2ND meeting of the European Research Consortium on ITP

NEW INSIGHTS INTO IMMUNE THROMBOCYTOPENIA

Paris Crowne Plaza Paris République

April 23-24, 2026

ERCI

2ND meeting of the European Research Consortium on ITP

NEW INSIGHTS INTO IMMUNE THROMBOCYTOPENIA

Paris Crowne Plaza Paris République

April 23-24, 2026

Other novel therapeutic approaches in ITP:
- Complement inhibition
- FcRn inhibition

Prof Sylvain AUDIA

Department of Internal Medicine and Clinical Immunology, Dijon
Referral Center for Autoimmune Cytopenia in Adults
sylvain.audia@chu-dijon.fr sylvain.audia@u-bourgogne.fr

CHU Centre Hospitalier Universitaire Dijon

Université Bourgogne Europe

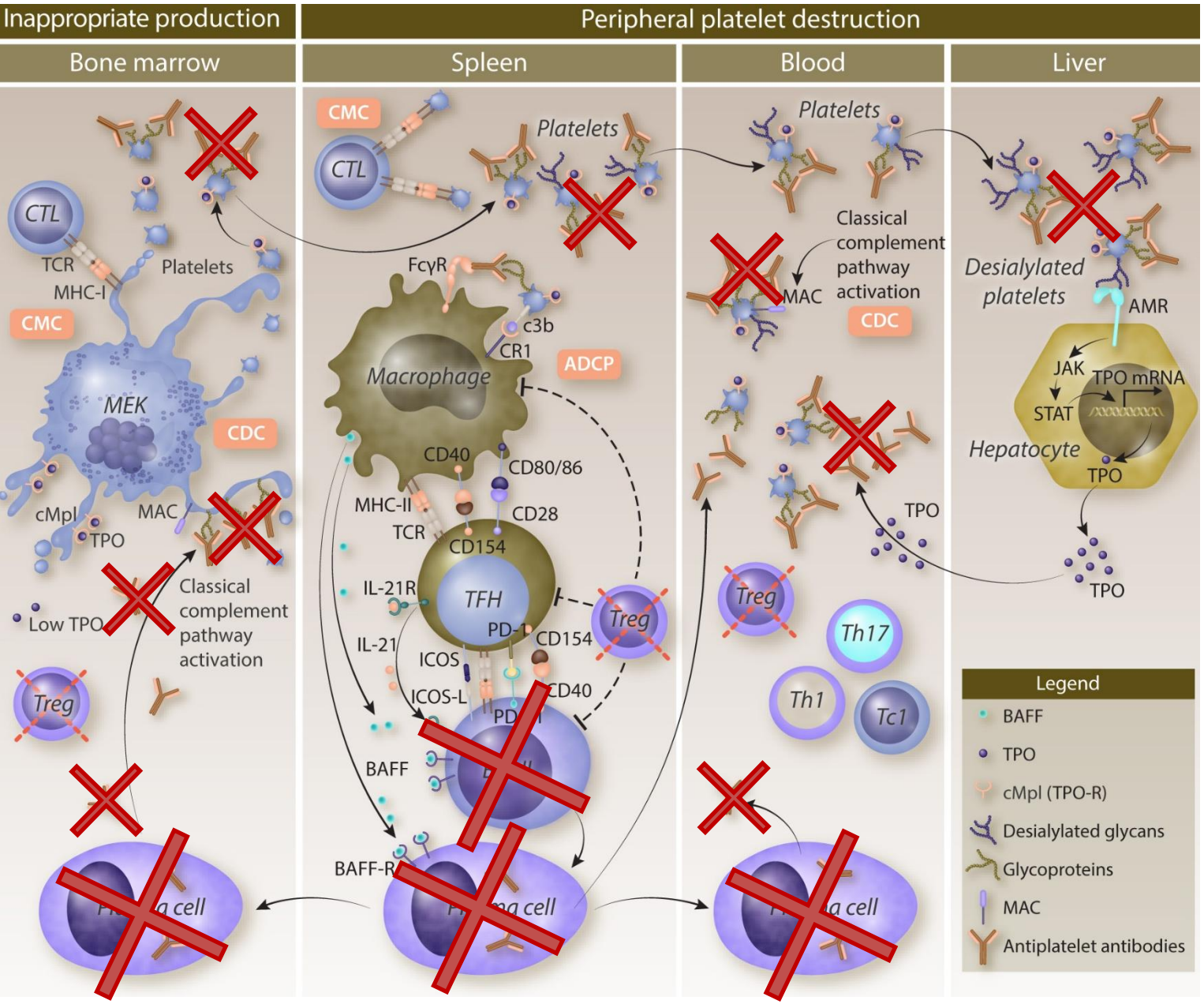
centre de référence maladies rares

CeReCAI Centre De Référence Cytopénies Auto-immunes de l'Adulte

MaRIH Filière de santé Maladies Rares Immuno-Hématologiques

Disclosures

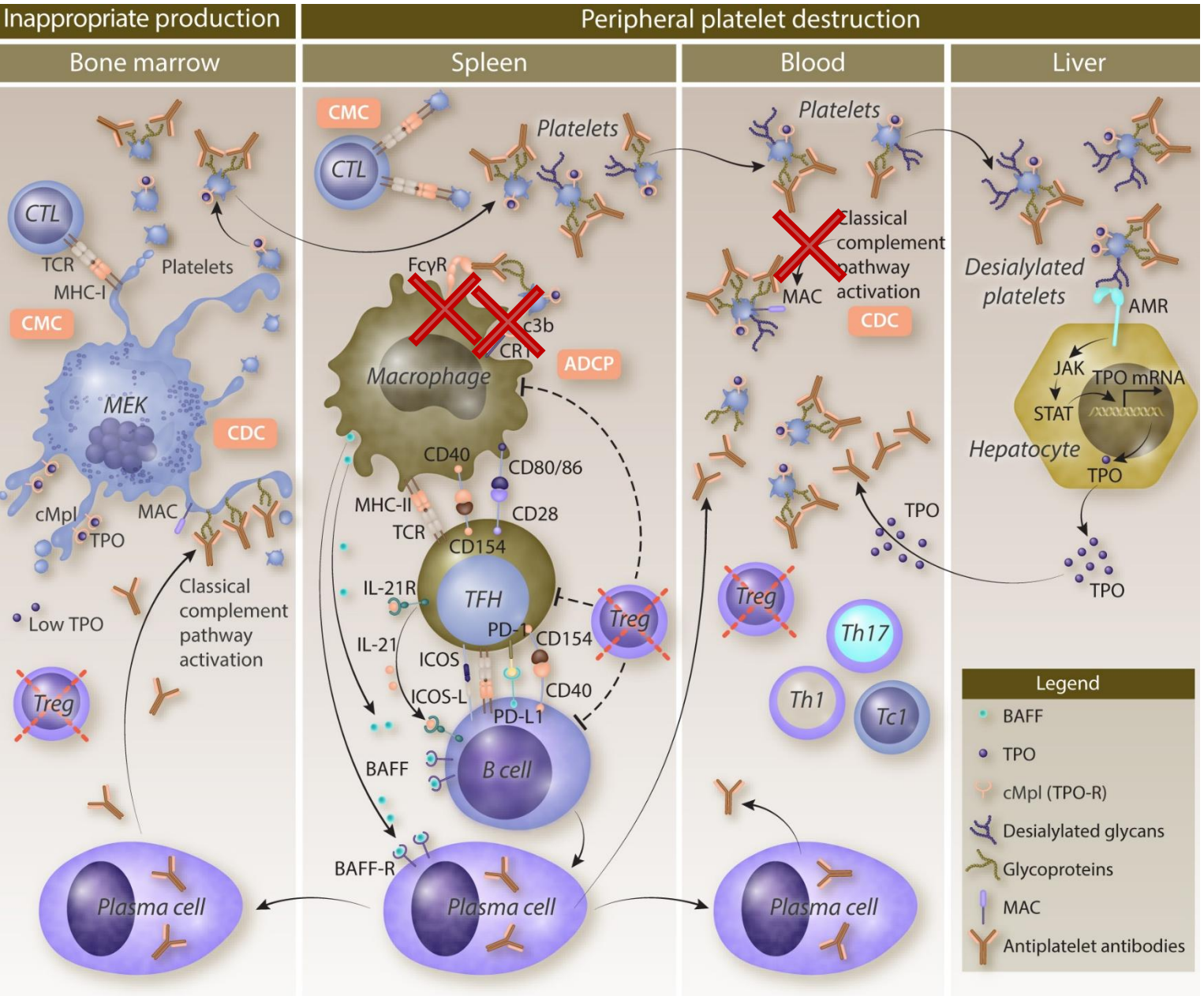
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Argenx			X			X	
Amgen						X	
Grifols			X			X	
Novartis	X		X			X	
Sanofi			X			X	



Targeting the humoral response in ITP

- **↘ antiplatelet Ab (APA) production**
  ⇒ B cell depleting therapies
- **↘ APA mechanisms of action**
  ⇒ IVIg
  ⇒ SYK inhibition
  ⇒ BTK inhibition
  ⇒ complement inhibition
  ⇒ FcRn blockade
  ⇒ ADCP inhibition

Audia *et al.*, Hemasphere 2021

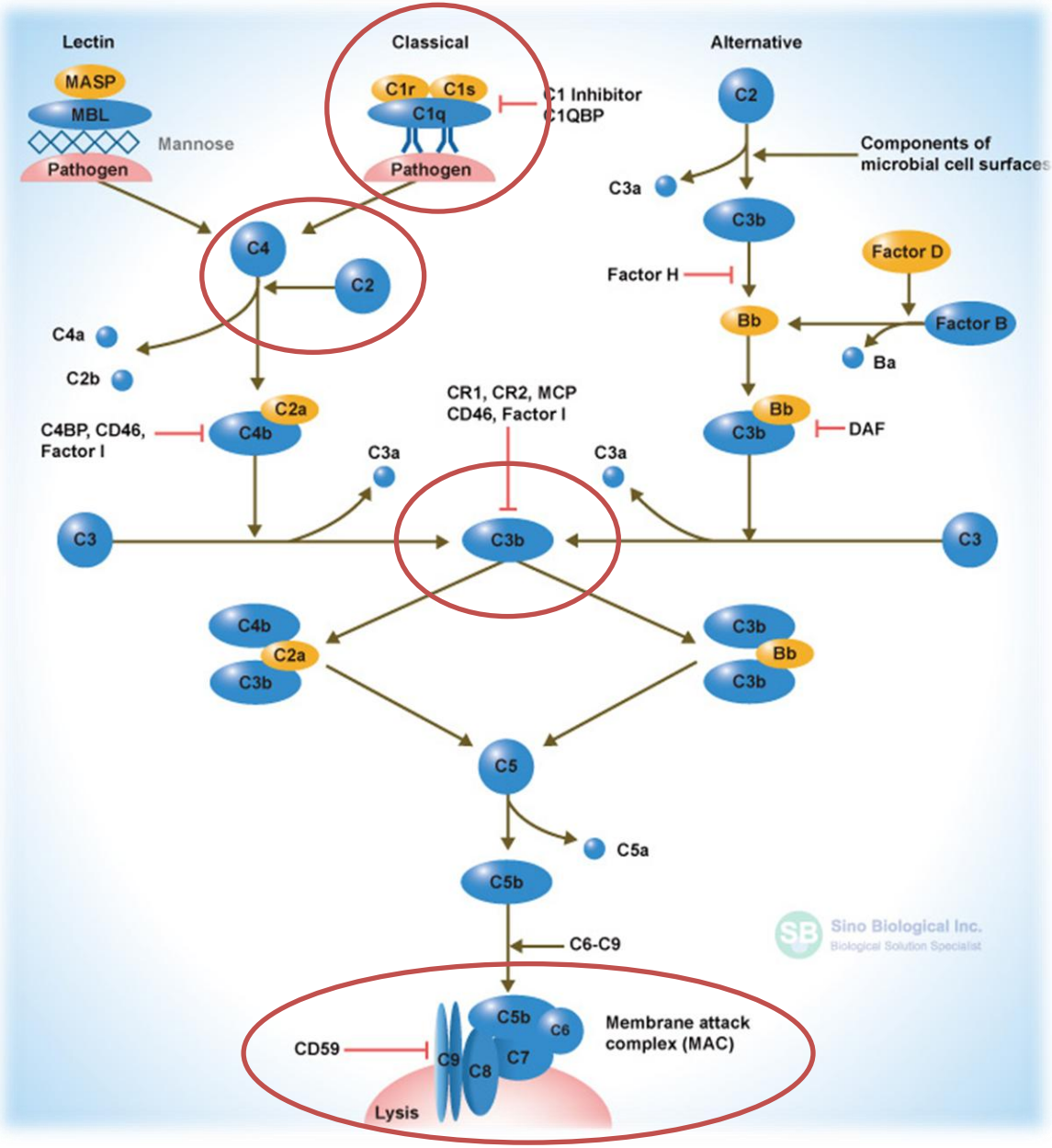


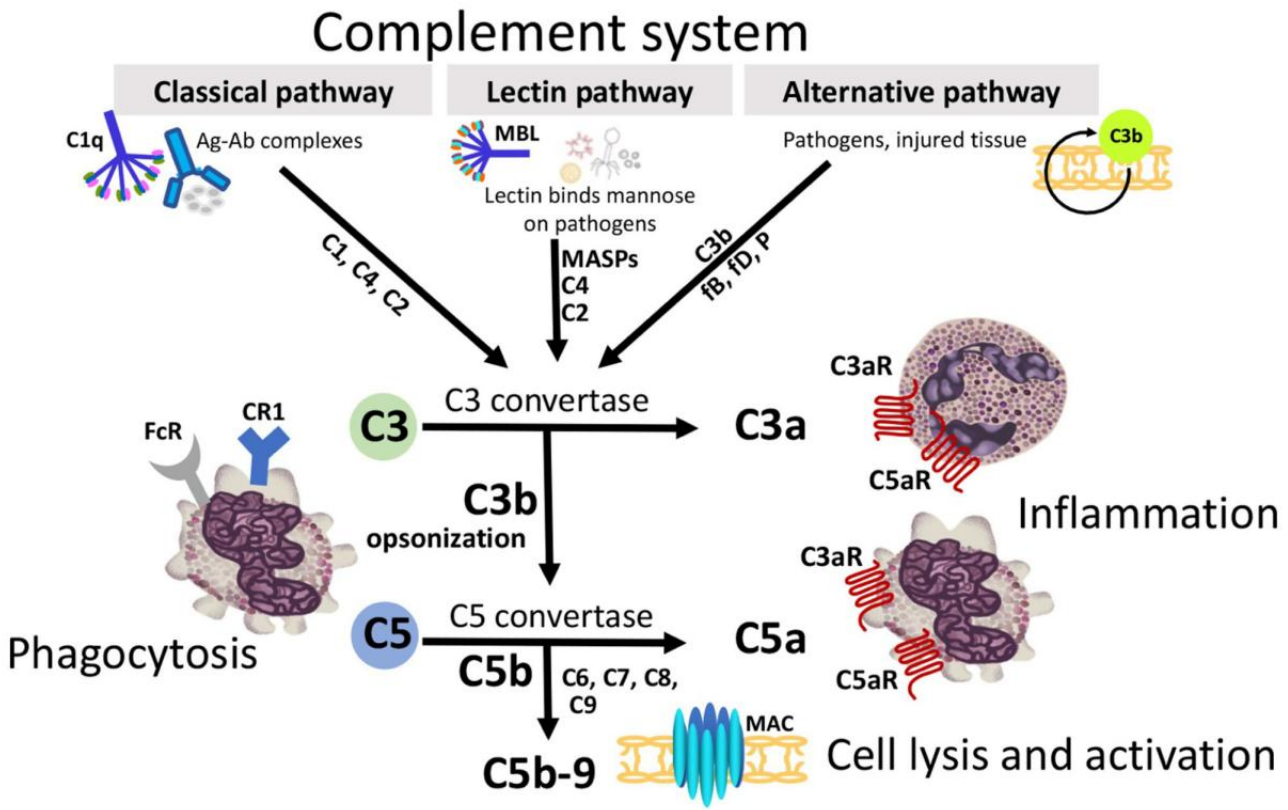
Targeting the humoral response in ITP

- **↘ antiplatelet Ab (APA) production**
  ⇒ B cell depleting therapies
- **↘ APA mechanisms of action**
  ⇒ IVIg
  ⇒ SYK inhibition
  ⇒ BTK inhibition
  ⇒ Complement inhibition

Audia *et al.*, Hemasphere 2021

Complement pathways

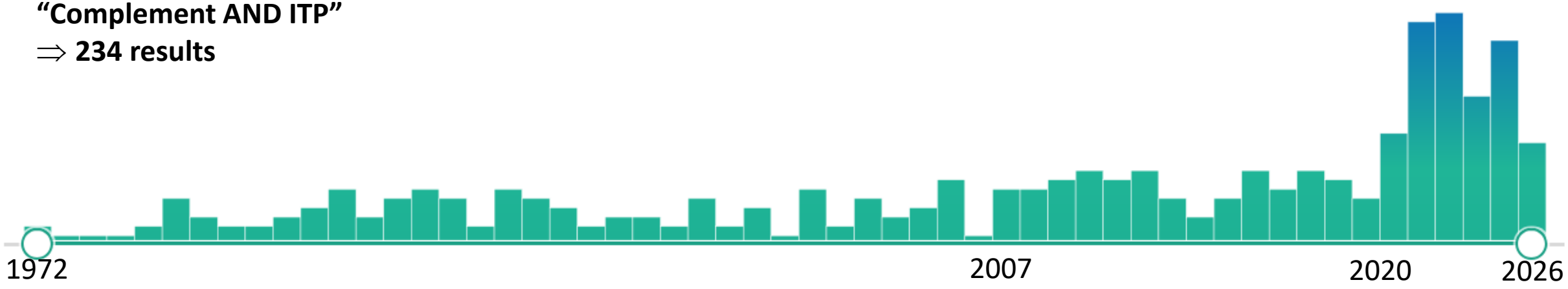




Girardi *et al.*, Frontiers Immunol 2020

Complement activation in ITP

"Complement AND ITP"
⇒ 234 results



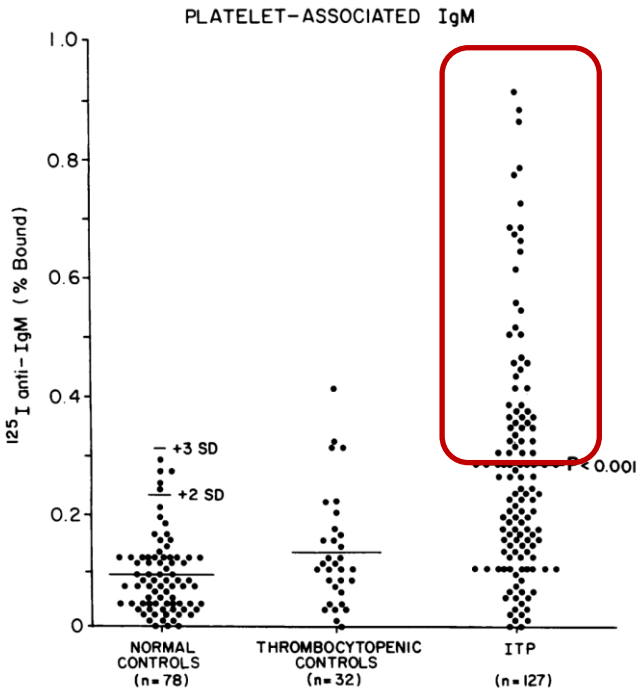
Articles	Topic
Hauch *et al*. Blood 1977	PA-complement
McMillan *et al*. BJH 1981	PA-complement
Myers *et al*. Blood 1982	PA-complement
Winiarski *et al*. Clin Exp Imm. 1983	PA-complement
Cines *et al*. J Clin Invest 1985	IgM antibodies
Tsubakio *et al*. BJH 1986	In vitro cpt activation/serum
Usuki *et al*. Int J Cell Cloning 1986	serum/megakaryocytes
Horstman *et al*. J Lab Clin Med 1994	lysis/opsonization
Peerschke *et al*. BJH 2010	Cpt & ↘A-IPF

