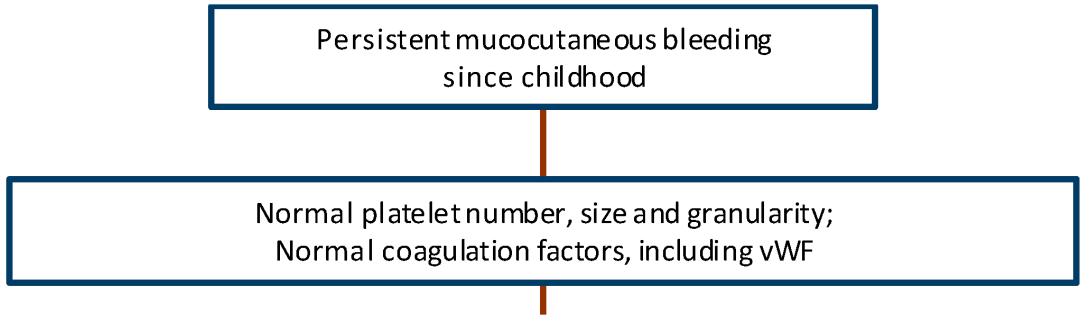
Psychological impact of bleeding

88 people with GT and **29 carers of children/young people** with GT aged <16 years

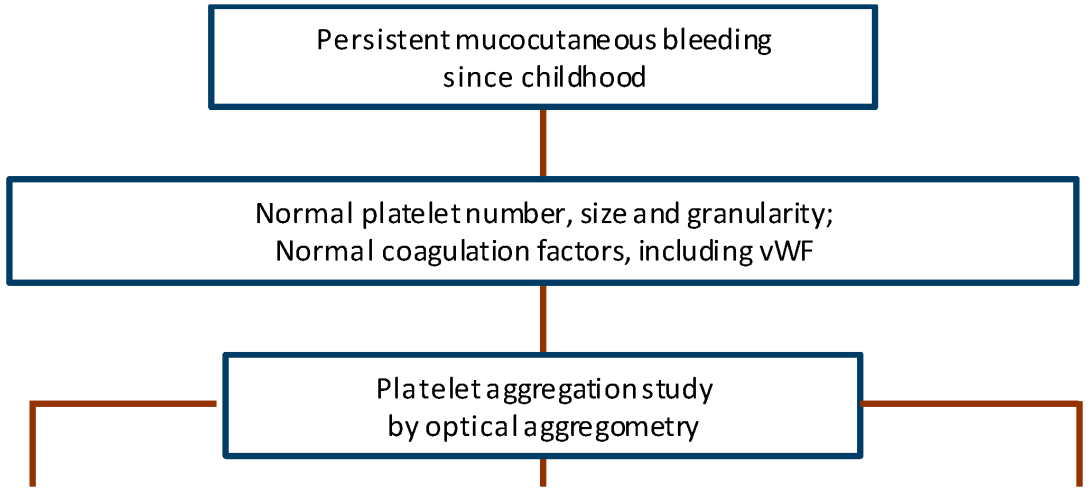


Khair K., Res Pract Thromb Haemost. 2024;8:e102586

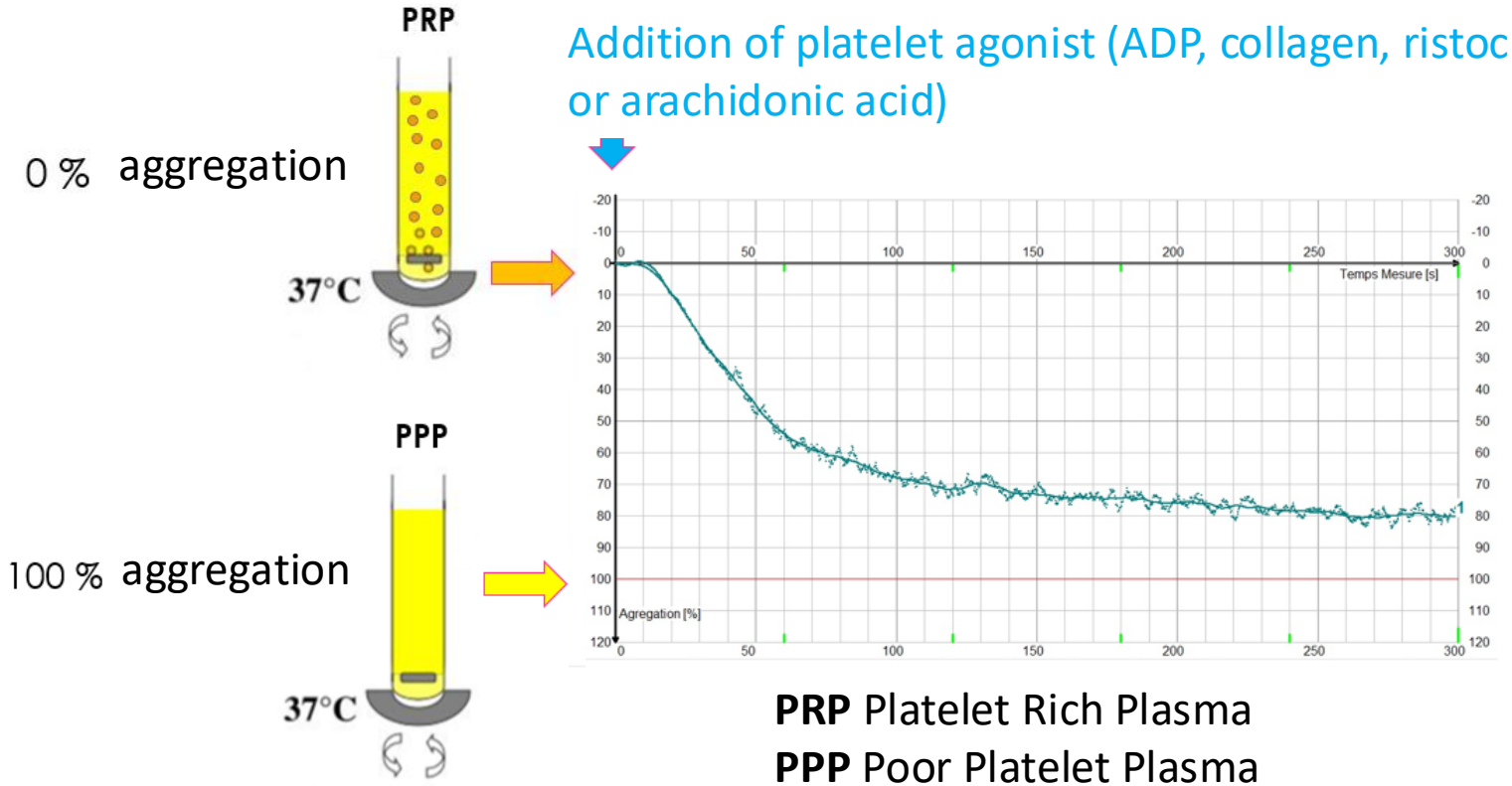
Diagnostic flowchart



Diagnostic flowchart



Light Transmission Aggregometry (LTA)

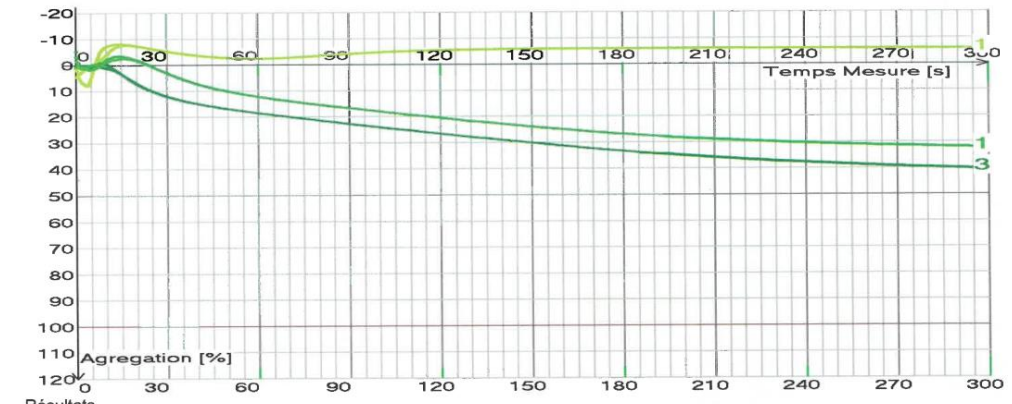


PRP Platelet Rich Plasma
PPP Poor Platelet Plasma

Visual of platelet aggregates formation by electron microscopy

A.Eckly, INSERM U949 Strasbourg

Absence or markedly reduced platelet aggregation with all agonists, except for ristocetin



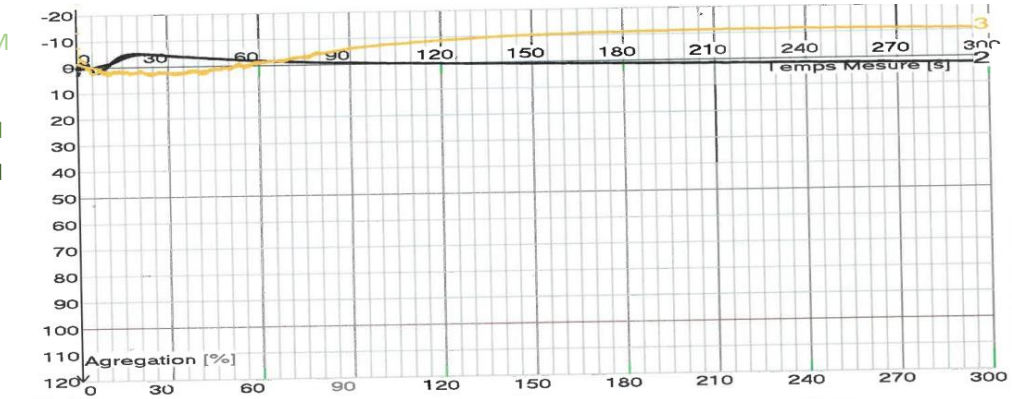
TRAP 10 µM

TRAP 25 µM

TRAP 50 µM

Résultats

No.	Date	Heure	Prénom	Nom	Test	Apact	Canal	SC Min [%]	Agrég. [s]	Agrég. Max [%]	Agrég. Pente [%/min]	Désagrégation Agrég.T2 [s]	Désagrégation Agrég.T2 [%]
9	11/06/2024	11:2			trap 10µM	Apact_02	1	0.00	20.0	-7.23	4.55	298.0	-5.86
15	11/06/2024	11:3			trap 50µM	Apact_01	3	0.00	300.2	40.15	36.61	298.0	40.10
16	11/06/2024	11:4			TRAP 25µM	Apact_01	1	-2.55	300.2	32.05	28.05	298.0	31.99

