2ND meeting of the European Research Consortium on ITP

NEW INSIGHTS INTO IMMUNE THROMBOCYTOPENIA

Paris Crowne Plaza Paris République

April 23-24, 2026

ERCI

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Management of secondary ITP

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

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Novartis						X	
Incyte	X						
GSK	X						
Amgen			x				

1. WHAT IS SECONDARY ITP ?

Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group

Francesco Rodeghiero,[1] Roberto Stasi,[2] Terry Gernsheimer,[3] Marc Michel,[4] Drew Provan,[5] Donald M. Arnold,[6] James B. Bussel,[7] Douglas B. Cines,[8] Beng H. Chong,[9] Nichola Cooper,[10] Bertrand Godeau,[4] Klaus Lechner,[11] Maria Gabriella Mazzucconi,[12] Robert McMillan,[13] Miguel A. Sanz,[14] Paul Imbach,[15] Victor Blanchette,[16] Thomas Kühne,[15] Marco Ruggeri,[1] and James N. George[17]

The term "secondary immune thrombocytopenia" or "secondary ITP" has been proposed to broadly include all forms of immune-mediated thrombocytopenias except primary ITP. Secondary forms include thrombocytopenias that are due to an underlying disease or to drug exposure. Some rare secondary immune thrombocytopenias, such as fetal and neonatal alloimmune thrombocytopenic purpura and posttransfusion purpura, would maintain their standard designation. For

blood

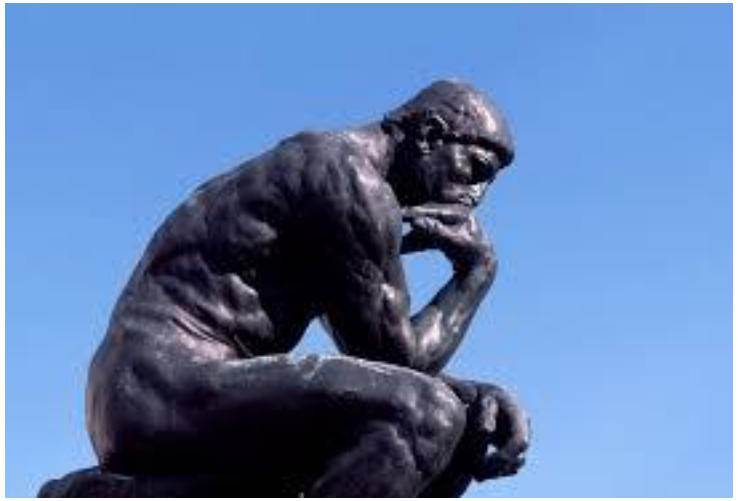
Blood 2009

Areas of uncertainty

- **Evans' syndrome ?** => combination of AIHA and ITP ± AIN, ES also classified as **primary of secondary**[1]
- **Thyroiditis** : should be rather seen as associated immune diseases occurring on a genetically predisposed background rather then true causes of ITP
- **ITP in pregnancy** => not truly secondary ITP but rather a transient predisposing state for developing ITP !
- **MGUS**[2] => fortuitous association or monoclonal gammopathy of clinical significance (as CAD) ? Needs further investigations…
- **Myelodysplastic syndrome** => some thrombocytopenic patients may respond to ITP treatment…
- Genetic predisposition ? Somatic mutations (elderly)?

[1] *Michel M et al. Blood.2009*
[2] *Mahevas M et al. Blood 2016*

The diagnosis of secondary ITP is clearest when remission follows an intervention to treat the underlying disorder such as eradication of infection (e.g., H. pylori).



In other situations, the relationship is assumed based on co-existence of other disorders (such as SLE and APS)

Waiting for new consensus/recommandations !

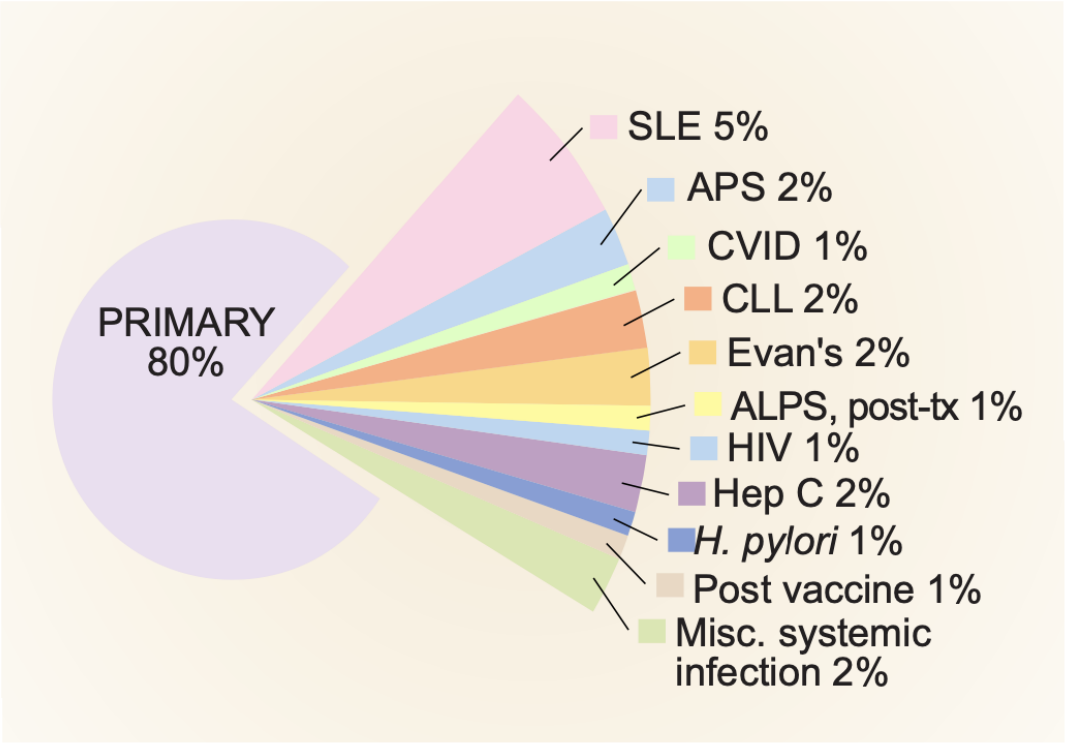
2. PREVALENCE OF SECONDARY ITP AND MAIN CAUSES ?

blood

Prepublished online Apr 24, 2009;
doi:10.1182/blood-2009-01-129155

The ITP syndrome: pathogenic and clinical diversity

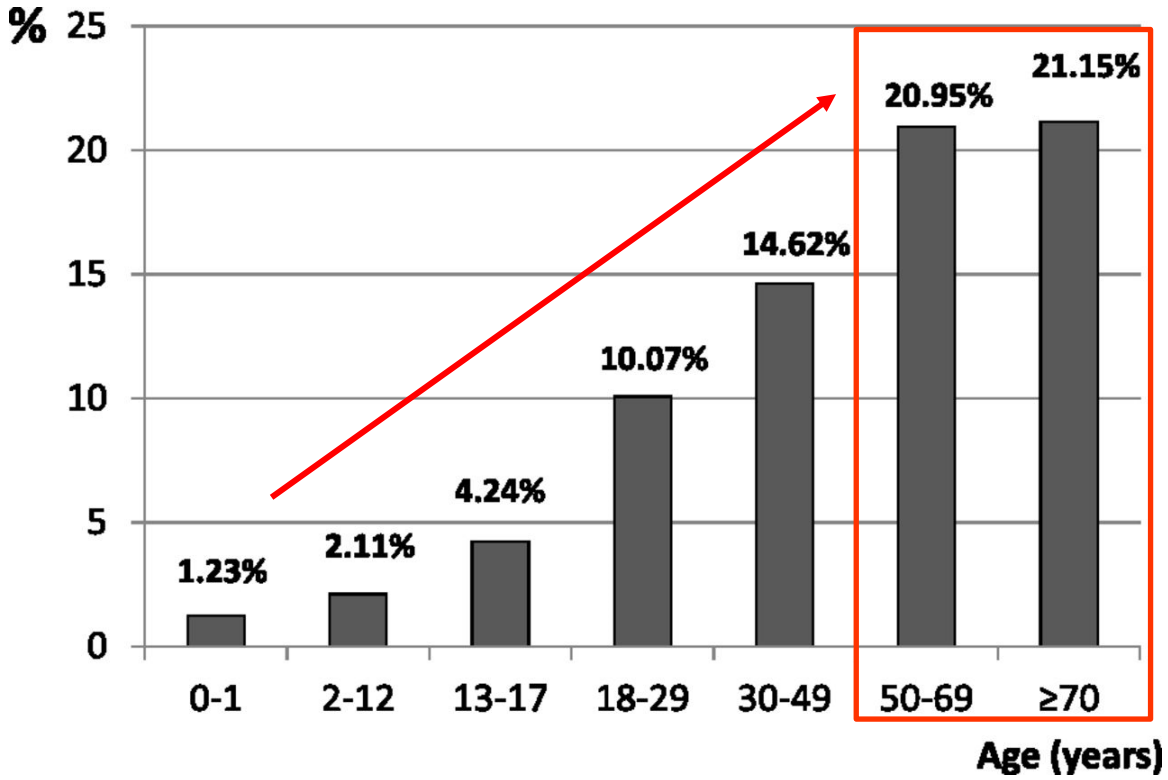
Douglas B. Cines, James B. Bussel, Howard A. Liebman and Eline T. Luning Prak



Data from France => **up to 20%** of secondary ITP

Cines et al. Blood 2009
Moulis G et al. Blood 2014

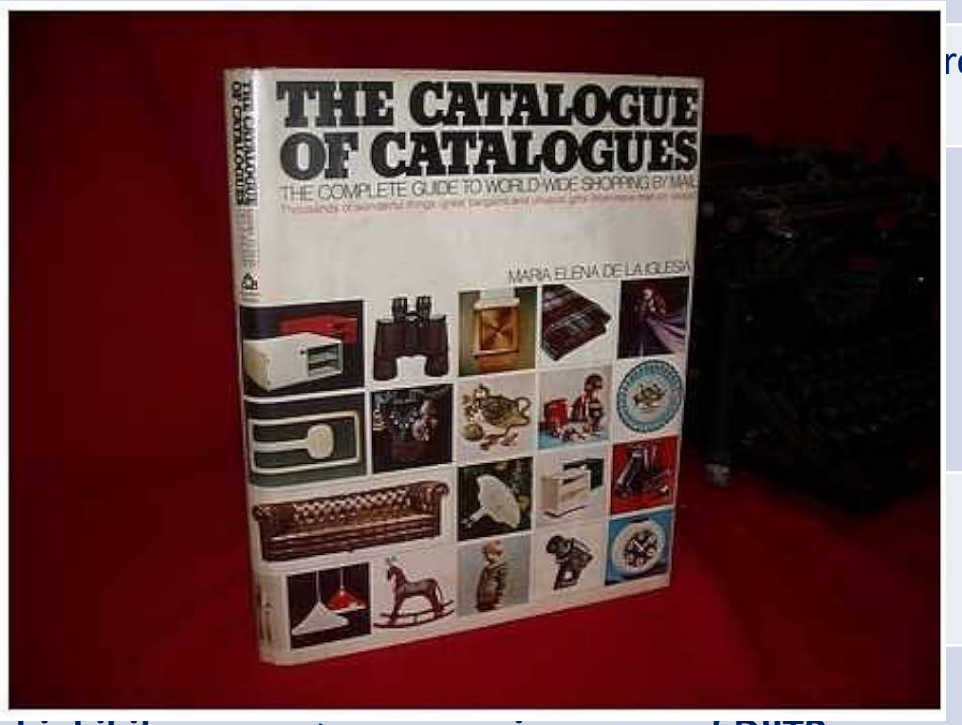
Cause*	ICD10 codes	n	Percent of secondary ITP (n = 518)	Percent of ITP (n = 2882)
In situ neoplasms	D00-D09	1	0.19%	0.03%
Malignant neoplasms	C00-C97	314	60.62%	10.89%
Hematological malignancies	C77, C81-C96	196	37.84%	6.80%
Lymphoma	C77, C81-C86	91	17.57%	3.16%
Hodgkin lymphoma	C81	16	3.09%	0.55%
B-cell chronic lymphocytic leukemia	C91.1	49	9.46%	1.70%
Multiple myeloma and malignant plasma cell neoplasms	C90	16	3.09%	0.55%
Waldenström macroglobulinaemia	C88.0	13	2.51%	0.45%
Myelodysplastic syndromes	D46	67	12.93%	2.32%
Antiphospholipid syndrome	D68.6	8	1.54%	0.28%
Viral hepatitis C or B	B16, B18.0-B18.2	9	1.74%	0.31%
Viral hepatitis C	B18.2	5	0.96%	0.17%
Viral hepatitis B	B16, B18.0-B18.1	4	0.77%	0.14%
Human immunodeficiency virus disease	B20-B24	27	5.21%	0.94%
Connective tissue disease	M32-M35.1	71	13.71%	2.46%
Systemic lupus erythematosus	M32	49	9.45%	1.70%
Systemic sclerosis	M34	3	0.58%	0.10%
Dermatopolymyositis	M33	2	0.39%	0.07%
Sicca syndrome	M35.0	16	3.09%	0.55%
Mixed connective tissue disease	M35.1	3	0.58%	0.10%
Rheumatoid arthritis	M05, M06.0, M06.2-M06.3, M06.8-M06.9	11	2.12%	0.38%
Sarcoidosis	D86	18	3.47%	0.62%
Immunodeficiency†	D80-D84	49	9.46%	1.70%



Moulis G et al. Blood 2014

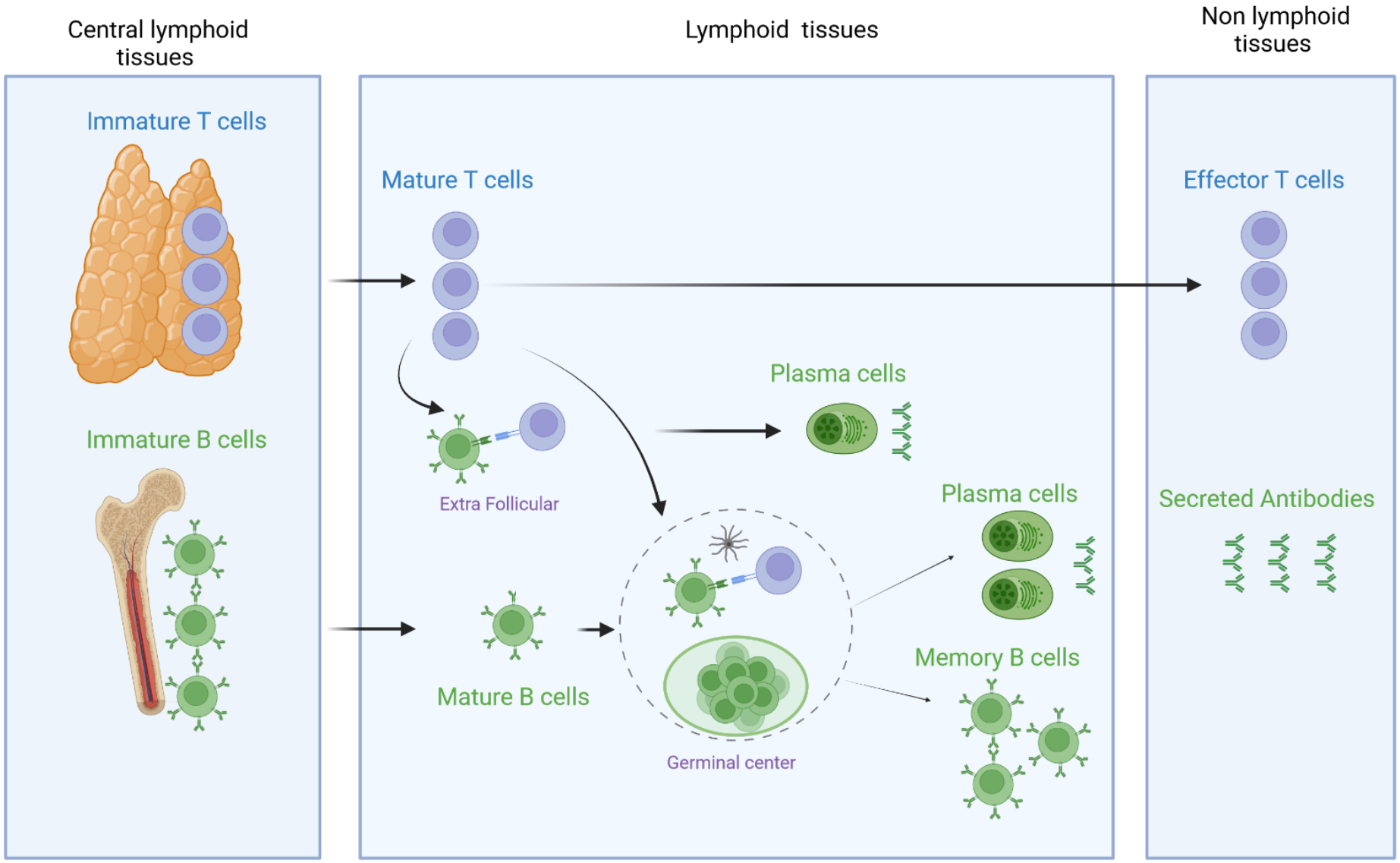
Main causes of secondary ITP (adults)