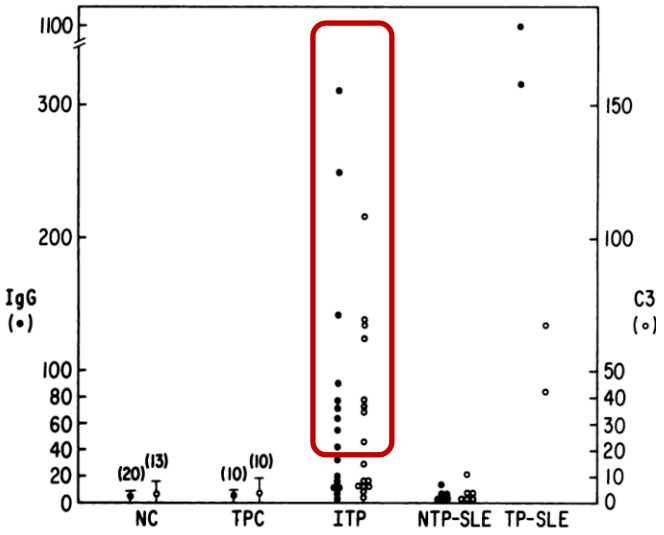
Articles	Topic
Najaoui *et al*. Eur J Haematol 2012	PA-Ab / PA-cpt
Peerschke *et al*. BJH 2010	in vitro C1s inhibitor
Unterberger *et al*. Platelets 2017	Ab against cpt inhibitors
Castelli *et al*. Clin Exp Immunol 2020	Cpt & ITP phases
Cheloff *et al*. Res Pract Thr Haemost 2020	Serum cpt level
Akesson *et al*. Platelets 2023	cpt & TPO-RA response
Broome *et al*. Blood Adv 2023	RCT sutimlimab
Nakata *et al*. Blood 2026	IgM Ab/IPF% & cpt
Roth *et al*. Am J Hematol 2026	RCT iptacopan

Complement activation & peripheral destruction of platelets

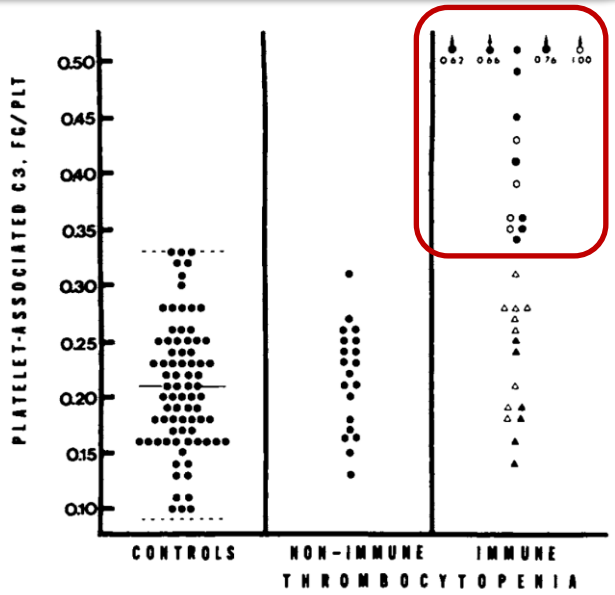
- **Deposition of C3 on platelet membrane during ITP**
  - Opsonization of platelets (C3b) => platelet phagocytosis
  - Platelet lysis by MAC (Tsubakio *et al*. BJH 1986)

- **IgG and C3 on platelet membrane**
- **Correlation btw PA-IgG and PA-C3 => classical CP activation**
- **Complement activation in ≈50% of patients**
- **Level of activation are highly variable**
- **IgM antibodies also participate**
- **Positive correlation btw IgM & cpt activation**



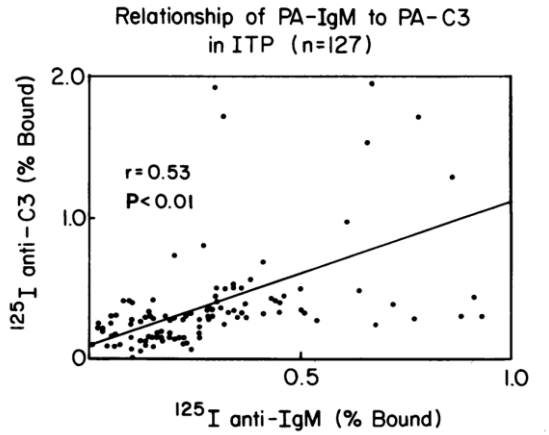


Hauch *et al*. Blood 1977



Myers *et al*. Blood 1982

	24 ITP
↗ PA-IgG = PA-C3	9 (38%)
↗ PA-IgG ↗ PA-C3	10 (42%)
0 PA-IgG ↗ PA-C3	5 (20%)

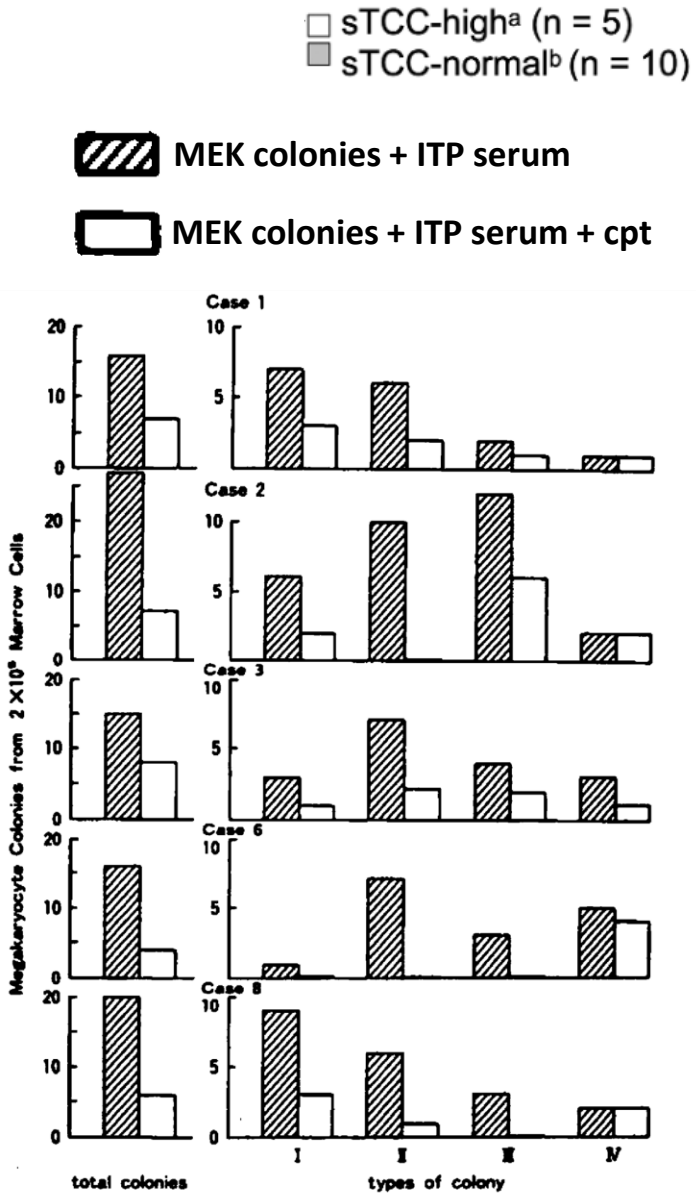


Cines *et al*. J Clin Invest 1985

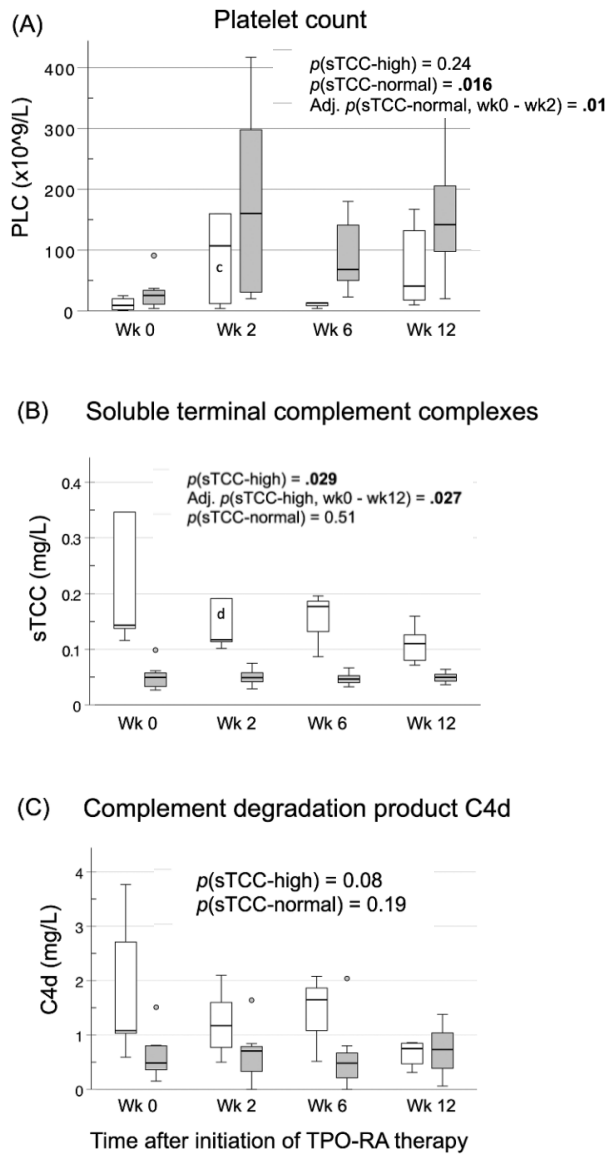
Complement activation & inhibition of megakaryopoiesis

Inhibition of megakaryopoiesis

- ↘ of MEK-colony formation by ITP serum + complement (Usuki *et al*. Int J Cell Cloning 1986)
- ↘ Absolute-Immature Platelet Fraction (A-IPF, bone marrow production) in ITP patients with high complement activation (Peerschke *et al*. BJH 2010)
- Complement activation associated with a lower response to TPO-RA (Akesson *et al*. Platelets 2023)



Usuki *et al*. Int J Cell Cloning 1986



Akesson *et al*. Platelets 2023

Decrease in serum complement fractions in ITP

Baseline characteristic	N=108	Value
Age, y, median (range)		53 (18-89)
Female, %		54
Platelet count (×10^9/L) at time of complement testing, median (range)		66 (2-595)
ITP duration in years at time of complement testing, median (range)		8.0 (0.0-59.6)
Post-splenectomy, n (%)		17 (16)
Platelet autoantibody[a] positive, n (%)		59 (75)
Anti-GPIIb/IIIa antibodies[a], n (%)		54 (71)
Anti-GPIb/IX antibodies,[a] n (%)		47 (63)
Anti-GPIa/IIa antibodies,[a] %		31 (41)
On ITP treatment at time of complement testing,[b] n (%)		56 (52)
Corticosteroids, n (%)		18 (17)
Romiplostim, n (%)		19 (18)
Eltrombopag, n (%)		16 (15)
Rituximab, n (%)		2 (2)
Fostamatinib, n (%)		2 (2)
Other, n (%)		8 (7)

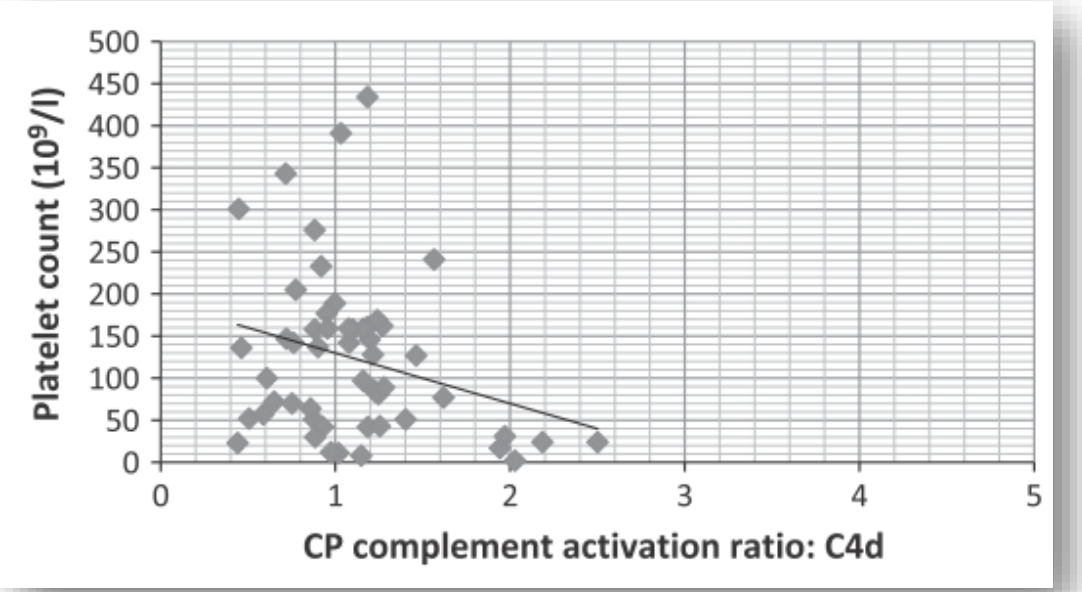
Assay	Patients with ITP	Healthy subjects	*P* value
Mean serum C3, mg/dL (95% CI)	104.2 (97.6-110.8)	116.8 (113.0-120.3)	<.001
Mean serum C4, mg/dL (95% CI)	20.4 (17.7-23.2)	24.1 (22.83-25.33)	<.001
Mean serum CH50, U/mL (95% CI)	62.9 (59.6-66.1)	68.4 (66.2-71.1)	.005

Serum level of classical complement pathway components (CH50, C3, C4):

- ✓ ↘ in ITP as compared to HC
- ✓ 32% below the lower range for ≥ 1 complement assay
- ✓ 10% had ↘ in all 3 complement assays

Cheloff *et al*. Res Pract Thr Haemost 2020

Therapeutic perspectives of complement inhibition in ITP



Complement deposition	C1s inhibition by TNT003 % Inhibition*
C1q	12·81 ± 13·23 ($P < 0·001$)
C4d	44 ± 43 ($P < 0·001$)
C3b	72 ± 17 ($P < 0·001$)
C5b-9	82 ± 14 ($P < 0·001$)

- **Classical complement pathway activation in ITP :**
  - ✓ **Complement activation in 47% of 55 ITP patients**
  - ✓ **Negative correlation with platelet count**
  - ✓ ***In vitro*, cpt activation was reversed by C1s inhibitor (murine TNT003 -> humanized sutimlimab)**

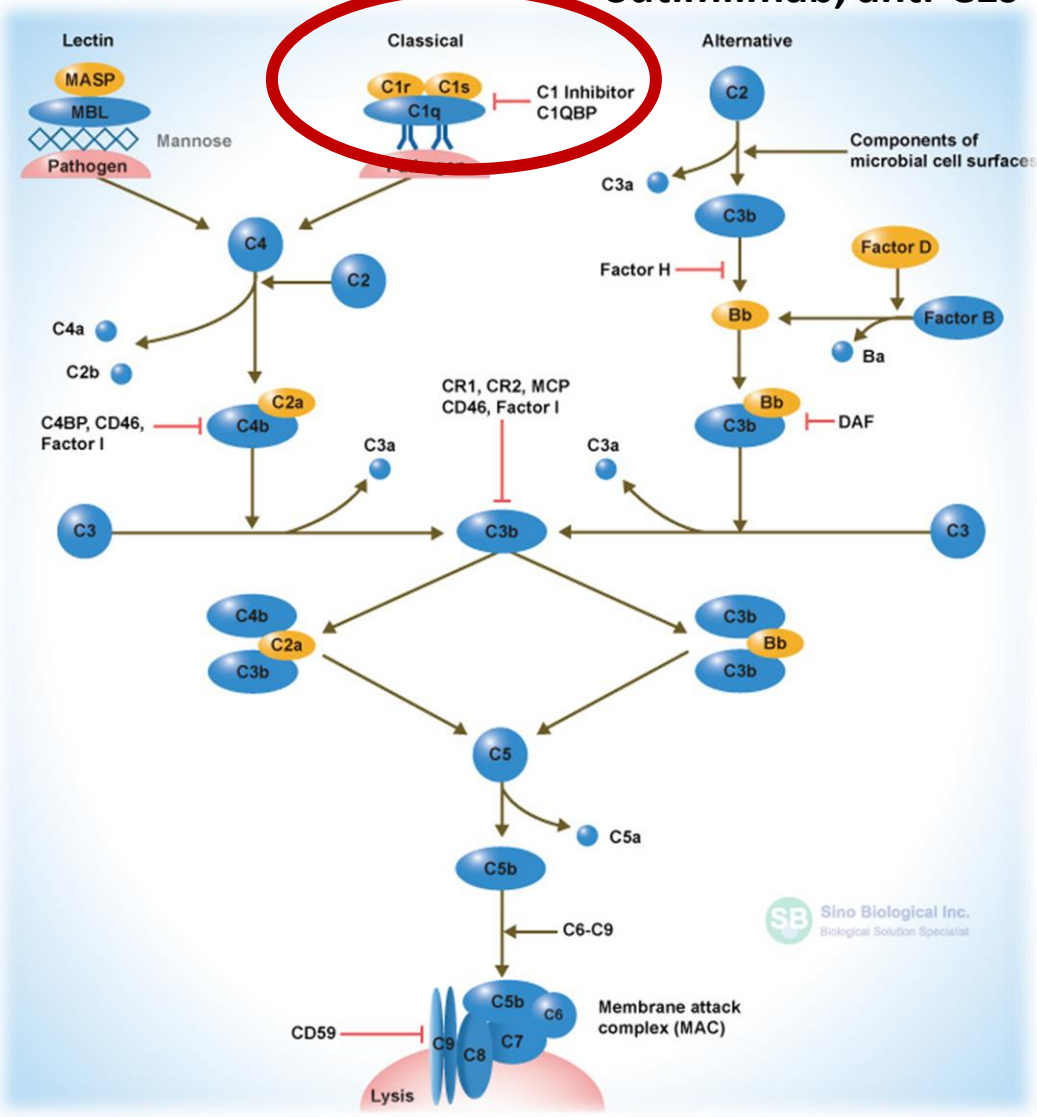
Peerschke *et al*. BJH 2010

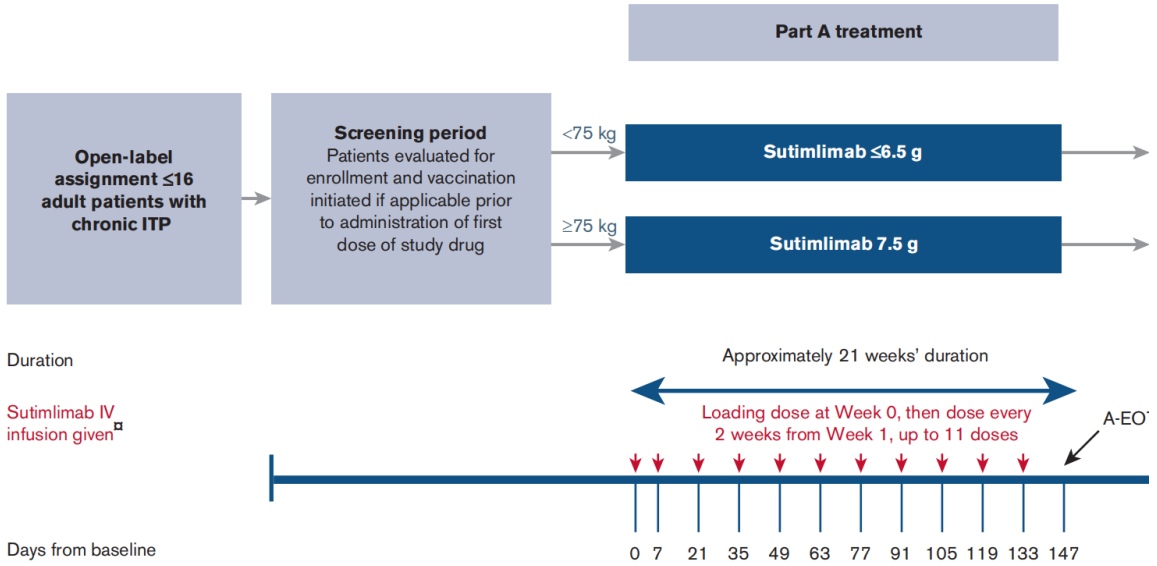
Safety and efficacy of classical complement pathway inhibition with sutimlimab in chronic immune thrombocytopenia

