



2ND meeting of the European Research Consortium on ITP

NEW INSIGHTS INTO IMMUNE
THROMBOCYTOPENIA

Paris Crowne Plaza Paris République

April 23-24, 2026



A large, stylized number '2' in a dark blue, brush-stroke font, with the letters 'ND' in a smaller, blue, sans-serif font positioned above it.

meeting of the European Research Consortium on ITP

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PREDICTIVE MARKERS OF TREATMENT RESPONSE: WHERE DO WE STAND?

Elisa Lucchini

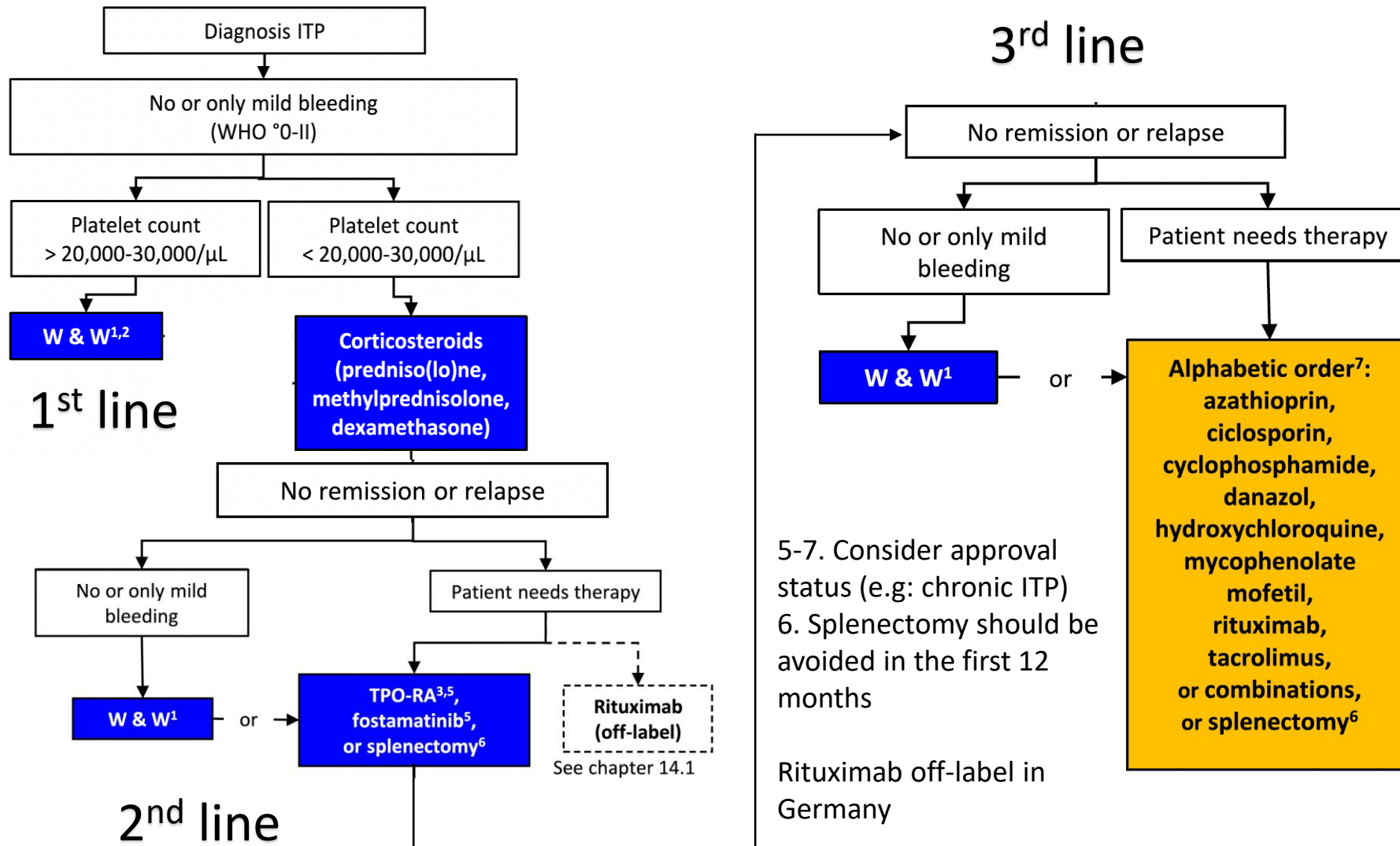
UCO Ematologia – Trieste (Italy)

Disclosures of Elisa Lucchini

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Roche							Honoraria
Amgen							Honoraria



German guidelines¹



Spanish guidelines²

«Fostamatinib is particularly suitable as a first option for second-line treatment in patients with high thromboembolic risk»

«Rituximab should be the secondary scenario in second-line options»

«There is no clear recommendation about how refractory patient treatments should be managed»

Target therapies

B-cells/phagocytosis		Plasmacells	Antibodies	Complement
Fixed duration	Continuous	Fixed duration	Continuous	Continuous
Rituximab	Fostamatinib	Daratumumab	Efgartigimod	Sutimlimab
Ianalumab	Rilzabrutinib	CM-313		Iptacopan
Belimumab		Mezagitamab		

TPO-RAs
Mainly continuous
Eltrombopag
Romiplostim
Avatrombopag

ATRA	Decitabine	Splenectomy	Combinations
Fixed duration	Fixed duration	Fixed duration	Ideally fixed duration

«broad spectrum» therapies

TREATMENT CHOICE IN ITP..



.. Still a TRIAL-AND-ERROR APPROACH

**Combination treatment could help
overcoming the problem**

BUT

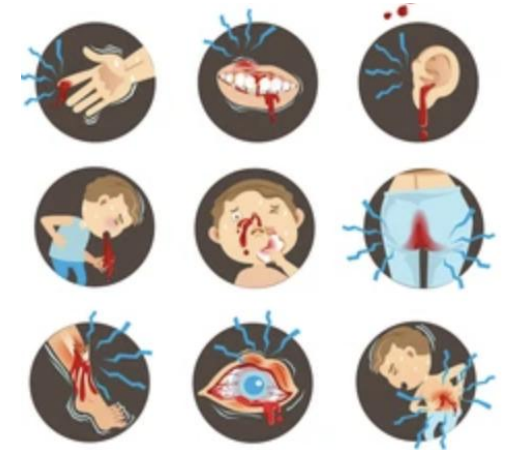
Is shooting in the dark the best option?

FACTORS PREDICTIVE of RESPONSE

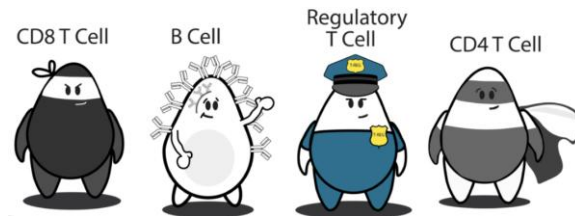


Related to the **patient**

Related to the **clinical** severity of the disease



Related to the **biology** of the disease



WHAT DO WE KNOW?