Underlying background	Causes
Infections	• Virus: HIV, HCV, (HBV, HAV), CMV, EBV, Parvovirus B19, Zika, SARS-COV2… • Bacteria: *H pylori*, Myc. tuberculosis, Mycoplasma pneumoniae..
Systemic autoimmune /inflammatory diseases	• **SLE,** antiph … ren syndrome,
Malignancies	• **Mostly B-c** • Hodgkin ly • Myeloma, • Angioimm • Renal carc
Primary immunodeficiency	• **CVID**; IgA • ALPS • Wisckott-A
Drugs	• Antibiotics • **Check-point inhibitors** **=> an emerging cause of DIITP** • Alemtuzumab • Vaccines
Miscellaneous	• Post-transplant (allogeneic BMT)

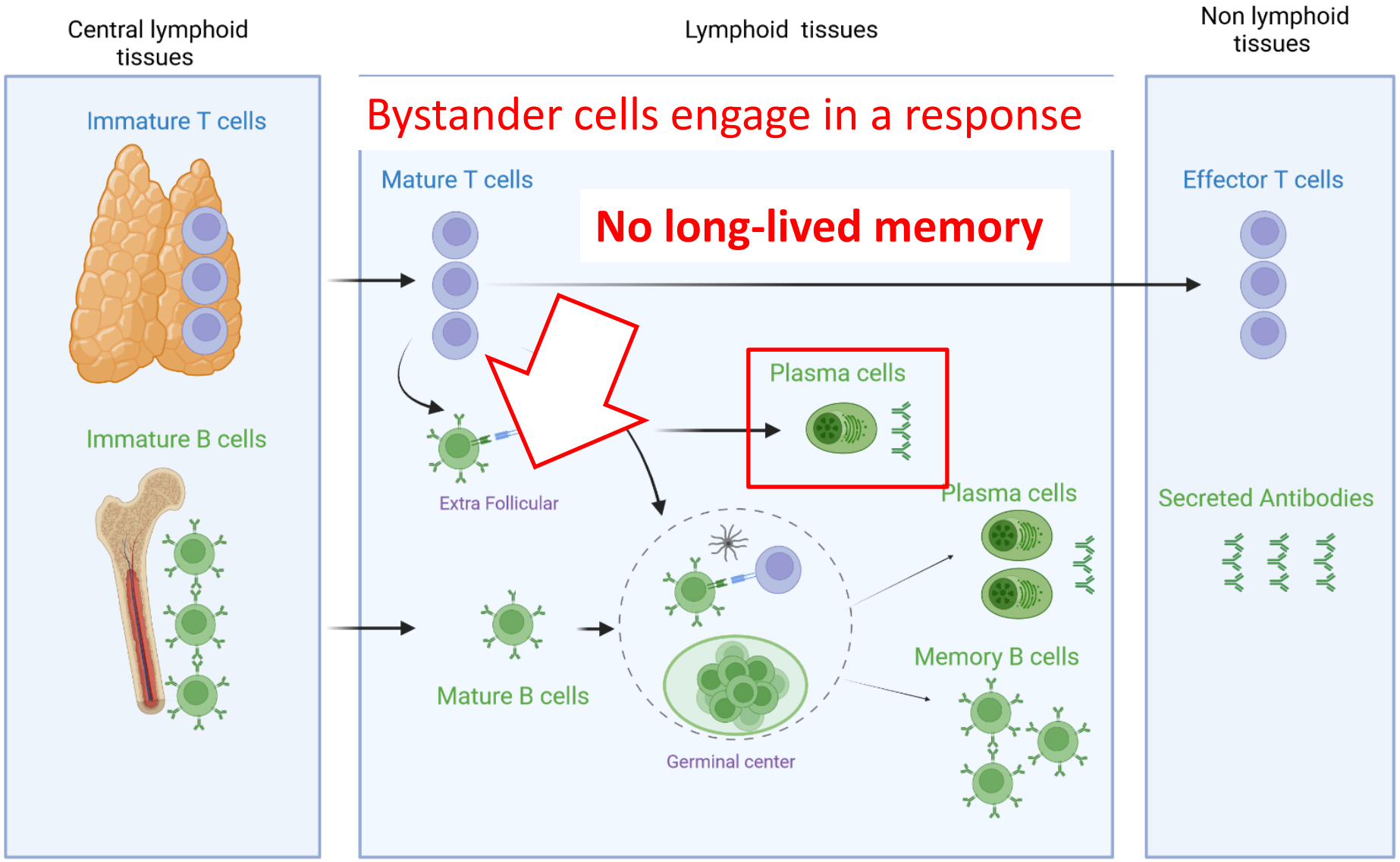


3. Can we learn something about the pathophysiology ?

Checkpoints Exist at Multiple Stages of the Immune Response



Checkpoints Exist at Multiple Stages of the Immune Response



bjh research paper

Molecular mimicry by *Helicobacter pylori* CagA protein may be involved in the pathogenesis of *H. pylori*-associated chronic idiopathic thrombocytopenic purpura

BJH2003

Role of molecular mimicry of hepatitis C virus protein with platelet GPIIIa in hepatitis C–related immunologic thrombocytopenia

Wei Zhang,[1] Michael A. Nardi,[2] William Borkowsky,[2] Zongdong Li,[1] and Simon Karpatkin[1]

Departments of [1]Medicine and [2]Pediatrics, New York University School of Medicine, NY

Blood 2009

Role of molecular mimicry to HIV-1 peptides in HIV-1–related immunologic thrombocytopenia

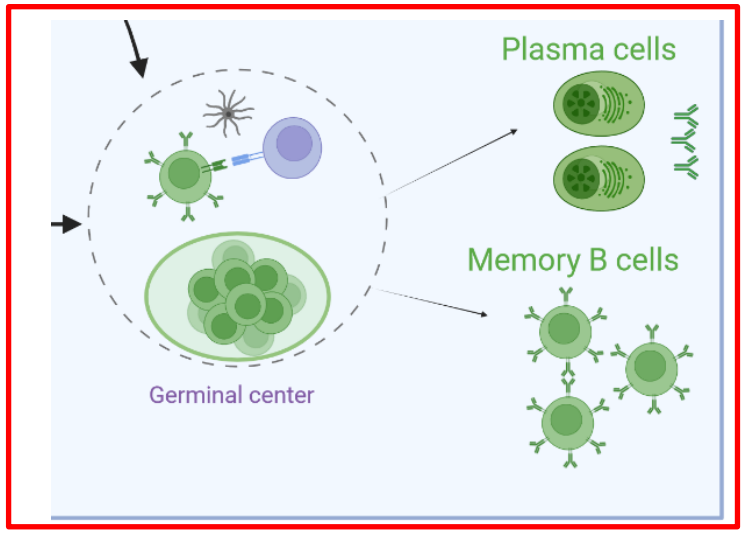
Zongdong Li, Michael A. Nardi, and Simon Karpatkin

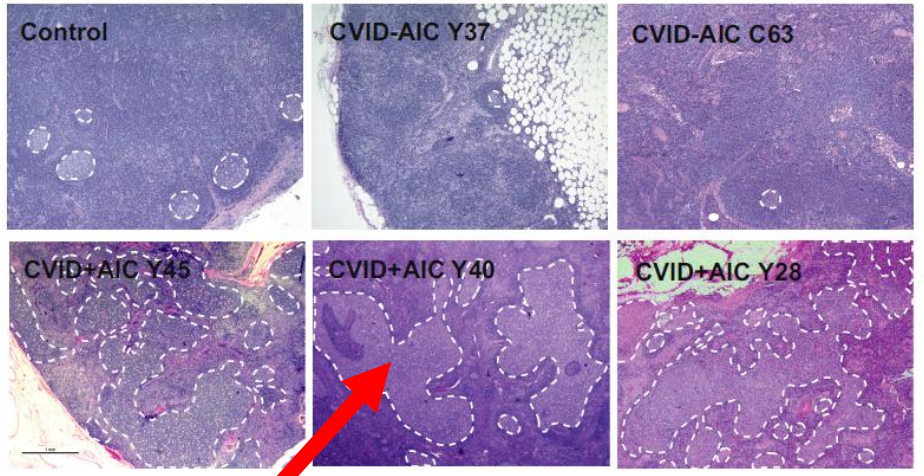
Blood 2005

Checkpoints Exist at Multiple Stages of the Immune Response

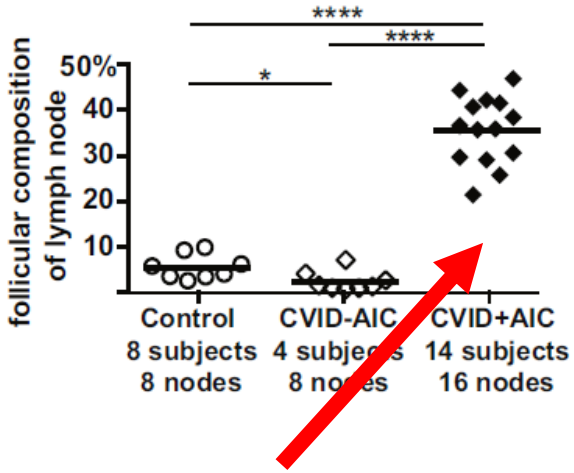
Common variable immunodeficiency

Germinal center activation





Germinal center !



Germinal center !

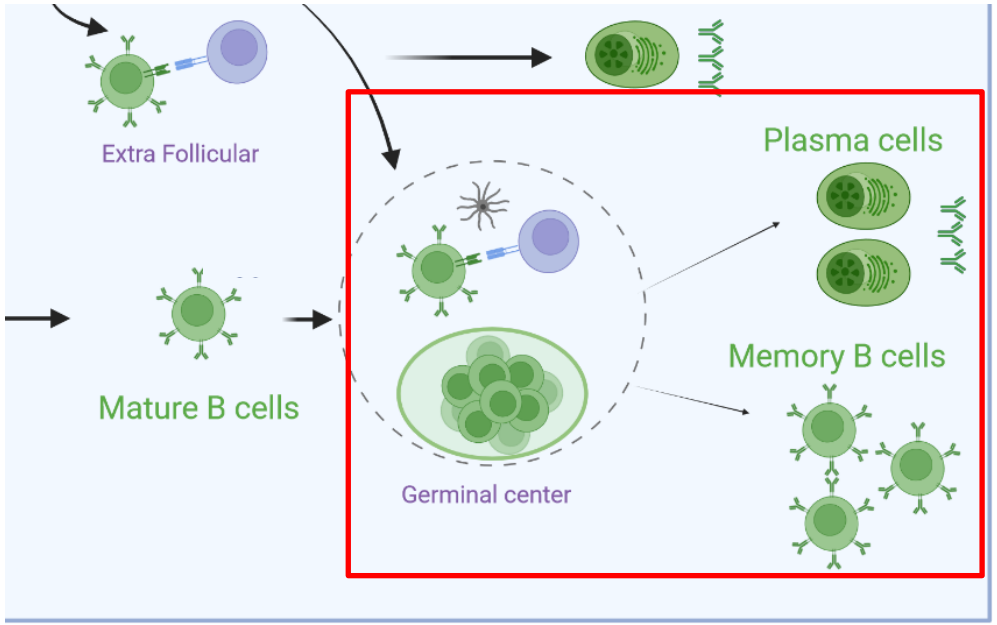
More generally inborn error of immunity

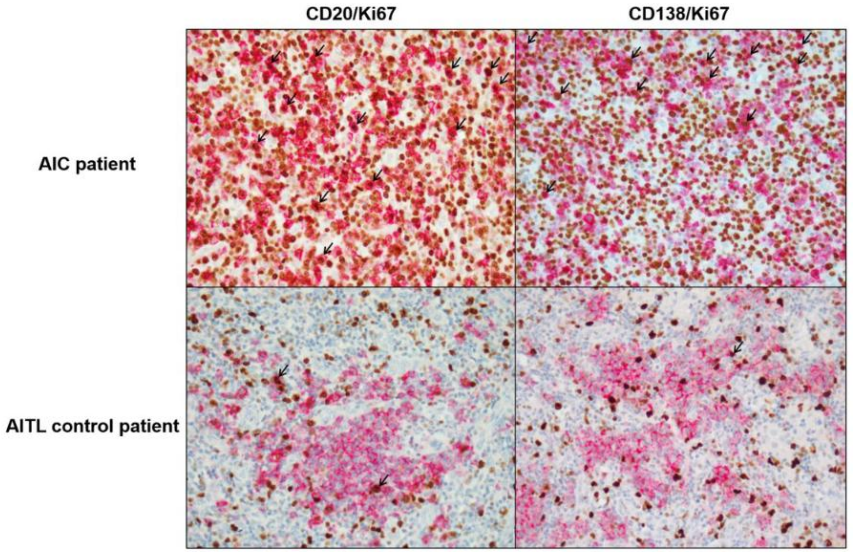
ITP patients with known genetic insufficiency in genes implicated in controlling B and T cell selection

Romberg; JACI 2018

Checkpoints Exist at Multiple Stages of the Immune Response

Angioimmunoblastic T-cell lymphoma



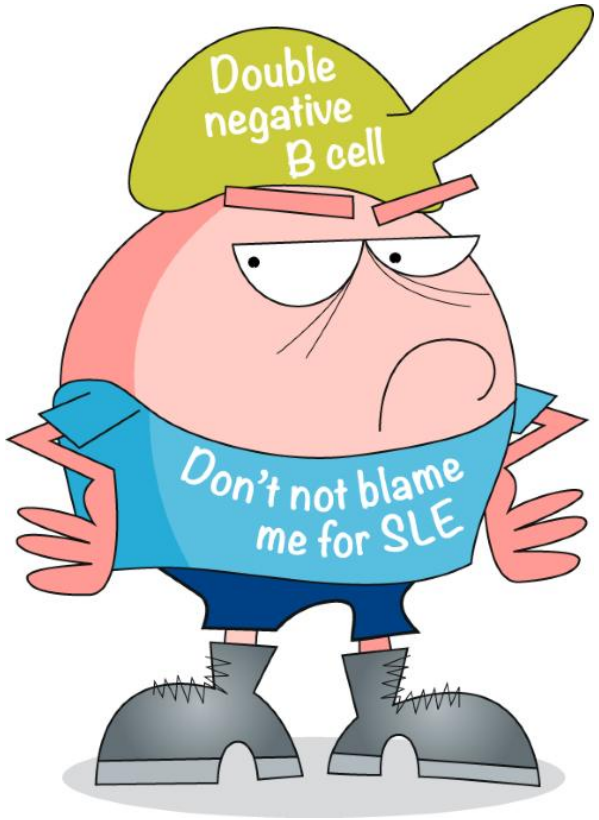


Plasmablast activation

PATHOGENIC TFH CELLS !