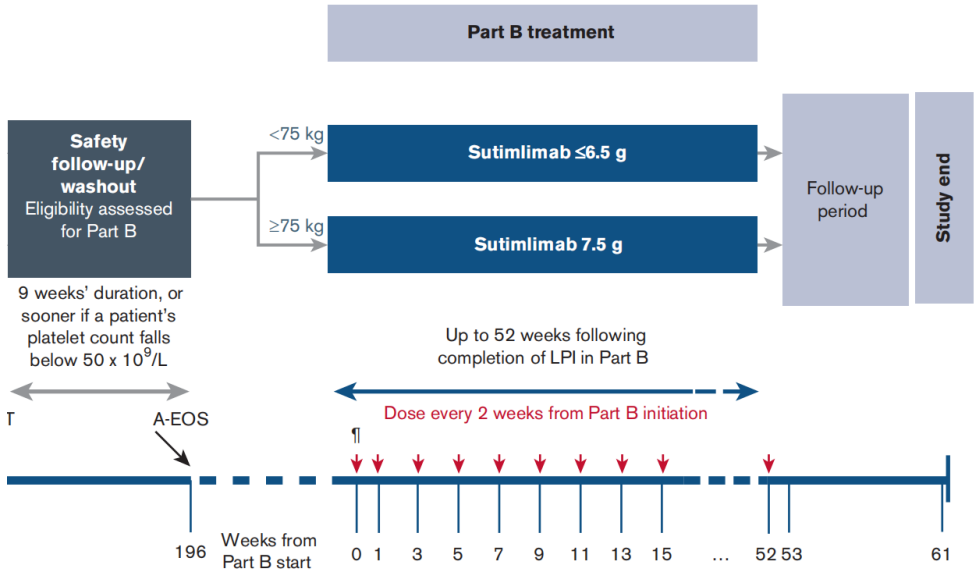
Catherine M. Broome,[1] Alexander Röth,[2] David J. Kuter,[3] Marie Scully,[4] Roy Smith,[5] Jennifer Wang,[6] Caroline Reuter,[6] William Hobbs,[6] and Ahmed Daak[6]

blood advances
28 MARCH 2023 • VOLUME 7, NUMBER 6

Sutimlimab, anti-C1s







Safety and efficacy of classical complement pathway inhibition with sutimlimab in chronic immune thrombocytopenia

Catherine M. Broome,[1] Alexander Röth,[2] David J. Kuter,[3] Marie Scully,[4] Roy Smith,[5] Jennifer Wang,[6] Caroline Reuter,[6] William Hobbs,[6] and Ahmed Daak[6]

blood advances

28 MARCH 2023 • VOLUME 7, NUMBER 6

Table 1. Patient demographic and baseline disease characteristics

Baseline characteristics, (N = 12)	
Age, median (range) y	41.5 (27-66)
Sex, female, n (%)	9 (75.0)
Race, n (%)	
White	8 (66.7)
Black or African American	3 (25.0)
Asian	1 (8.3)
Weight, kg [n = 11], mean (range)	78.3 (57-114)
Disease duration at screening, y [n = 7], median (range)	4.7 (2.0-36.4)
Platelet count,* median (range), $\times 10^9$/L	19 (1-57)
Number of prior treatments, median (range)	5.5 (2-10)
Prior treatment received, n (%)	
Rituximab	10 (83.3)
Corticosteroids	8 (66.7)
TPO-RA	
Romiplostim	8 (66.7)
Eltrombopag	8 (66.7)
IVIg	7 (58.3)
Fostamatinib	2 (16.7)
Rilzabrutinib†	1 (8.3)
Prior splenectomy, n (%)	4 (33.3)

*Average of all platelet counts at screening, including day 0.
†Investigational Bruton's tyrosine kinase inhibitor.

Safety and efficacy of classical complement pathway inhibition with sutimlimab in chronic immune thrombocytopenia

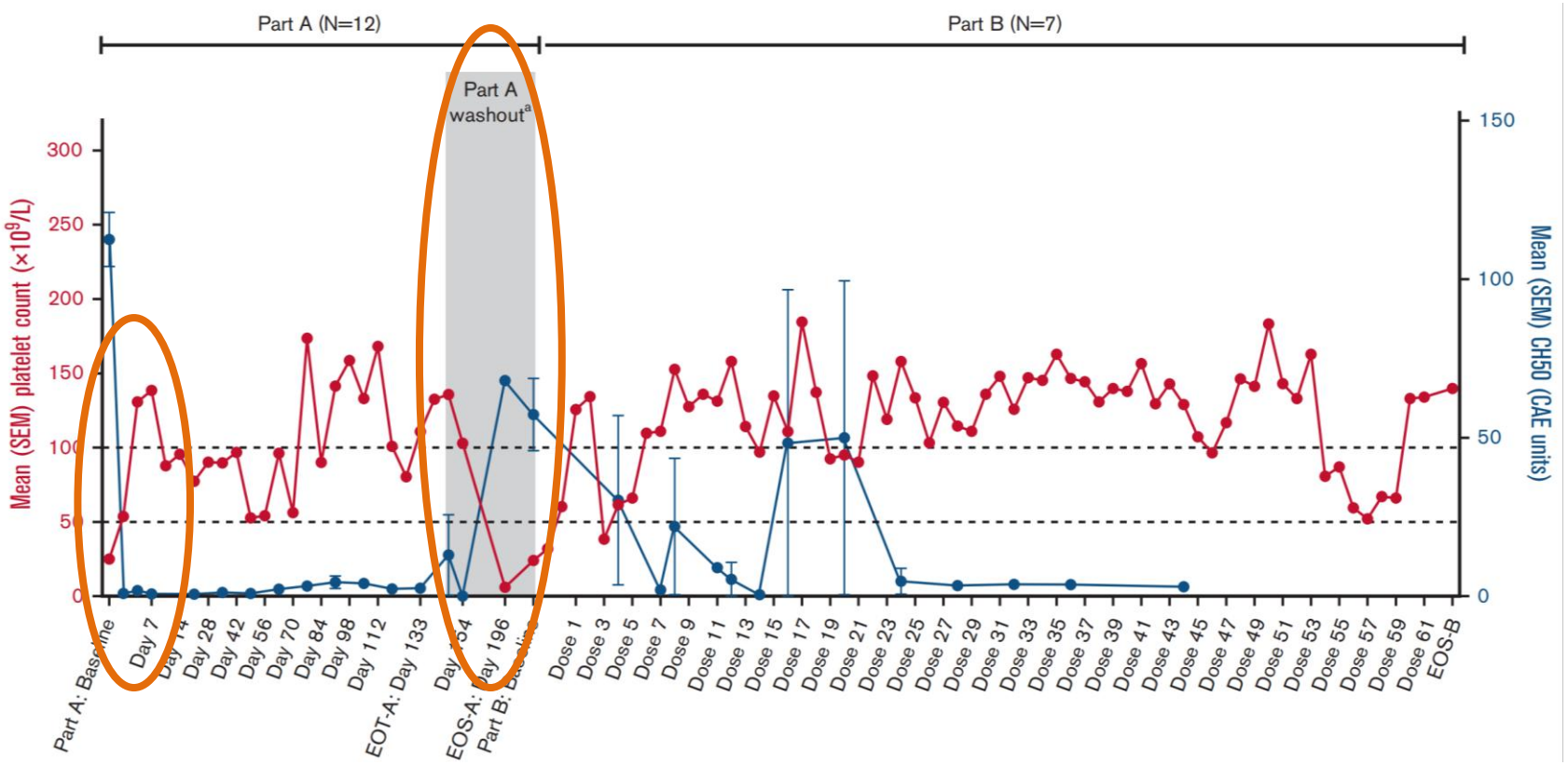
Catherine M. Broome,[1] Alexander Röth,[2] David J. Kuter,[3] Marie Scully,[4] Roy Smith,[5] Jennifer Wang,[6] Caroline Reuter,[6] William Hobbs,[6] and Ahmed Daak[6]

blood advances
28 MARCH 2023 • VOLUME 7, NUMBER 6

Table 1. Patient demographic and baseline disease characteristics

Baseline characteristics, (N = 12)	
Age, median (range) y	41.5 (27-66)
Sex, female, n (%)	9 (75.0)
Race, n (%)	
White	8 (66.7)
Black or African American	3 (25.0)
Asian	1 (8.3)
Weight, kg [n = 11], mean (range)	78.3 (57-114)
Disease duration at screening, y [n = 7], median (range)	4.7 (2.0-36.4)
Platelet count,* median (range), $\times 10^9$/L	19 (1-57)
Number of prior treatments, median (range)	5.5 (2-10)
Prior treatment received, n (%)	
Rituximab	10 (83.3)
Corticosteroids	8 (66.7)
TPO-RA	
Romiplostim	8 (66.7)
Eltrombopag	8 (66.7)
IVIg	7 (58.3)
Fostamatinib	2 (16.7)
Rilzabrutinib†	1 (8.3)
Prior splenectomy, n (%)	4 (33.3)

*Average of all platelet counts at screening, including day 0.
†Investigational Bruton's tyrosine kinase inhibitor.



- **Response : 5/12 (42%)**
- **Rapid: 24 hours (25 to 54.10^9/L)**
- **Suspensive: relapse after withdrawal**
- **Prolonged Resp. on ttt: 2 years follow-up**

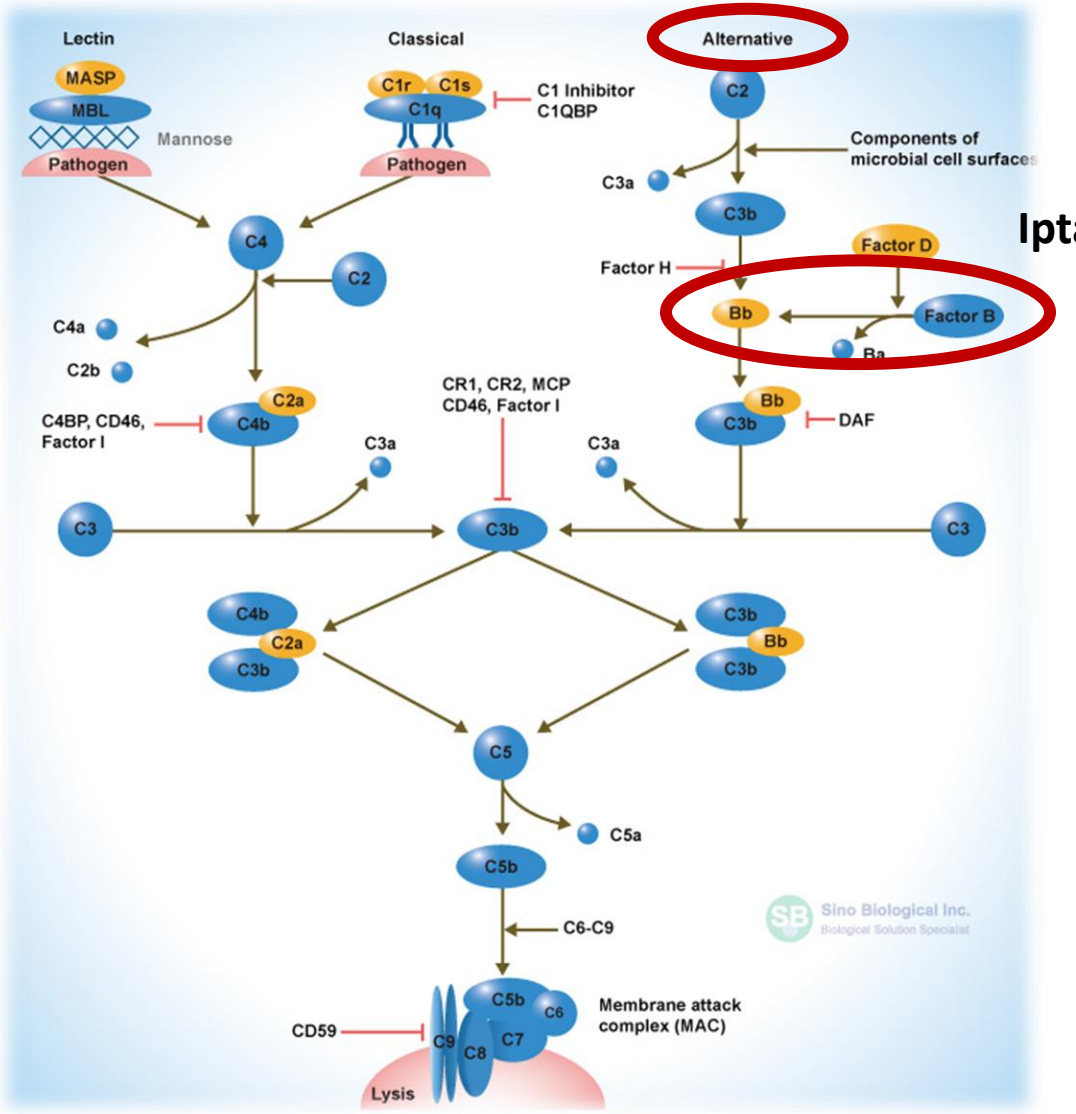
⇒ **Need for biomarkers identifying responders**

Iptacopan for Immune Thrombocytopenia and Cold Agglutinin Disease: A Global Phase 2 Basket Clinical Trial

AJH

American Journal of Hematology, 2026; 101:242–254

Alexander Röth[1] | Wilma Barcellini[2] | Christine Ademokun[3] | Junho Jang[4] | Maria Luisa Lozano[5] | David Valcarcel Ferreiras[6] | Cristina Pascual-Izquierdo[7] | Shripad Chitnis[8] | Sofiya Matviykiv[9] | Alessandra Vitaliti[9] | Chi Chen[10] | Vasiliki Katsanou[9] | Raghav Chawla[9] | Hanny Al-Samkari[11]



Iptacopan, anti-B

Alternative complement pathway

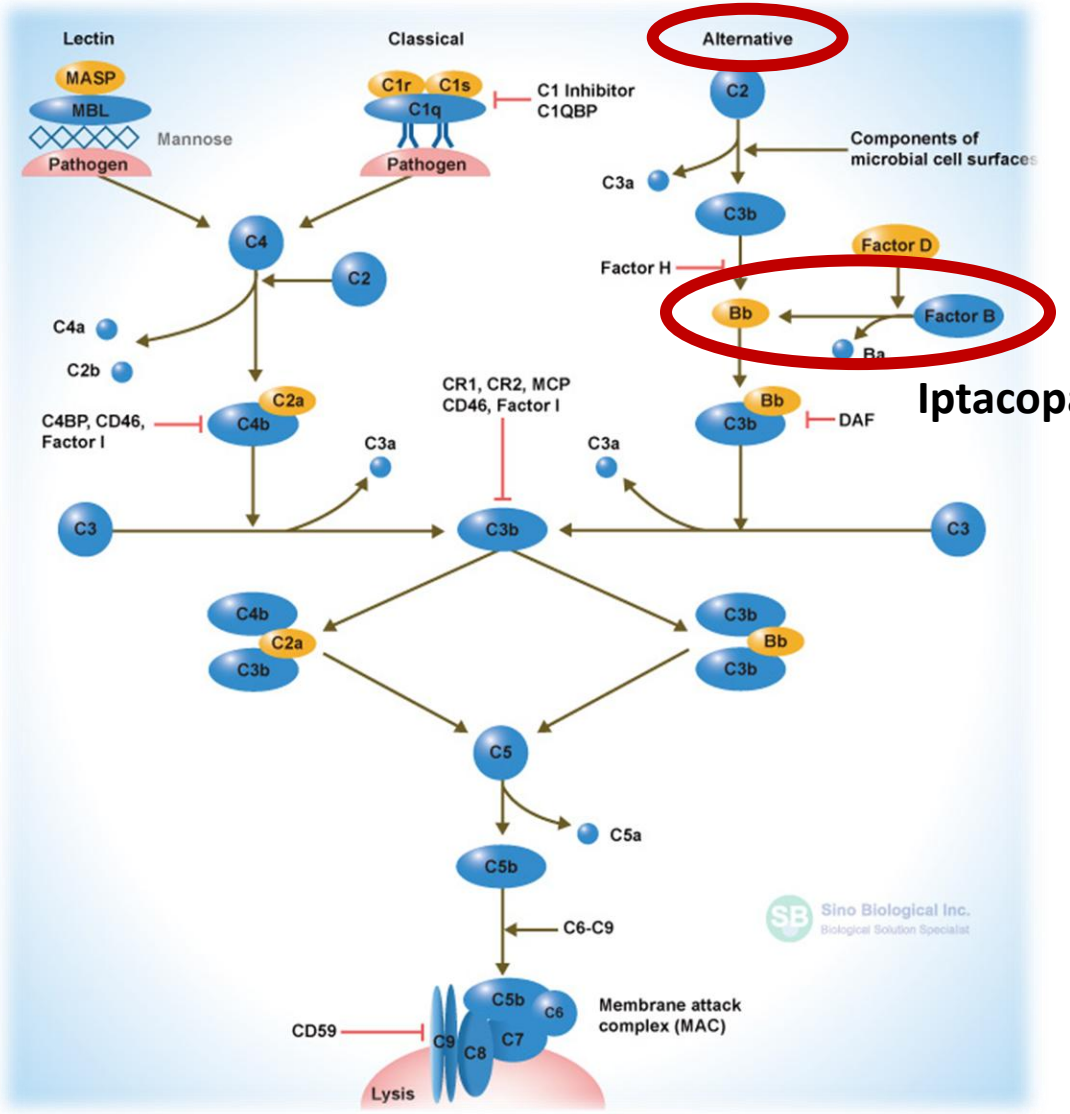
- **Continually activated / regulated**
- **↗ activation by exogenous components**
- **C3b (than can be generated from the classical CP) also participates to its activation**
- **Its inhibition has demonstrated its efficacy in PNH (Peffault de Latour *et al*. NEJM 2024 & Risitano *et al*. Lancet Haematol 2025)**