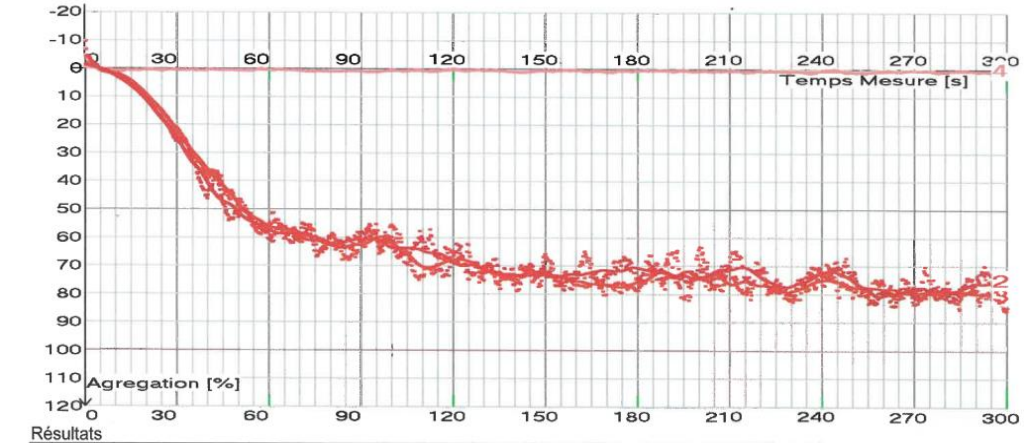


Collagen 2 µg/mL

Arachidonic acid 1 mM

Résultats

No.	Date	Heure	Prénom	Nom	Test	Apact	Canal	SC Min [%]	Agrég. Max [s]	Agrég. Max [%]	Agrég. Pente [%/min]	Agrég. Temps de latence [s]	Désagrégation Agrég.T2 [s]	Désagrégation Agrég.T2 [%]
10	11/06/2024	11:27:25	A		Arachidonique 1mM	Apact_02	2	-4.98	297.0	2.16	5.53		298.0	2.15
11	11/06/2024	11:27:58	A		Collagen 2µg/ml	Apact_02	3	0.00	28.8	2.44	3.80	20.0	298.0	-10.92

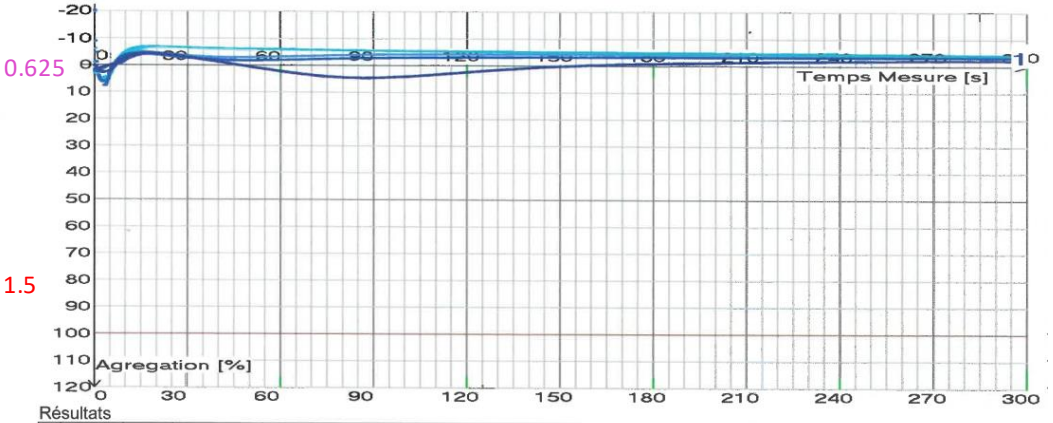


Ristocetin 0.625

Ristocetin 1.5

Résultats

No.	Date	Heure	Prénom	Nom	Test	Apact	Canal	SC Min [%]	Agrég. Max [s]	Agrég. Max [%]	Agrég. Pente [%/min]	Désagrégation Agrég.T2 [s]	Désagrégation Agrég.T2 [%]
7	11/06/2024	11:25			ristocétine 1.20 mg/ml	Apact_01	3	0.00	300.2	81.41	83.80	298.0	81.07
8	11/06/2024	11:26			Ristocetin 0.625mg/ml	Apact_01	4	0.00	89.2	0.85	2.89	298.0	0.77
14	11/06/2024	11:36			Ristocetin 1.5mg/ml	Apact_01	2	0.00	258.4	80.75	95.73	298.0	75.94



ADP 0.5 µM

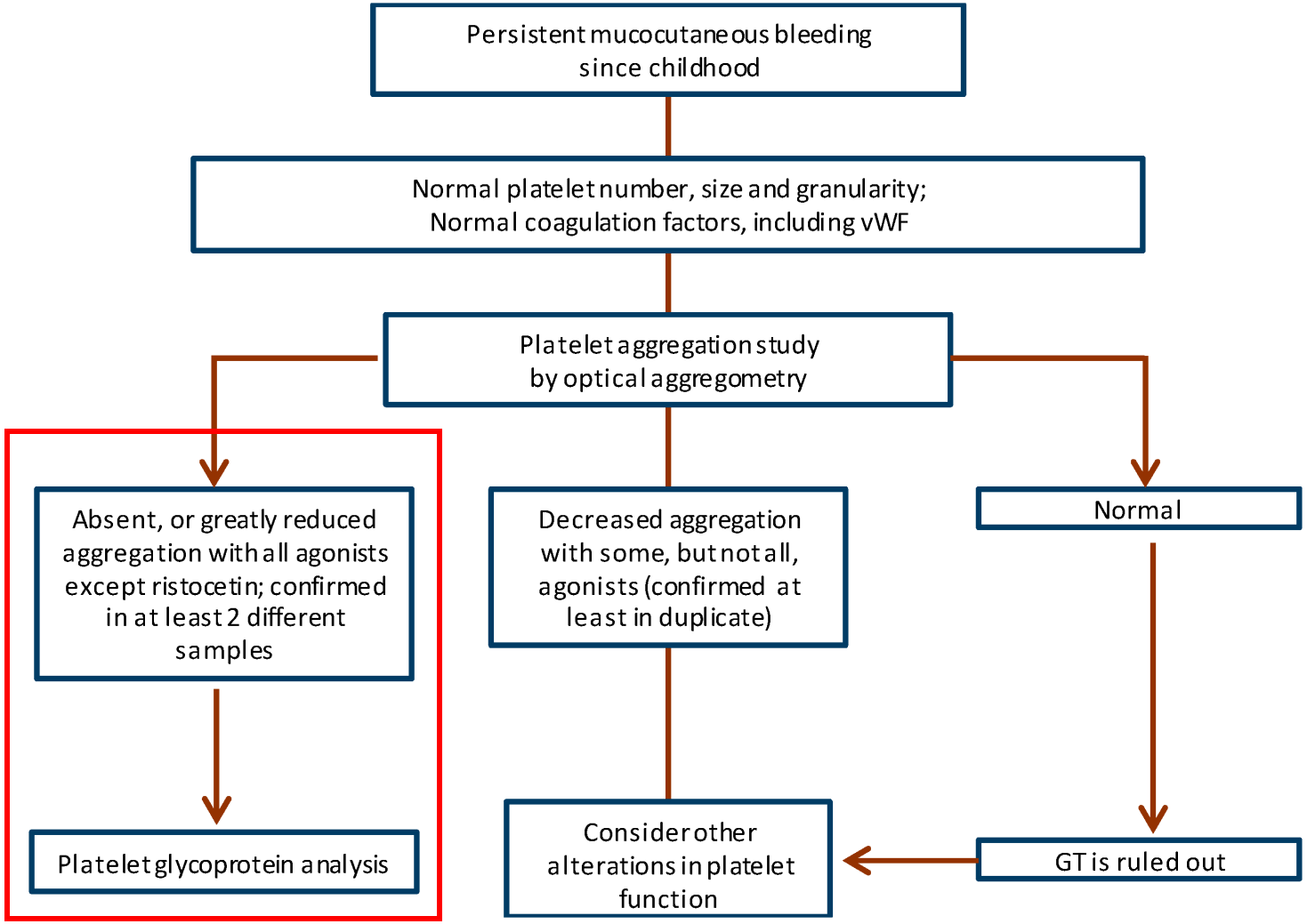
ADP 2.5 µM

ADP 5 µM

Résultats

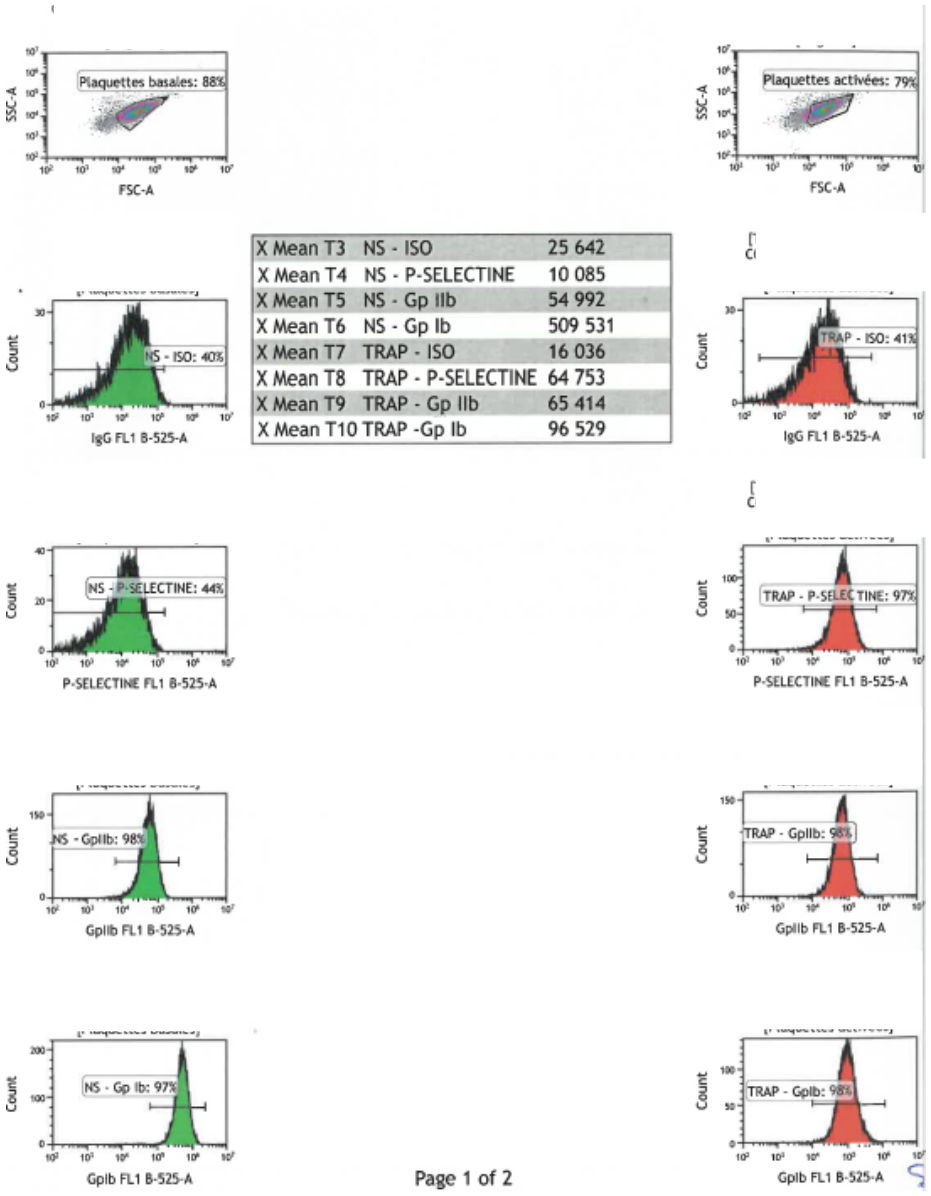
No.	Date	Heure	Prénom	Nom	Test	Apact	Canal	SC Min [%]	Agrég. Max [s]	Agrég. Max [%]	Agrég. Pente [%/min]	Agrég. Temps de latence [s]	Désagrégation Agrég.T2 [s]	Désagrégation Agrég.T2 [%]
5	11/06/2024	11:24:			ADP 2,5 µM	Apact_01	1	0.00	5.0	0.00	1.24	12.0	298.0	
6	11/06/2024	11:24:			ADP 0.5 µM	Apact_01	2	0.00	5.0	0.00	-5.50		298.0	-4.07
12	11/06/2024	11:34:			ADP 5 µM	Apact_02	4	0.00	5.0	0.00	2.86		298.0	-3.36
13	11/06/2024	11:36:			ADP 10 µM	Apact_01	1	-4.31	86.6	4.50	10.64		298.0	-2.34