CAN WE PREDICT RESPONSE TO STEROIDS?

Biomarkers for predicting response to corticosteroid therapy for immune thrombocytopenic purpura

127 patients who received first-line steroid therapy (98% prednisolone)

Responders (plt count $\geq 30 \times 10^9/L$ within 3 weeks): **53.5%**

Age ≥ 81 yrs

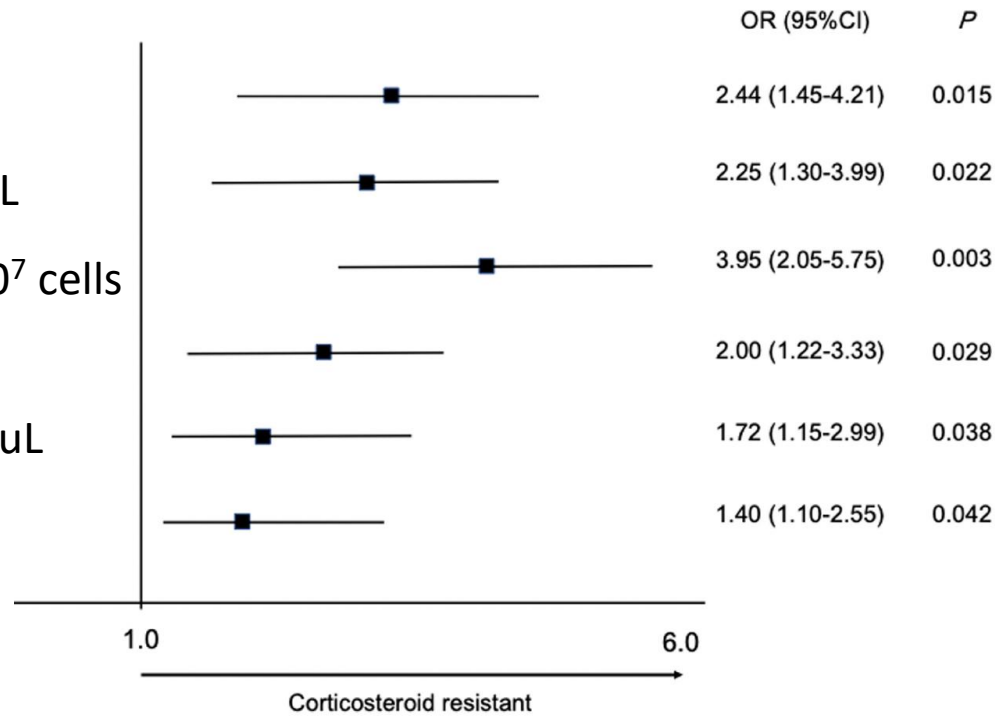
Plt count $< 9 \times 10^9/L$

PAIgG ≥ 445 ng/ 10^7 cells

PDW ≥ 14.0 g/dL

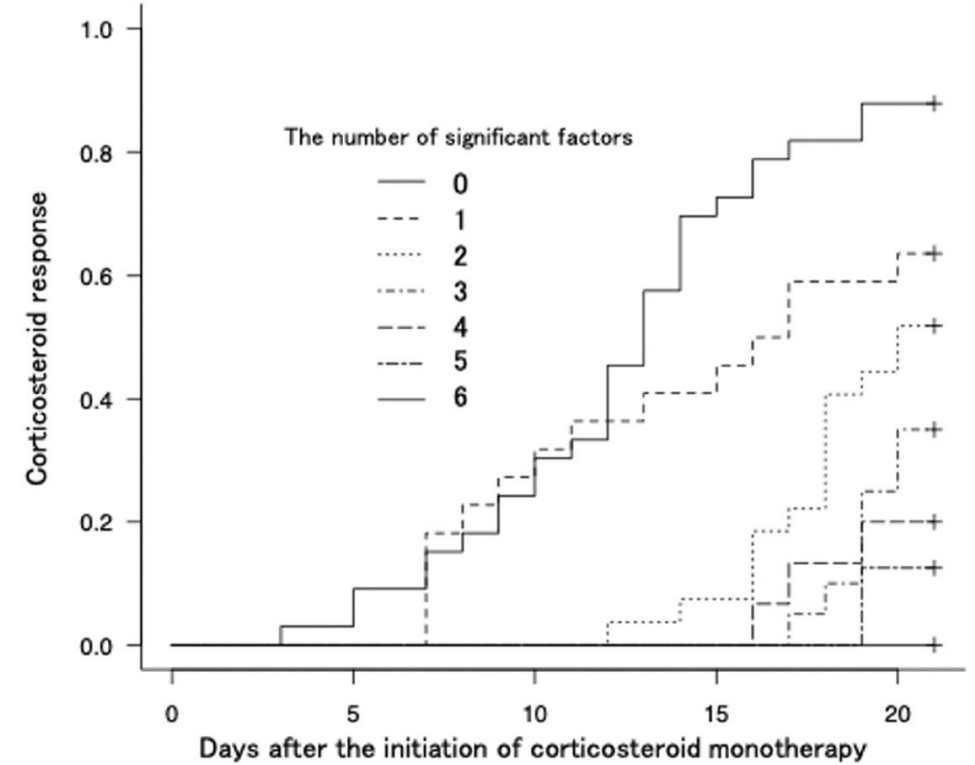
MK count $< 85.5/uL$

LMR ≥ 3.52



LMR: lymphocyte-monocyte ratio

Relationship between the number of significant factors and steroid response

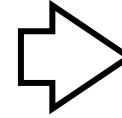


Days	0	1	2	3	4	5	6
0	33	32	25	10	4		
1	22	22	16	13	9		
2	27	27	27	25	15		
3	20	20	20	20	15		
4	15	15	15	15	12		
5	8	8	8	8	7		
6	2	2	2	2	2		

Antiplatelet antibodies

The association between platelet glycoprotein-specific antibodies and response to short-term high-dose dexamethasone with prednisone maintenance treatment in adult patients with primary immune thrombocytopenia

Hou YQ et al. Annals of Medicine 2022

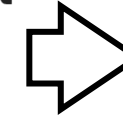


NO significant difference in **ORR** between antibody-positive and antibody-negative groups

Higher CR rate in antibody-positive group, driven by **anti-GPIIb/IIIa** positivity

Relationship between the expression of autoantibodies against platelet membrane glycoprotein and therapeutic effect in primary immune thrombocytopenia

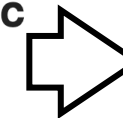
Liu XF et al. Chinese J Hematol. 2013



Higher CR rate to corticosteroids + IVIg in newly diagnosed ITP patients with positive **GP IIb/IIIa**