Iptacopan for Immune Thrombocytopenia and Cold Agglutinin Disease: A Global Phase 2 Basket Clinical Trial

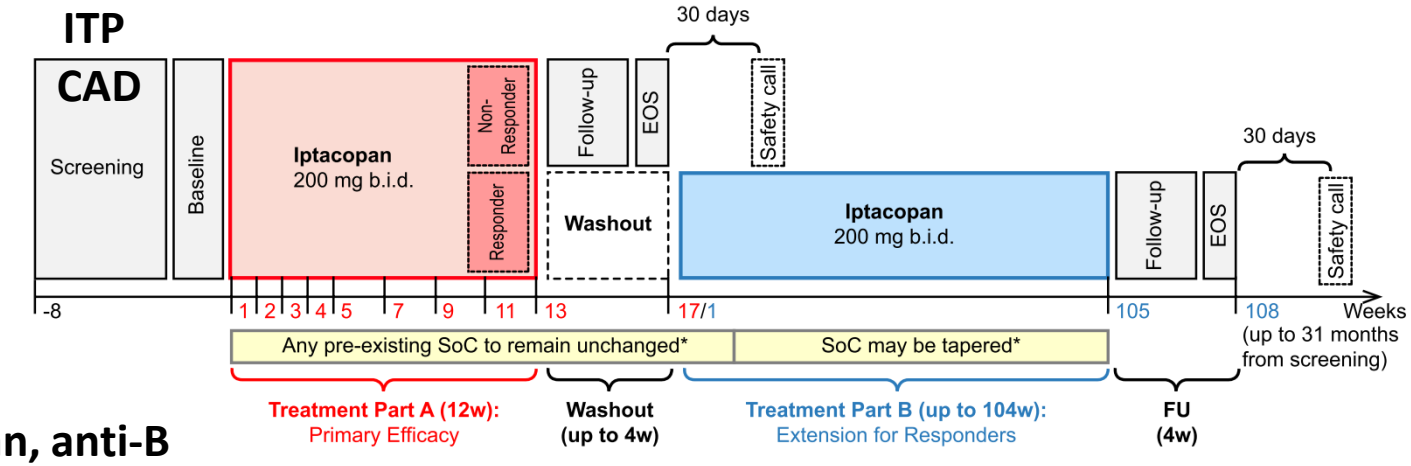
AJH

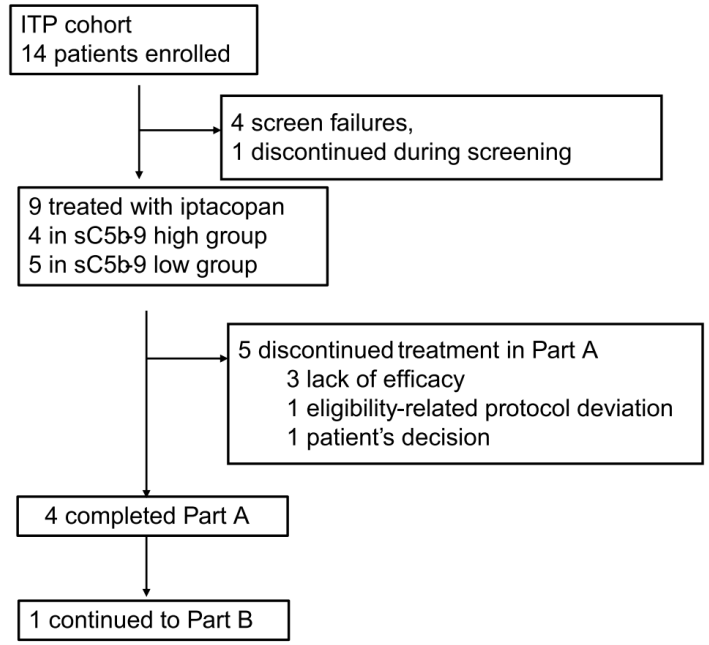
American Journal of Hematology, 2026; 101:242–254

Alexander Röth[1] | Wilma Barcellini[2] | Christine Ademokun[3] | Junho Jang[4] | Maria Luisa Lozano[5] | David Valcarcel Ferreiras[6] | Cristina Pascual-Izquierdo[7] | Shripad Chitnis[8] | Sofiya Matviykiv[9] | Alessandra Vitaliti[9] | Chi Chen[10] | Vasiliki Katsanou[9] | Raghav Chawla[9] | Hanny Al-Samkari[11]



Iptacopan, anti-B





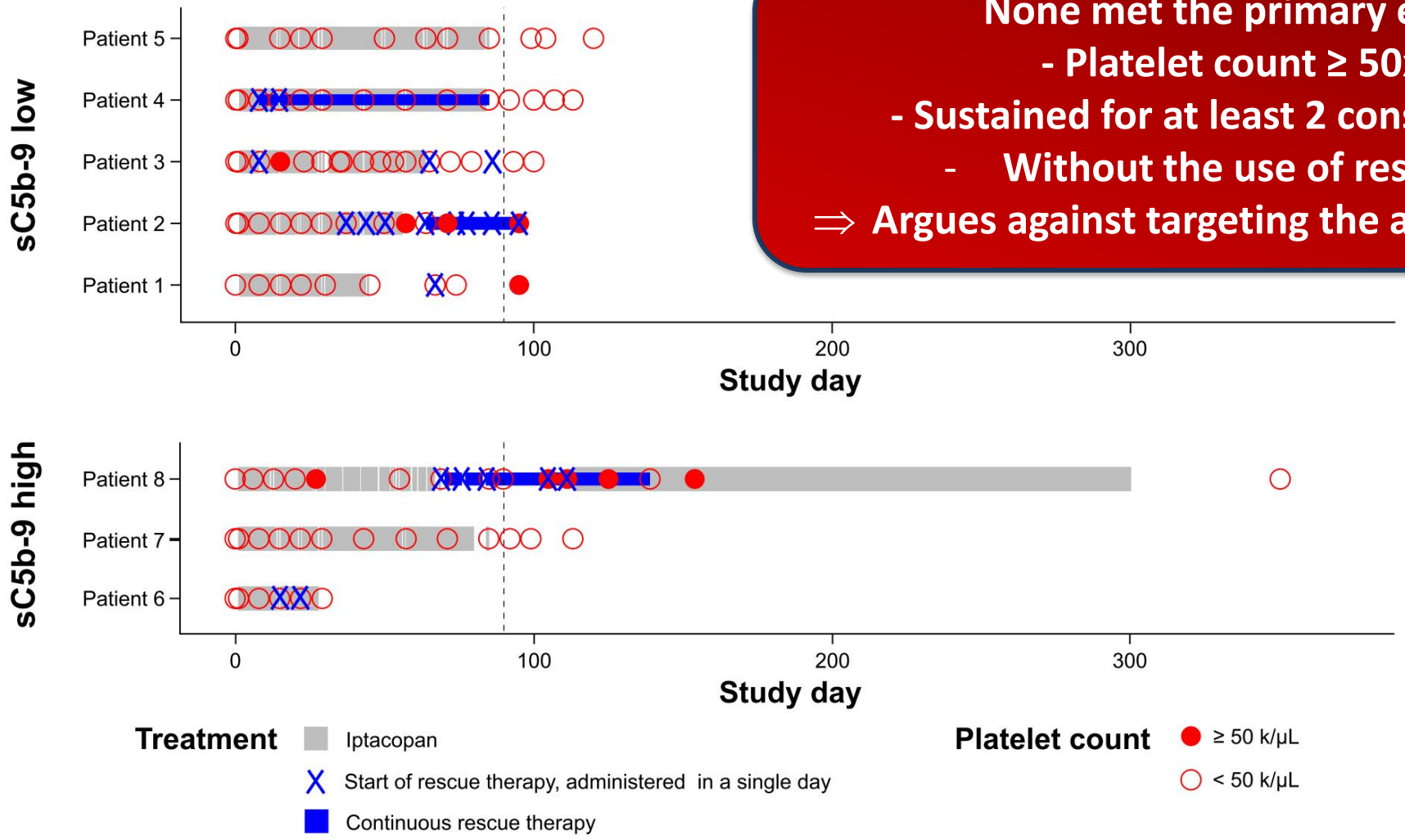
Iptacopan for Immune Thrombocytopenia and Cold Agglutinin Disease: A Global Phase 2 Basket Clinical Trial

Alexander Röth[1] | Wilma Barcellini[2] | Christine Ademokun[3] | Junho Jang[4] | Maria Luisa Lozano[5] | David Valcarcel Ferreiras[6] | Cristina Pascual-Izquierdo[7] | Shripad Chitnis[8] | Sofiya Matviykiv[9] | Alessandra Vitaliti[9] | Chi Chen[10] | Vasiliki Katsanou[9] | Raghav Chawla[9] | Hanny Al-Samkari[11]

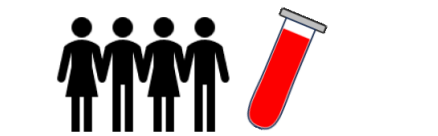
AJH

American Journal of Hematology, 2026; 101:242–254

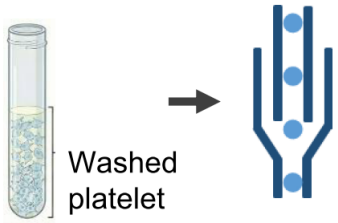
None met the primary endpoint :
- Platelet count ≥ 50x10⁹ /L
- Sustained for at least 2 consecutive weeks
- Without the use of rescue therapy
⇒ Argues against targeting the alternative CP in ITP



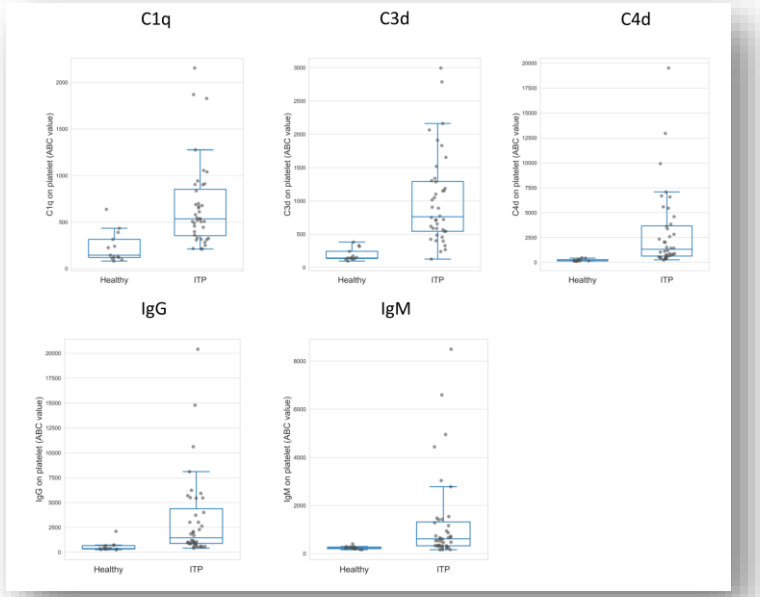
Potential biomarkers of response to complement inh. in ITP

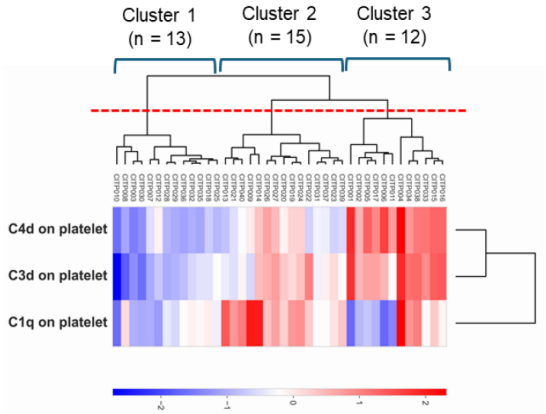


40 patients with primary ITP



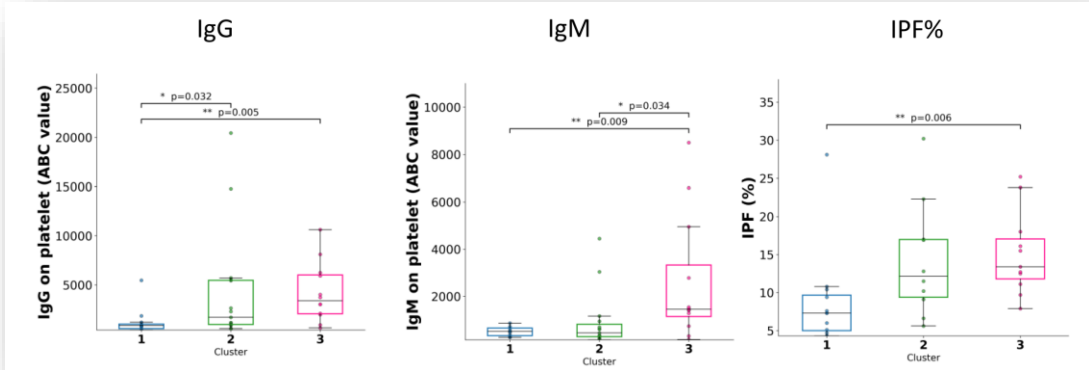
Flow Cytometry





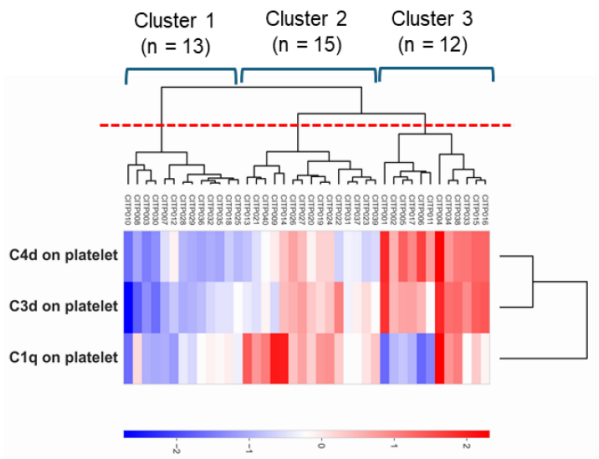
- **Cluster 1**:all negative
- **Cluster 2**: elevated C1q with negative to low C3d and C4d
- **Cluster 3**: high C3d and C4d

- Complement deposition on platelets in ITP
- Presence of PA-IgG and PA-IgM
- Identification of 3 clusters
- Cluster #3 showed :
  - ✓ High complement deposition
  - ✓ Associated with PA-IgM
  - ✓ Associated with high Immature Platelet Fraction (IPF%)
- No correlation with serum cpt fractions (C3, C4, sC5b-9)



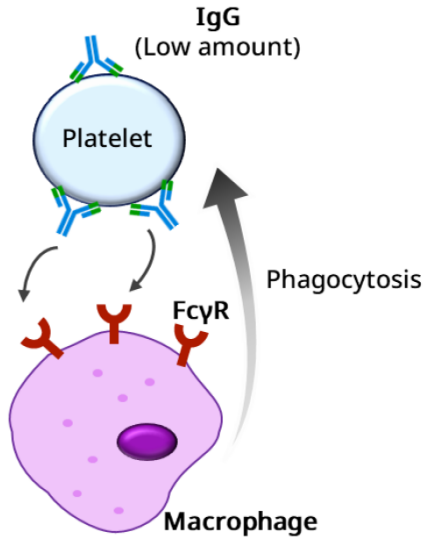
Nakata *et al*. Blood 2026

Levels of complement activation could modulate platelet destruction



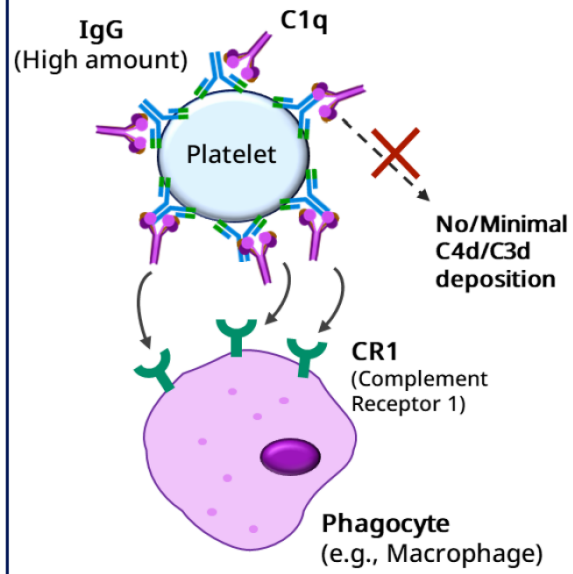
- **Cluster 1**:all negative
- **Cluster 2**: elevated C1q with negative to low C3d and C4d
- **Cluster 3**: high C3d and C4d

Cluster 1: FcγR-mediated Sequestration



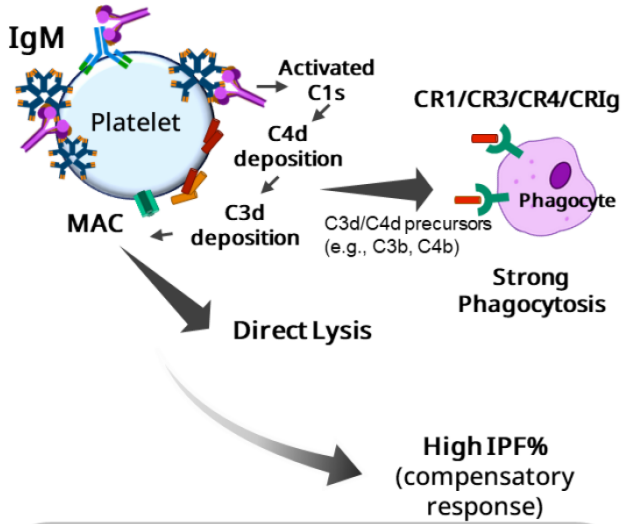
Mechanism Note:
- ✓ Classical mechanism of ITP
- ✓ Low complement activation
- ✓ FcγR-dependent clearance

Cluster 2: C1q-mediated Modulation



Mechanism Note:
In addition to FcγR-dependent mechanisms:
- ✓ "Stalled" Activation: Terminates at C1q complex
- ✓ C1q directly binds to CR1 independent of downstream factors
- ✓ Enhanced Phagocytosis / Signaling