Diagnostic flowchart



Biomolecules **2025**, *15*, 1528

PLATELET GLYCOPROTEINS – FLOW CYTOMETRY



X Mean T3	NS - ISO	25 642
X Mean T4	NS - P-SELECTINE	10 085
X Mean T5	NS - Gp IIb	54 992
X Mean T6	NS - Gp Ib	509 531
X Mean T7	TRAP - ISO	16 036
X Mean T8	TRAP - P-SELECTINE	64 753
X Mean T9	TRAP - Gp IIb	65 414
X Mean T10	TRAP -Gp Ib	96 529

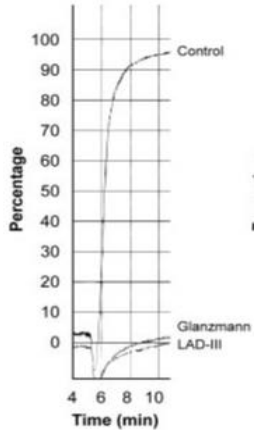
Resting	Number of sites	
GMP 140 (CD62P) *Cytométrie en flux, DXflex, PLT Gp/receptors/Biocytex*	0	<1000
GP IIb (CD41) *Cytométrie en flux, DXflex, PLT Gp/receptors/Biocytex*	**3818**	35600-54100
GP Ib (CD42b) *Cytométrie en flux, DXflex, PLT Gp/receptors/Biocytex*	**62112**	22450-42490

Activation TRAP 60µmol/L	Number of sites	
GMP 140 (CD62P) *Cytométrie en flux, DXflex, PLT Gp/receptors/Biocytex*	6339	2740-6800
GP IIb (CD41) *Cytométrie en flux, DXflex, PLT Gp/receptors/Biocytex*	**6425**	46490-77333
GP Ib (CD42b) *Cytométrie en flux, DXflex, PLT Gp/receptors/Biocytex*	10450	10170-23150

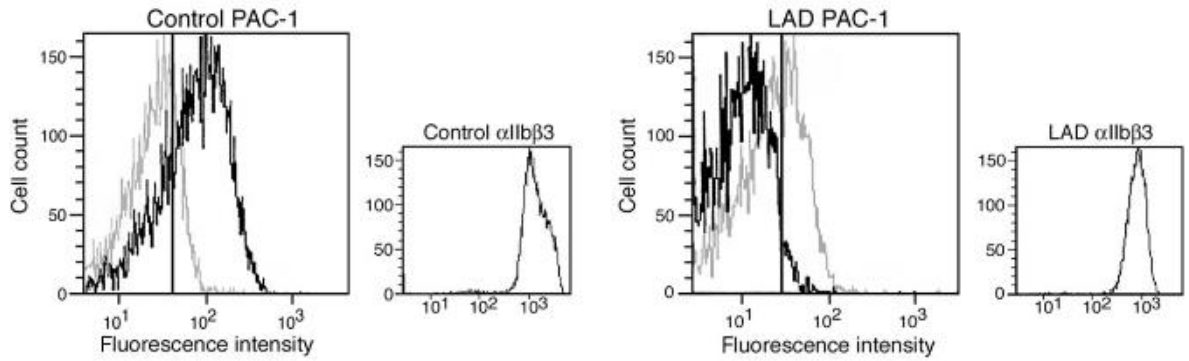
GLANZMANN THROMBASTHENIA IN ALL ITS FORMS

Disease Description	Comments
Type I Subgroup	
- Absence of platelet aggregation and little or no clot retraction. Levels of αIIbβ3 <5% or absent. Platelet Fg storage pool lacking or negligible. AR inheritance.	- The most common type of GT, given by defects in *ITGA2B* and *ITGB3 genes*. With *ITGA2B* defects αvβ3 may still be present and functional. Patients susceptible to form isoantibodies reactive with αIIbβ3 and/or αvβ3 after blood transfusion or pregnancy.
Type II Subgroup	
- Absence of platelet aggregation but clot retraction can be partial or normal. Residual αIIbβ3 historically defined as 5–15% of normal levels. Platelet Fg pool can be substantial. AR inheritance.	- Frequency variable within populations but usually less than 20% of the patients. Given by defects in *ITGA2B* and *ITGB3*. Clot retraction defects and the platelet Fg storage capacity are mutation dependent.
Variant Forms	
- Absence of platelet aggregation but clot retraction and Fg storage highly variable. Residual αIIbβ3 mainly >50% or even normal but non-functional with little or no activation-dependent Fg binding as also shown by a lack of PAC-1 binding. AR inheritance.	- Rare. Can be given by defects in *ITGA2B* but mostly by *ITGB3* variants. Extracellular mutations directly or indirectly abrogate Fg-binding sites. Intracellular mutations stop signals for αIIbβ3 activation. Clot retraction and Fg storage are mutation dependent. Can be confused with defects in *FERMT3* and *RASGRP2* that prevent kindlin-3 (LAD-III disease) and CalDAG-GEFI signaling.

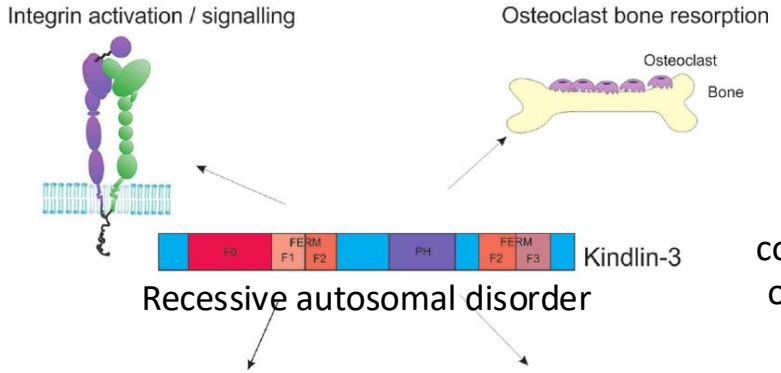
LEUKOCYTE ADHESION DEFICIENCY (LAD-III)



van de Vijver E, Blood, 2012



Pasvolsky, JEM, 2007



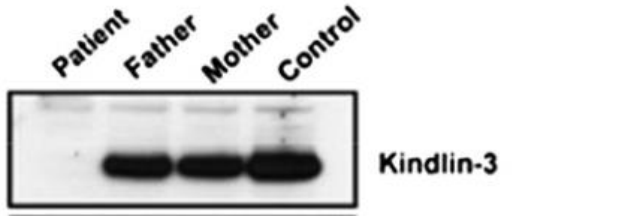
Osteopetrosis

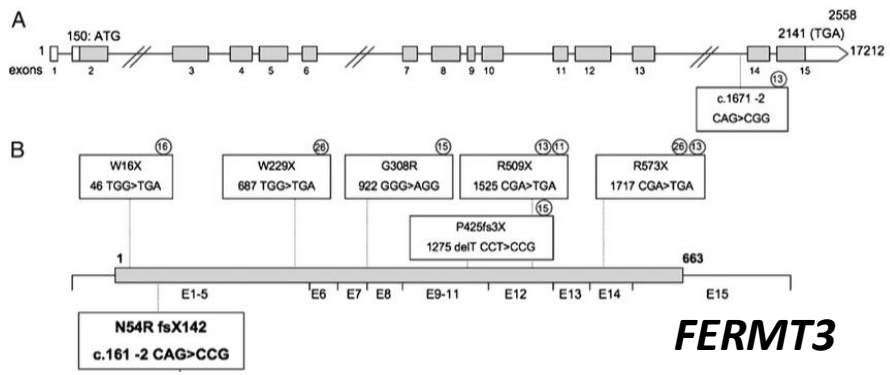
Essential cytoplasmic cofactor for the activation of β_1, β_2 and β_3 integrins

Severe bleeding phenotype

Recurrent infections

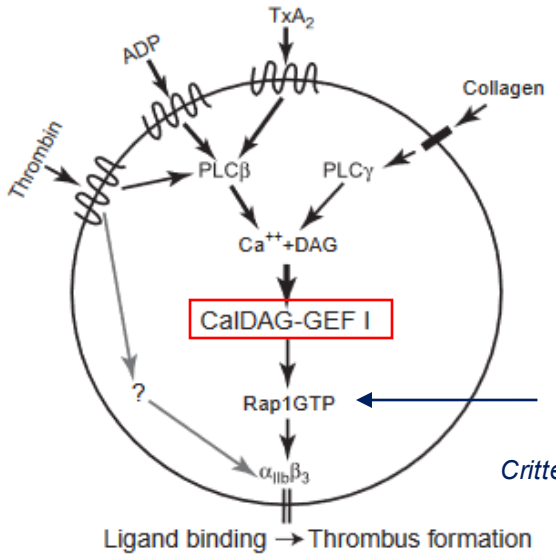
Fagerholm SC, Am J Clin Exp Immunol, 2014