Study on the relationship of platelet specific–autoantibodies with therapeutic outcomes by dexamethasone in immune thrombocytopenia purpura

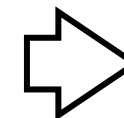
Chen Y et al. Chinese J Hematol. 2015



Patients with anti-GPIb have worse response to dexamethasone

Relative efficacy of steroid therapy in immune thrombocytopenia mediated by anti-platelet GPIIb/IIIa versus GPIb α antibodies

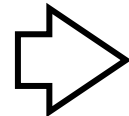
Zeng Q et al. American J Hematol. 2011



Worse response to dexamethasone in anti-GPIb positive
Response observed in patients with **anti-GPIIb/IIIa** or without detectable antibodies

Antiplatelet antibodies

The association between platelet glycoprotein-specific antibodies and response to short-term high-dose dexamethasone with prednisone maintenance treatment in adult patients with primary immune thrombocytopenia Hou YQ et al. Annals of Medicine 2022



NO significant difference in **ORR** between antibody-positive and antibody-negative groups

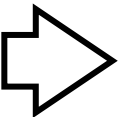
No standardized method for antiplatelet antibodies testing
Could negative patients not be true ITP?

Higher CR rate in antibody-positive group, **anti-GPIIb/IIIa** positivity

Relationship between the expression of membrane glycoprotein and thrombocytopenia Liu XF et al. Chin

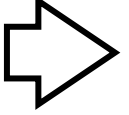
Higher CR rate to corticosteroids + IVIg in newly diagnosed ITP patients with positive **GP IIb/IIIa**

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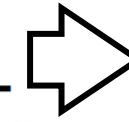


Worse response to dexamethasone in anti-GPIb positive
Response observed in patients with **anti-GPIIb/IIIa** or without detectable antibodies

Lymphocyte subpopulations

The predictive value of regulatory T cells on glucocorticoid sensitivity in patients with immune thrombocytopenia: a multicentre, prospective clinical study

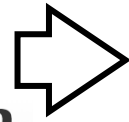
Li L et al. BJH. 2021



Significantly higher levels of **CD8+CD25+ Tregs** in steroid-sensitive patients (> 0.09%)

CD8+CD25+ Tregs as a predictor of glucocorticoid sensitivity in patients with immune thrombocytopenia

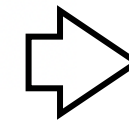
El-Sayed Abd El-Ghani S et al. Expert Review of hematology. 2025



This study could not confirm the predictive value of **CD8+CD25+** Tregs in glucocorticoid sensitivity

Higher CD56+ or CD2+ lymphocyte percentage predicts poor steroid response in patients with immune thrombocytopenia

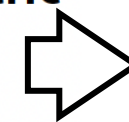
Wu JF et al. Thrombosis research. 2019



In good responders: **high CD19+**
In non responders: **high CD56+** (>24.5%) **or CD2+** (>85.7%)

Prediction of response to first-line therapy with ITP by flow cytometric analysis of bone marrow lymphocyte phenotypes

Satoko Oka¹ · Kazuo Ono² · Masaharu Nohgawa¹ International Journal of Hematology. 2020



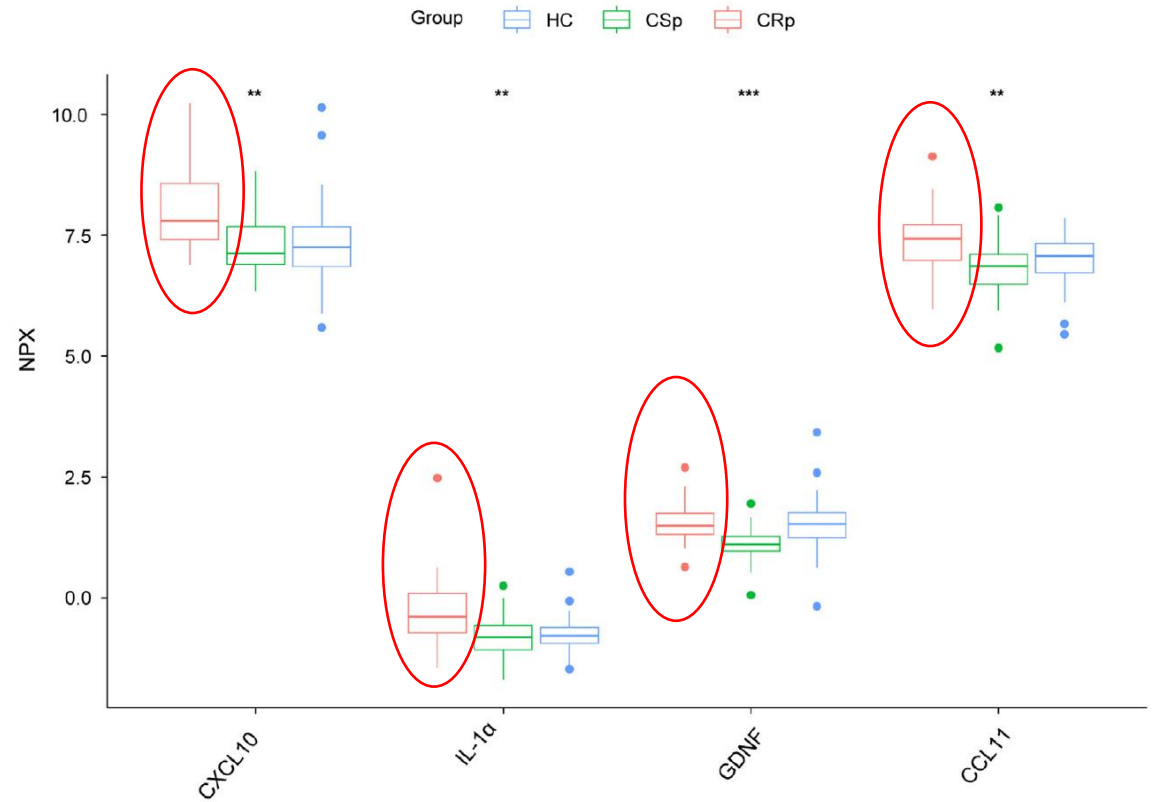
No difference in absolute numbers of CD3, CD19, CD4, CD8 and NK cells
Abnormal CD4:CD8 ratio in responders

Identification of key biomarkers for initial corticosteroid resistance in newly diagnosed primary immune thrombocytopenia

Analysis of plasma protein biomarkers (92 inflammation-related cytokines) from newly diagnosed ITP patients, 30 CS-sensitive and 26 CS-resistant