Crickx EJH 2019

Checkpoints Exist at Multiple Stages of the Immune Response



Lymphoid tissues

Systemic lupus

Mature T cells

Extra Follicular

Plasma cells

Mature B cells

Germinal center

Plasma cells

Memory B cells

(C) aNAV, DN2 and plasmablasts expanded in patients with anti-dsDNA autoantibody positive

SLE patients

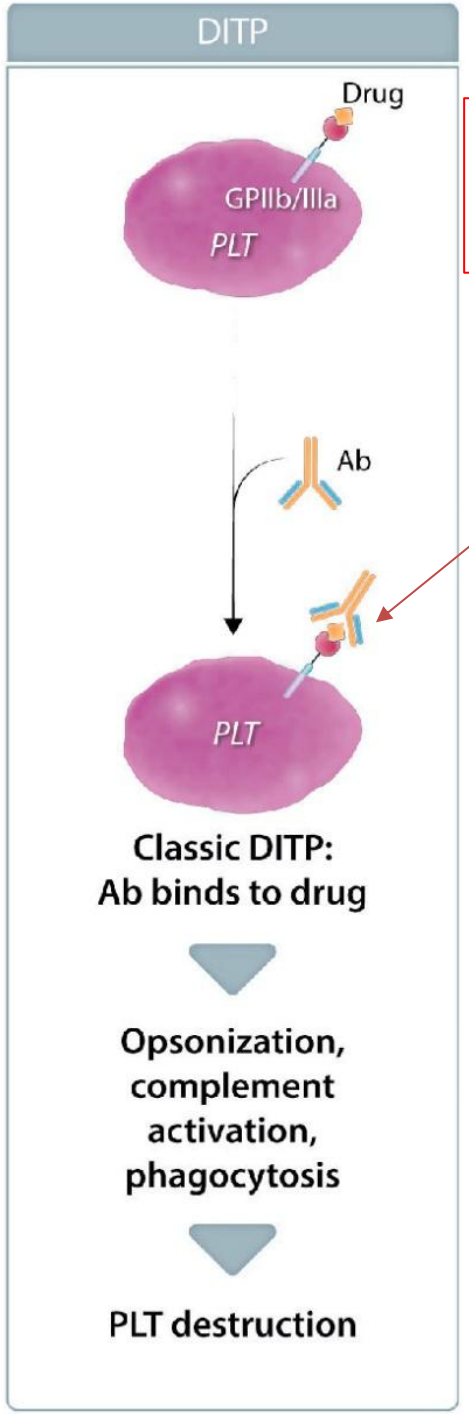
Anti-dsDNA autoantibodies

Activated naive

Double negative 2

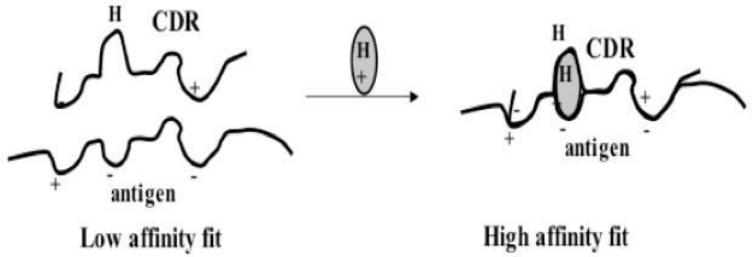
Plasmablasts

Switched memory B cells



Antibody recognize a complex GP/drug

Antibody change affinity with complex GP/drug



Aster JHT2010
Marini. Haematologica 2022

DITP

Drug

GPIIb/IIIa

PLT

Ab

PLT

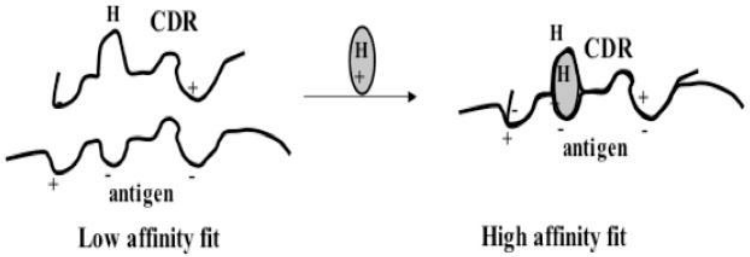
Classic DITP: Ab binds to drug

Opsonization, complement activation, phagocytosis

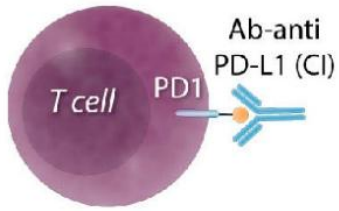
PLT destruction

Antibody recognize a complex GP/drug

Antibody change affinity with complex GP/drug



ICI- induced ITP



B-cell activation

B cell

Ab production

PLT

PLT opsonization and destruction

Checkpoint inhibitor
T cell tolerance breakdown

Aster JHT2010
Marini. Haematologica 2022

4. DOES SEARCHING FOR AN UNDERLYING DISEASE / CONDITION / IMMUNOLOGICAL STATUS MATTER FOR THE MANAGEMENT OF ITP?

Main causes of secondary ITP (adults)

Underlying background	Causes
Infections	• Virus: HIV, HCV, (HBV, HAV), CMV, EBV, Parvovirus B19, Zika, SARS-COV2… • Bacteria: *H pylori*, Myc. tuberculosis, Mycoplasma pneumoniae..

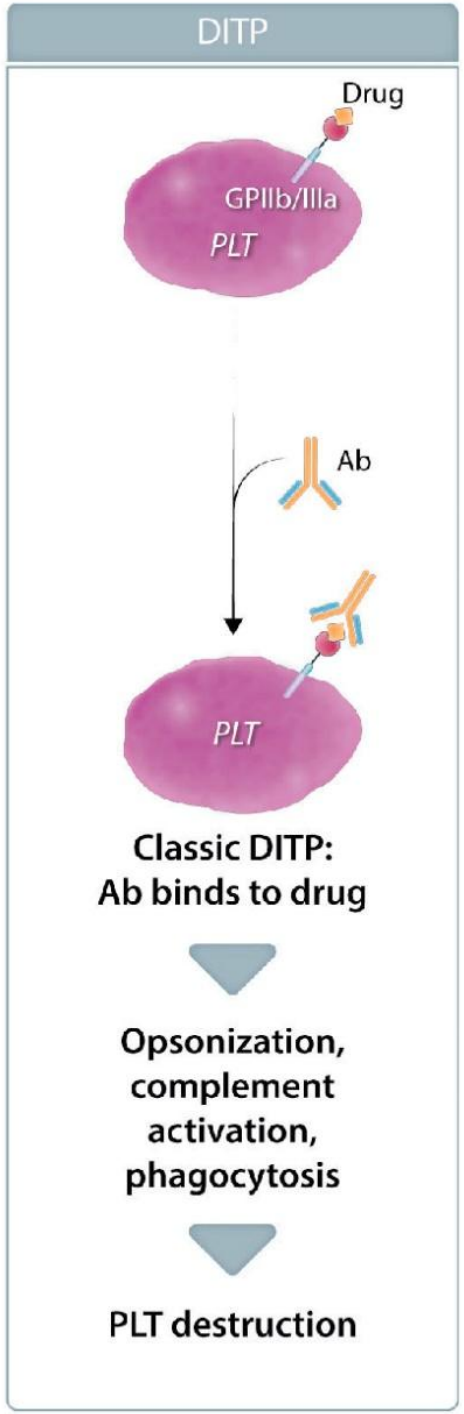
Wait until the disease is spontaneously cured (ex COVID)

Treat infection if its course is chronic (ex HP in Japan, HIV, VHC)

Could evolve as a chronic disease

Main causes of secondary ITP (adults)

Underlying background	Causes
Drugs	• Antibiotics, NSAIDs, anticonvulsivants, diuretics.. • **Check-point inhibitors => an emerging cause of DIITP** • Alemtuzumab • Vaccines



When should DITP be suspected?

- **Drug administration preceded thrombocytopenia; recovery from thrombocytopenia is complete and sustained after drug discontinued**
- **Other etiologies of thrombocytopenia excluded**
- **Re-exposure to the drug resulted in recurrent thrombocytopenia**

An updated list of drugs suspected to be associated with immune thrombocytopenia based on the WHO pharmacovigilance database

Ségolène Fuentes,[1] Basile Chrétien,[2] Charles Dolladille,[2,3] Joachim Alexandre,[2,3] Anaël Dumont,[1] Alexandre Nguyen,[1] Hubert de Boysson,[1,4] Stéphane Chèze,[5] Gwénola Maigné,[1] Achille Aouba,[1,4] and Samuel Deshayes[1,4]

Aster JHT2010
Marini. Haematologica 2022

Immune thrombocytopenia in patients treated with immune checkpoint inhibitors

Context of Research

Comprehensive data on immune checkpoint inhibitor–associated ITP (ICI-ITP) are lacking

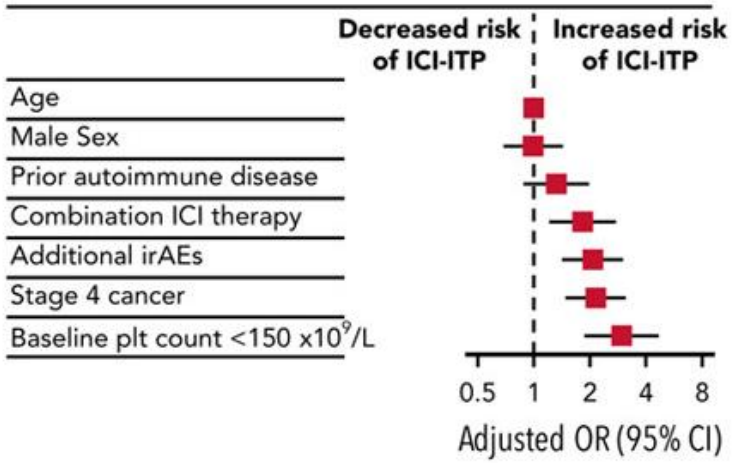
Findings

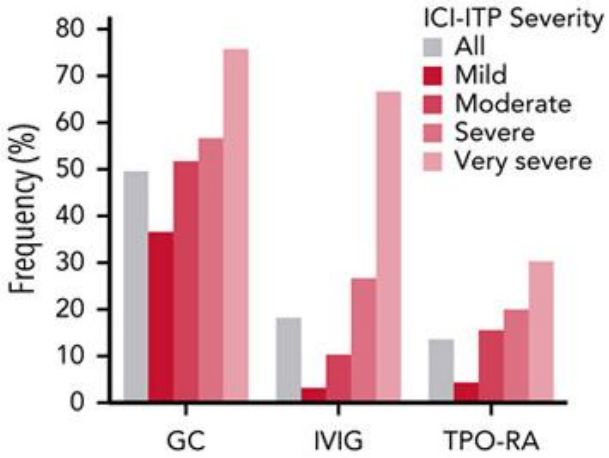
- Among **86 467 patients** who initiated treatment with ICIs across **29 U.S. hospitals** between 2016–2023, ICI-ITP occurred in 214 (**0.25% incidence**)
- **Risk factors** for ICI-ITP included combination ICI therapy, additional irAEs, stage 4 cancer, and lower baseline platelet count
- ICI-ITP occurred at a **median of 8 weeks (IQR, 4–18) after ICI initiation**

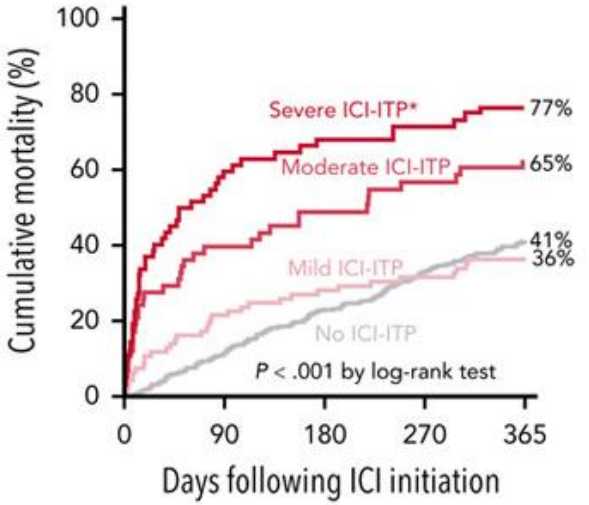
Aim of This Study

To identify the incidence, risk factors, clinical features, treatments, and outcomes associated with ICI-ITP

- **Glucocorticoids (GCs), IVIG, and TPO-RAs** were the most common treatments administered
- Recovery from ICI-ITP occurred in 161 patients (75.2%) at a median of 2.3 weeks
- Of 76 patients rechallenged with ICIs, 23 (30.3%) had **recurrent ICI-ITP**
- ICI-ITP and its severity were independently and monotonically associated with **higher mortality**







Similar with Delanoy. Lancet Heamatol 2019

Leaf, blood 2026

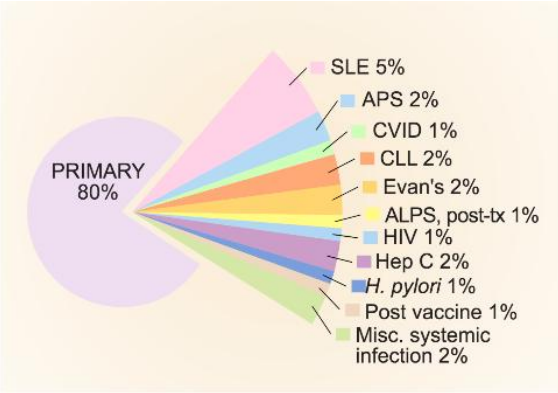
Main causes of secondary ITP (adults)

Underlying background	Causes
Infections	• Virus: HIV, HCV, (HBV, HAV), CMV, EBV, Parvovirus B19, Zika, SARS-COV2… • Bacteria: *H pylori*, Myc. tuberculosis, Mycoplasma pneumoniae..
Systemic autoimmune /inflammatory diseases	• **SLE,** antiphospholipid syndrome, systemic sclerosis, primary Sjögren syndrome, **sarcoidosis**…
Malignancies	• **Mostly B-cell lymphoma**: **CLL**, MZL, mantle-cell lymphoma • Hodgkin lymphoma • Myeloma, **CMML** • Angioimmunoblastic T-cell lymphoma • Renal carcinoma, other solid tumors..
Primary immunodeficiency	• **CVID**; IgA deficiency • ALPS • Wisckott-Aldrich syndrome
Drugs	• Antibiotics, NSAIDs, anticonvulsivants, diuretics.. • **Check-point inhibitors** **=> an emerging cause of DIITP** • Alemtuzumab • Vaccines
Miscellaneous	• Post-transplant (allogeneic BMT)

ITP secondary to SLE/APS

- **SLE represents an estimated 2–5% of the various forms of secondary ITP**

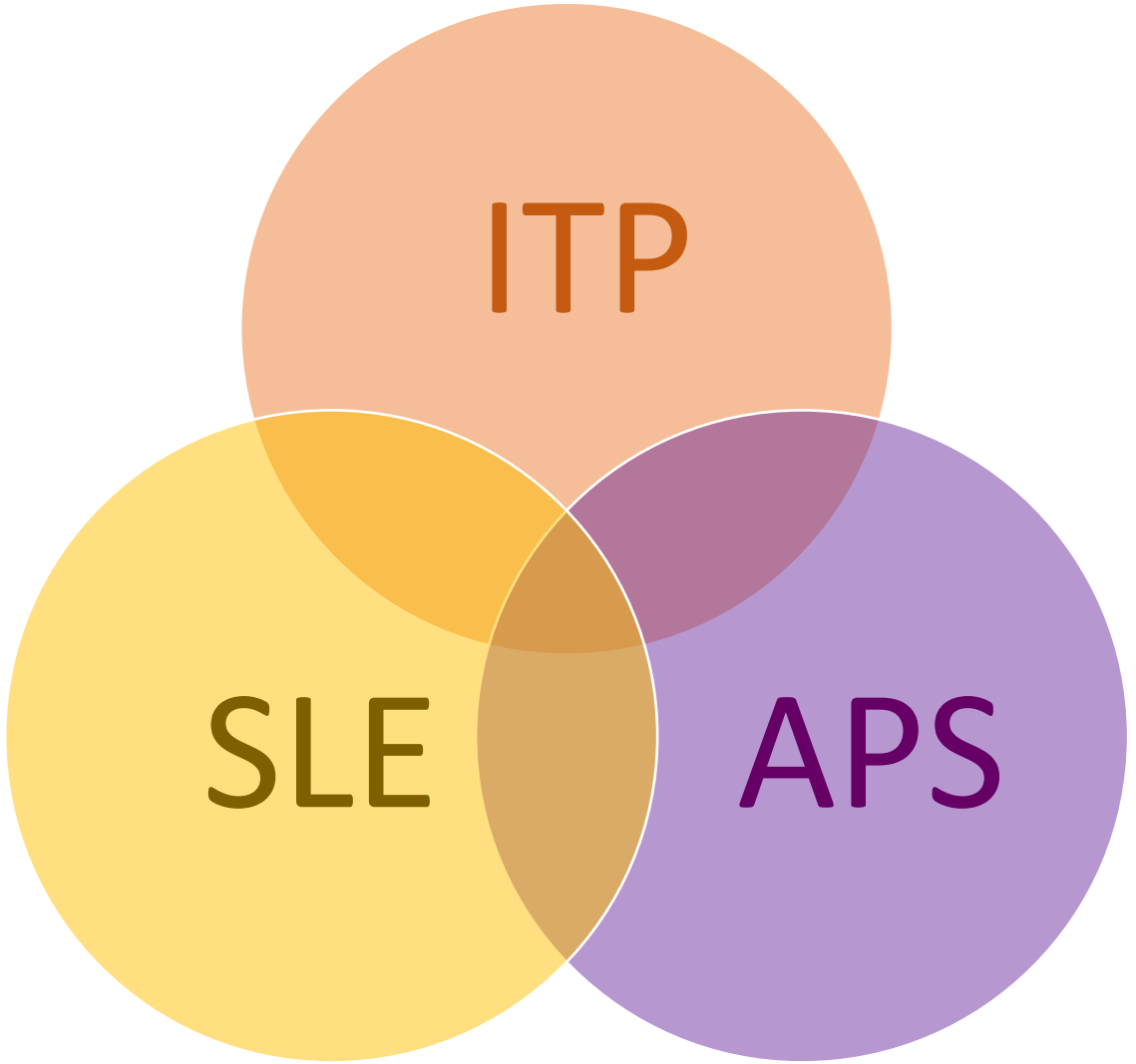
Cines et al, Blood 2009, Moulis et al, blood 2014



- **ANA titre ≥1:160 = 30-40% of adult's ITP**

- But the **incidence** of systemic lupus after a diagnosis of primary ITP **seems low** in two cohorts of patients with primary ITP based on nationwide electronic health records in Taiwan (n = 723) and in France (n = 9589). **The 5-year cumulative incidences were 4.8% and 1.9** (95% CI: 1.6–2.2) respectively.