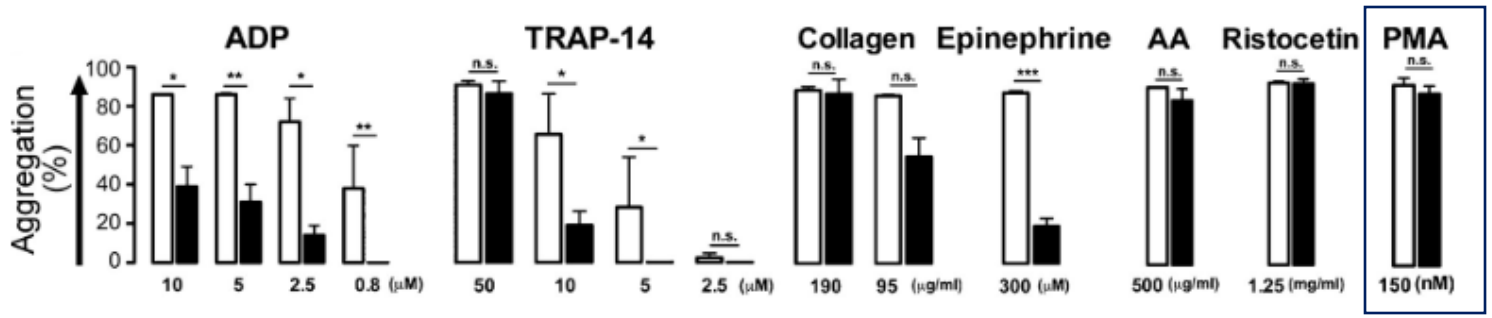
Robert P, J immunol, 2011

CALDAG-GEFI DEFICIENCY

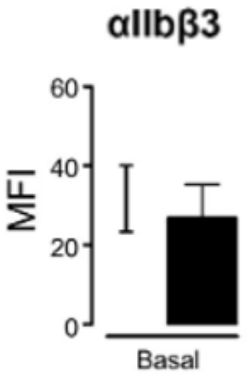


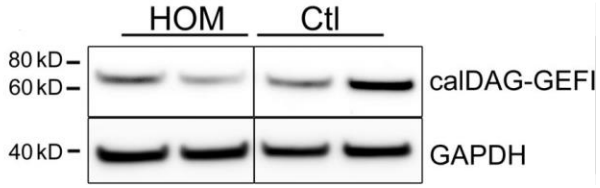
PMA

Crittenden JR, Nature Medicine, 2004



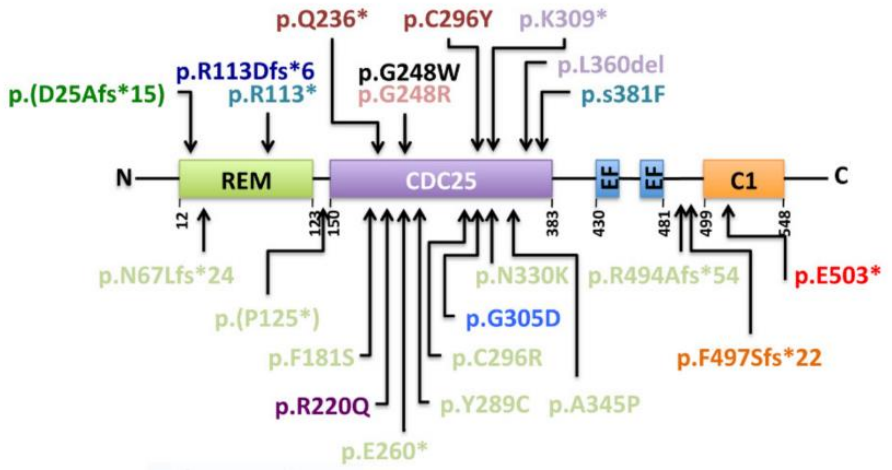
Canault M, JEM, 2014





Canault M, JEM, 2014

RASGRP2-AR



Canault M, Int. J. Mol. Sci., 2020

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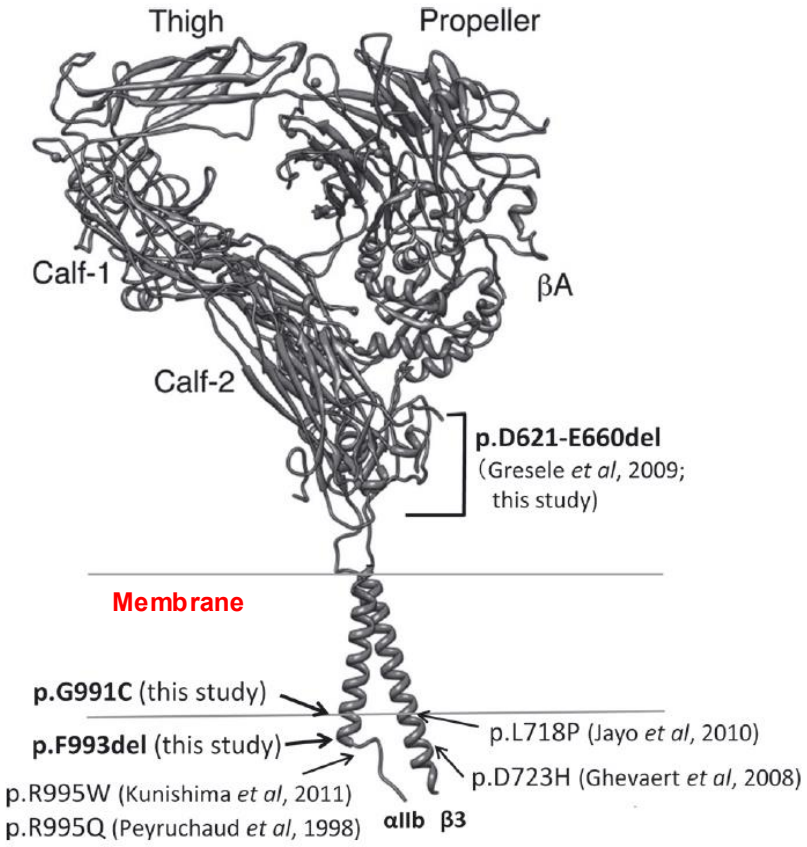
Upregulated αIIbβ3 and Macrothrombocytopenia (MTP)	
- Much reduced platelet aggregation with clot retraction and Fg storage again variable. Residual αIIbβ3 normally >30% but with spontaneous binding of PAC-1 (but rarely Fg). MTP mostly moderate with subpopulations of enlarged even giant platelets. AD inheritance.	- Rare. Patients with up-regulated αIIbβ3 interfering with megakaryocyte maturation and platelet biogenesis with enlarged platelets in variable numbers. Bleeding mostly due to defective αIIbβ3 function. Single allele mutations on *ITGA2B* but mostly *ITGB3*. Often these affect cytoplasmic domains.

Notes: The above criteria are basic for each subtype, but there is much overlap between them and clear boundaries do not exist. PAC-1 is an activation dependent IgM monoclonal antibody to αIIbβ3.

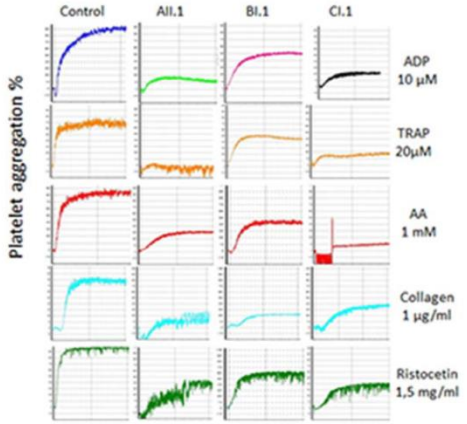
Abbreviations: AR, autosomal recessive; AD, autosomal dominant; LAD-III, leukocyte adhesion deficiency syndrome type III.

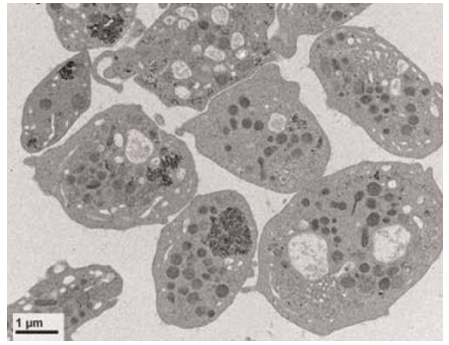
Nurden Journal of Blood Medicine 2021:12