CXCL-10
IL-1 α
GDNF
CCL11

Expressed at significant higher levels in **CS-resistant** patients



Platelet desialylation

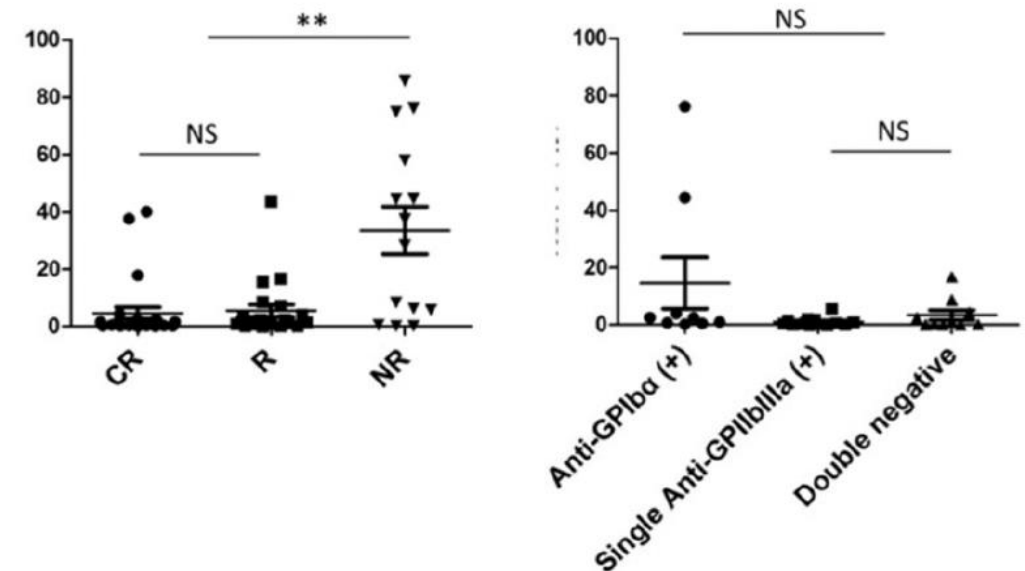
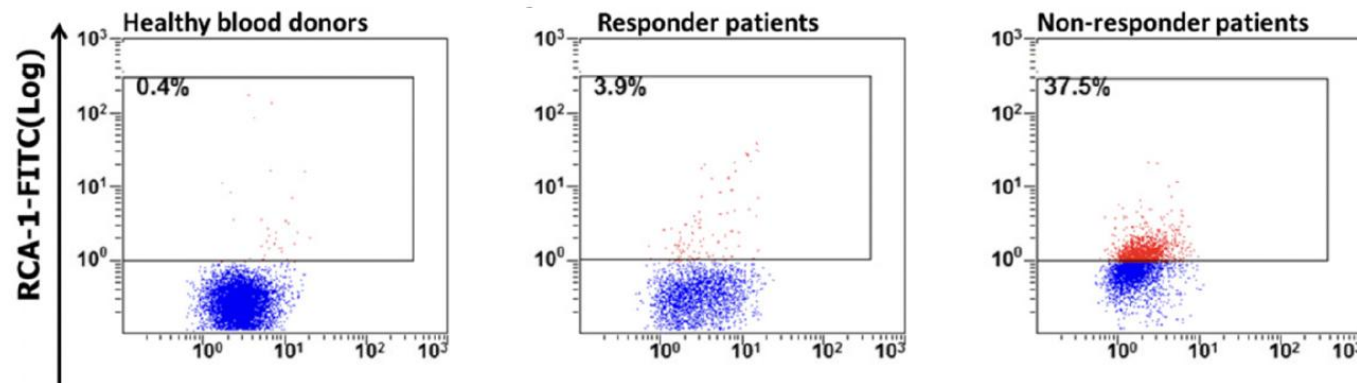
Platelet desialylation correlates with efficacy of first-line therapies for immune thrombocytopenia

61 ITP patients treated with standard first-line therapy

Desialylated galactose and beta-GlcNAc detected using RCA-1 and ECL

Significantly higher desialylation in non-responders

Increased platelet desialylation in patients with anti-GPIIb antibodies compared to anti-GPIIb/IIIa and without detectable antibodies



Fecal microbiota

Correlation Between Fecal Microbiota and Corticosteroid Responsiveness in Primary Immune Thrombocytopenia: an Exploratory Study

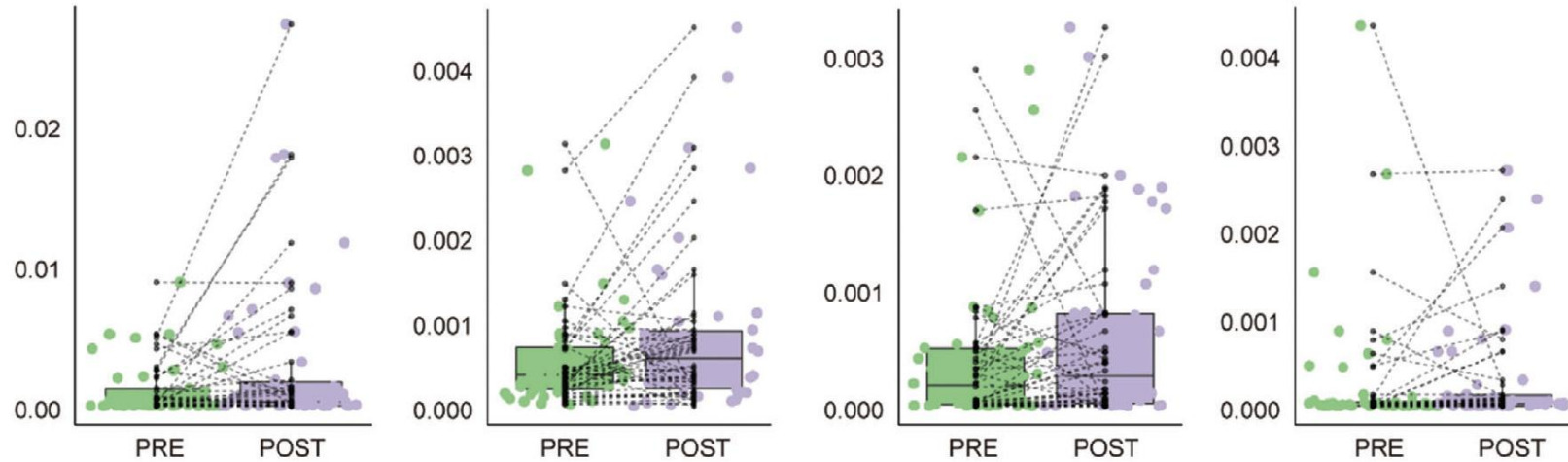
Four species exhibited significant association with treatment

Ruminococcus callidus
Wilcoxon: p -value = 0.042
MaAsLin: p -value = 0.004

uncultured Eubacterium sp.
Wilcoxon: p -value = 0.014
MaAsLin: p -value = 2.72e-08

Firmicutes bacterium CAG:114
Wilcoxon: p -value = 0.018
MaAsLin: p -value = 0.0004