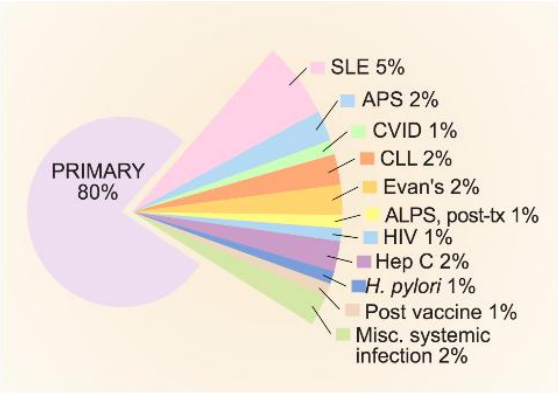
Zhu et al, ARD 2020, Maquet et al ARD 2021



ITP secondary to SLE/APS

- **2-5% estimated fraction of the various forms of secondary ITP**

Cines et al, Blood 2009, Moulis et al, blood 2014



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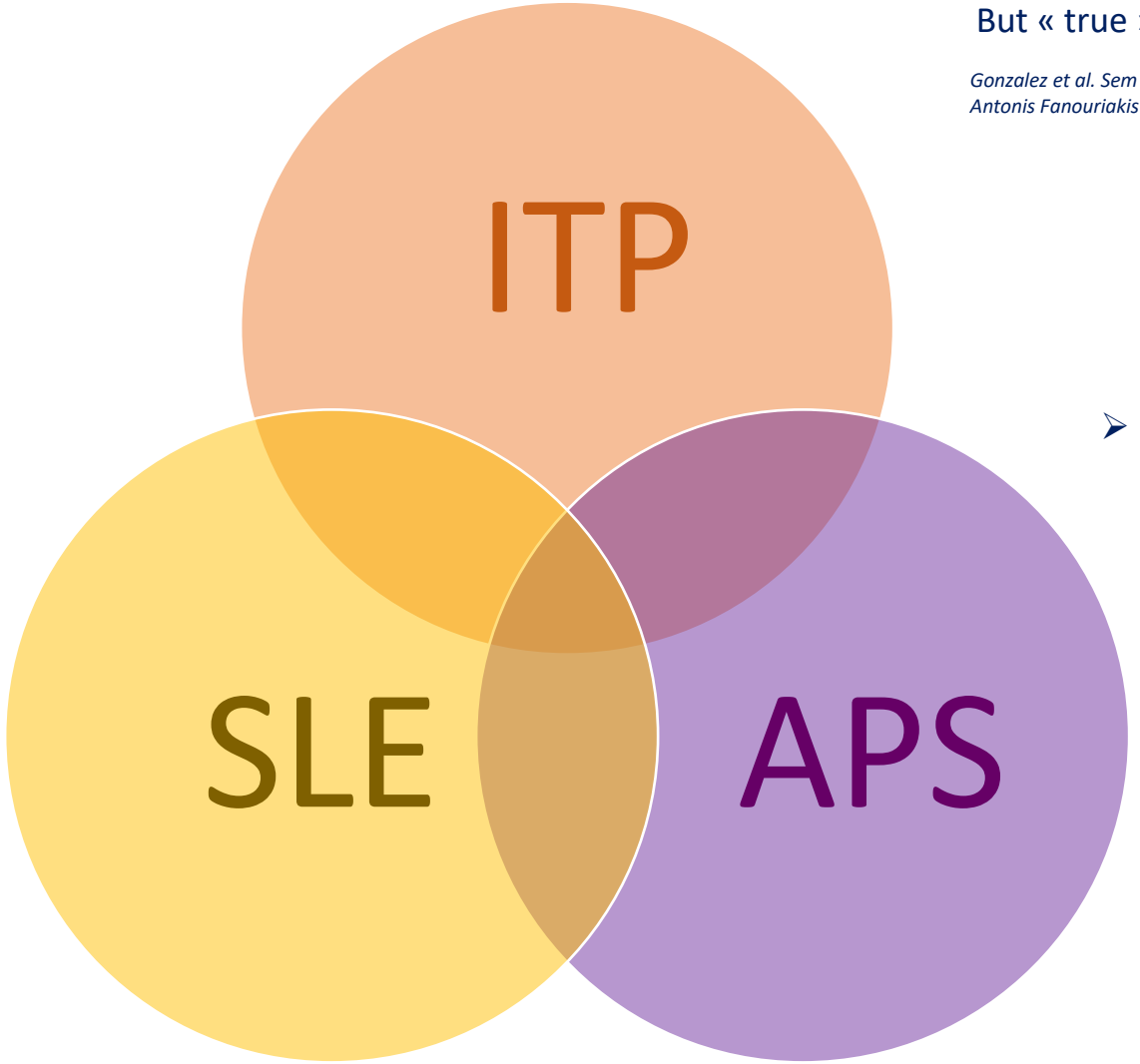
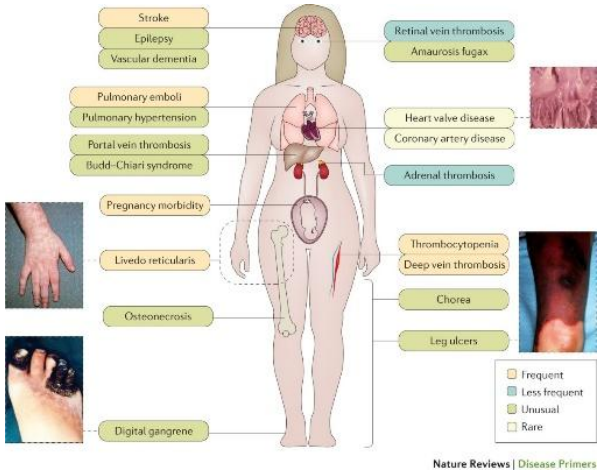


- **Thrombocytopenia is common during SLE** (15-25 %)
  But « true » ITP is rare in only 3-5 % of cases

Gonzalez et al. Sem in Arthritis Rheumatism 2024
Antonis Fanouriakis et al. Ann Rheum Dis 2021

- **Thrombocytopenia is common during Antiphospholipid syndrome (APS) (15-30%)**
  But ITP is rare

Cohen et al, JTH 2020, Sorin et al, submitted



Are there implications for clinical practice?”

Hydroxychloroquine good second-line treatment for ITP and positive antinuclear antibodies

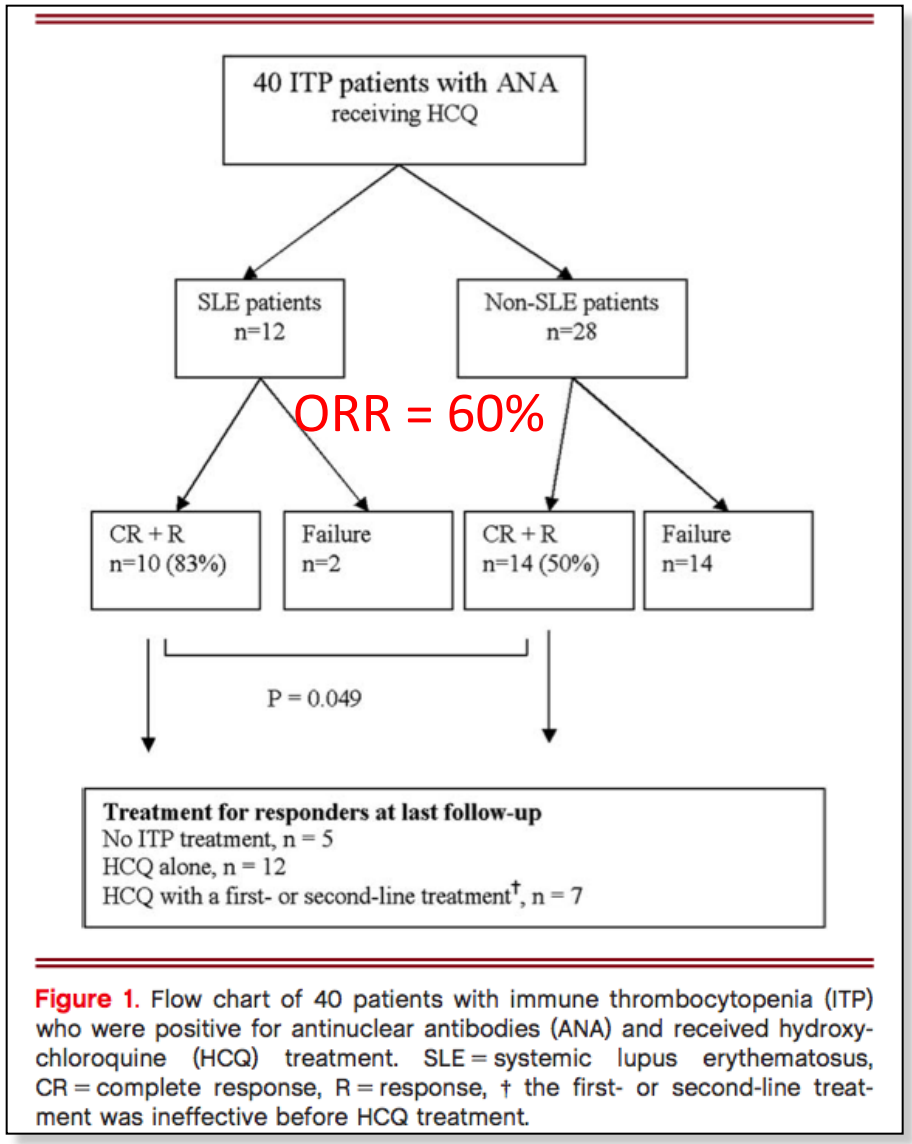


Figure 1. Flow chart of 40 patients with immune thrombocytopenia (ITP) who were positive for antinuclear antibodies (ANA) and received hydroxychloroquine (HCQ) treatment. SLE = systemic lupus erythematosus, CR = complete response, R = response, † the first- or second-line treatment was ineffective before HCQ treatment.

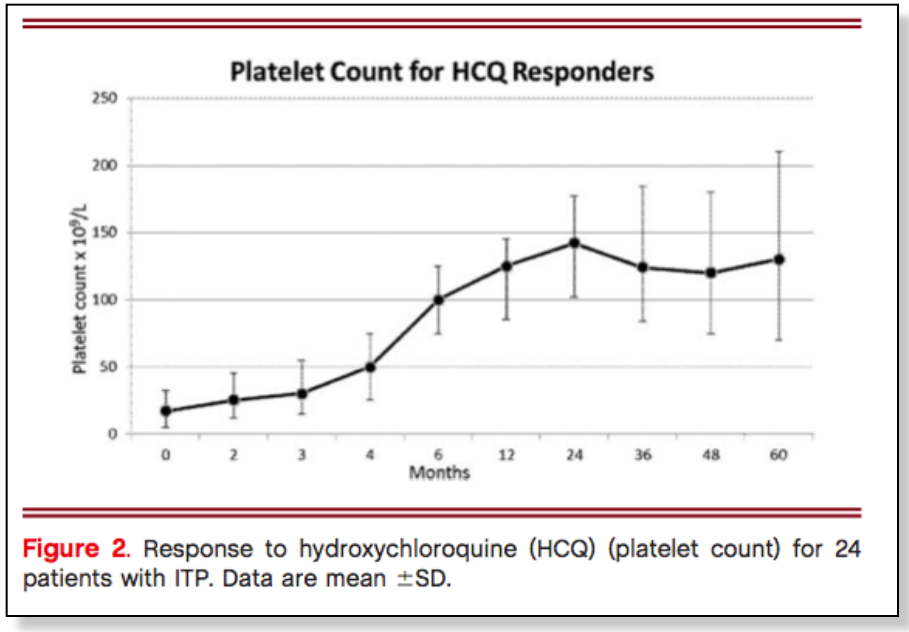


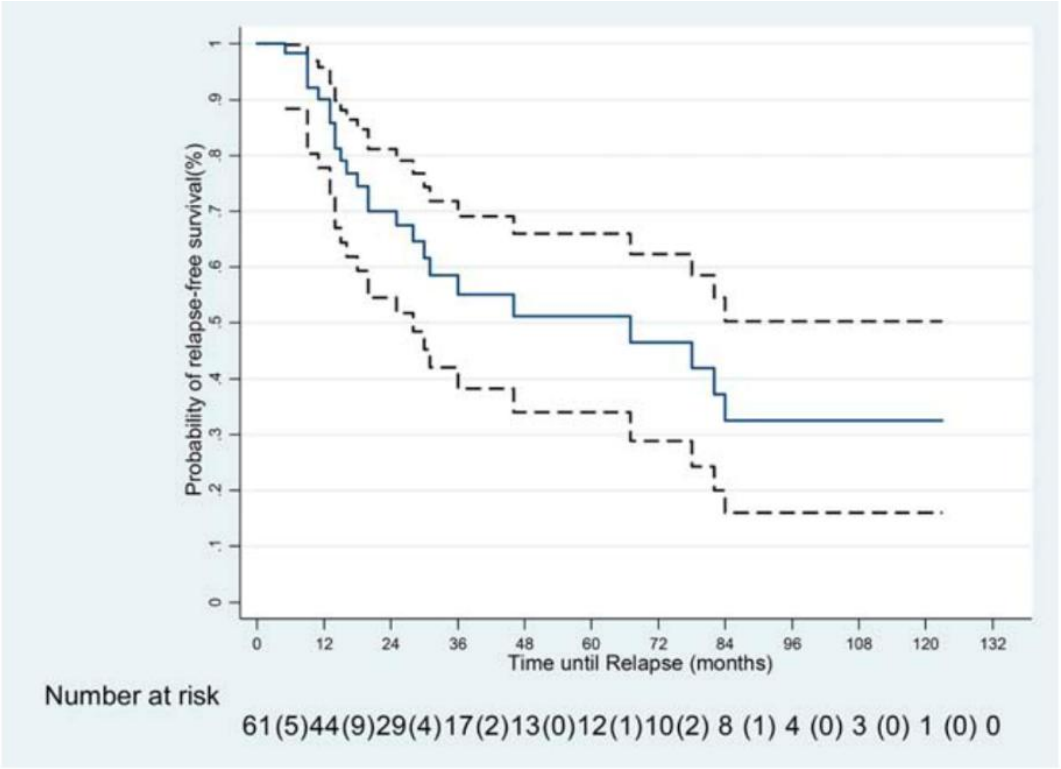
Figure 2. Response to hydroxychloroquine (HCQ) (platelet count) for 24 patients with ITP. Data are mean ±SD.

« …No patient stopped HCQ because of a side-effect. HCQ appears to be a safe and effective second line treatment for patients with SLE-ITP or ITP and high titer of ANA… »

Khellaf *et al*, Am J Hematol 2014

Can Rituximab be Useful for Treating SLE-Associated Immune Cytopenias? Results from a Retrospective Multicenter Study on 71 Patients

- **40 ITP cases**
- Average of 3.1 ± 1.3 treatments prior to RTX including steroids (100%), and hydroxychloroquine (90.3%).
- **ORR : 87%**
- Median follow-up after the first injection of RTX was 24.6 months [12.6-61.2].
- **41% of the initial responders relapsed** and **re-treatment with RTX was successful in 94%.**
- No cases of of opportunistic infections of RTX-induced neutropenia were observed.



Serris et al, Am J Hematol 2018

French experience of TPO-RAs in ITP associated with SLE and APS

We assessed the safety and the efficacy of TPO-Ras in a large retrospective cohort

- Three groups of ITP patients:
  - ✓ SLE or incomplete SLE without APL Ab
  - ✓ SLE or incomplete SLE with APL Ab but no APS
  - ✓ Primary or secondary APS (i.e. associated with SLE)

→ Thrombotic events (TE) after first TPO-Ras initiation

Marques et al , Am J Hematol 2025

French experience of TPO-RAs in ITP associated with SLE and APS

	SLE or lupus antibodies without APL Ab (n=37)
Presence of APL Ab	**0**
Associated TE risk factor*	66.7%
History of previous TE	21.6%
TPO-RAs	ELT 59.5%, ROM 18.9% ELT and ROM: 21.6%
Duration of FU (median years, IQR)	3.70 (2.38)
Number of TE during FU (%)	**3 (8.1%)**
Type of TE	Venous: 2, arterial : 2
Duration of TPO-RAs before TE (median DAYS, IQR)	365 (94-1095)

Only 3 patients in this group experienced TEs despite a high prevalence of TE risk factors.

This percentage is similar to the incidence of TE reported in ITP and connective tissue diseases.