GLANZMANN THROMBASTHENIA-LIKE SYNDROME ASSOCIATED WITH MACROTHROMBOCYTOPENIA

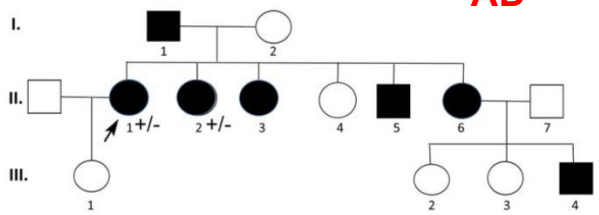


H. Kashiwagi *et al.*
Molecular Genetics & Genomic Medicine
2013; 1(2): 77–86

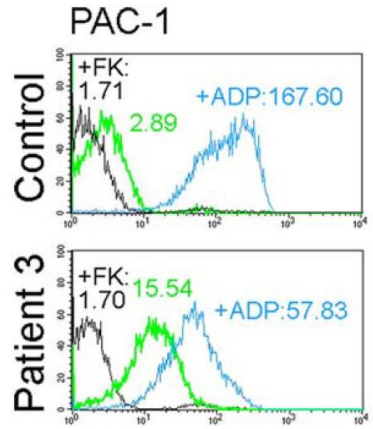




AD

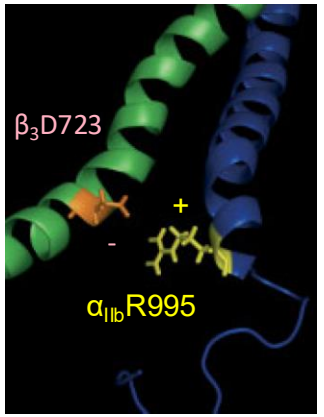


FAVIER ET AL. *Am J Hematol.* 2018;93:195–204



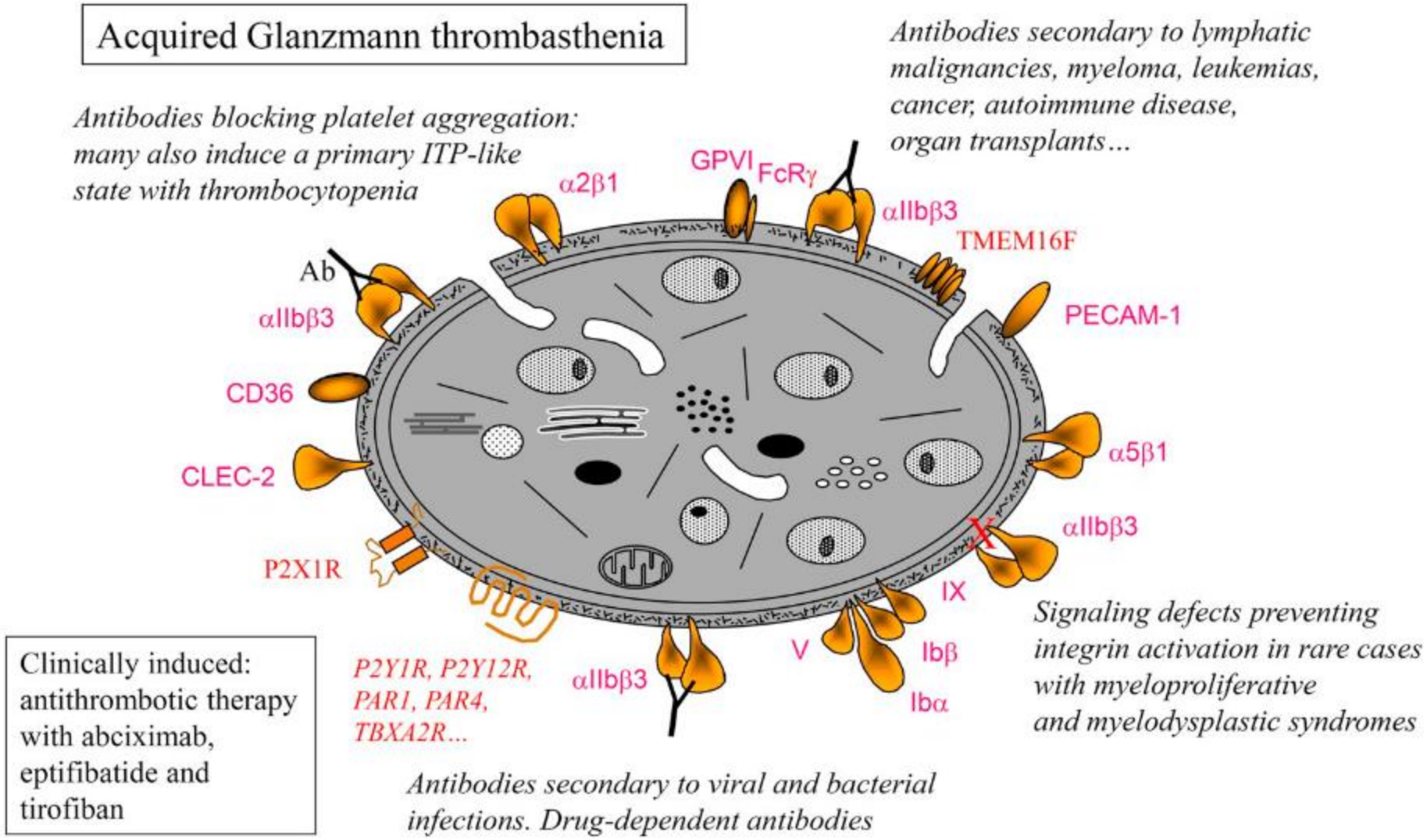
Kunishima, Blood, 2011

Spontaneous integrin activation

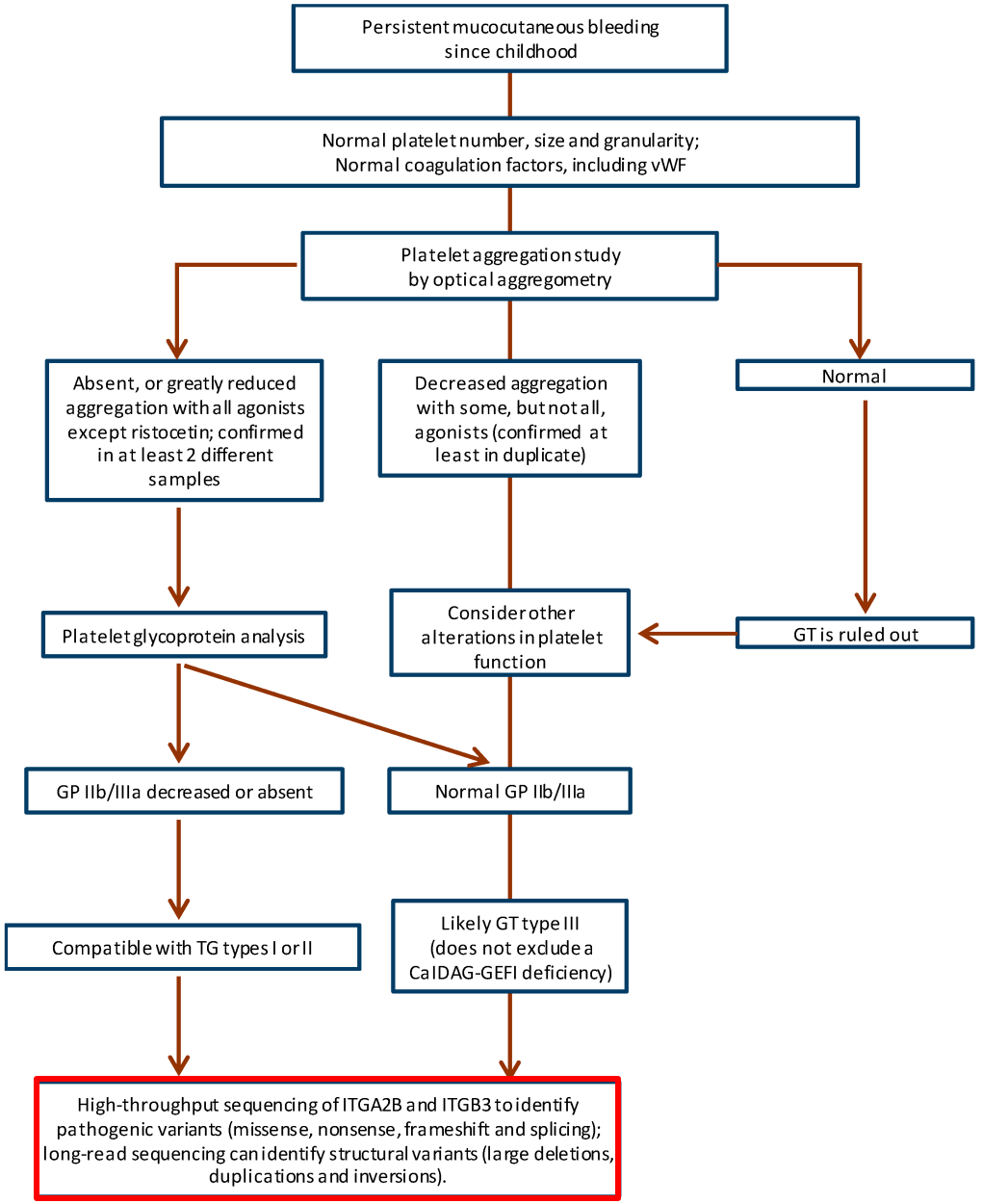


Nurden A, STH, 2011

ACQUIRED GLANZMANN THROMBASTHENIA

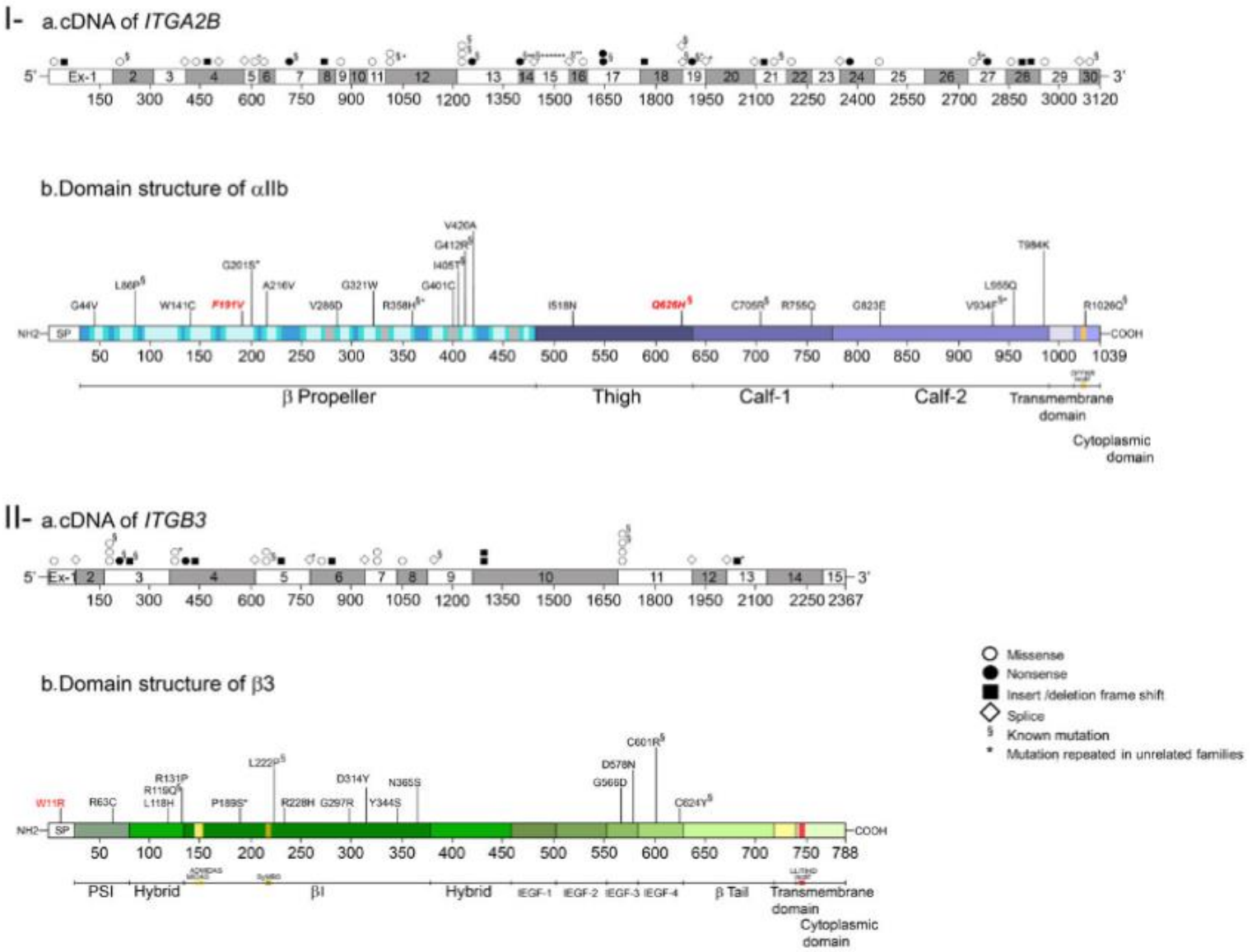


Diagnostic flowchart from clinical findings to genetic confirmation



Biomolecules **2025**, *15*, 1528

MUTATION SPECTRUM FOR *ITGA2B* AND *ITGB3* GENES



NURDEN A., HUMAN MUTATION, Vol. 36, No. 5, 548–561, 2015

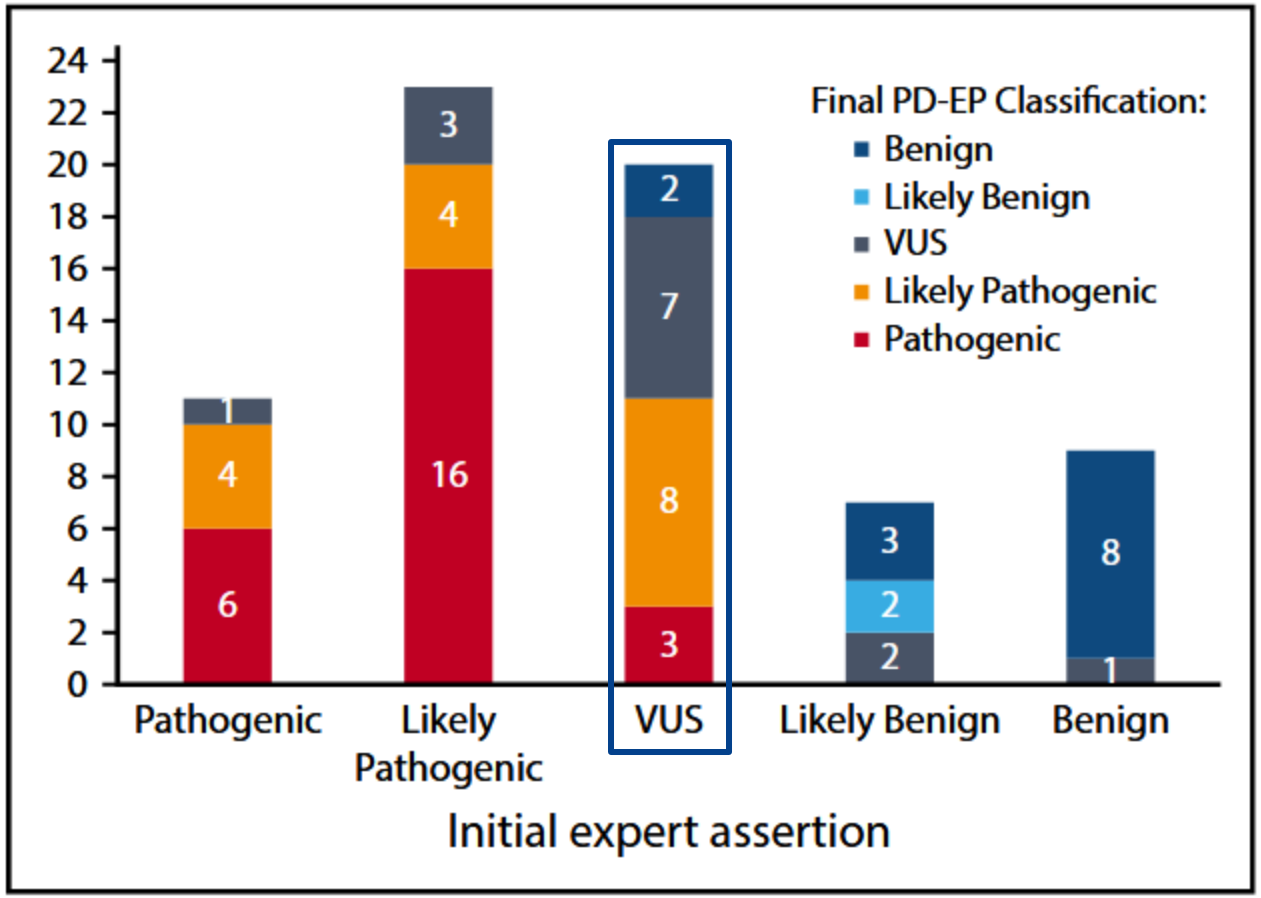
Specifications of the variant curation guidelines for *ITGA2B/ITGB3*: ClinGen Platelet Disorder Variant Curation Panel

Chairs

Juliana Perez Botero MD

Sarah Westbury BA, BM BCh, PhD, FRCPath

- To make ACMG/AMP rule specifications for *ITGA2B* and *ITGB3*
- Classifications of 70 pilot *ITAG2B/ITGB3* variants

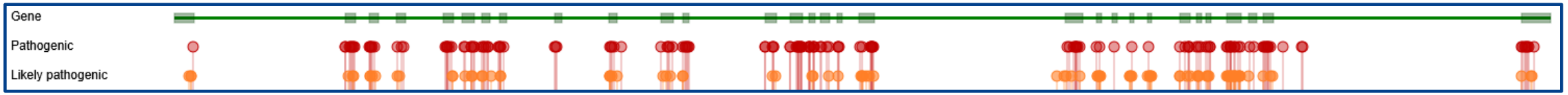


Reduction of VUS from 29% to 20%