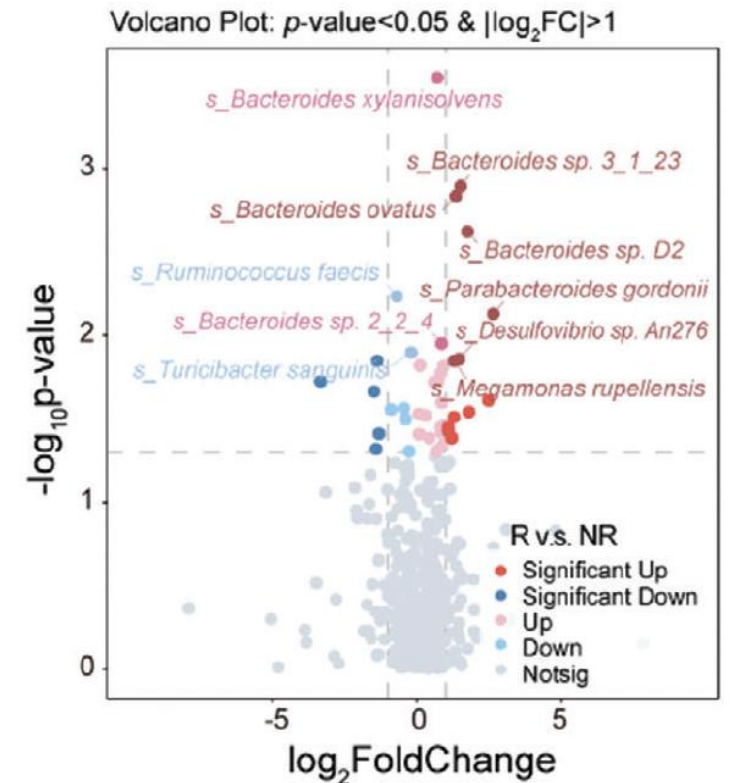
Alistipes ihumii
Wilcoxon: p -value = 0.038
MaAsLin: p -value = 0.0004



Enrolment of Participants

212 pts with primary ITP
157 treated with corticosteroids
Baseline and after treatment samples

Six species significantly more abundant in R group
Two species more abundant in NR

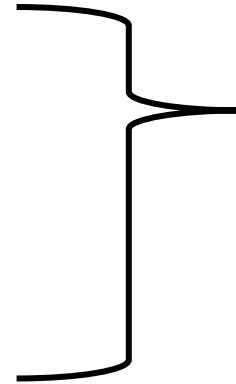


CAN WE PREDICT RESPONSE TO RITUXIMAB?

Clinical parameters

Factors associated with response and sustained response:

- Duration of ITP < 12-24 months^{1,2,3}
- Response achieved (CR)^{1,3}
- Age and gender: young females^{1,2,3}



But not confirmed in other reports^{4,5,6}

Antinuclear-antibody positivity (> 1:180) --> strong predictor of rituximab response⁷

Antiplatelet antibodies

bjh correspondence

GPIIb/IIIa autoantibody predicts better rituximab response in ITP Feng et al. BJH 2017

- Higher response rate in patients with anti **GPIIb/IIIa**
- No difference in response based on anti-GPIb/IX antibodies

Lack of detectable platelet autoantibodies is correlated with nonresponsiveness to rituximab treatment in ITP patients Porcelijn et al Blood 2017

Anti-GPIb/IX autoantibodies are associated with poor response to dexamethasone combined with rituximab therapy in primary immune thrombocytopenia patients Ding B et al. Platelets 2023

OR and CR rates significantly higher in patients without anti-GPIb/IX antibodies at 4 wks and 6 months

bjh research paper

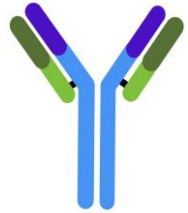
The effect of rituximab on anti-platelet autoantibody levels in patients with immune thrombocytopenia Arnold BJH 2017

Rituximab associated with significant reduction in anti-GPIIb/IIIa levels
Neither the presence of an autoantibody at baseline nor the loss of the autoantibody after treatment was associated with a response

Other factors



Low number of circulating NK cells (<150/mm³) predicts CR to rituximab¹, but not confirmed in other studies^{2,3}



IgG-Fc glycosylation does not predict treatment response to rituximab⁴

FC-gamma-RIIIa polymorphisms do not influence rituximab response⁵

Machine learning models found that **antinuclear antibodies** titres, **thyroglobulin antibody**, **corticosteroid response** and **bleeding severity** were positive predictors, while **thyroid peroxidase antibody**, **CD3+**, **CD4+**, **IL-17+ T cells** and **duration of disease** before rituximab were negative predictors⁶

***in pediatric ITP**

1.Rivière E et al. BJH 2022; 2.Monzon-Manzano E et al. BJH 2020; 3.Ebbo M et al. Clin Immunol. 2017

4.Schmidt D et al. Sci Rep 2020; 5.Ellithy HN et al. Hematology 2018; 6.Ma J et al. BJH 2024

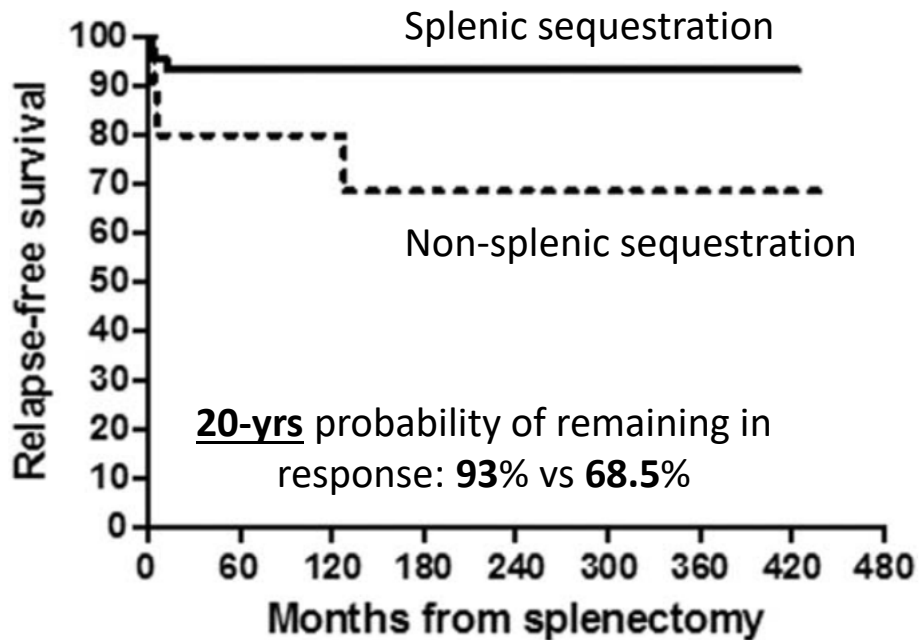
**CAN WE PREDICT RESPONSE TO
SPLENECTOMY?**

Response to splenectomy

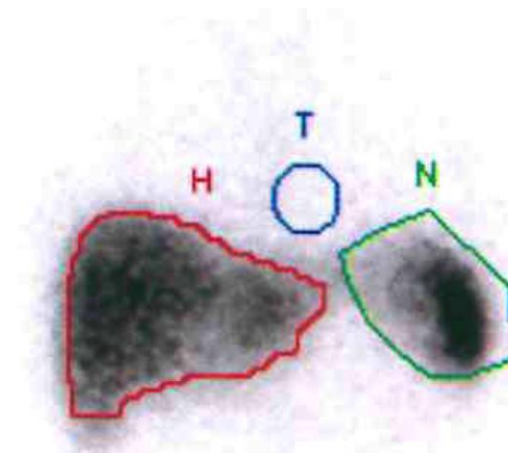
Factors predictive of response to splenectomy¹⁻³:

- Younger age (<60-65 yrs)
- Higher platelet count at splenectomy
- Less number of former therapies

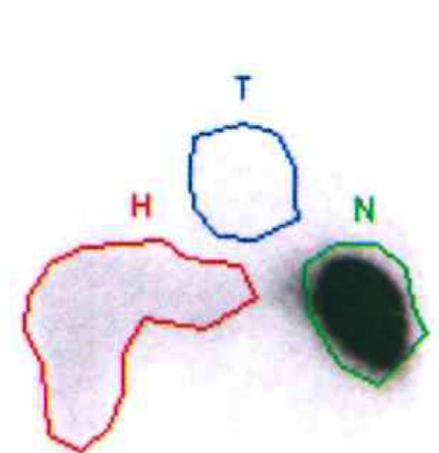
Role of platelet kinetics and ¹¹¹indium labeled platelets⁴



Mixed sequestration⁵



Splenic sequestration

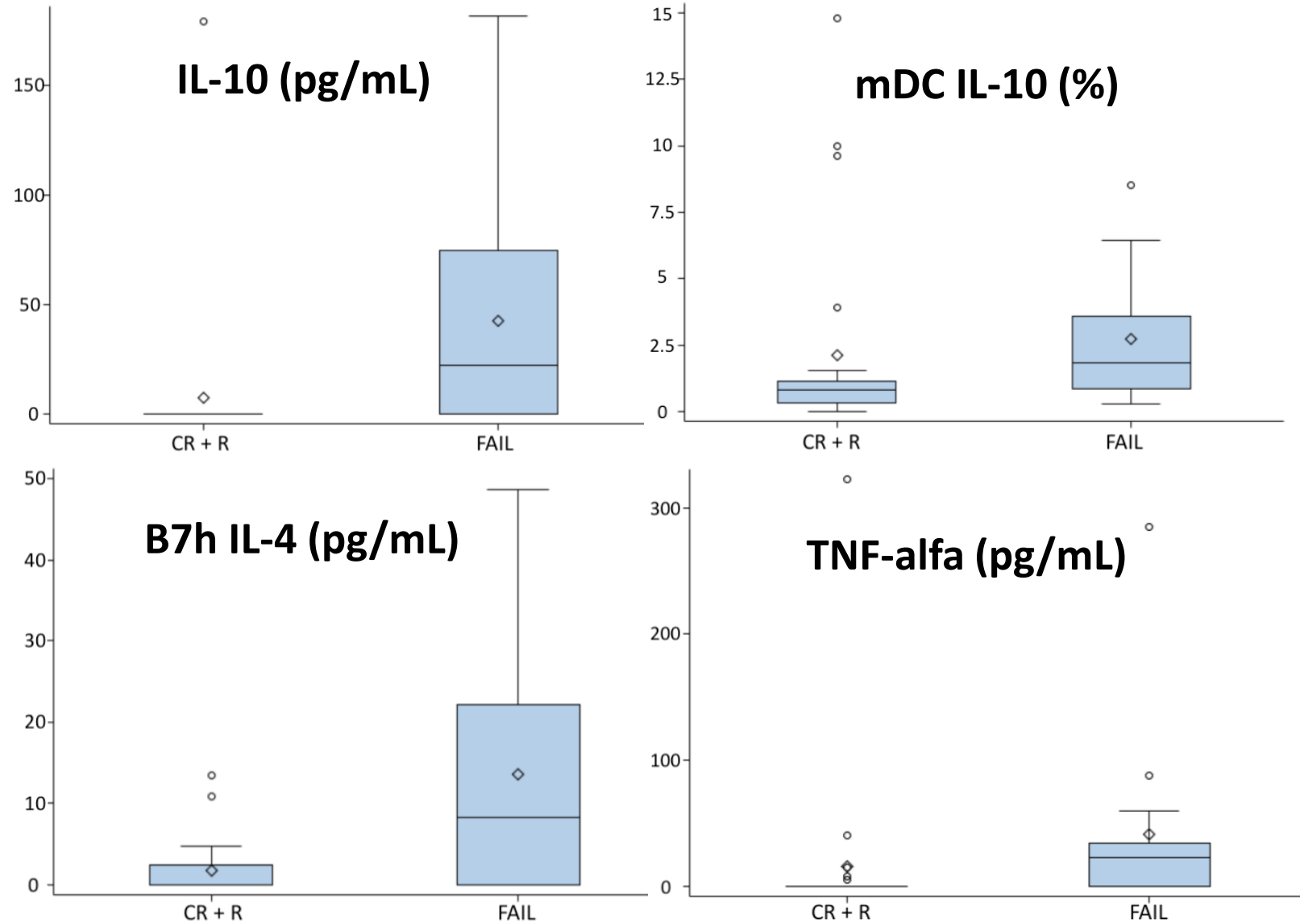


CAN WE PREDICT RESPONSE TO TPO-RAs?


Association between baseline levels and response to eltrombopag

Higher levels of baseline IL-10, IL-4 and TNF-alfa in non responders

- IL-10 and IL-4: secreted by Th2 lymphocytes; ↑ antibody-production
- TNF-alfa: pro-inflammatory cytokine



Thrombopoietin level predicts response to treatment with eltrombopag and romiplostim in immune thrombocytopenia

Hanny Al-Samkari  | David J. Kuter  AJH 2018

- TPO level inversely correlated with response
- TPO threshold ≤ 136 pg/mL for eltrombopag and ≤ 209 pg/mL for romiplostim were predictive for response
- Non-responders had median higher levels of TPO

Complement activation negatively affects the platelet response to thrombopoietin receptor agonists in patients with immune thrombocytopenia: a prospective cohort study

Akesson A et al. Platelets. 2023

Higher baseline levels of terminal complement complex were associated with inadequate response to TPO-RAs and more use of rescue therapy.