These data are reassuring regarding the use of TPO-RA in SLE patients without APL Abs

** TE risk factors: tobacco, obesity, diabetes, Estrogen-progestogen pills, family history of thrombosis*

Marques et al , Am J Hematol 2025

French experience of TPO-RAs in ITP associated with SLE and APS

	SLE or lupus antibodies without APL Ab (n=37)	Definite or incomplete SLE with APL but no APS (n=27)
Presence of APL Ab	**0**	LA: 37%, triple +: 11.1%
Associated TE risk factor*	66.7%	52%
History of previous TE	21.6%	14.8%
TPO-RAs	ELT 59.5%, ROM 18.9% ELT and ROM: 21.6%	ELT: 37%, ROM 11.1%, ELT and ROM: 51.9%
Duration of FU (median years, IQR)	3.70 (2.38)	3.69 (4,37)
Number of TE during FU (%)	**3 (8.1%)**	**6 (22.2%)**
Type of TE	Venous: 2, arterial : 2	Venous: 4, Arterial: 5
Duration of TPO-RAs before TE (median DAYS, IQR)	365 (94-1095)	187 (7-4380)

** TE risk factors: tobacco, obesity, diabetes, Estrogen-progestogen pills, family history of thrombosis*

Marques et al , Am J Hematol 2025

French experience of TPO-RAs in ITP associated with SLE and APS

	SLE or lupus antibodies without APL Ab (n=37)	Definite or incomplete SLE with APL but no APS (n=27)	APS (primary or associated with SLE) (n=16)
Presence of APL Ab	**0**	LA: 37%, triple +: 11.1%	LA: 69.9%, triple +: 43.8%
Associated TE risk factor*	66.7%	52%	76%
History of previous TE	21.6%	14.8%	100%
TPO-RAs	ELT 59.5%, ROM 18.9% ELT and ROM: 21.6%	ELT: 37%, ROM 11.1%, ELT and ROM: 51.9%	ELT: 43.8%, ROM: 25% ELT and ROM: 31.3%
Duration of FU (median years, IQR)	3.70 (2.38)	3.69 (4,37)	2.12 (4.36)
Number of TE during FU (%)	**3 (8.1%)**	**6 (22.2%)**	**8 (50%)**
Type of TE	Venous: 2, arterial : 2	Venous: 4, Arterial: 5	Venous: 1, Arterial: 7
Duration of TPO-RAs before TE (median DAYS, IQR)	365 (94-1095)	187 (7-4380)	30 (15-122)

** TE risk factors: tobacco, obesity, diabetes, Estrogen-progestogen pills, family history of thrombosis*

Marques et al , Am J Hematol 2025

French experience of TPO-RAs in ITP associated with SLE and APS

	SLE or lupus antibodies without APL Ab (n=37)	Definite or incomplete SLE with APL but no APS (n=27)	APS (primary or associated with SLE) (n=16)
Presence of APL Ab	**0**	LA: 37%, triple +: 11.1%	LA: 69.9%, triple +: 43.8%
Associated TE risk factor*	66.7%	52%	76%
History of previous TE			
TPO-RAs			
Duration of FU (median years, IQR)			
Number of TE during FU (%)			
Type of TE	Venous: 2, arterial : 2	Venous: 4, Arterial: 5	Venous: 1, Arterial: 7
Duration of TPO-RAs before TE (median DAYS, IQR)	365 (94-1095)	187 (7-4380)	30 (15-122)

Warning for thrombosis events

TPO-RA Should be avoid in APS

12 of the 17 patients had a lupus anticoagulant

** TE risk factors: tobacco, obesity, diabetes, Estrogen-progestogen pills, family history of thrombosis*

Marques et al , Am J Hematol 2025

Key points SLE/APS

- **At diagnosis of ITP, antinuclear antibodies testing is usefull.**

- In patients with a history of thrombosis, screening for antiphospholipid syndrome (APS) is required, including anticardiolipin antibodies, anti-β2 glycoprotein I antibodies, and lupus anticoagulant.

Key points SLE/APS

- **At diagnosis of ITP, antinuclear antibodies testing is usefull.**
- In patients with a history of thrombosis, screening for antiphospholipid syndrome (APS) is required, including anticardiolipin antibodies, anti-β2 glycoprotein I antibodies, and lupus anticoagulant.
- Standard long-term treatment of SLE is based on hydroxychloroquine +/- rituximab used in refractory cases. The role of obinutuzumab is currently under investigation.
- **AR-TPO are not recommended in APS**, particularly in patients with triple positivity, and should be avoided in lupus patients with antiphospholipid antibodies.
- New therapeutic strategies, such as fostamatinib, are under evaluation, and their exact role in clinical practice remains to be defined.

CVID: data from the largest series of the literature

	Ramirez-Vargas 2013 (n = 43)	Defi cohort (France) 2008 (n=314)	Quinti 2007 (n=224)	Hermaszewski 1993 (n=247)	Cunningham 1999 (n=248)
Respiratory tract		**91%**		**94%**	
Sinusitis	83%	63	54%	72	
Pneumonia	83%	58	56%		78
GI tract manifestations					
Giardia	**44%**	**47%**	**41%**	**39%**	**21%**
Campylobacter	7/19	14		8	3
Salmonella sp.	1/19	8		5	4
Lymphoid hyperpl.	3/19	8		7	1
Crohn'like disease				7	4
	5	4		4	6
Liver disease		**17%**		**20%**	**12%**
Splénomégalie		**38%**	**26%**	**38%**	
Auto-immunity	**23%**	**31%**	**26%**		**23%**
ITP	4%	15%	6%		6%
AIHA	2%	6%	4%	5%	5%
Polyarthritis	2%	6%	2%	3%	4%
Vitiligo	4%	4%	13%	3%	
Granulomatosis		**13%**		**5%**	**8%**
Lymphoma		**6%**	**2%**	**4%**	**9%**

Efficacy and safety of rituximab in common variable immunodeficiency-associated immune cytopenias: a retrospective multicentre study on 33 patients

Delphine Gobert,[1] James B. Bussel,[2] Charlotte Cunningham-Rundles,[3] Lionel Galicier,[4] Agnès Dechartres,[5] Alice Berezne,[6] Bernard Bonnotte,[7] Thierry DeRevel,[8] Christophe Auzary,[9] Roland Jaussaud,[10] Claire Larroche,[11] Alain LeQuellec,[12] Marc Ruivard,[13] Pascal Seve,[14] Amar Smail,[15] Jean-François Viallard,[16] Bertrand Godeau,[1] Olivier Hermine[17] and Marc Michel[1]

RTX very effective but
Require IvIG replacement therapy +++

Summary

Patients with common variable immunodeficiency (CVID) are at high risk of developing immune thrombocytopenia (ITP) and/or autoimmune haemolytic anaemia (AHA). Given their underlying immunodeficiency, immunosuppressive treatment of these manifestations may increase the risk of infection. To assess efficacy and safety of rituximab in patients with CVID-associated ITP/AHA, a multicentre retrospective study was performed. Thirty-three patients, 29 adults and four children, were included. Patients received an average of 2·6 treatments prior to rituximab including steroids, intravenous immunoglobulin and splenectomy (21%). The median ITP/AHA duration at time of first rituximab administration was 12 months [range 1–324] and the indication for using rituximab was ITP (22 cases), AHA ($n = 5$) or both ($n = 7$); 1 patient was treated sequentially for ITP and then AHA. The overall initial response rate to rituximab was 85% including 74% complete responses. After a mean follow-up of 39 ± 30 months after rituximab first administration, 10 of the initial responders relapsed and re-treatment with rituximab was successful in 7/9. Severe infections occurred after rituximab in eight adults (24%), four of whom were not on immunoglobulin replacement therapy. In conclusion, rituximab appears to be highly effective and relatively safe for the management of CVID-associated severe immune cytopenias.

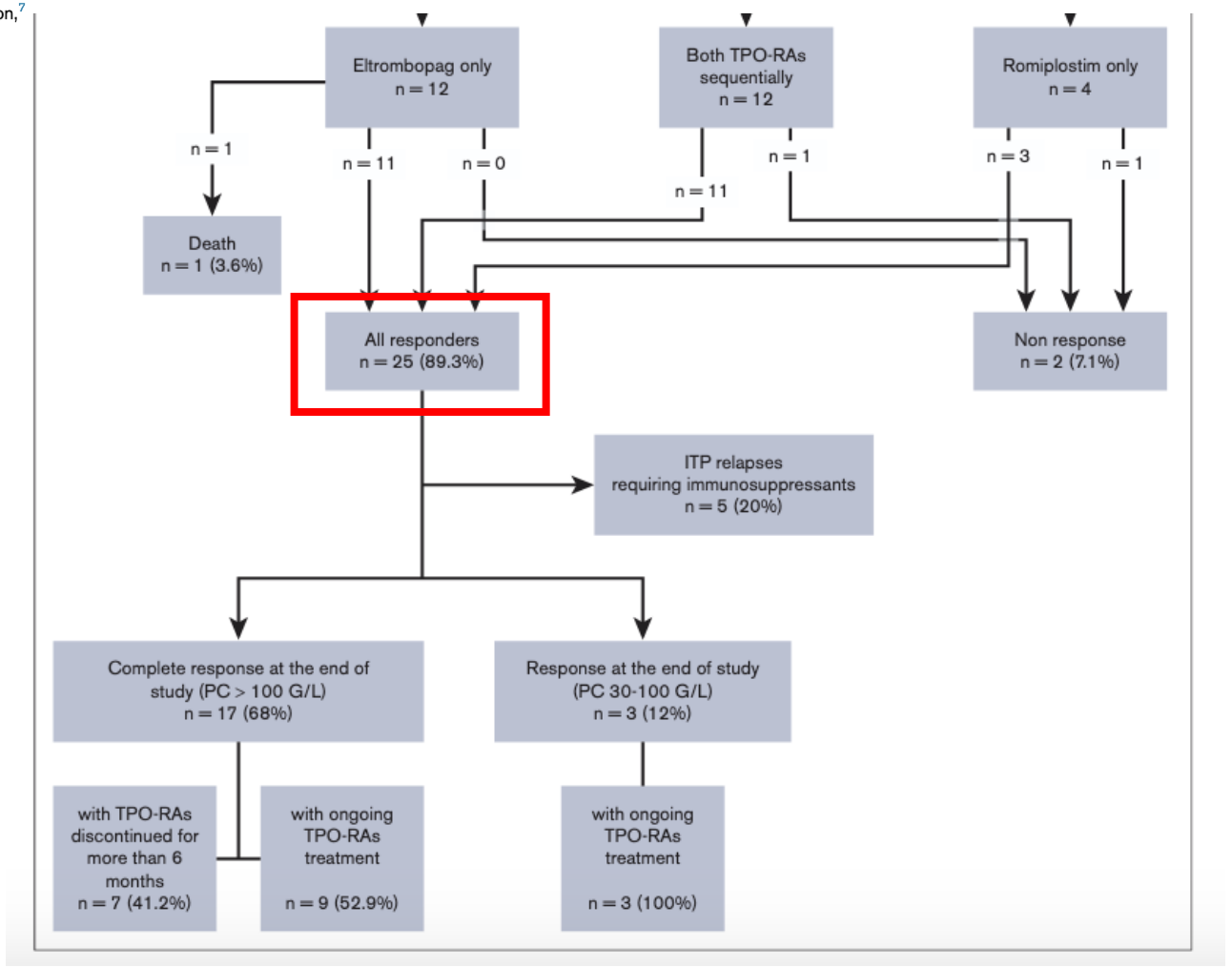
blood advances

Efficacy and safety of TPO receptor agonists in treatment of ITP associated with predominantly antibody deficiencies

Margaux Soulard,[1] Lionel Galicier,[2] Nizar Mahlaoui,[3,4] Claire Fieschi,[2] Samuel Deshayes,[5] Delphine Gobert,[6] Clément Gourguechon,[7] Hélène Henique,[8] Sebastien Humbert,[9] Carole Lacout,[10] Ronan Le Calloch,[11] Marc Michel,[12] Marie-lea Piel-julian,[13] Jean François Viallard,[14] Alain Lescoat,[1] Bertrand Godeau,[12] and Antoinette Perlat[1]

Table 1. Patients characteristics

Characteristics	N = 28	
Male	17	(60.7%)
Age at PID diagnosis (y)	30	(14-68)
Age at ITP diagnosis (y)	31	(5-68)
Follow-up duration after ITP diagnosis (mo)	81	(11-324)
Type of PID		
CVID	24	(85.7%)
Including LOCID	3	(10.7%)
HIGM	1	(3.6%)
CTLA4 deficiency	1	(3.6%)
PI3KCD mutation	1	(3.6%)
KMT2D mutation (Kabuki syndrome)	1	(3.6%)
Immunoglobulin serum levels at the time of PID diagnosis (mg/dL)		
IgG	326	(85-486)
IgA	27	(0-146)
IgM	39	(4-500)



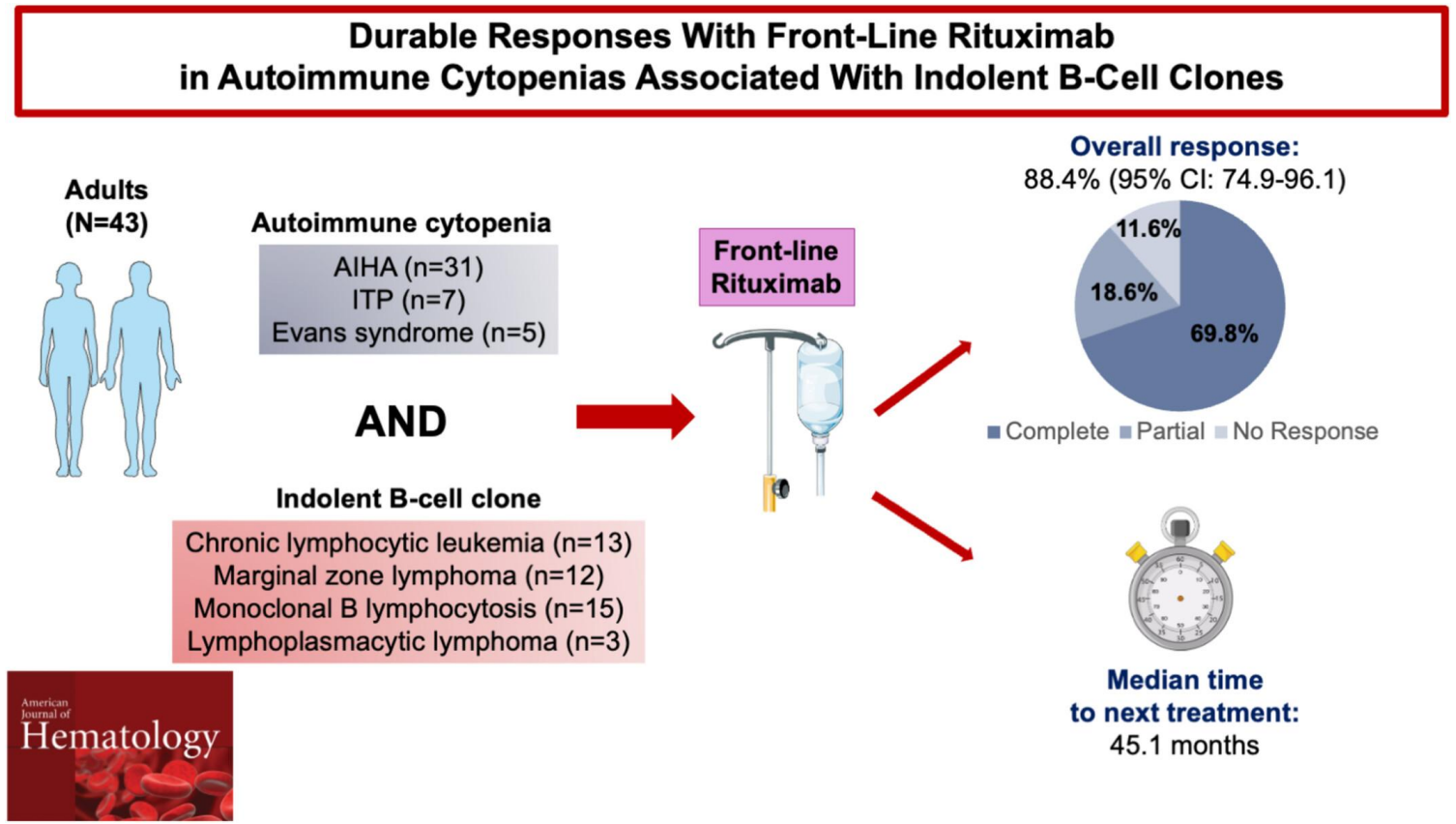
TPO-RA are effective, but data remain limited.