Cluster 3: Classical Pathway Amplification

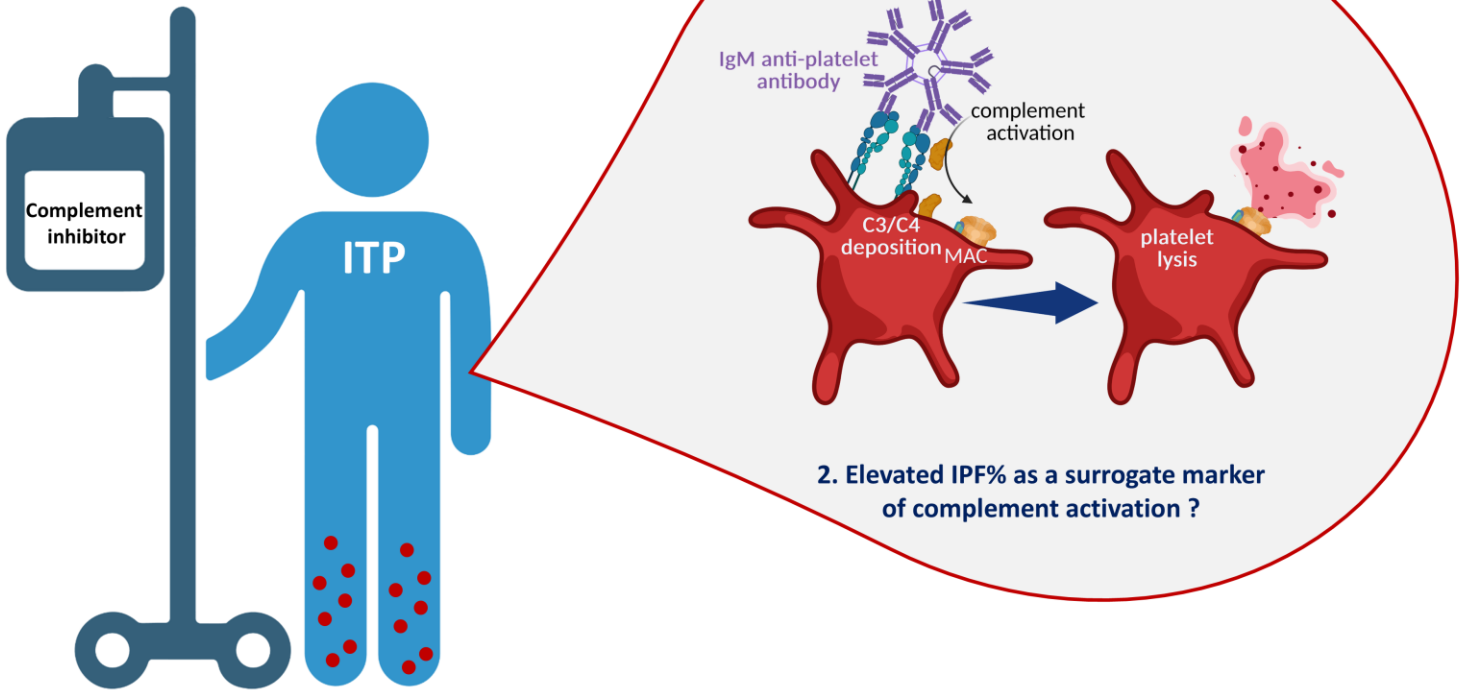


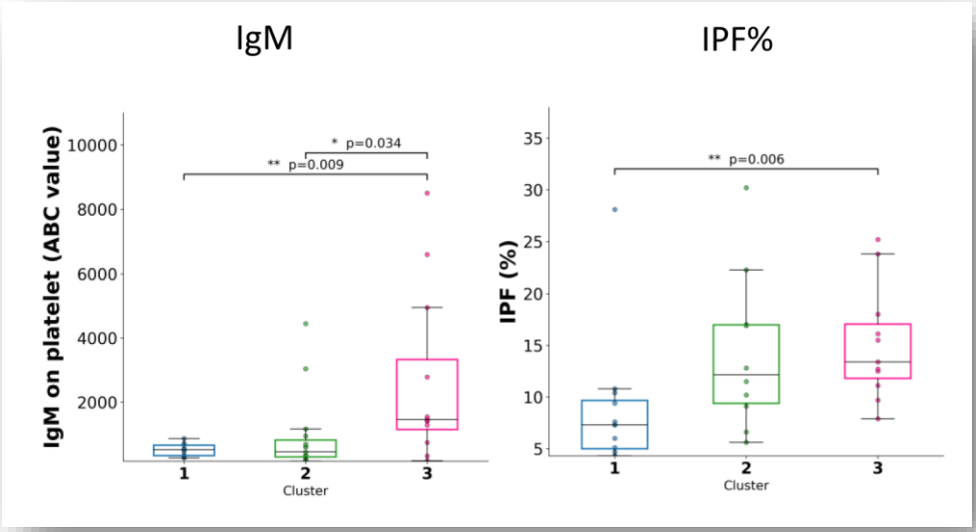
Mechanism Note:
In addition to FcγR-dependent mechanisms:
- ✓ Full CP Activation: High C3d/C4d, MAC formation
- ✓ Both destruction (lysis and phagocytosis)
- ✓ Correlates with high IPF%

Nakata *et al*. Blood 2026

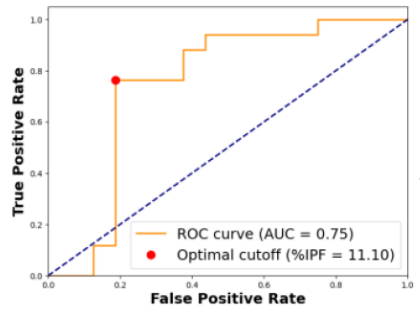
Potential biomarkers of response to complement inh. in ITP ?

Toward an identification of a cluster of ITP patients who could benefit from complement-targeting therapies ?





ROC analysis for predicting high platelet C4d deposition



High IPF% is a surrogate marker for complement activation

- **Controversial data as IPF was shown to be decreased due to CDC against megakaryocytes (Peerschke *et al*. BJH 2010)**
- **No correlation btw circulating antiplatelet antibodies and their detection in bone marrow (Shrestha *et al*. Blood Adv 2020)**

Audia *et al*. Blood 2026

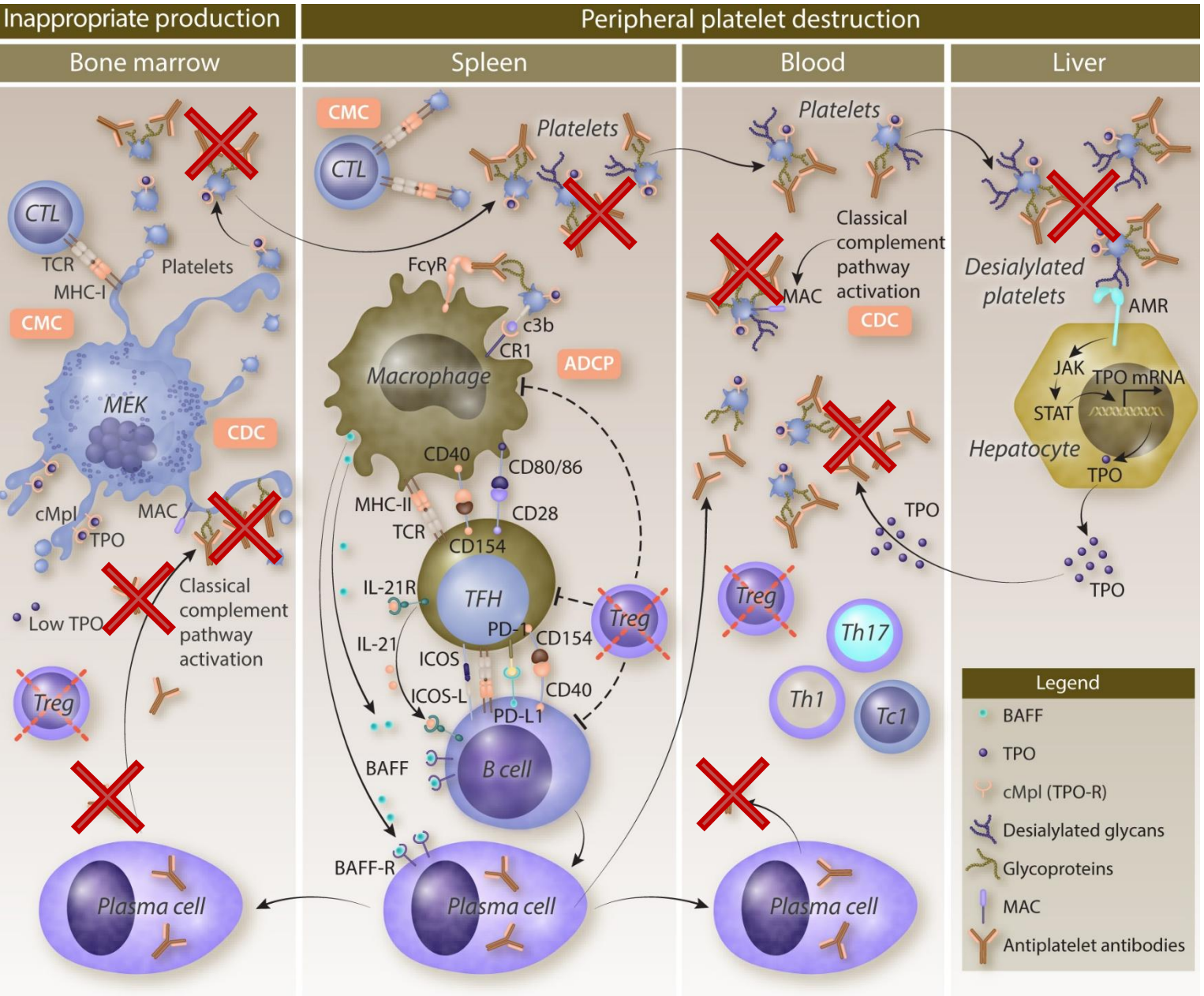
Complement pathway in ITP: summary

- Complement activation participates to :
  - ↗ platelet peripheral destruction (complement-mediated lysis, opsonization => phagocytosis)
  - ↘ BM platelet production

- Frequency : ≈ 50% of ITP patients

- Therapeutic perspectives :
  - Classical pathway complement inhibitors: sutimlimab (C1s inhibitor)
  - Further developments ?
  - In a subset of patients who need to be identified

- Potential biomarkers :
  - High IPF% as a surrogate marker of IgM Ab/cpt-mediated peripheral destruction of platelets ?
  - IgM antibodies : not measured routinely
  - Limited value of serum levels of complement fractions (C3, C4)

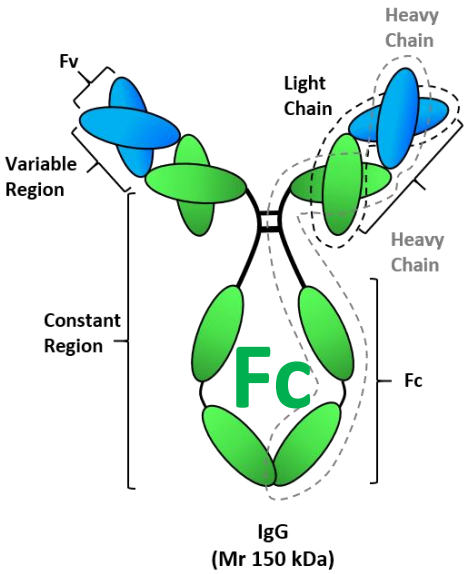


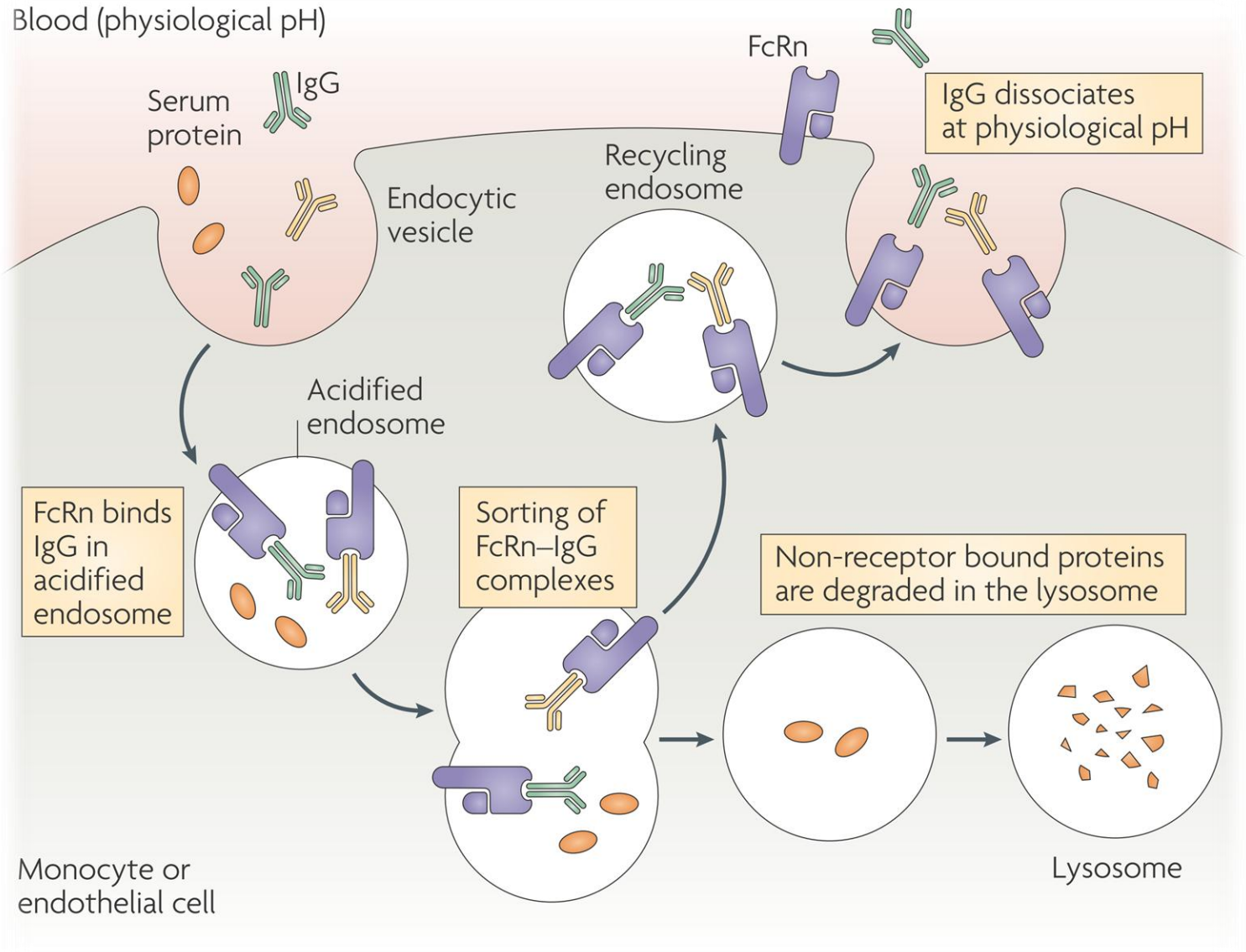
Targeting the humoral response in ITP

- **↘ antiplatelet Ab (APA) production**
  ⇒ B cell depleting therapies
- **↘ APA mechanism of action**
  ⇒ IVIg
  ⇒ SYK inhibition
  ⇒ BTK inhibition
  ⇒ Complement inhibition
- **↗ APA clearance**
  ⇒ IVIg
  ⇒ FcRn inhibition

Audia *et al.*, Hemasphere 2021

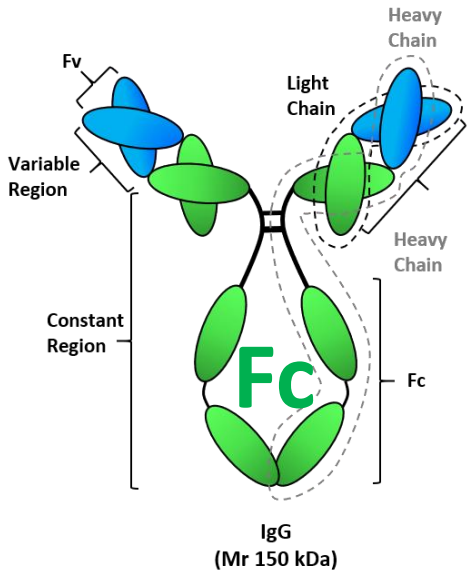
Role of FcRn (neonatal Fc Receptor)