Levels of C4d positively correlated with terminal complement complex levels, reflecting the engagement of classical pathway

Can we predict SROT?

Clinical factors associated with SROT

	Clinical factors predictive of response
UK study¹	None (platelet count, age, gender, time)
ESTIT²	None
TAPER³	None (time since ITP diagnosis, age, gender, time to achieve CR, plt count at start of tapering)
STOPAGO⁴	Plt count $<150 \times 10^9/L$ and chronic ITP were associated with non sustained response
Korea study⁵	Higher peak platelet count ($>100 \times 10^9/L$) and prior IVIG response High autoimmune burden associated with lower SROT
STOP TPO-RA⁶	Higer platelet count and lower stable dose of romi at tapering start associated with SROT

1.Newland A et al. BJH 2015 4.Guillet S et al. Blood 2023

2.Lucchini E et al. BJH 2021 5.Yoon JH et al. JTH 2025

3.Cooper N et al. AJH 2022 6.Nelson VS e al. BJH 2025

Can we predict SROT?

Biological factors associated with SROT

	Biological factors predictive of response
UK study ¹	/
ESTIT ²	No association between B and T cells subsets, and cytokines (IFN-gamma, IL-10, IL-17a, IL-9, IL-22, IL-4, IL-2), TPO serum levels between patients who achieved SROT or not.
TAPER ³	/
STOPAGO ⁴	No differences in terms of B cells, T cells (including Treg cells), antiplatelet antibodies (anti GPIIb/IIIa/IbIX), TNF-alfa, IL-1beta, IL-6, IL-8, perforine, granzyme B, in patients who achieved SROT, SCROT and in non-sustained-response group. <u>CD69 (marker of T cell activation) in CD8+ memory T cells upregulated among patients with non-sustained-response</u>
Korea study ⁵	/
STOP TPO-RA ⁶	No difference in baseline TPO levels between patients who achieved or not SROT; no difference in antibodies levels

1. Newland A et al. BJH 2015

2. Lucchini E et al. BJH 2021

3. Cooper N et al. AJH 2022

4. Guillet S et al. Blood 2023

5. Yoon JH et al. JTH 2025

6. Nelson VS et al. BJH 2025

CAN WE PREDICT RESPONSE TO...?

SYK-inhibitors

Anti-CD38

**Anti-
BAFF/BAFF-R**

BTK-inhibitors

Anti-FcRn



Need for antiplatelet-
antibodies

B Cell-directed therapies

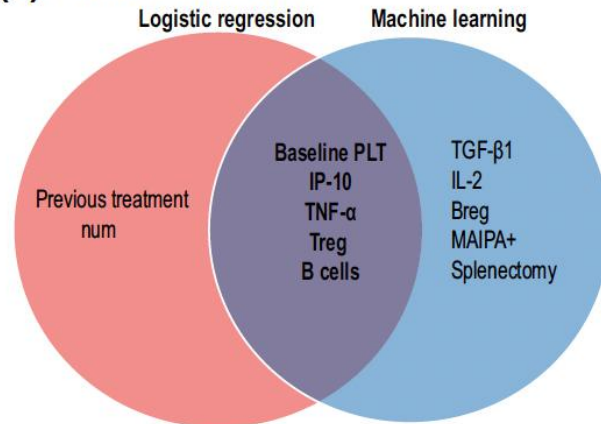
A novel scoring model for predicting efficacy and guiding individualised treatment in immune thrombocytopenia

Patients treated with corticosteroids (n=260); TPO-RAs (n=262); Rituximab (n=92)
Divided into training set, internal validation and external validation sets

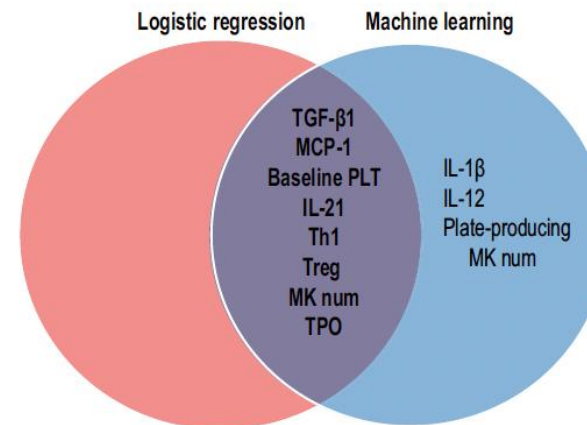
61 clinical and biological variables analyzed

5 classical ML models constructed for analysis & cross-validation with logistic regression