GENETIC BASIS

ITGA2B

222 variants

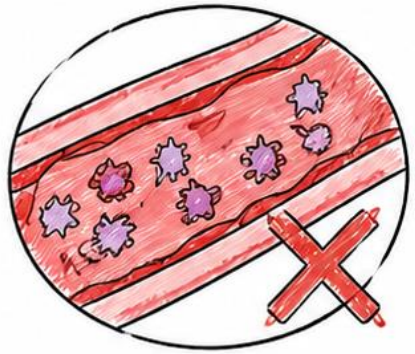


ITGB3

147 variants

ClinGen
Clinical Genome Resource

Glanzmann thrombasthenia follow-up



DEFECTIVE PLATELET AGGREGATION

↓

↑ BLEEDING RISK

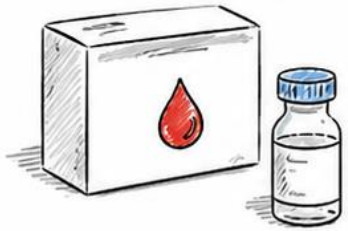
FOLLOW-UP REGULAR VISITS

CLINICAL ASSESSMENT

- ☑ Bleeding history
- ☑ Symptoms
- ☑ Quality of life
- ☑ Treatment review

LABORATORY MONITORING

- Platelet count
- Platelet function (aggregation studies)
- Hemoglobin / Ferritin



MANAGEMENT

- Avoid antiplatelet drugs
- Hemostatic treatment as needed
- Patient education

PREVENTION

- Avoid trauma
- Inform healthcare providers
- Medical alert

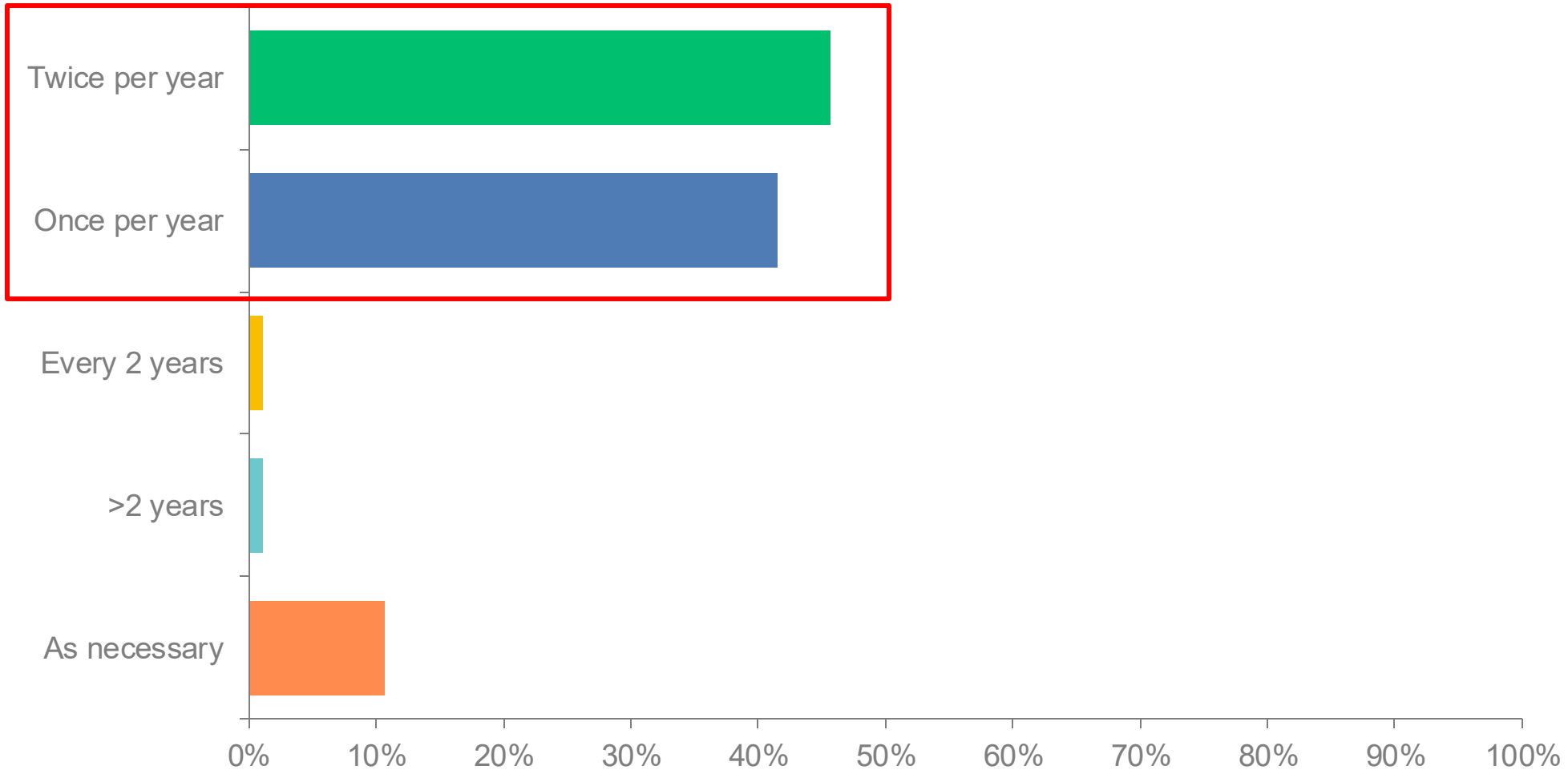
MULTIDISCIPLINARY CARE

- Hematologist
- Dentist
- Genetic counseling
- Support and resources

European Management of Glanzmann's Thrombasthenia: A Survey of Current Clinical Practice

Mathieu Fiore[1,2,3] | Andrea Artoni[4] | Robert Klamroth[5] | Mary Mathias[6] | Roger Schutgens[7] | Roseline d'Oiron[8] | EAHAD Glanzmann Thrombasthenia Working Group

6. What frequency of follow-up by the specialised centre do you usually recommend in the long term, apart from any intercurrent event?