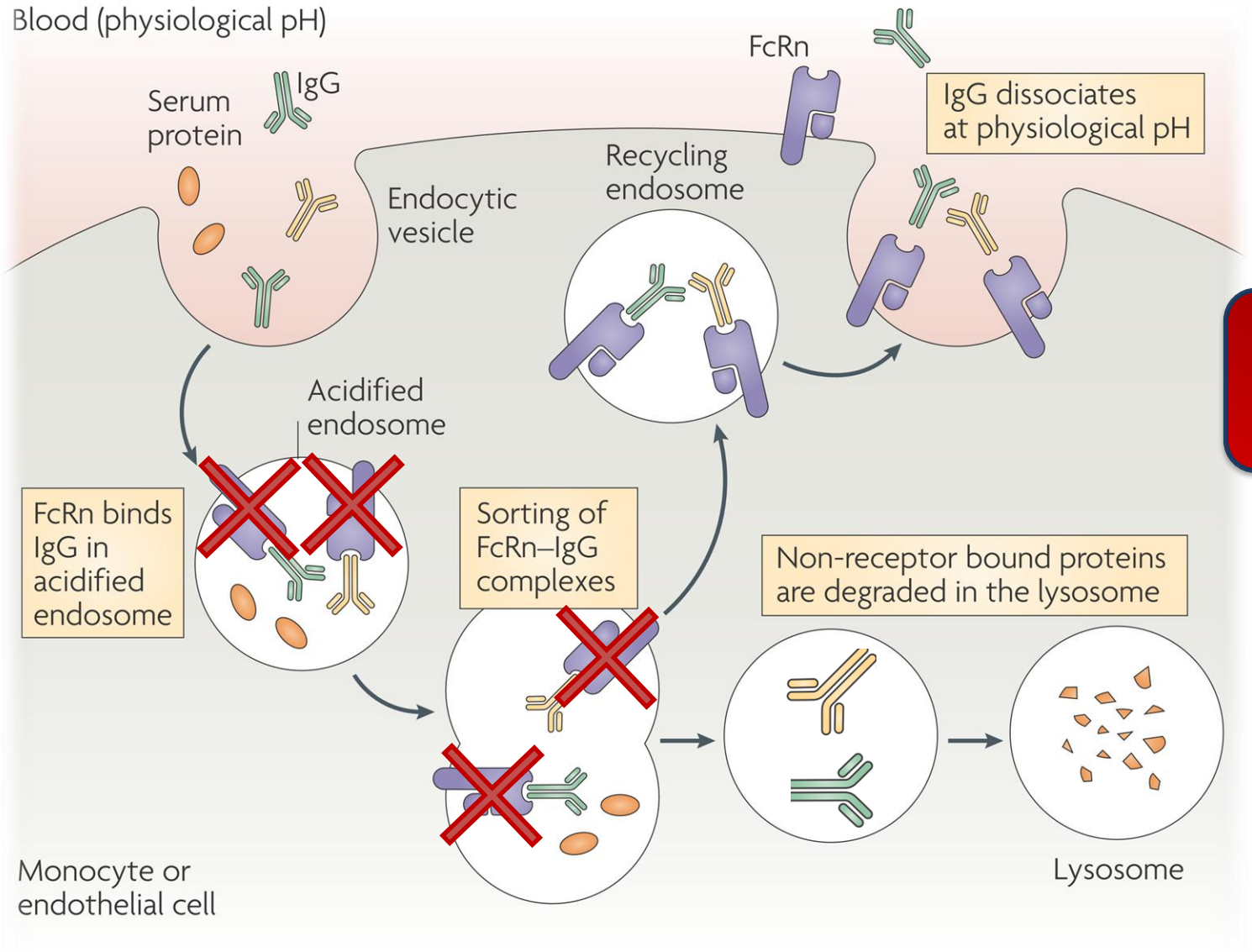




Roopenian *et al.*, Nature Rev. 2007

FcRn inhibition : ↗ clearance of pathogenic Ab

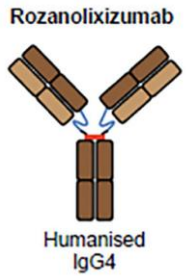


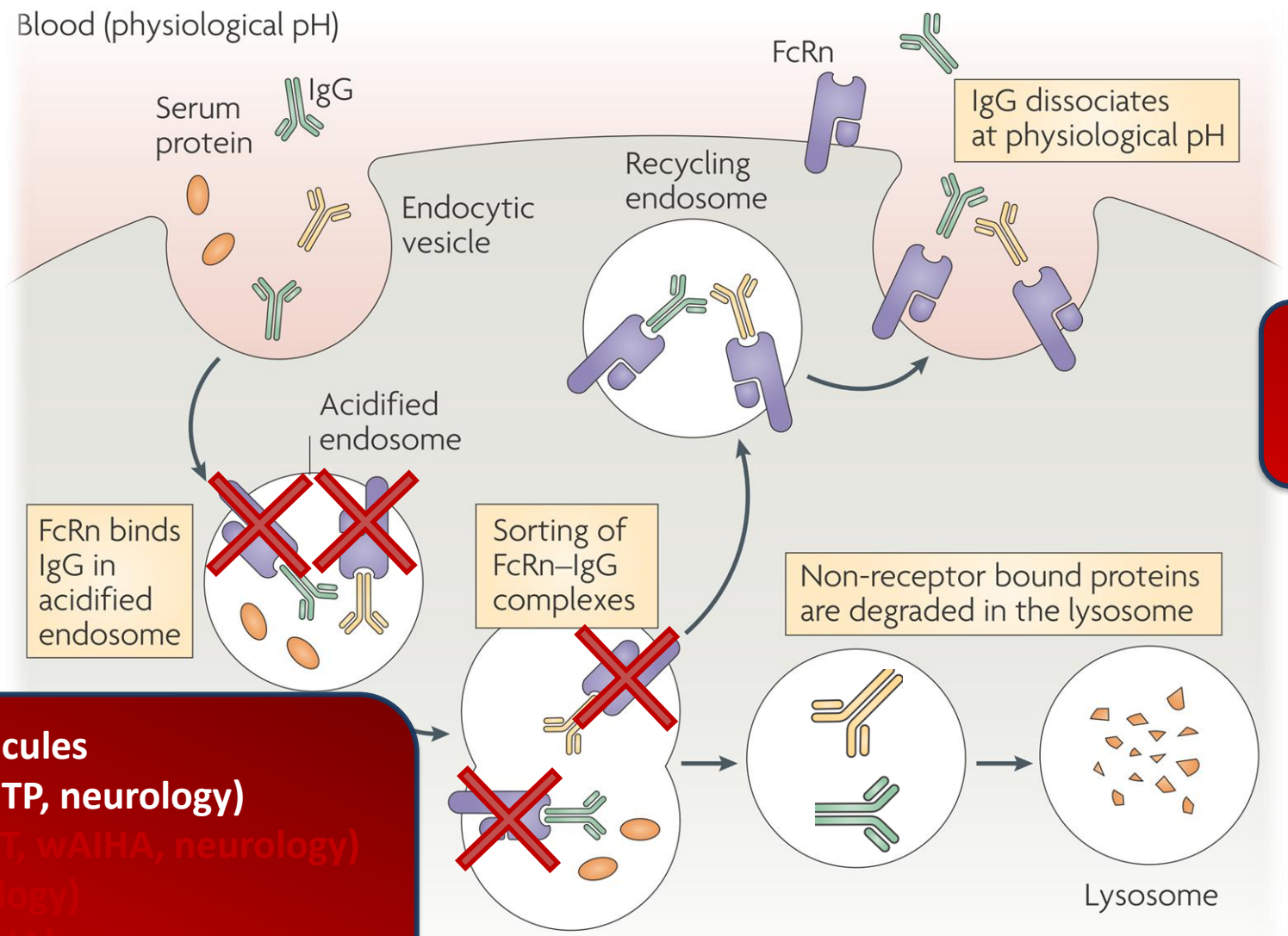


FcRn inhibition
- **↘ pathogenic IgG**
- **↘ total IgG**

Roopenian *et al.*, Nature Rev. 2007

FcRn inhibition : ↗ clearance of pathogenic Ab





FcRn inhibition
- ↘ pathogenic IgG
- ↘ total IgG

Molecules
- **Rozanolixizumab (ITP, neurology)**
- **Nipocalimab (FNAIT, wAIHA, neurology)**
- **Batoclimab (neurology)**
- **Efgartigimod (wAIHA)**
- **Efgartigimod (ITP, neurology)**

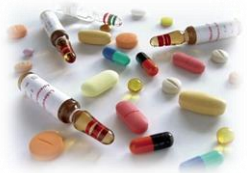
Roopenian *et al.*, Nature Rev. 2007
Zuercher *et al*. Autoimm Review 2019

Phase 2 multiple-dose study of an FcRn inhibitor, rozanolixizumab, in patients with primary immune thrombocytopenia

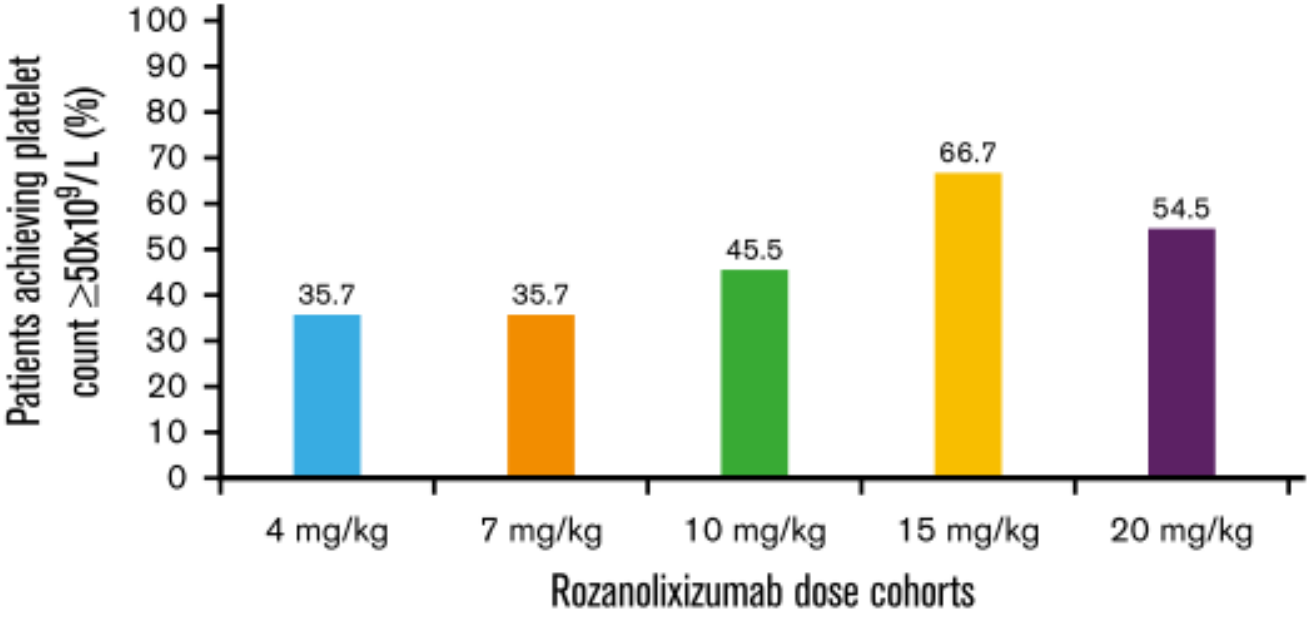
Tadeusz Robak,[1] Maciej Kaźmierczak,[2] Isidro Jarque,[3,4] Vasile Musteata,[5] Jacek Treliński,[1] Nichola Cooper,[6] Peter Kiessling,[7] Ute Massow, Franz Woltering,[7] Rose Snipes,[8] Juan Ke,[9] Grant Langdon,[10] James B. Bussel,[11] and Stephen Jolles[12]

blood advances

8 SEPTEMBER 2020

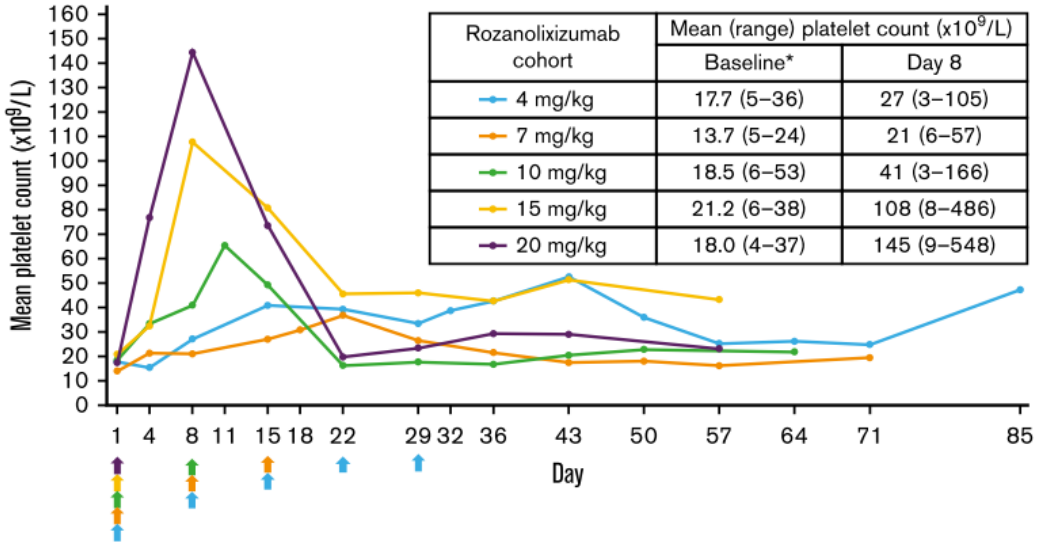


Platelets > 50 G/L

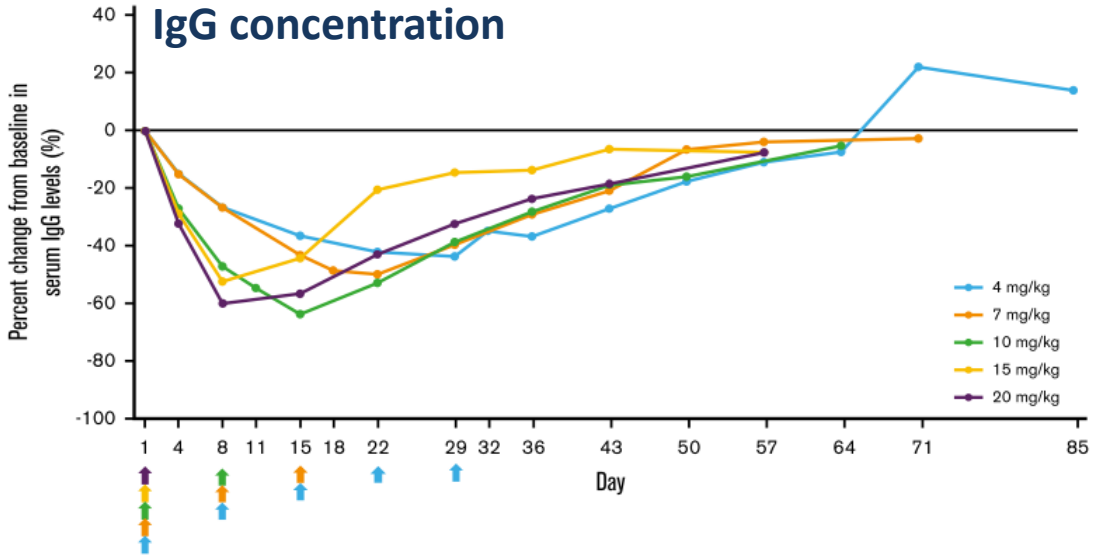


Platelet count

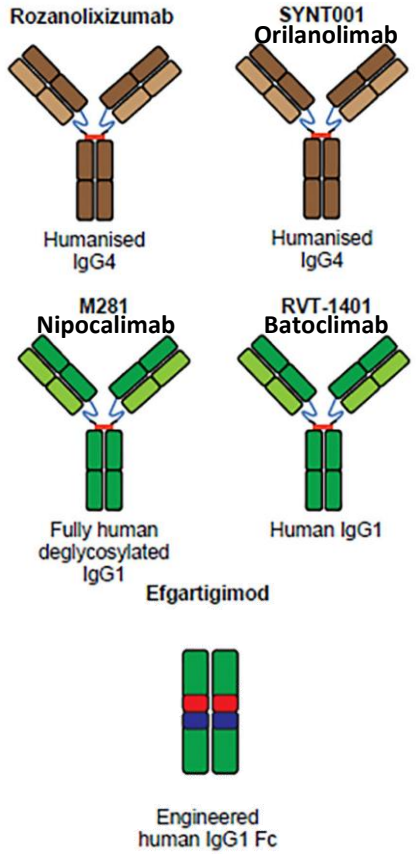
Rozanolixizumab cohort	Mean (range) platelet count (x10⁹/L)	
	Baseline*	Day 8
4 mg/kg	17.7 (5–36)	27 (3–105)
7 mg/kg	13.7 (5–24)	21 (6–57)
10 mg/kg	18.5 (6–53)	41 (3–166)
15 mg/kg	21.2 (6–38)	108 (8–486)
20 mg/kg	18.0 (4–37)	145 (9–548)

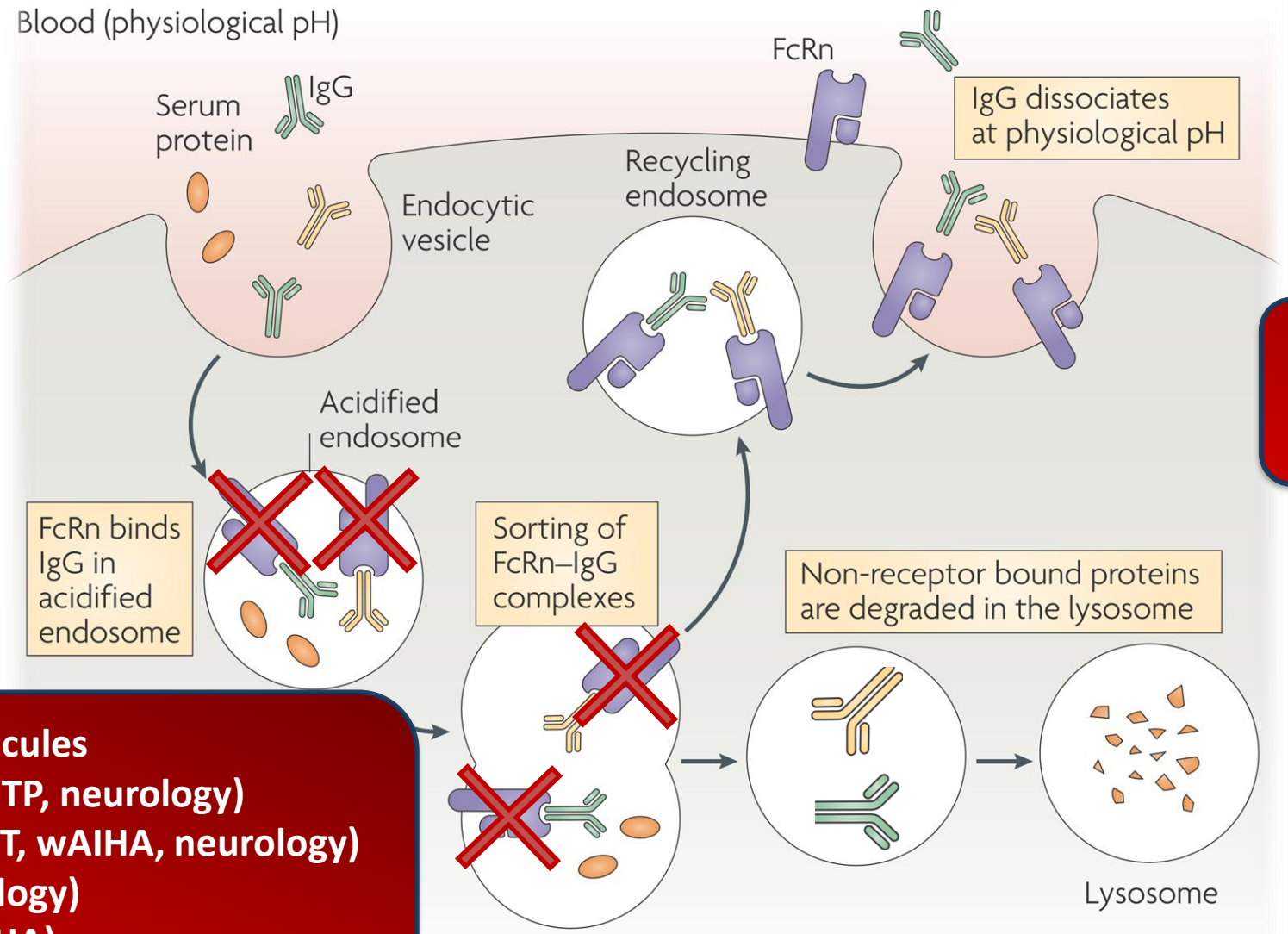


IgG concentration



FcRn inhibition : ↗ clearance of pathogenic Ab





FcRn inhibition
- ↘ pathogenic IgG
- ↘ total IgG

Molecules
- Rozanolixizumab (ITP, neurology)
- Nipocalimab (FNAIT, wAIHA, neurology)
- Batoclimab (neurology)
- Orilanolimab (wAIHA)
- Efgartigimod (ITP (Japan), neurology)