Soulard, Blood advance, 2024

Main causes of secondary ITP (adults)

Underlying background	Causes
Infections	• Virus: HIV, HCV, (HBV, HAV), CMV, EBV, Parvovirus B19, Zika, SARS-COV2… • Bacteria: *H pylori*, Myc. tuberculosis, Mycoplasma pneumoniae..
Systemic autoimmune /inflammatory diseases	• **SLE,** antiphospholipid syndrome, systemic sclerosis, primary Sjögren syndrome, **sarcoidosis**…
Malignancies	• **Mostly B-cell lymphoma**: **CLL**, MZL, mantle-cell lymphoma • Hodgkin lymphoma • Myeloma, **CMML** • Angioimmunoblastic T-cell lymphoma • Renal carcinoma, other solid tumors..
Primary immunodeficiency	• **CVID**; IgA deficiency • ALPS • Wiskott-Aldrich syndrome
Drugs	• Antibiotics, NSAIDs, anticonvulsivants, diuretics.. • **Check-point inhibitors => an emerging cause of DIITP** • Alemtuzumab • Vaccines
Miscellaneous	• Post-transplant (allogeneic BMT)

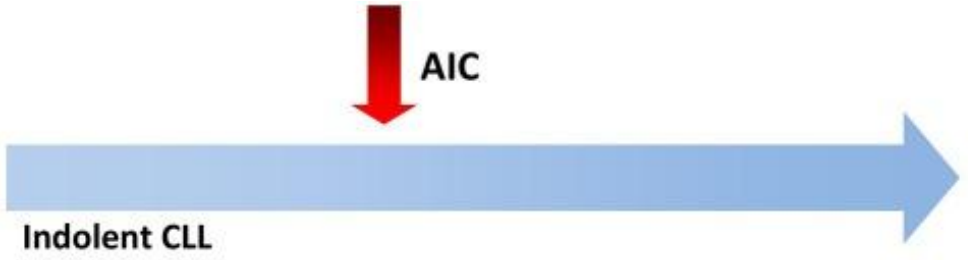
ITP and hematologic malignancies: therapeutic implications



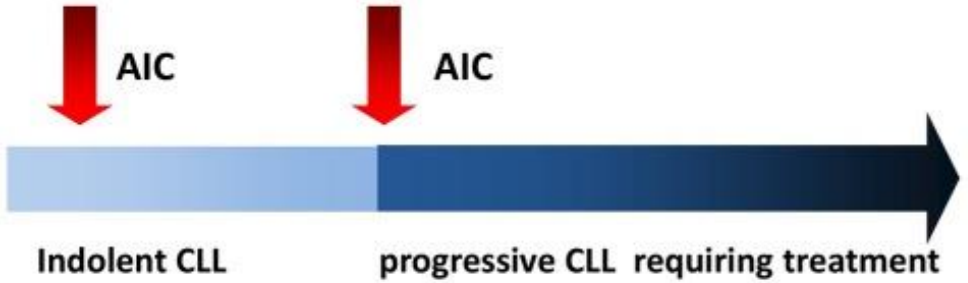
In indolent (quiescent) B-cell lymphomas, there may be a benefit to early targeting of the B-cell clone

Zadro, Am J Hematol, 2025

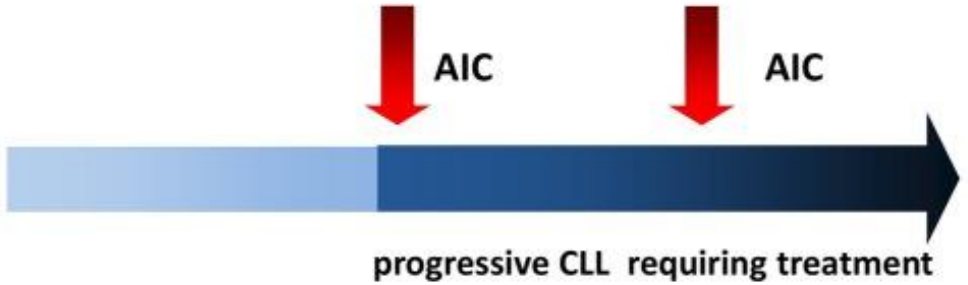
ITP and hematologic malignancies: therapeutic implications



- Treat AIC, if necessary
- Isolate AIC is not an indication to treat CLL



- Treat CLL and AIC with combination therapy
- Choose CLL-therapy with "low-AIC inducing effect"

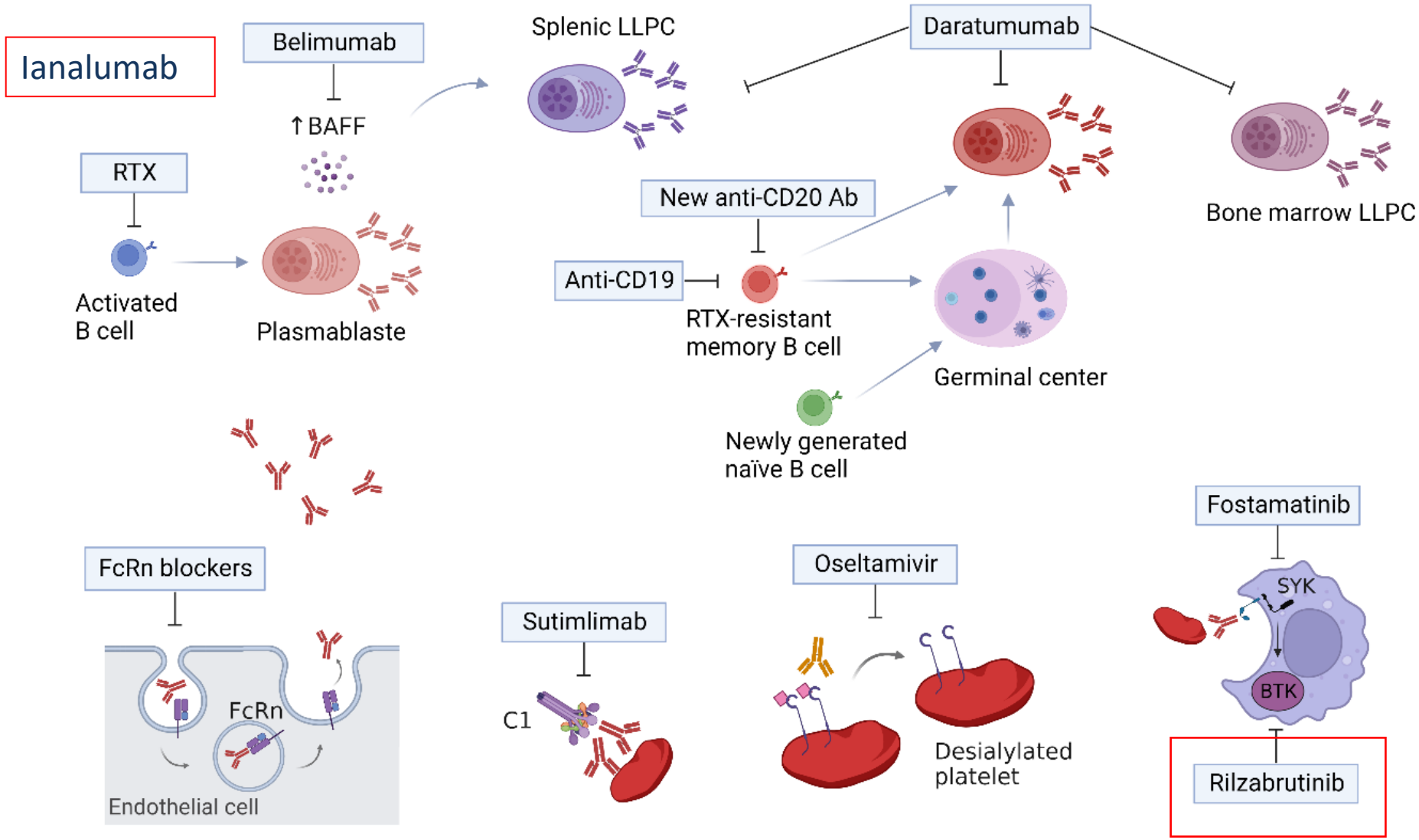


- Anemia/thrombocytopenia in Binet stage C CLL have a worse prognosis than AIHA/ITP
- AIC therapy may up-grade Binet stage to A or B

Fatizzo,Frontiers oncol 2020

Place for new therapies in secondary ITP ?

SLE



SLE/APS
CLL
Hematologic malignancies

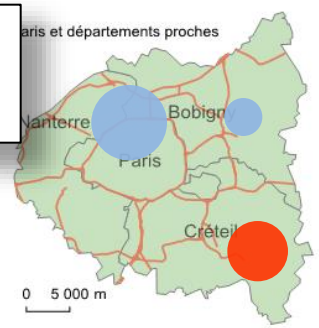
Roeser, BJH 2023

Take home messages

- Secondary ITP represents **15 - 20%** of all ITP cases in adults
- Highlights the diversity of the underlying pathophysiological mechanisms and underscores the importance of improving our understanding
- Treatment of secondary ITP is not consensual and not evidence-based and it is mostly extrapolated from the data of primary ITP
- The status of the underlying disease (active or not) as well as the risk/benefit ratio of each treatment strategy (higher risk of thrombosis and/or infection) must be taken into consideration

Acknowledgement

All the french physicians who participate to CERECAI network and CARMEN register



References centers of ITP network in France

Main site

Reference centers

Competence centers

Treating the underlying cause is an important principle of treatment for secondary ITP; however, this is often challenging and not always effective for improving the thrombocytopenia.

CMV-associated ITP, IVIG is recommended, Anti-CMV medications have been effective, primarily ganciclovir, which is often used in combination with IVIG; however, ganciclovir can
thro
trea

Helicobacter pylori-associated ITP: In 1998, Gasbarrini et al [77] found that eradication of *H. pylori* increased platelet count in a small number of thrombocytopenic patients. The most accepted mechanism is cross-reactive antibodies or molecular mimicry of the CagA

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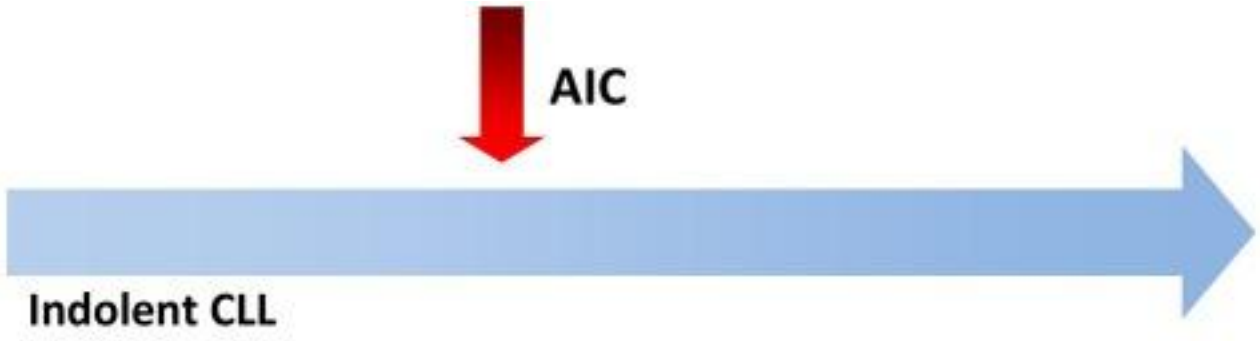
Clinical characteristics, management and outcome of COVID-19-associated immune thrombocytopenia: a French multicentre series

pylori infection is detected, eradication does not often lead to improvement in platelet coun [79] likely because of population differences in HLA class II or different strains of *H. pylori* .

ITP and hematologic malignancies: therapeutic implications



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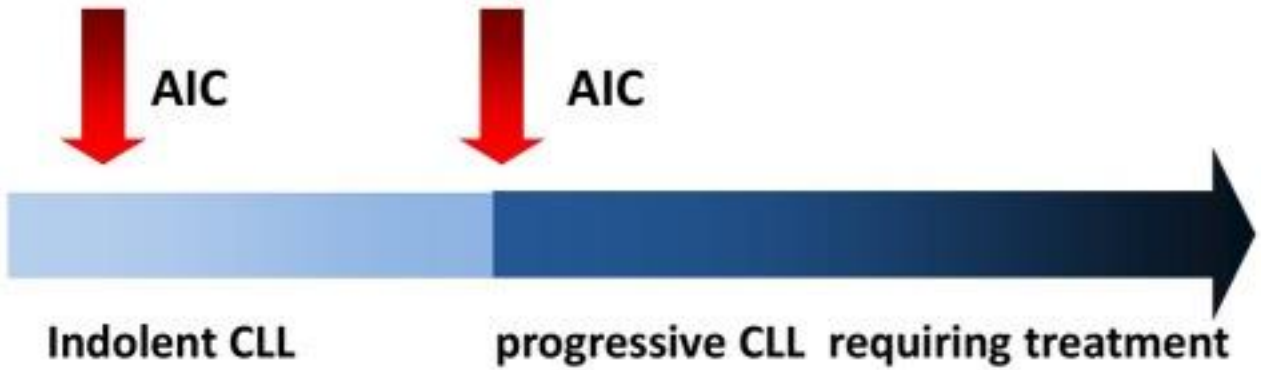

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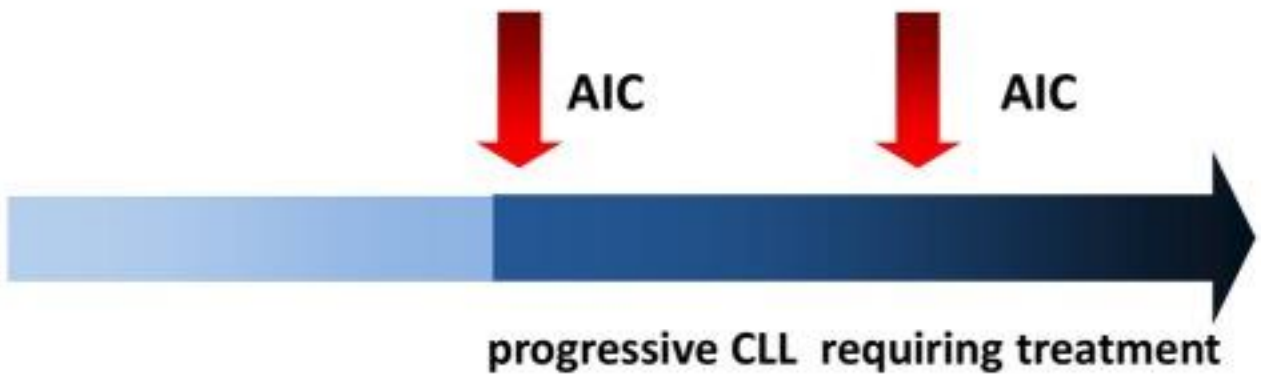

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- AIC therapy may up-grade Binet stage to A or B

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AT+	AIHA DAT− (n = 7)	ITP (n = 20)	All (n = 70)
	5	9	30
	7	28	
	0	1	7
	0	3	3
	1	0	2
	2	10	31
	1	8	17
	1	1	7
	0	1	5
	3	0	10

Main causes of secondary ITP (adults)

Underlying background	Causes
Infections	• Virus: HIV, HCV, (HBV, HAV), CMV, EBV, Parvovirus B19, Zika, SARS-COV2… • Bacteria: *H pylori*, Myc. tuberculosis, Mycoplasma pneumoniae..
Systemic autoimmune /inflammatory diseases	• **SLE,** antiphospholipid syndrome, systemic sclerosis, primary Sjögren syndrome, **sarcoidosis**…
Malignancies	• **Mostly B-cell lymphoma**: **CLL**, MZL, mantle-cell lymphoma • Hodgkin lymphoma • Myeloma, **CMML** • Angioimmunoblastic T-cell lymphoma • Renal carcinoma, other solid tumors..
Primary immunodeficiency	• **CVID**; IgA deficiency • ALPS • Wiskott-Aldrich syndrome
Drugs	• Antibiotics, NSAIDs, anticonvulsivants, diuretics.. • **Check-point inhibitors** **=> an emerging cause of DIITP** • Alemtuzumab • Vaccines
Miscellaneous	• Post-transplant (allogeneic BMT)

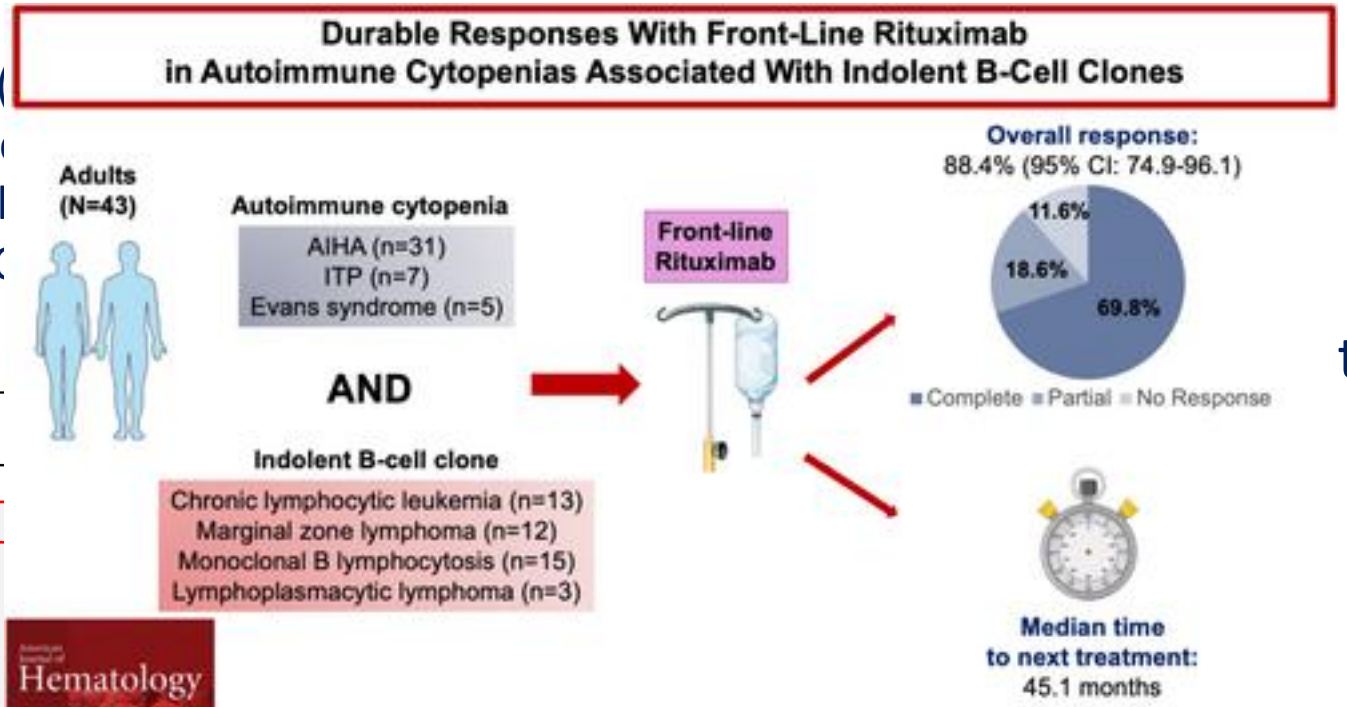
Screening for ANA at ITP onset is relevant !