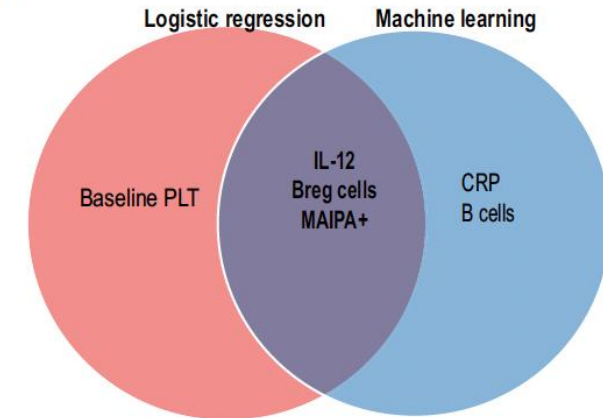
(J) Glucocorticoid

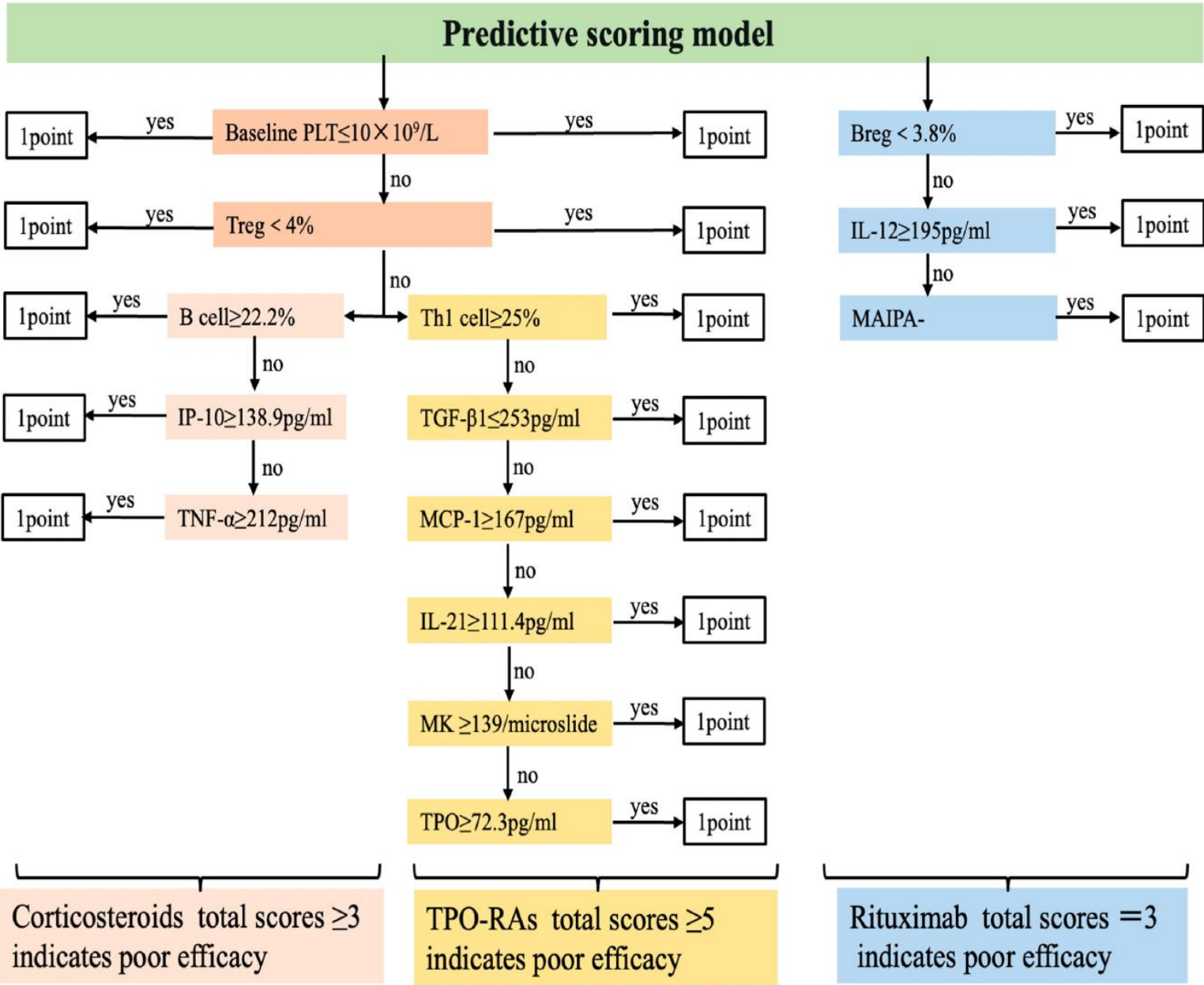


(K) TPO-RAs



(L) Rituximab





- Single-center and Chinese population only → needs external validation
- Does not take into account drug dosage and combinations
- 95% of patients had undergone at least one treatment before → is this score applicable to treatment-naive patients?

Are we ready for biomarkers evaluation?

Antiplatelet antibodies

MAIPA assay is considered the gold standard for platelet antibodies detection:

- **Direct:** platelet-rich plasma, at least 20×10^6 plt needed, fresh sample
- **Indirect:** serum

- Specificity > 95% → conformational changes of the antigen; limited panel of antibodies
- Sensitivity 80% → too low platelets; low antigen expression; antigen not accessible

- Limited to be a «rule-in» test
- Detected autoantibodies may not indicate disease severity
- Not available broadly
- What about secondary ITP?

Other options:

- PIFT: flow cytometry for platelet-associated IgG; also with low platelet counts; low specificity
- B-cell clonality: need to prove that B-cell clones produce pathogenic antibodies

Are we ready for biomarkers evaluation?

Platelet desialylation & apoptosis^{1,2}

Assessed on platelet-rich-plasma by flow cytometry

- Need of fresh material → possible platelet degradation
- Not enough material if platelet counts very low
- No «gold-standard» assay
- No direct correlation between the degree of desialylation and platelet apoptosis

Complement markers^{3,4}

- Pre-analytical factors (complement proteins are heat-labile); easy degradation or ex-vivo activation
- Lack of standardization
- Time-consuming and complex procedures to perform traditional hemolytic assays

Are we ready for biomarkers evaluation?

Lymphocyte subpopulations and cytokines

- Relatively easy to perform
- Problems interpreting the results
- Costs

Features of a good prognostic marker:

- ✓ Strong association with clinical outcomes
- ✓ Reproducibility across different cohorts
- ✓ Easy to use and cost-effective

GIMEMA BIO-ITP study

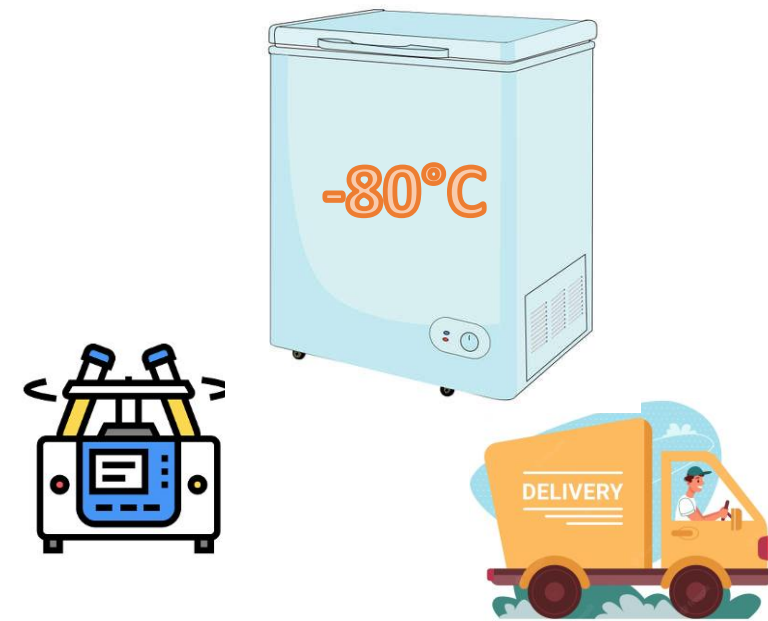
Multicenter, biological, prospective, non pharmacologic study aimed to characterize from a biological point of view ITP patients.

Adult patients with previously untreated, primary ITP, in need for first line treatment are enrolled.

Peripheral blood, fecal and bone marrow samples are collected at specific timepoints.

Antipletelet antibodies
Cytokine profile
Lymphocyte subpopulations
T-cell activation markers
B and T-cell clonality
Complement activation markers

Desialylation
Platelet apoptosis
TPO serum levels
Platelet parameters
Fecal microbiota
Genetic panel



Acknowledgements

UCO Ematologia, ASUGI, Trieste

- Mario Ballerini
- Laura Ballotta
- Manuela Caizzi
- Eleonora De Bellis
- Giovanni De Sabbata
- Davide Griguolo
- Sara Mohamed
- Monica Poiani
- Simona Puglisi
- Eugenio Sbisà
- Rossella Stella
- Cristina Ancora
- Matteo Turollo
- Rebecca Stefani
- Francesco Zaja