Roopenian *et al.*, Nature Rev. 2007
Zuercher *et al*. Autoimm Review 2019

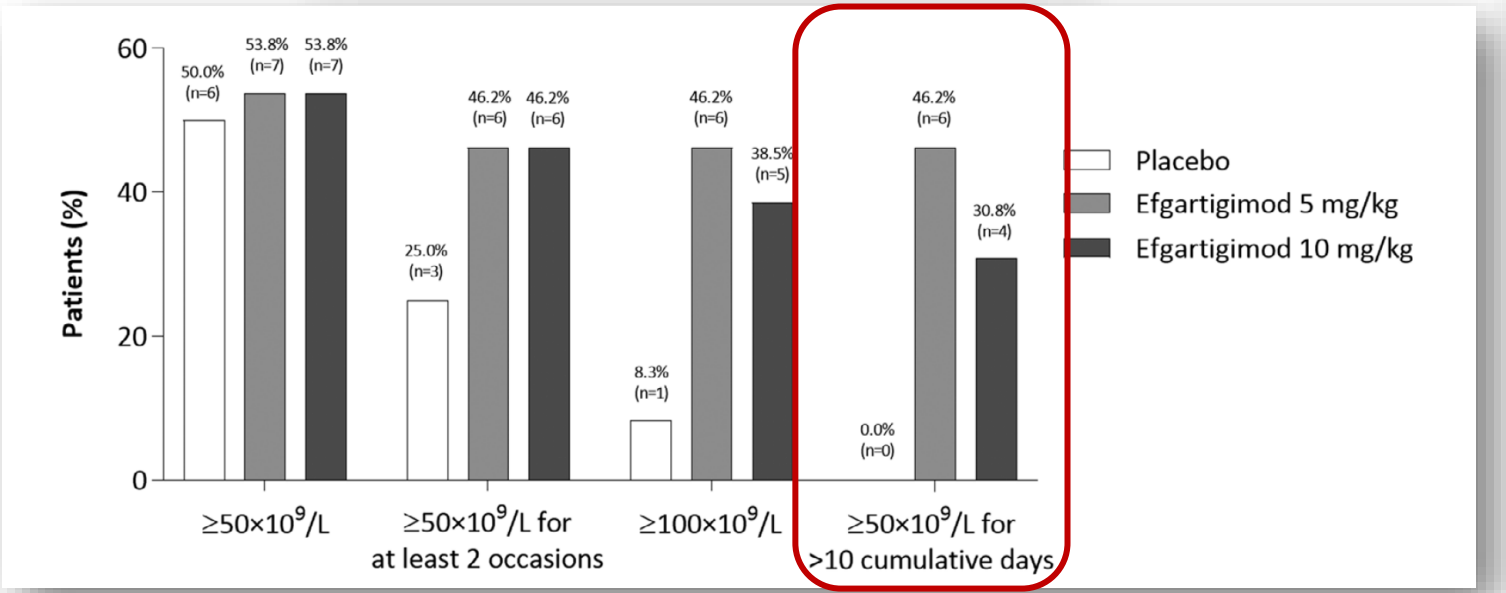
Phase 2 study of efgartigimod, a novel FcRn antagonist, in adult patients with primary immune thrombocytopenia

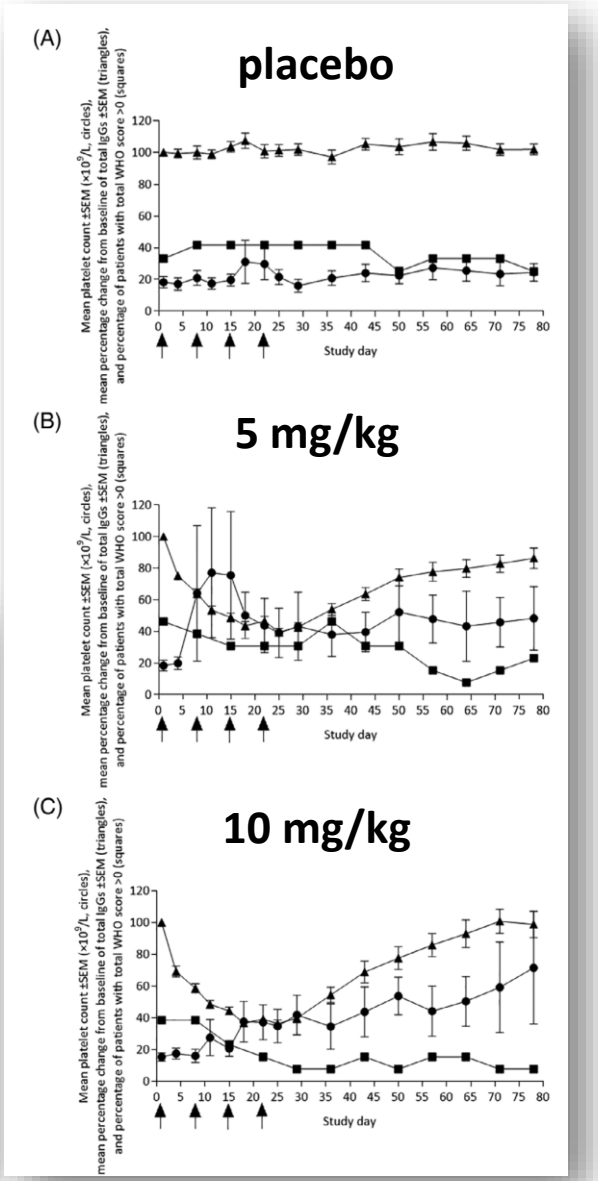
Adrian C. Newland[1] | Blanca Sánchez-González[2] | László Rejtő[3] | Miklos Egyed[4] | Nataliya Romanyuk[5] | Marie Godar[6] | Katrien Verschueren[6] | Domenica Gandini[6] | Peter Ulrichts[6] | Jon Beauchamp[6] | Torsten Dreier[6] | E. Sally Ward[7,8] | Marc Michel[9] | Howard A. Liebman[10] | Hans de Haard[6] | Nicolas Leupin[6] | David J. Kuter[11]

AJH

Am J Hematol. 2019;1–10.

human IgG1 antibody Fc-fragment, a natural ligand of the neonatal Fc receptor (FcRn), engineered for increased affinity to FcRn, while preserving its characteristic pH-dependent binding. Efgartigimod blocks FcRn, preventing IgG recycling, and causing targeted IgG degradation. In this Phase 2 study, 38 patients were randomized 1:1:1 to receive four weekly intravenous infusions of either placebo (N = 12) or efgartigimod at a dose of 5 mg/kg (N = 13) or 10 mg/kg (N = 13). This short treatment cycle of efgartigimod in patients with ITP, predominantly refractory to previous lines of therapy, was shown to be well tolerated, and demonstrated a favorable safety profile consistent with Phase 1 data. Efgartigimod induced a rapid reduction of total IgG levels (up to 63.7% mean change from baseline), which was associated with clinically relevant increases in platelet counts (46% patients on efgartigimod vs 25% on placebo achieved a platelet count of ≥50 × 10^9/L on at least two occasions, and 38% vs 0% achieved ≥50 × 10^9/L for at least 10 cumulative days), and a reduced proportion of patients with bleeding. Taken together, these data warrant further evaluation of FcRn antagonism as a novel therapeutic approach in ITP.





Platelets

Delta IgG

Bleedings

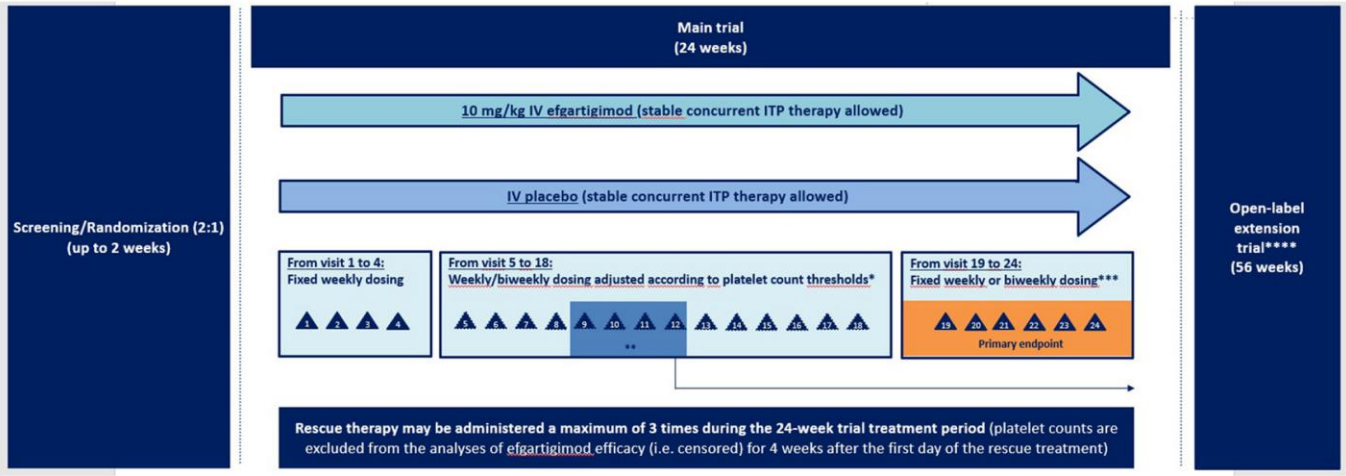
Newland *et al.*, AJH. 2020

Efficacy and safety of the neonatal Fc receptor inhibitor efgartigimod in adults with primary immune thrombocytopenia (ADVANCE IV): a multicentre, randomised, placebo-controlled, phase 3 trial

www.thelancet.com Vol 402 November 4, 2023

THE LANCET FULL-TEXT ARTICLE

*Catherine M Broome, Vickie McDonald, Yoshitaka Miyakawa, Monica Carpenedo, David J Kuter, Hanny Al-Samkari, James B Bussel, Marie Godar, Jaume Ayguasanosa, Kristof De Beuf, Francesco Rodeghiero, Marc Michel, Adrian Newland, with the ADVANCE Investigator Study Group**



	Efgartigimod 10 mg/kg (n=86)	Placebo (n=45)	Total (N=131)
Age, years			
Mean	46·9 (16·55)	51·7 (17·93)	48·6 (17·12)
Median	47·0 (19–85)	55·0 (18–82)	47·0 (18–85)
Sex at birth			
Male	39 (45%)	21 (47%)	60 (46%)
Female	47 (55%)	24 (53%)	71 (54%)
Ethnicity			
Japanese	5 (6%)	3 (7%)	8 (6%)
Hispanic or Latino	4 (5%)	1 (2%)	5 (4%)
Not Hispanic or Latino	77 (90%)	40 (89%)	117 (89%)
Not reported	0	1 (2%)	1 (1%)
Time since diagnosis, years			
Mean	10·3 (12·05)	11·1 (13·08)	10·6 (12·37)
Median	4·15 (0·3–54·1)	6·07 (0·5–53·4)	4·57 (0·3–54·1)
Disease duration category			
Chronic	78 (91%)	40 (89%)	118 (90%)
Persistent	8 (9%)	5 (11%)	13 (10%)
Baseline platelet count, $\times 10^9$ per L			
Mean	17·3 (10·19)	14·2 (9·19)	16·3 (9·93)
Median	17·0 (0·0–51·0)	12·0 (2·0–31·0)	17·0 (0·0–51·0)
Number of previous immune thrombocytopenia therapies received			
1	14 (16%)	4 (9%)	18 (14%)
2	13 (15%)	12 (27%)	25 (19%)
≥3	59 (69%)	29 (64%)	88 (67%)
Previous immune thrombocytopenia therapy types			
Corticosteroids	82 (95%)	40 (89%)	122 (93%)
Intravenous Ig or anti-D Ig	42 (49%)	29 (64%)	71 (54%)
Thrombopoietin receptor agonists	48 (56%)	29 (64%)	77 (59%)
Anti-CD20 (rituximab)	31 (36%)	14 (31%)	45 (34%)
Other immunosuppressants	21 (24%)	18 (40%)	39 (30%)
Danazol	10 (12%)	6 (13%)	16 (12%)
Dapsone	1 (1%)	2 (4%)	3 (2%)

(Table 1 continues in next column)

	Efgartigimod 10 mg/kg (n=86)	Placebo (n=45)	Total (N=131)
(Continued from previous column)			
Fostamatinib	3 (3%)	1 (2%)	4 (3%)
Splenectomy	32 (37%)	17 (38%)	49 (37%)
Receiving concurrent immune thrombocytopenia therapy at baseline	43 (50%)	22 (49%)	65 (50%)
Concurrent immune thrombocytopenia therapy types at baseline			
Corticosteroids	22 (26%)	12 (27%)	34 (26%)
Intravenous Ig or anti-D Ig	2 (2%)*	1 (2%)*	3 (2%)*
Thrombopoietin receptor agonists	20 (23%)	9 (20%)	29 (22%)
Anti-CD20 (rituximab)	0	1 (2%)*	1 (1%)*
Other immunosuppressants	8 (9%)	6 (13%)	14 (11%)
Danazol	2 (2%)	1 (2%)	3 (2%)
Ascorbic acid	0	1 (2%)	1 (1%)
WHO bleeding score†			
No bleeding	44 (51%)	16 (36%)	60 (46%)
Grade 1	38 (44%)	25 (56%)	63 (48%)
Grade 2 or higher	4 (5%)	4 (9%)	8 (6%)

Data are mean (SD), median (range), or n (%). *Three patients had prohibited medications classified as continued concurrent immune thrombocytopenia therapies: two with intravenous Ig and one with intravenous Ig and rituximab. These therapies were started before signing the informed consent form. Because the end date for these therapies was not recorded in the database, these patients were classified as receiving these medications as continued concurrent immune thrombocytopenia therapies. However, it was confirmed via data query resolution that the end date for these immune thrombocytopenia therapies occurred before the protocol-specified washout period before random assignment. †Grade 0 (no bleeding); grade 1 (petechial bleeding); grade 2 (mild blood loss); grade 3 (gross blood loss); and grade 4 (debilitating blood loss). WHO-classified bleeding events do not consider platelet counts.[24]

Table 1: **Participant characteristics at baseline (full analysis set)**

Broome *et al.*, Lancet 2023

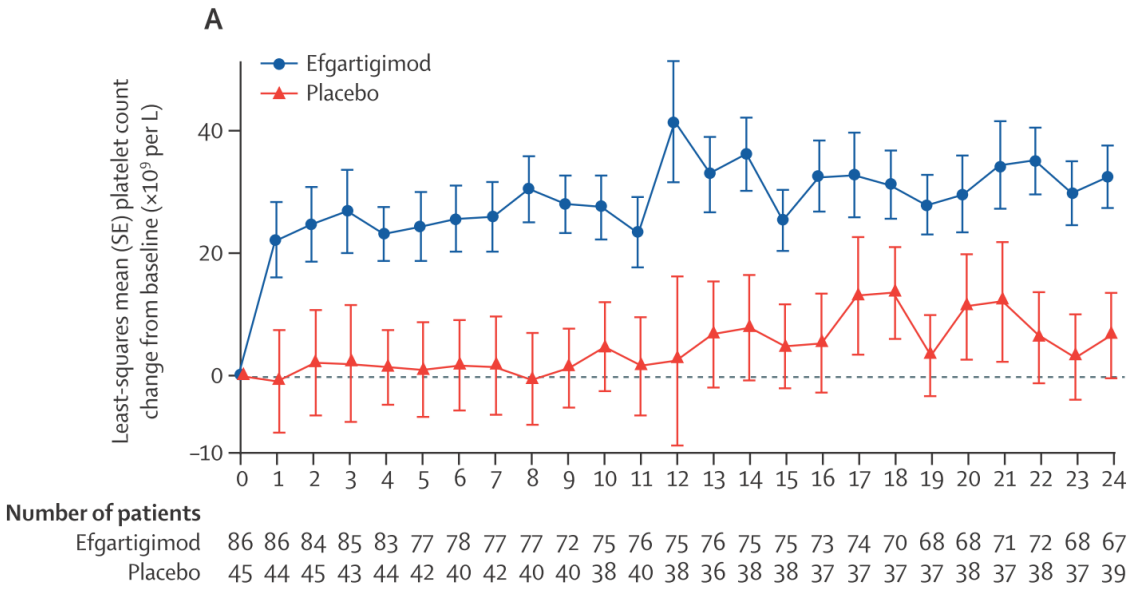
Efficacy and safety of the neonatal Fc receptor inhibitor efgartigimod in adults with primary immune thrombocytopenia (ADVANCE IV): a multicentre, randomised, placebo-controlled, phase 3 trial

www.thelancet.com Vol 402 November 4, 2023

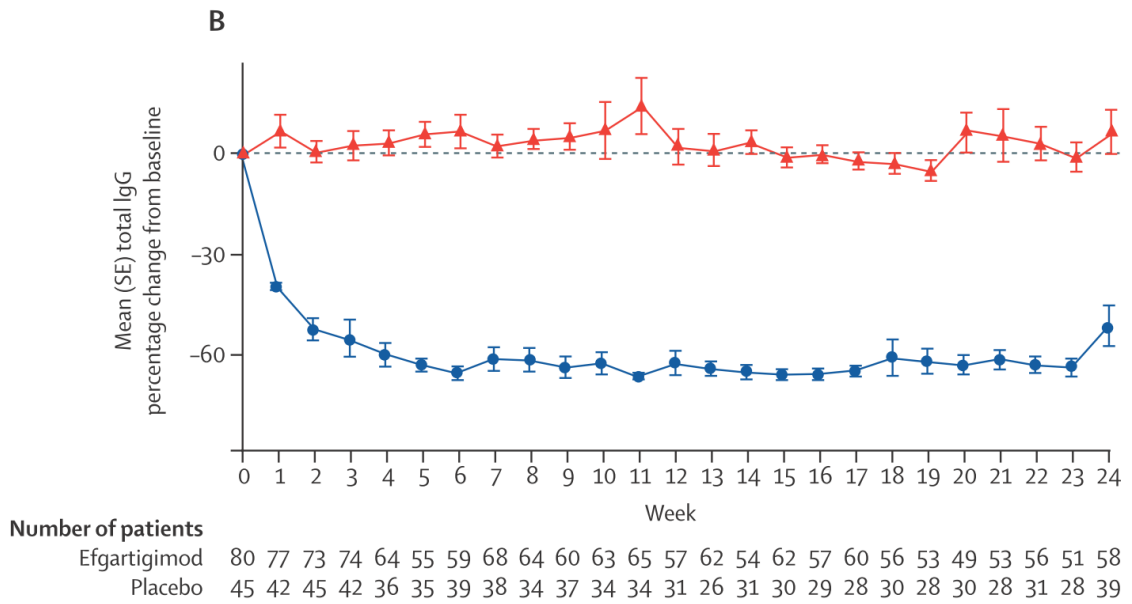
THE LANCET
FULL-TEXT ARTICLE

*Catherine M Broome, Vickie McDonald, Yoshitaka Miyakawa, Monica Carpenedo, David J Kuter, Hanny Al-Samkari, James B Bussel, Marie Godar, Jaume Ayguasanosa, Kristof De Beuf, Francesco Rodeghiero, Marc Michel, Adrian Newland, with the ADVANCE Investigator Study Group**

Platelet count



Total IgG



Broome *et al.*, Lancet 2023

Efficacy and safety of the neonatal Fc receptor inhibitor efgartigimod in adults with primary immune thrombocytopenia (ADVANCE IV): a multicentre, randomised, placebo-controlled, phase 3 trial

www.thelancet.com Vol 402 November 4, 2023

THE LANCET
FULL-TEXT ARTICLE

*Catherine M Broome, Vickie McDonald, Yoshitaka Miyakawa, Monica Carpenedo, David J Kuter, Hanny Al-Samkari, James B Bussel, Marie Godar, Jaume Ayguasanosa, Kristof De Beuf, Francesco Rodeghiero, Marc Michel, Adrian Newland, with the ADVANCE Investigator Study Group**

	Efgartigimod 10 mg/kg (n=86)	Placebo (n=45)	Adjusted difference in response (95% CI)	p value
Primary endpoint in chronic population (n=118)				
Sustained platelet count response*	17/78 (22%)	2/40 (5%)	16 (2·6–26·4)	0·032†
Key secondary endpoints in chronic population (n=118)				
Extent of disease control in the chronic population‡				
Mean number of cumulative weeks	6·1 (7·66)	1·5 (3·23)	..	0·0009§
Median number of cumulative weeks (IQR)	2·0 (0·0–11·0)	0·0 (0·0–1·0)	..	..
Key secondary endpoints in overall population (N=131)				
Sustained platelet count response*	22 (26%)	3 (7%)	19 (5·7–29·6)	0·011§
Incidence of WHO-classified bleeding events¶				
Mean number of visits with WHO-classified bleeding events ≥1	6·2 (6·39)	8·3 (8·01)	..	0·83
Median number of visits with WHO-classified bleeding events ≥1 (IQR)	4·0 (1·0–10·0)	5·0 (2·0–14·0)	..	..
Durable sustained platelet count response‖	19 (22%)	3 (7%)	16 (2·8–25·8)	NA**
Additional secondary endpoints†† in overall population (N=131)				
Patients with overall platelet count response at any time‡‡	42 (49%)	7 (16%)	33 (16·1–46·9)	0·0003
Patients with overall platelet count response until week 12§§	30 (35%)	2 (4%)	31 (17·7–41·3)	0·0001
Extent of disease control¶¶				
Median (range)	1·00 (0·00–12·00)	0·00 (0·00–12·00)	..	<0·0001
Mean (SD)	3·3 (4·12)	0·5 (1·91)	..	..
Time to response				
Median number of days‖‖ (95% CI)	113·0 (57·0–NC)	NC (NC–NC)	..	..
Median number of days‖‖ 25th quartile (95% CI)	22·0 (15·0–50·0)	NC (92·0–NC)	..	..
Median number of days‖‖ 75th quartile (95% CI)	NC (NC–NC)	NC (NC–NC)	..	..
Patients with two consecutive platelet counts ≥50 × 10⁹ per L	42 (49%)	9 (20%)	..	..
Cumulative number of weeks over the 24-week treatment period with a platelet count of ≥30 × 10⁹ per L and ≥20 × 10⁹ per L higher than baseline				
In the overall population, median (range)	6·00 (0·00–24·00)	0·00 (0·00–23·00)	..	<0·0001
In patients with a baseline platelet count of <15×10⁹ per L,*** median (range)	5·00 (0·00–24·00)	0·00 (0·00–23·00)	..	0·018
IWG-related platelet count				
Complete response†††	24 (28%)	2 (4%)	..	..
Response‡‡‡	44 (51%)	9 (20%)	..	..
Initial response§§§	27 (31%)	3 (7%)	..	..
Change in concurrent immune thrombocytopenia therapy¶¶¶	4 (5%)	6 (13%)	..	..