N=94

Haemophilia, 2025; 31:1261–1270

Key objectives of clinical follow-up

1. To assess bleeding phenotype
2. To screen for clinical signs associated with iron deficiency
3. To monitor and discuss treatment options
4. To coordinate care with other healthcare professionals
5. To review the bleeding diary and emergency card
6. To continue patient therapeutic education
7. To assess and improve patients' understanding of their disease
8. To facilitate access to social and professional activities

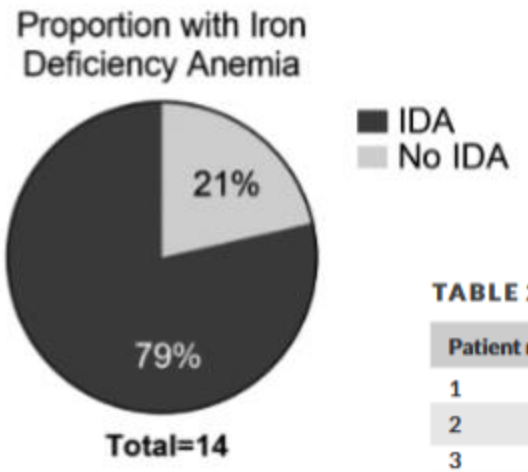
Investigations required for routine evaluation of patients with Glanzmann thrombasthenia

Diagnostic parameters	Role
CBC (PLT, Hb, MCV)	To screen for anemia
Ferritinemia	To screen for iron deficiency

PLT: platelet count; Hb: hemoglobin; MCV: mean corpuscular volume

Iron deficiency anemia and bleeding management in pediatric patients with Bernard-Soulier syndrome and Glanzmann Thrombasthenia: A single-institution analysis

Haemophilia WFH



BSS (n = 2) or **GT (n = 12)**

TABLE 2 Hematologic indices of all patients with BSS and GT[a]

Patient no.	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fl)	RDW (%)	Iron (μg/dL)	TIBC (μg/dL)	Iron saturation (%)	Ferritin (ng/ml)
1	11.1 (9.5-12.2)	33.4 (28.6-36.3)	91.0 (85.3-92.3)	13.4 (13.2-13.6)	76 (43-108)	393 (381-405)	19 (11-27)	15.5 (14.2-16.8)
2	10.7 (10.4-10.9)	31.5 (31.1-32.1)	75.2 (74.4-75.8)	16.0 (15.4-16.3)	52 (29-79)	381 (339-413)	14 (7-20)	19.9 (12.4-26.3)
3	10.6 (10.3-11.7)	32.8 (32.3-35.0)	82.1 (78.0-83.3)	15.3 (14.4-15.9)	33 (33)	481 (481)	7 (7)	10.9 (10.9)
4	11.0 (7.4-12.4)	32.4 (25.4-39.3)	79.7 (65.3-80.6)	14.6 (13.2-18.4)	65 (20-116)	492 (403-543)	15 (4-26)	5.4 (4.5-50.7)
5	8.4 (7.6-9.1)	25.6 (23.2-27.7)	81.8 (79.0-84.4)	17.0 (16.5-17.3)	42 (14-95)	409 (332-447)	12 (4-34)	8.0 (4.1-24.0)
6	12.7 (11.6-13.1)	36.5 (34.0-38.3)	80.2 (77.7-81.0)	13.4 (13.0-13.6)	-	-	-	-
7	8.0 (7.3-9.1)	28.2 (26.1-30.4)	79.4 (74.5-81.2)	18.4 (17.5-18.8)	15 (12-17)	445 (409-468)	3 (2-5)	6.8 (5.4-12.2)
8	10.6 (9.2-12.0)	32.5 (27.4-34.6)	80.5 (73.9-89.7)	12.9 (12.3-14.7)	48 (48)	318 (318)	14 (14)	18.5 (18.5)
9	10.2 (9.7-10.5)	30.5 (29.9-32.6)	77.3 (76.0-79.2)	15.8 (14.6-16.6)	44 (11-231)	293 (273-437)	15 (3-83)	16.8 (6.2-27.9)
10	13.2 (12.8-13.9)	39.2 (37.1-42.0)	84.5 (82.9-85.3)	13.2 (12.9-13.4)	-	-	-	-
11	13.8 (13.5-17.1)	39.8 (37.8-47.5)	84.6 (79.0-87.9)	12.8 (12.3-13.3)	-	-	-	-
12	13.3 (9.8-14.0)	39.1 (30.9-41.2)	75.3 (66.3-77.7)	17.0 (15.3-18.0)	38 (11.4-91.0)	548 (511-664)	7 (2-18)	7.9 (3.7-14.4)
13	13.5 (13.5)	41.6 (41.6)	91.0 (91.0)	14.6 (14.6)	-	-	-	-
14	10.4 (10.0-10.8)	30.4 (29.6-31.4)	82.9 (78.6-85.4)	16.2 (16.0-16.5)	-	-	-	-
Median Values of Cohort	11.1	33.4	81.8	14.6	46	401	15	11.7

Data presented as medians (*95% confidence intervals*).
Fl, femtoliters (1×10^{-15}); MCV, mean corpuscular volume; RDW, red cell distribution width; TIBC, total iron binding content.
[a]Hematologic indices presented represent baseline values for all individuals.

LEE ET AL. *Haemophilia*. 2022;28:633–641.

European Management of Glanzmann's Thrombasthenia: A Survey of Current Clinical Practice

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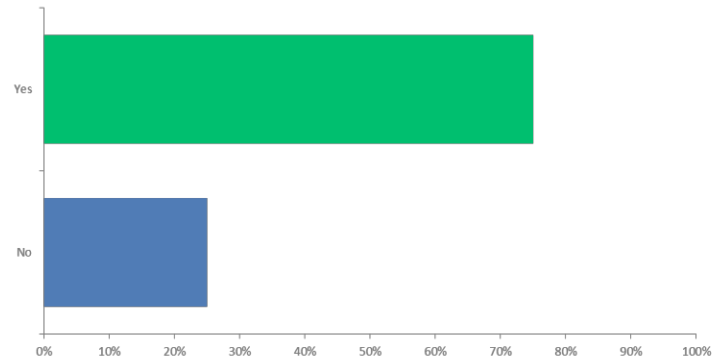
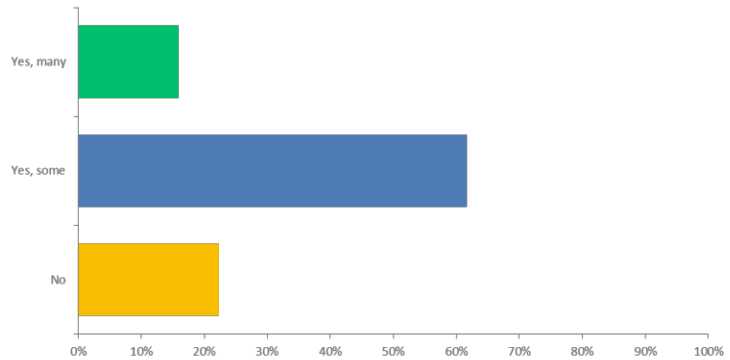
Q54: Do you prescribe chronic oral iron supplementation?



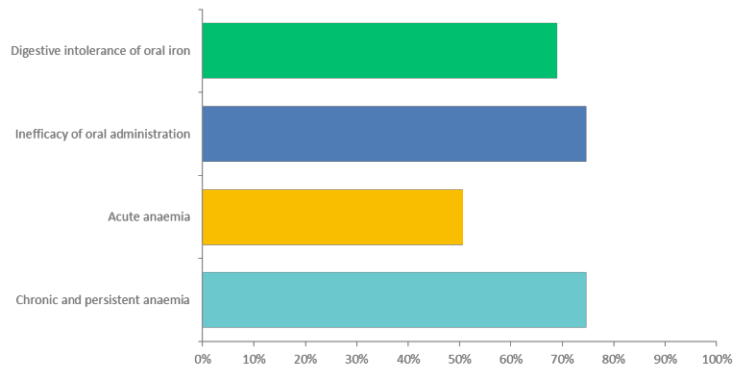
- Answered: 92 Skipped: 3

Q55: Do your patients require intravenous iron supplementation?



- Answered: 94 Skipped: 1

Q56: If yes, in which situation? (Please check all that apply.)



- Answered: 71 Skipped: 24

Haemophilia, 2025; 31:1261–1270

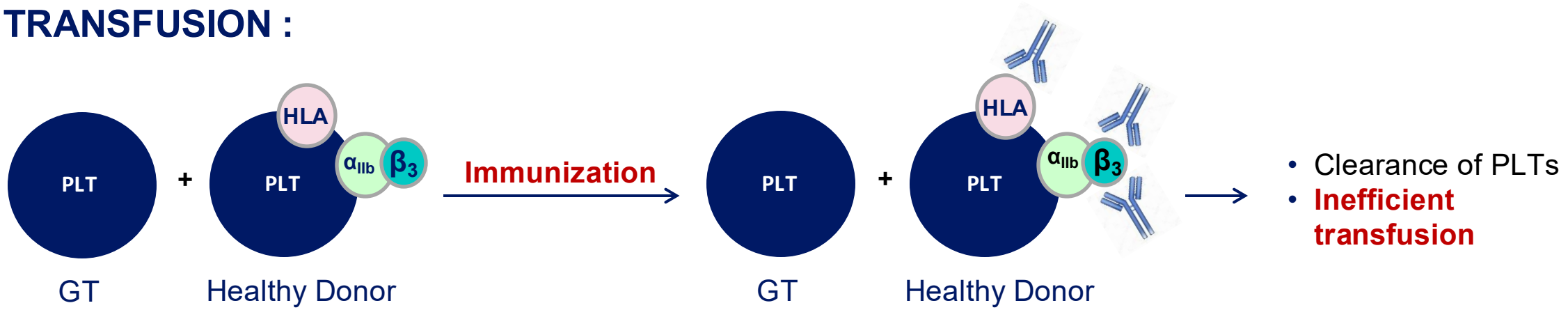
Investigations required for routine evaluation of patients with Glanzmann thrombasthenia

Diagnostic parameters	Role
CBC (PLT, Hb, MCV)	To screen for anemia and iron deficiency
Ferritinemia	To screen for anemia and iron deficiency
Anti-HLA antibodies screening	To select treatment strategies, ensure efficacy, and anticipate tolerance of platelet concentrates administration
Anti-$\alpha_{IIb}\beta_3$ antibodies screening (MAIPA)	To select treatment strategies, ensure efficacy, and anticipate tolerance of platelet concentrates administration To evaluate the risk of fetal/neonatal thrombocytopenia