Even in the absence of definite SLE, ITP patients with positive ANA may be successfully treated **hydroxychloroquine alone ± low dose of prednisone**

ITP and hematologic malignancies: therapeutic implications

168 patients with autoimmune cytopenia from 2000 to 2022, 58 ITP

- Chronic lymphocytic leuke
- Marginal zone lymphoma (
- Monoclonal B-cell lympho
- Waldenström macroglobul
- Mantle cell lymphoma (MC



Severe adverse event	Total n=168			
Total, n (%)	63 (37.7)			
Infectious,§ n (%)	34 (19.6)			
Pulmonary	13 (7.7)			
Gastrointestinal	6 (3.6)			
Urogenital	4 (2.4)			
Cardiovascular	3 (1.8)			
Dermatological	2 (1.2)			
Neurological	2 (1.2)			
Musculoskeletal	1 (0.6)	0 (0.0)	1 (2.3)	0 (0.0)
Other	7 (4.2)	3 (3.7)	3 (7.0)	1 (2.3)
Non infectious, n (%)	39 (23.2)	15 (18.5)	12 (27.9)	12 (27.3)
Cardiovascular	9 (5.4)	6 (7.4)	2 (4.7)	1 (2.3)
Thrombosis	4 (2.4)	1 (1.2)	3 (7.0)	0 (0.0)
Neutropenia	3 (1.8)	0 (0.0)	2 (4.7)	1 (2.3)
Encephalopathy	1 (0.6)	1 (1.2)	0 (0.0)	0 (0.0)
Kidney Failure	1 (0.6)	0 (0.0)	1 (2.3)	0 (0.0)
Allergy	1 (0.6)	0 (0.0)	1 (2.3)	0 (0.0)

B-cell lymphomas, to early targeting of clone

Zadro, Am J Hematol, 2025; Herishanu, BJH, 2021

Updated international consensus report on the investigation and management of primary immune thrombocytopenia

Table 1: Recommendations for the diagnosis of ITP in children and adults

Basic evaluation in all patients	Tests of potential utility in the management of an ITP patient	Tests of unproven or uncertain benefit‡
Patient history	Glycoprotein-specific antibody (can be used in difficult cases; has poor sensitivity and is not a primary diagnostic test)	TPO level
Family history	**Antiphospholipid antibodies (including anticardiolipin and lupus anticoagulant)** if there are clinical features of antiphospholipid syndrome	Reticulated platelets/ immature platelet fraction
Physical examination	**Antithyroid antibodies and thyroid function**	Platelet survival study
Complete blood count and reticulocyte count	Pregnancy test in women of childbearing potential	Bleeding time
Peripheral blood film	**Antinuclear antibodies**	Serum complement
Quantitative immunoglobulin level measurement*	**Viral PCR for EBV, CMV and parvovirus**	
Blood group (Rh)	Bone marrow examination (in selected patients; refer to text)	
HIV†	**Direct antiglobulin test**	
HCV†	**H. pylori†**	

†Recommended by the majority of the panel for adult patients in the appropriate geographic setting.

‡These tests have no proven role in the differential diagnosis of ITP from other thrombocytopenias and do not guide patient management.

Diagnosis workup : tests to rule out other causes of thrombocytopenia or search for secondary ITP (adults) => **French guidelines** for ITP

Causes	Tests
Liver disease, portal hypertension, hypersplenism	Abdominal ultrasound ± doppler (non systematic)
Infections	**HIV*, HCV*, HBV*** (pre-therapeutical), • EBV, CMV, Parvovirus B19 serology and PCR only in selected cases (infectious prodroma, mononucleosis syndrome on the smear…) • Breath test for Hp in selected patients (> 50 y and/or gastric symptoms)
Underlying autoimmune disease (SLE, APS, Evans syndrome..)	**Antinuclear Abs*** + anti ENA • Lupus anticoagulant, anti-cardiolpin Abs, anti-β2gpI (ANA ++ or previous history of thrombosis) • TSH, anti-Tpo Abs • Direct antiglobulin test
Primary immunodeficiency (CVID,IgA deficiency)	**IgG, IgM and IgA levels***+ B-cell immunophenotyping in case of hypogammaglobulinemia

https://www.has-sante.fr/portail/jcms/c_2772874/fr/purpura-thrombopenique-immunologique-de-l-enfant-et-de-l-adulte

Cytomegalovirus can make immune thrombocytopenic purpura refractory

Table III. Diagnostic and other clinical features in the four cases of CMV-related ITP in this study.

Clinical features/Laboratory findings	Case 1	Case 2	Case 3	Case 4
Increase in platelet number as CMV PCR normalizes	+	+	+	+
Steroids result in worsening ITP/ no benefit	+	+	+	+
Nadir platelet count ($\times 10^9$/l)	2	2	5	1
Transaminitis	+	+	+	+
Immunodeficiency present	−	−	−	−
Improvement in platelet count with ganciclovir/cytogam	+	+	+	+
Need for splenectomy	−	+	−	+
Presence of ICH	+	−	−	+
Bone marrow characteristics	Megakaryocytic hyperplasia	No significant megakaryocytic hyperplasia	No significant megakaryocytic hyperplasia	Megakaryocytic hyperplasia
Presented with CMV like illness-myalgia, fever, headache, malaise, throat pain	+	−	−	−
Severity of bleeding worse than others with ITP with similar degree of thrombocytopenia	+	+	+	+
HIV testing negative	+	+	+	+
Episodes of intermittent neutropenia	+	−	−	−
Atypical lymphocytes on smear	−	−	+	−

ITP, idiopathic thrombocytopenic purpura; CMV, cytomegalovirus; PCR, polymerase chain réaction; ICH, intracerebral haemorrhage; HIV, human immunodeficiency virus.

Efficacy and safety of rituximab for systemic lupus erythematosus-associated immune cytopenias: A multicenter retrospective cohort study of 71 adults

Alexandra Serris[1] | Zahir Amoura[2] | Florence Canouï-Poitrine[3,4] | Benjamin Terrier[5] | Eric Hachulla[6] | Nathalie Costedoat-Chalumeau[5] | Thomas Papo[7] | Olivier Lambotte[8] | David Saadoun[9] | Miguel Hié[4] | Philippe Blanche[5] | Bertrand Lioger[10] | Jacques-Eric Gottenberg[11] | Bertrand Godeau[1] | Marc Michel[1]

Am J Hematol. 2018;93:424–429.

Abstract

The aim of the study was to assess the efficacy and safety of rituximab (RTX) for treating systemic lupus erythematosus (SLE)-associated immune cytopenias. This multicenter retrospective cohort study of adults from French referral centers and networks for adult immune cytopenias and SLE involved patients ≥18 years old with a definite diagnosis of SLE treated with RTX specifically for SLE-associated immune cytopenia from 2005 to 2015. Response assessment was based on standard definitions. In total, 71 patients, 61 women (85.9%), with median age 36 years [interquartile range 31-48], were included. The median duration of SLE at the time of the first RTX administration was 6.1 years [2.6-11.6] and the reason for using RTX was immune thrombocytopenia (ITP) for 44 patients (62.0%), autoimmune hemolytic anemia (AIHA) for 16 (22.5%), Evans syndrome for 10 (14.1%), and pure red cell aplasia for one patient. Before receiving RTX, patients had received a mean of 3.1 ± 1.3 treatments that included corticosteroids (100%), and hydroxychloroquine (88.5%). The overall initial response rate to RTX was 86% (91% with ITP, 87.5% with AIHA, and 60% with Evans syndrome), including 60.5% with complete response. Median follow-up after the first injection of RTX was 26.4 months [14.3-71.2]. Among 61 initial responders, relapse occurred in 24 (39.3%); for 18, RTX retreatment was successful in 16 (88.8%). Severe infections occurred after RTX in three patients, with no fatal outcome. No cases of RTX-induced neutropenia were observed. In conclusion, RTX seems effective and relatively safe for treating SLE-associated immune cytopenias.

Risk of thrombosis with anti-phospholipid syndrome in systemic lupus erythematosus treated with thrombopoietin-receptor agonists

Zelie Guitton[1], Louis Terriou[1], Jean-Christophe Lega[2], Raphaele Nove-Josserand[2], Miguel Hie[3], Zahir Amoura[3], James B. Bussel[4], Mohamed Hamidou[5], Eric Rosenthal[6], Bertrand Lioger[7], Dominique Chauveau[8], Axel Chaminade[9], Nadine Magy-Bertrand[10], Marc Michel[11], Sylvain Audia[12], Bertrand Godeau[11,*] and Matthieu Mahevas[11,*]

- Multicentre retrospective study
- **N = 18 patients** with SLE-associated
- ITP treated with Tpo-Ras, 55% with Positive aPl, 27% with definite APS
- Response observed in 17/18 **(94%)**

TABLE 1 Characteristics of patients with SLE-ITP who received TPO-RAs and presented TEs

Age, years/ sex	Previous therapies for ITP and SLE	APS/aPLs	Type of TPO-RAs	Dose	Response	Type of TE	Antithrombotic treatment at the occurrence of TE	Duration of TPO-RA exposure at TE onset	Platelet count at TE ($\times 10^9$/l)	Management of TPO-RA/TEs
52/F	HCQ, CS, AZA, IVIG, RTX	APS aCL + LA Obstetrical events	Avatrombopag Eltrombopag Romiplostim	NS 75 mg 4 µg/bw	CR CR CR	Stroke	Aspirin	5	100	Avatrombopag continued LVMH, then warfarin and clopidogrel
28/F	CS, HCQ, AZA, MMF, IVIG, RTX, CYC	APS aCL + aβ2GP1 Arterial and venous events	Eltrombopag Romiplostim	75 mg 3 µg/bw	CR CR	– Myocardial infarction	Aspirin (warfarin withdrawn for 1 month)	1	484	Romiplostim withdrawn Aspirin, clopidogrel and warfarin
24/F	HCQ, CS, MMF, AZA, IVIG, dapsone, RTX	–	Romiplostim	9 µg/bw	CR	Intracranial sinus thrombosis	None	1	166	Romiplostim withdrawn LMWH
						Pulmonary embolism	Non-compliance with LMWH	12	186	LMWH, then warfarin
60/F	HCQ, CS, MMF, IVIG, RTX	aPLs aCL	Eltrombopag	75 mg	CR	Myocardial infarction	None	10	94	Eltrombopag withdrawn Aspirin and clopidogrel
67/F	CS, HCQ, AZA, RTX, splenectomy	APS LA + aβ2GP1 obstetrical and venous events	Eltrombopag	50 mg	CR	Catastrophic APS	Rivaroxaban	6	269	Eltrombopag withdrawn Aspirin and UFH, plasma exchange, CS, IGIV

aβ2GP1: anti-beta-2-glycoprotein 1; CR: complete response; F: female; LMVH: low-molecular-weight heparin; LA: circulating anticoagulant; M: male; NR: no response; NS: not specified; R: response; RTX: rituximab; SLE-ITP: SLE-associated immune thrombocytopenia; TE: thrombotic event; TPO-RA: thrombopoietin-receptor agonist.

Rheumatology 2018;57:1432–1438

TABLE 2 Literature review of 15 case reports describing the use of TPO-RAs for SLE-ITP

Reference	Age, years	Sex	Previous treatments	aPLs (type of event if APS)	Antithrombotic treatment	TPO-RA	Dose	Response	Time to response (days)	Side-effects	Platelet count at TE/delay
Magnano *et al.* 1	69	F	CS, IVIG, Spl, RTX	None	None	Eltrombopag	25 mg	CR	14	None	–
2	39	F	CS, IVIG, CYC, AZA, RTX	None	None	Romiplostim	7 μg/bw	CR	14	None	–
Gonzalez-Nieto	44	M	CS, IVIG, CYC, AZA, RTX	LA (arterial event)	NS	Romiplostim	2 μg/bw	CR	21	None	–
Alkaabi	34	F	CS, IVIG, RTX, CYC	Aβ2GP1	NS	Romiplostim	3 μg/bw	CR	6	None	–
Tomov	19	F	CS, IVIG, RTX	None	None	Romiplostim	UK	CR	NS	Renal thrombotic microangiopathy	60×10^9/l at 42 days
Borrell	72	F	CS, MMF, IVIG, RTX, Spl	aCL, aβ2GP1	None	Romiplostim	UK	CR	NS	Left popliteal deep vein thrombosis	177×10^9/l at 90 days
LaMoreaux	14	M	CS, IVIG, RTX, Spl	aCL, LA	None	Romiplostim	UK	CR	NS	Catastrophic APS	111×10^9/l at 77 days
Cela	55	F	CS, RTX, CSA	NS	None	Eltrombopag	50 mg	CR	14	None	–
Gudbrandsdottir	NS	NS	NS	NS	NS	NS	UK	NR	–	NS	–
Maroun 1	44	F	CS, IVIG, HCQ	aCL	None	Eltrombopag	UK	CR	21	None	–
2	46	F	HCQ, CS	None	Aspirin	Eltrombopag	50 mg	CR	7	Urticaria	–
3	51	F	CS, IVIG, RTX	None	None	Eltrombopag	50 mg	CR	NS	None	–
Scheinberg	30	F	CS, CYC, AZA, IVIG, RTX	NS	None	Eltrombopag	50 mg	CR	3	None	–
Boulon	61	F	CS, IVIG, AZA, CYC, Spl	LA (obstetrical and venous events)	AVK	Eltrombopag	50 mg	CR	30	Pulmonary embolism	119×10^9/l at 30 days
Martínez	39	F	CS, HCQ, MMF, AZA, RTX	NS	None	Eltrombopag	50 mg	CR	30	None	–

Aba: abatacept; aβ2GP1: anti-beta-2-glycoprotein 1; AVK: antivitamin K; CR: complete response; Elt: eltrombopag; F: female; M: male; NR: non-response; NS: not specified; Romipl: romiplostim; RTX: rituximab; R: response; SLE-ITP: SLE associated immune thrombocytopenia; Spl: splenectomy; Toci: tocilizumab; TPO-RA: thrombopoietin-receptor agonist.

Rheumatology key messages

- Thrombopoietin-receptor agonists are very effective in SLE immune thrombocytopenia.
- Serious unexpected venous and arterial thrombosis were observed in patients with APS or aPLs.
- aPLs should be systematically screened before initiation of thrombopoietin-receptor agonists in patients with SLE.

CVID: data from the largest series of the literature

	Ramirez-Vargas 2013 (n = 43)	Defi cohort (France) 2008 (n=314)	Quinti 2007 (n=224)	Hermaszewski 1993 (n=247)	Cunningham 1999 (n=248)
Respiratory tract		**91%**		**94%**	
Sinusitis	83%	63	54%	72	
Pneumonia	83%	58	56%		78
GI tract manifestations					
Giardia	**44%**	**47%**	**41%**	**39%**	**21%**
Campylobacter	7/19	14		8	3
Salmonella sp.	1/19	8		5	4
Lymphoid hyperpl.	3/19	8		7	1
Crohn'like disease				7	4
	5	4		4	6
Liver disease		**17%**		**20%**	**12%**
Splénomégalie		**38%**	**26%**	**38%**	
Auto-immunity	**23%**	**31%**	**26%**		**23%**
ITP	4%	15%	6%		6%
AIHA	2%	6%	4%	5%	5%
Polyarthritis	2%	6%	2%	3%	4%
Vitiligo	4%	4%	13%	3%	
Granulomatosis		**13%**		**5%**	**8%**
Lymphoma		**6%**	**2%**	**4%**	**9%**

Efficacy and safety of rituximab in common variable immunodeficiency-associated immune cytopenias: a retrospective multicentre study on 33 patients

Delphine Gobert,[1] James B. Bussel,[2] Charlotte Cunningham-Rundles,[3] Lionel Galicier,[4] Agnès Dechartres,[5] Alice Berezne,[6] Bernard Bonnotte,[7] Thierry DeRevel,[8] Christophe Auzary,[9] Roland Jaussaud,[10] Claire Larroche,[11] Alain LeQuellec,[12] Marc Ruivard,[13] Pascal Seve,[14] Amar Smail,[15] Jean-François Viallard,[16] Bertrand Godeau,[1] Olivier Hermine[17] and Marc Michel[1]

Summary

Patients with common variable immunodeficiency (CVID) are at high risk of developing immune thrombocytopenia (ITP) and/or autoimmune haemolytic anaemia (AHA). Given their underlying immunodeficiency, immunosuppressive treatment of these manifestations may increase the risk of infection. To assess efficacy and safety of rituximab in patients with CVID-associated ITP/AHA, a multicentre retrospective study was performed. Thirty-three patients, 29 adults and four children, were included. Patients received an average of 2·6 treatments prior to rituximab including steroids, intravenous immunoglobulin and splenectomy (21%). The median ITP/AHA duration at time of first rituximab administration was 12 months [range 1–324] and the indication for using rituximab was ITP (22 cases), AHA ($n = 5$) or both ($n = 7$); 1 patient was treated sequentially for ITP and then AHA. The overall initial response rate to rituximab was 85% including 74% complete responses. After a mean follow-up of 39 ± 30 months after rituximab first administration, 10 of the initial responders relapsed and re-treatment with rituximab was successful in 7/9. Severe infections occurred after rituximab in eight adults (24%), four of whom were not on immunoglobulin replacement therapy. In conclusion, rituximab appears to be highly effective and relatively safe for the management of CVID-associated severe immune cytopenias.