Efficacy

- **Primary endpoint**
  - ✓ **% chronic ITP patients with sustained response**
  - ✓ **i.e. ≥ 50x10^9/L for ≥ 4/6 visits btw W19-24**
- **Secondary endpoints**
  - ✓ **Cumulative weeks with PC ≥ 50x10^9/L**
  - ✓ **Sustained response in overall population**
  - ✓ ***Bleeding events***
  - ✓ **Durable sustained response ≥ 6/8 visits btw W17-24**
- **IWG criteria response**
  - ✓ **51% (44/86) vs. 20% (9/45)**
- **Recue therapies**
  - ✓ **34% vs. 49%**

Broome *et al.*, Lancet 2023

Efficacy and safety of the neonatal Fc receptor inhibitor efgartigimod in adults with primary immune thrombocytopenia (ADVANCE IV): a multicentre, randomised, placebo-controlled, phase 3 trial

www.thelancet.com Vol 402 November 4, 2023

THE LANCET
FULL-TEXT ARTICLE

*Catherine M Broome, Vickie McDonald, Yoshitaka Miyakawa, Monica Carpenedo, David J Kuter, Hanny Al-Samkari, James B Bussel, Marie Godar, Jaume Ayguasanosa, Kristof De Beuf, Francesco Rodeghiero, Marc Michel, Adrian Newland, with the ADVANCE Investigator Study Group**

	Efgartigimod 10 mg/kg (n=86)	Placebo (n=45)
Any TEAE	80 (93%)	43 (96%)
Any serious TEAE	7 (8%)	7 (16%)
Any grade 3 or higher TEAE	11 (13%)	9 (20%)
Any fatal TEAE	0	0
Any treatment-related TEAE according to principal investigator	15 (17%)	10 (22%)
Any serious treatment-related TEAE according to principal investigator	0	0
Any procedure-related TEAE according to principal investigator	3 (3%)	2 (4%)
Any TEAE leading to discontinuation of study drug	4 (5%)	1 (2%)
Any TEAE leading to study discontinuation	3 (3%)	0
Any bleeding	61 (71%)	39 (87%)
Any infection	25 (29%)	10 (22%)
Infusion-related reaction event	10 (12%)	5 (11%)
TEAEs of interest		
Headache	14 (16%)	6 (13%)
Haematuria	14 (16%)	7 (16%)
Petechiae	13 (15%)	12 (27%)
Purpura	7 (8%)	4 (9%)
Asthenia	6 (7%)	0
Hypertension	5 (6%)	0
Nausea	5 (6%)	2 (4%)
Fatigue	4 (5%)	1 (2%)

Data are n (%). TEAE=treatment-emergent adverse event.

Table 3: **Summary of TEAEs**

Safety

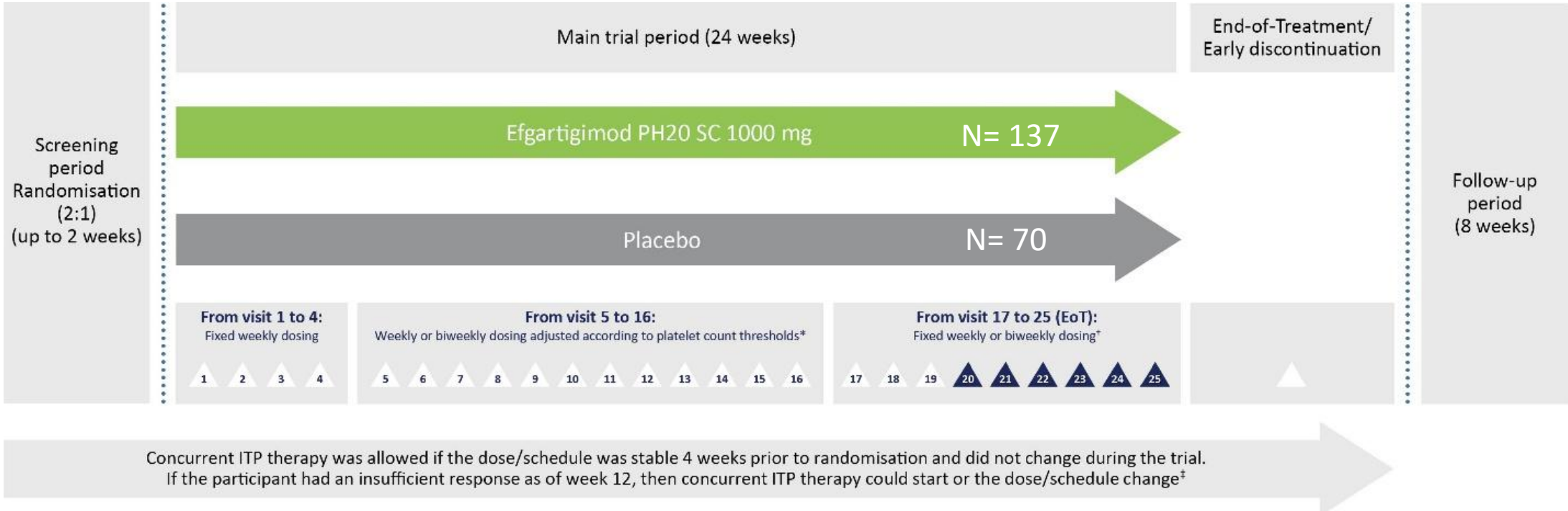
- **Well-tolerated**
- **No death**
- **No increased risk of infections**

Broome *et al.*, Lancet 2023

Efficacy and Safety of Subcutaneous Efgartigimod PH20 in Adults With Primary Immune Thrombocytopenia (ADVANCE SC): A Multicenter, Randomized, Double-Blinded, Placebo-Controlled, Phase 3 Trial

American Journal of Hematology, 2026; 0:1–13

Nichola Cooper[1] | Catherine M. Broome[2] | Yoshitaka Miyakawa[3] | Vickie McDonald[4] | Hanny Al-Samkari[5] | Abderrahim Khelif[6] | Spero R. Cataland[7] | Wilma Barcellini[8] | Renchi Yang[9] | Heng Mei[10] | Filip Matthijssens[11] | Anna Hultberg[11] | Giorgia Ciurlia[11] | Domenica Gandini[11] | Jaume Ayguasanosa[11] | Kristof De Beuf[11] | Ségolène Pastouret[11] | Waleed Ghanima[12] | Francesco Rodeghiero[13] | James B. Bussel[14] | the ADVANCE SC Investigator Trial Group



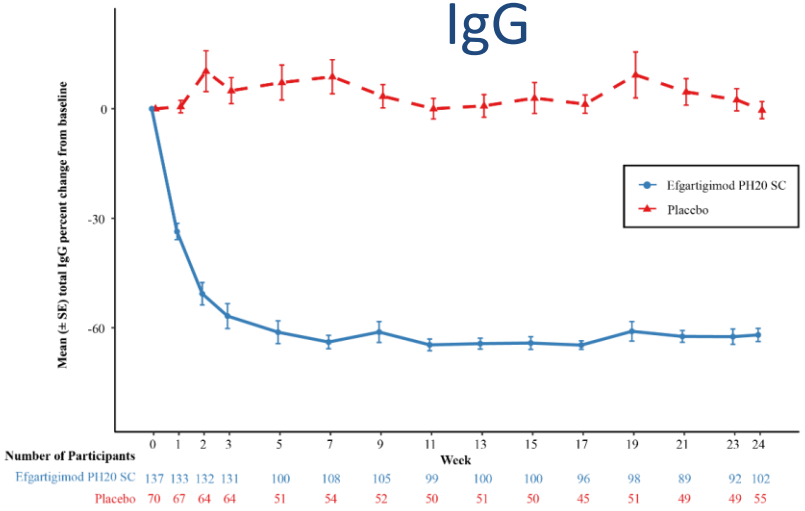
Cooper *et al.*, AJH. 2026

Efficacy and Safety of Subcutaneous Efgartigimod PH20 in Adults With Primary Immune Thrombocytopenia (ADVANCE SC): A Multicenter, Randomized, Double-Blinded, Placebo-Controlled, Phase 3 Trial

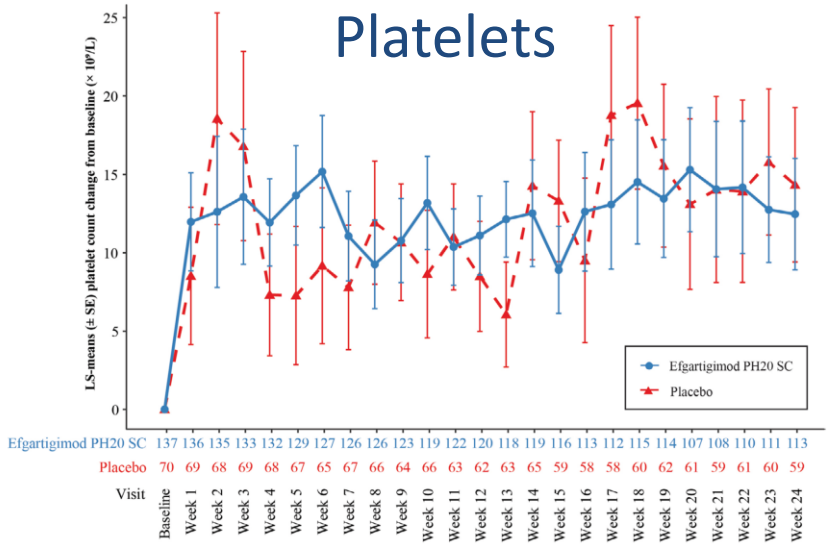
American Journal of Hematology, 2026; 0:1–13

Nichola Cooper[1] | Catherine M. Broome[2] | Yoshitaka Miyakawa[3] | Vickie McDonald[4] | Hanny Al-Samkari[5] | Abderrahim Khelif[6] | Spero R. Cataland[7] | Wilma Barcellini[8] | Renchi Yang[9] | Heng Mei[10] | Filip Matthijssens[11] | Anna Hultberg[11] | Giorgia Ciurlia[11] | Domenica Gandini[11] | Jaume Ayguasanosa[11] | Kristof De Beuf[11] | Ségolène Pastouret[11] | Waleed Ghanima[12] | Francesco Rodeghiero[13] | James B. Bussel[14] | the ADVANCE SC Investigator Trial Group

IgG



Platelets



N=207 (137 vs. 70)	Efgartigimod PH20 SC	Placebo	Significant[a]	Summary statistic (95% CI)[b]	P-value
PRIMARY ENDPOINT					
Sustained platelet count response[c]	17/124 (**13.7**)	11/68 (**16.2**)	No	0.757 (0.299, 1.950)	0.51[d]
KEY SECONDARY ENDPOINTS					
Extent of disease control[e]	**0.5** (0.0–4.5)	**0.0** (0.0–4.0)	NA	0 (0, 0)	0.49[f]
Sustained platelet count response[g]	22/137 (**16.1**)	11/70 (**15.7**)	NA	0.967 (0.406, 2.402)	0.93[d]
Durable sustained platelet count response[h]	17/137 (**12.4**)	10/70 (**14.3**)	NA	0.871 (0.341, 2.293)	0.74[d]
Incidence of WHO bleeding events[i]	**9.0** (3.0–15.0)	**10.0** (4.0–14.0)	NA	0 (−2.000, 2.000)	0.77[f]

	Efgartigimod PH20 SC (*N* = 137); PYFU 58.36		Placebo (*N* = 70); PYFU 30.21	
	n (%)	ER	*n* (%)	ER
Any AE	130 (94.9)	22.53	65 (92.9)	22.64
Any SAE	14 (10.2)	0.41	10 (14.3)	0.36
Any Grade ≥ 3 AE	22 (16.1)	0.81	14 (20.0)	0.60
Any fatal AE[a]	1 (0.7)	0.02	0	0
Any treatment-related AE	58 (42.3)	4.20	24 (34.3)	2.25
Any procedure-related AE	33 (24.1)	1.76	15 (21.4)	1.03
Any serious treatment-related AE	1 (0.7)[b]	0.03	0	0
Any AE for which treatment was discontinued[c]	3 (2.2)	0.12	0	0
Any bleeding	112 (81.8)	12.12	60 (85.7)	14.47
Any infection	65 (47.4)	1.78	25 (35.7)	1.69
Any injection site reaction	51 (37.2)	2.95	18 (25.7)	1.36
Any injection-related reaction	29 (21.2)	1.76	8 (11.4)	0.40

Cooper *et al.*, AJH. 2026

Efficacy and Safety of Subcutaneous Efgartigimod PH20 in Adults With Primary Immune Thrombocytopenia (ADVANCE SC): A Multicenter, Randomized, Double-Blinded, Placebo-Controlled, Phase 3 Trial

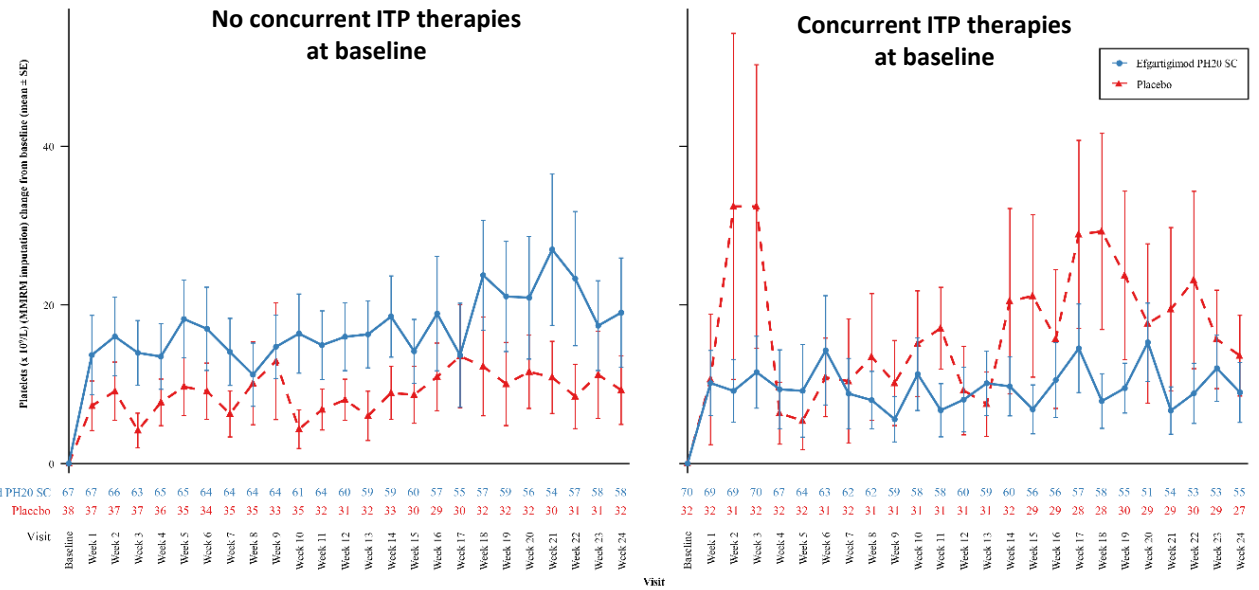
American Journal of Hematology, 2026; 0:1–13

AJH

Nichola Cooper[1] | Catherine M. Broome[2] | Yoshitaka Miyakawa[3] | Vickie McDonald[4] | Hanny Al-Samkari[5] | Abderrahim Khelif[6] | Spero R. Cataland[7] | Wilma Barcellini[8] | Renchi Yang[9] | Heng Mei[10] | Filip Matthijssens[11] | Anna Hultberg[11] | Giorgia Ciurlia[11] | Domenica Gandini[11] | Jaume Ayguasanosa[11] | Kristof De Beuf[11] | Ségolène Pastouret[11] | Waleed Ghanima[12] | Francesco Rodeghiero[13] | James B. Bussel[14] | the ADVANCE SC Investigator Trial Group

Hypotheses for differences btw IV and SC trials :

- High response rate in placebo group (16% in the SC vs. 5% in IV trial) due to concurrent ttt, shorter duration of ITP?
- Different mechanisms of action
  - ✓ IV: could also inhibit FcγR (“IVIg-like”)
  - ✓ SC: action only mediated by FcRn inhibition
- No neutralizing antibodies detected
- Predose concentration were similar (≈15 µg/mL)



⇒ Phase 3 ADVANCE NEXT IV study

Cooper *et al.*, AJH. 2026

FcRn inhibition in ITP: summary

- FcRn inhibitors :
  - Strong rational for their use in Ab-mediated diseases
  - Positive results in a subset of ITP patients
  - Expected to be only a suspensive therapy
  - Repeated IV injections are required
  - Responsible for a decrease in total IgG => no higher risk of infections in CT / long-term ?
  - Further developments in ITP?

Tanks for your attention !