PLT: platelet count; Hb: hemoglobin; MCV: mean corpuscular volume

Anti–HLA/$\alpha_{IIb}\beta_3$ PLATELET ANTIBODIES

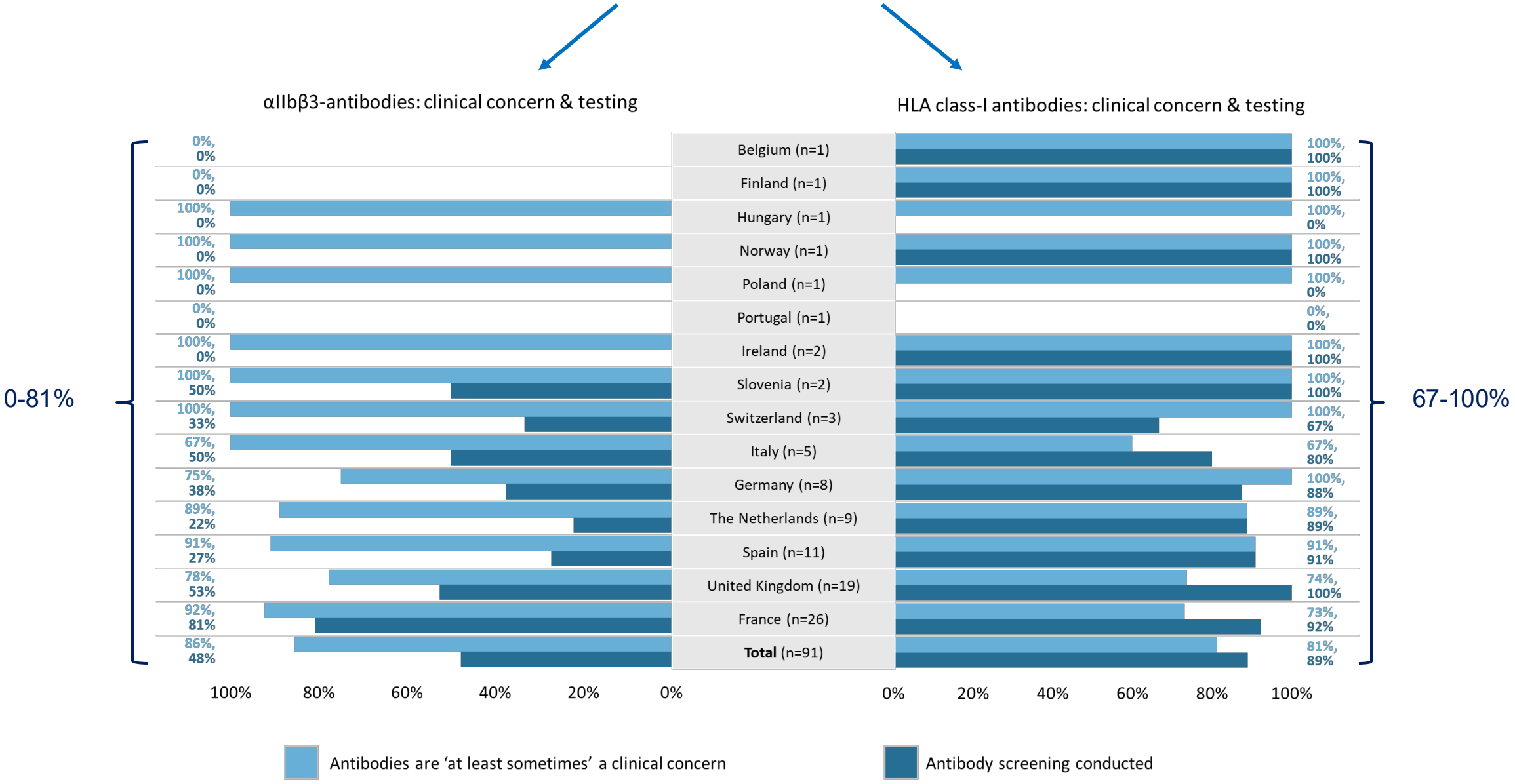
TRANSFUSION :



- Clearance of PLTs
- **Inefficient transfusion**

Fiore, BJH, 2018; Nurden, Transfus Med Rev, 2018

Anti–HLA/$\alpha_{IIb}\beta_3$ PLATELET ANTIBODIES

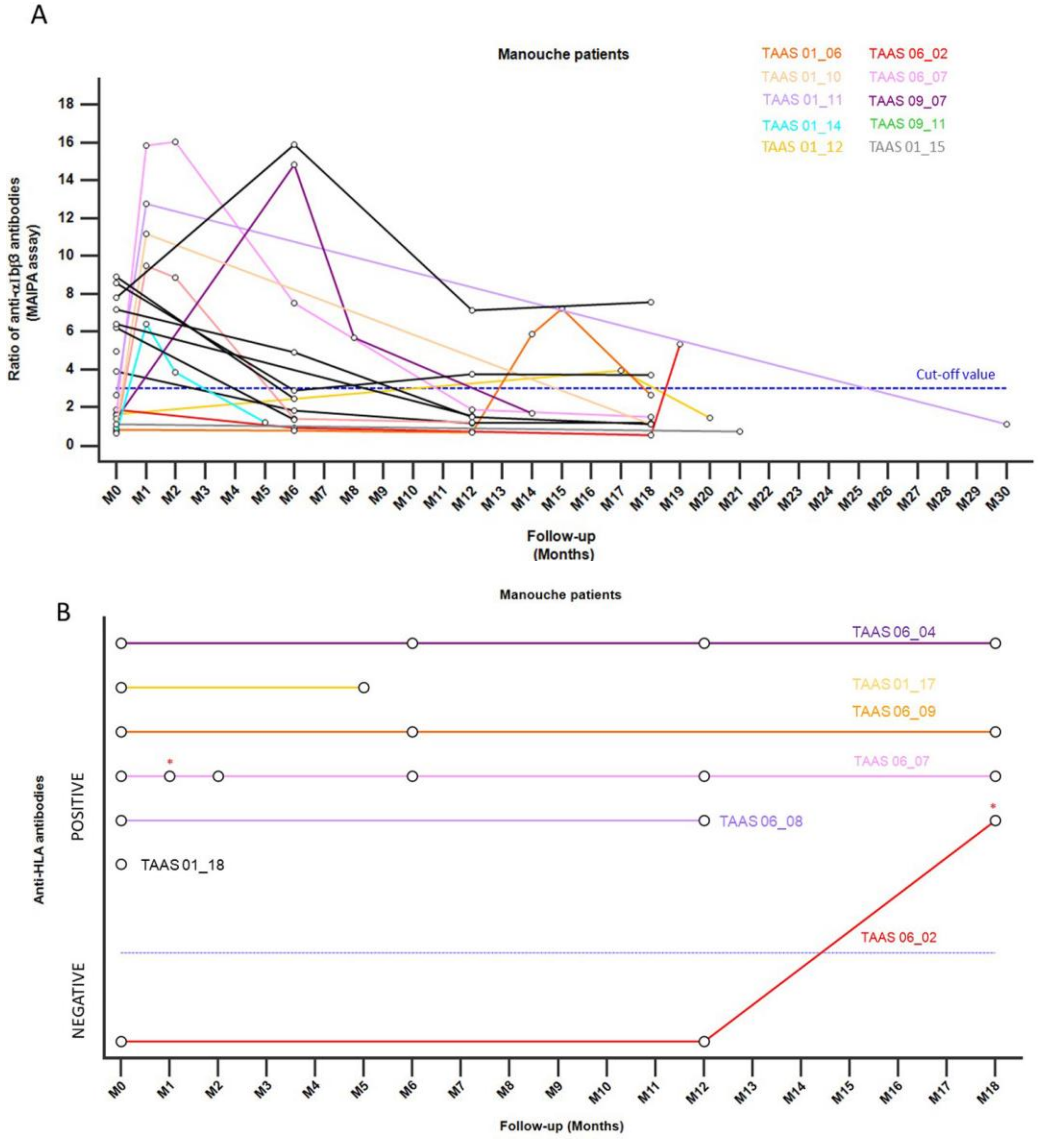


Haemophilia, 2025; 31:1261–1270

Natural history of antiplatelet antibody formation in patients with Glanzmann thrombasthenia: a French multicenter prospective study

Dominique Desprez[1] | Roseline d'Oiron[2] | Sophie Voisin[3,4] | Céline Falaise[4,5] | Marie-Christine Alessi[4,6] | Paul Saultier[4,7] | Géraldine Lavigne[8] | Arnaud Essaydi[9] | Marie-Joelle Apithy[9] | Arnaud Dupuis[9] | Valérie Goin[4] | Yoann Huguenin[4,10] | Mathieu Fiore[4,11]

Variables	All (*n* = 55)	Manouche patients (*n* = 28)	Other patients (*n* = 27)
Age, median (IQR)	32 (12-52)	37 (22-54)	24 (10-50)
Sex, *n* (%)			
Male	22 (40%)	11 (39%)	16 (59%)
Female	33 (60%)	17 (61%)	11 (41%)
Ethnic origin, *n* (%)			
Manouche	28 (51%)	28 (100%)	0
Caucasian	13 (23.5%)	0	13 (48%)
North African, Middle East	13 (23.5%)	0	13 (48%)
Sub-Saharan Africa	1 (2%)	0	1 (4%)
Type of GT, *n* (%)			
Type I	50 (91%)	28 (100%)	22 (81%)
Type II	4 (7%)	0	4 (15%)
Variant	1 (2%)	0	1 (4%)
Gene, *n* (%)			
ITGA2B	47 (85%)	28 (100%)	19 (70%)
ITGB3	8 (15%)	0	8 (30%)
Allelic status, *n* (%)			
Homozygous	43 (78%)	28 (100%)	15 (55%)
Compound heterozygous	12 (22%)	0	12 (44%)
Type of variants, *n* = 35 (%)			
Missense	16 (46%)	0	16 (47%)
Nonsense	6 (17%)	0	6 (18%)
Splice	9 (26%)	1 (100%)	8 (23%)
Indel	3 (8%)	0	3 (9%)
Others	1 (3%)	0	1 (3%)
Patients with biallelic null variants, *n* (%)			
No	22 (40%)	0	22 (81%)
Yes	33 (60%)	28 (100%)	5 (19%)
Blood products administration, *n* (%)	50 (91%)	24 (86%)	26 (96%)
Platelet transfusion	45 (82%)	21 (75%)	24 (92%)
RBC administration	45 (82%)	23 (82%)	22 (85%)
Full-term pregnancies[a], *n* (%)	12 (46%)	6 (46%)	6 (46%)
Antiplatelet antibodies			
Anti-HLA Abs, *n* (%)	11/42 (26%)	6/23 (26%)	5/19 (26%)
Anti-αIIbβ3Abs, *n* (%)	8/55 (14%)	8/28 (29%)	0/27



Anti-$\alpha_{IIb}\beta_3$ Abs

Anti-HLA Abs

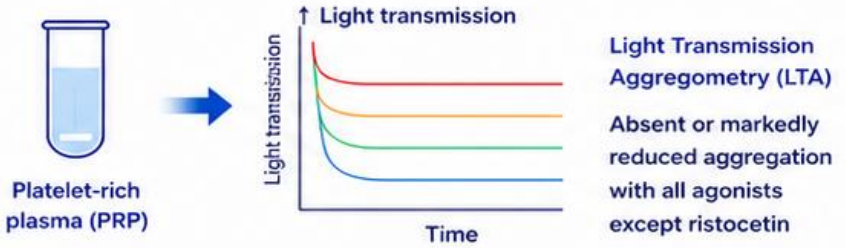
J Thromb Haemost. 2026;■:1–13

GLANZMANN THROMBASTHENIA

DIAGNOSTIC APPROACH & MANAGEMENT PRINCIPLES

1. DIAGNOSTIC APPROACH

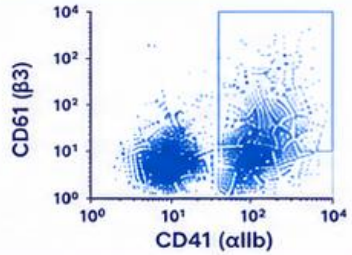
A. FUNCTIONAL TESTING



Light Transmission Aggregometry (LTA)

Absent or markedly reduced aggregation with all agonists except ristocetin

B. PLATELET GLYCOPROTEIN ANALYSIS



Flow cytometry (platelet glycoproteins)

Markedly reduced or absent αIIbβ3 expression

C. DIAGNOSTIC CONFIRMATION

Genetic analysis: ITGA2B / ITGB3

ACMG/AMP guidelines support variant interpretation

Differential diagnosis with other disorders of αIIbβ3 activation or expression

2. PRINCIPLES OF FOLLOW-UP

To assess bleeding phenotype

To screen for clinical and biological signs associated with anemia and iron deficiency

To regularly screen for anti-HLA and anti-GPIIb-IIIa antibodies

Patient-centered care

THANK YOU

CRPP Centre de Référence Pathologies Plaquettaires

MHEMO La Filière des maladies rares de l'hémostase

ebn ERN | EuroBloodNet

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