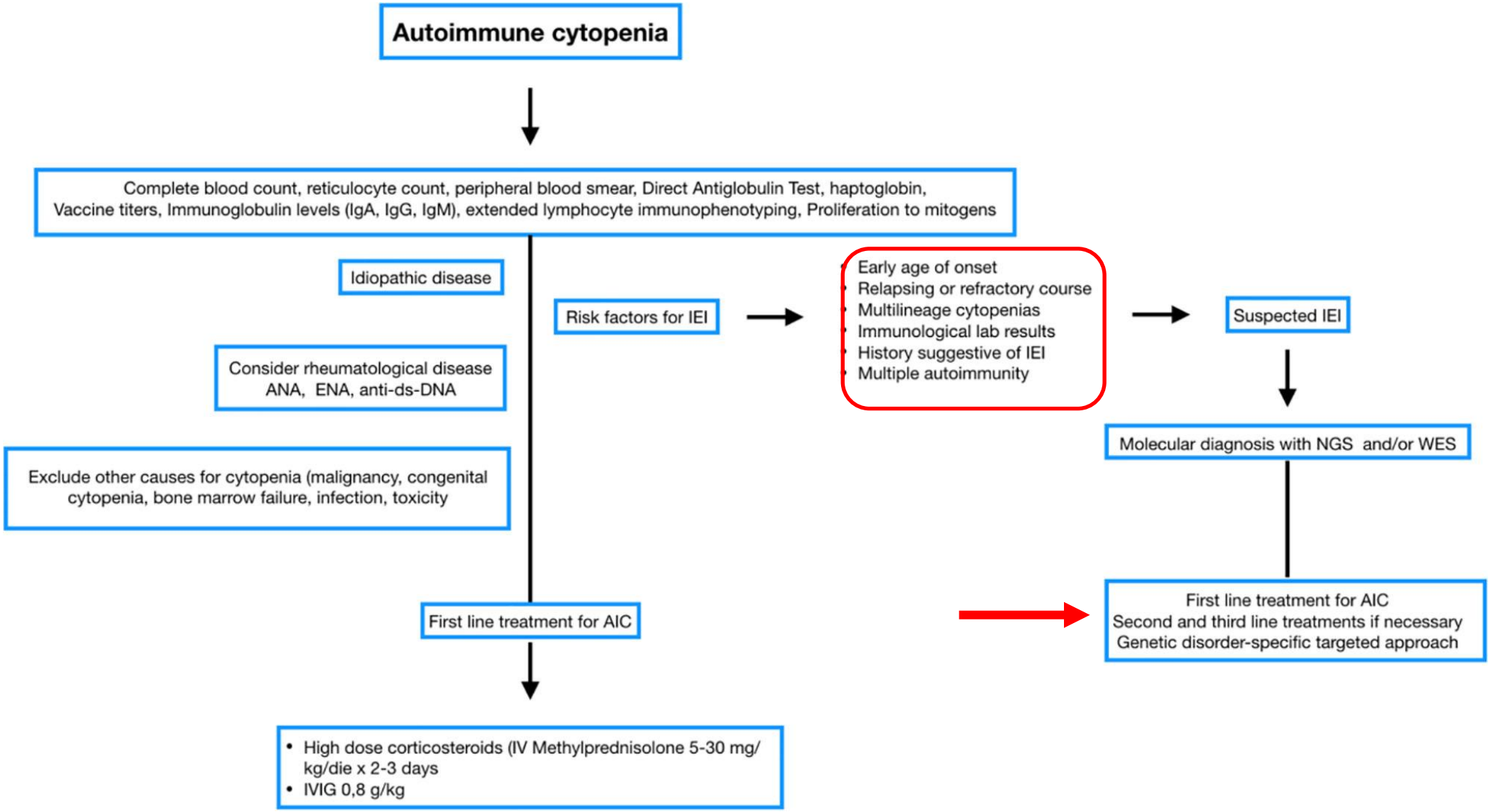


FIGURE 1 | Flow chart Immune cytopenia management. Blood and immunological test at onset. Genetic studies for bilinear cytopenia and relapses.

Overview of the talk

- What is secondary ITP ?
- Prevalence and main causes of secondary ITP
- Can we learn something about the pathophysiology ?
- Does searching for an underlying disease / condition / immunological status matter for the management of ITP ?

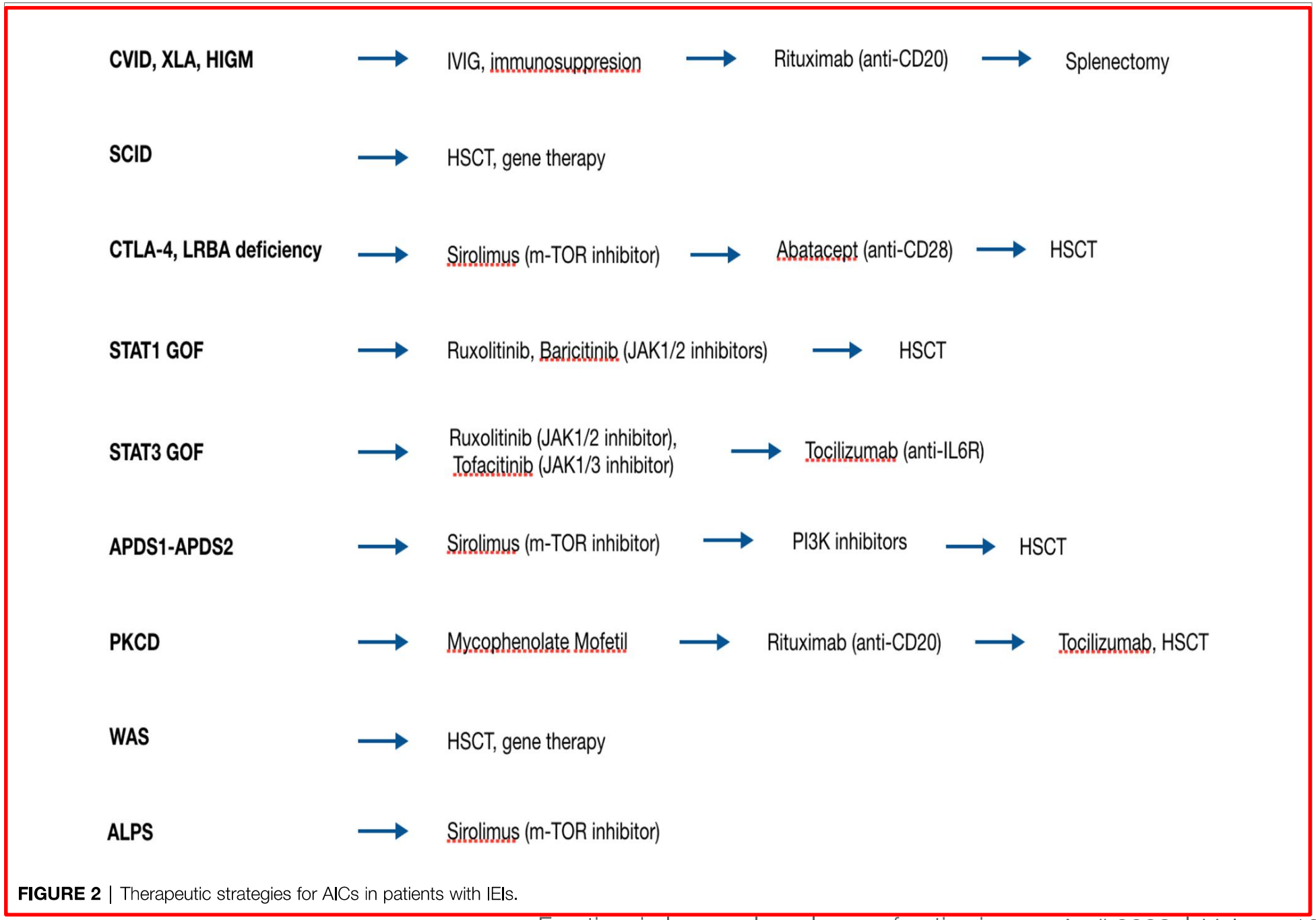


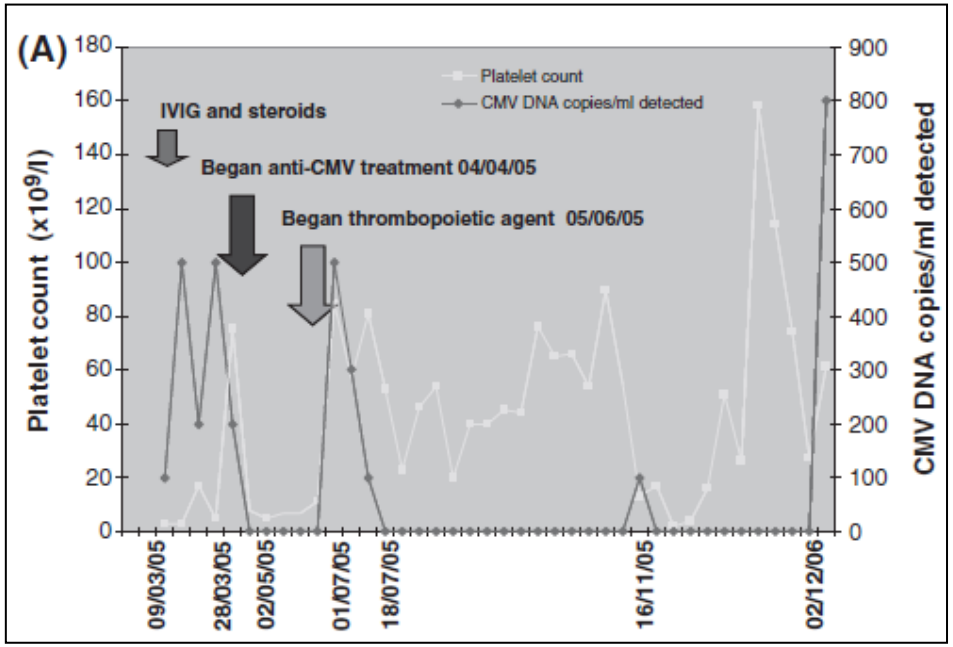
FIGURE 2 | Therapeutic strategies for AICs in patients with IEIs.

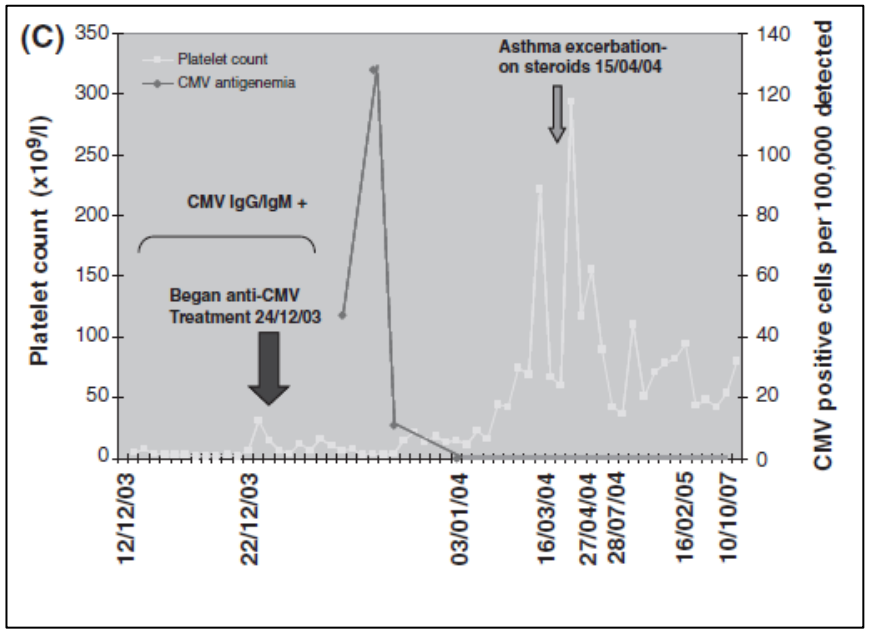
Cytomegalovirus can make immune thrombocytopenic purpura refractory

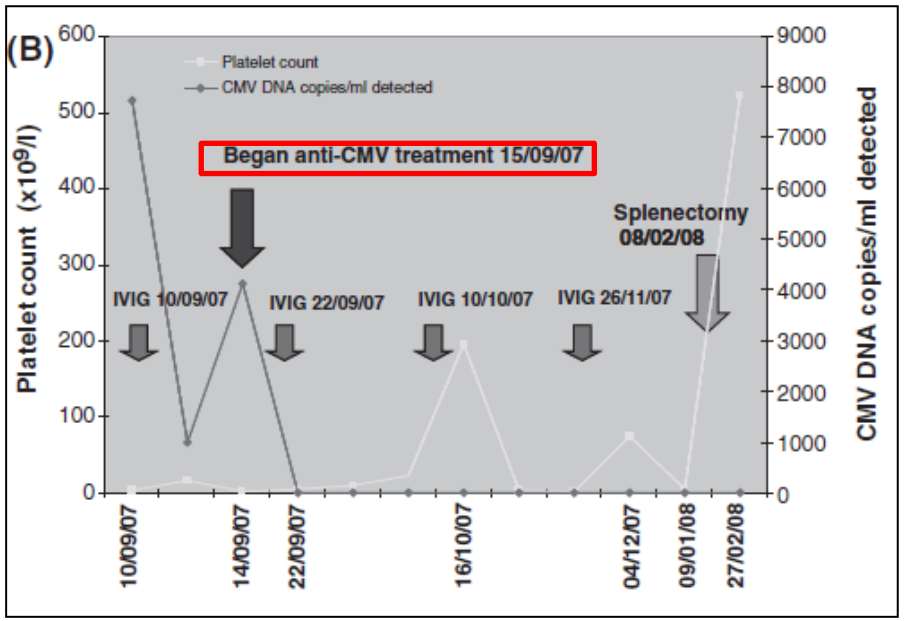
Table III. Diagnostic and other clinical features in the four cases of CMV-related ITP in this study.

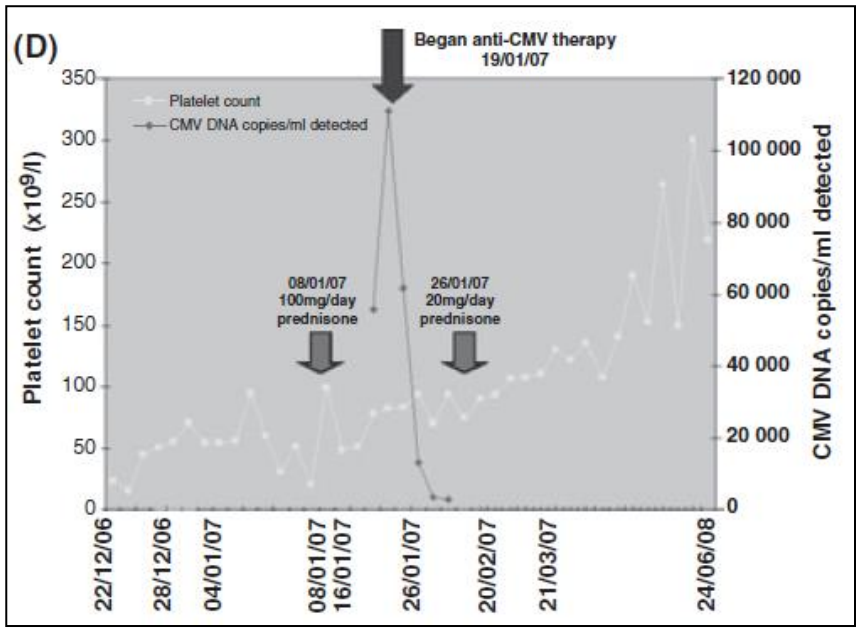
Clinical features/Laboratory findings	Case 1	Case 2	Case 3	Case 4
Increase in platelet number as CMV PCR normalizes	+	+	+	+
Steroids result in worsening ITP/ no benefit	+	+	+	+
Nadir platelet count ($\times 10^9$/l)	2	2	5	1
Transaminitis	+	+	+	+
Immunodeficiency present	−	−	−	−
Improvement in platelet count with ganciclovir/cytogam	+	+	+	+
Need for splenectomy	−	+	−	+
Presence of ICH	+	−	−	+
Bone marrow characteristics	Megakaryocytic hyperplasia	No significant megakaryocytic hyperplasia	No significant megakaryocytic hyperplasia	Megakaryocytic hyperplasia
Presented with CMV like illness-myalgia, fever, headache, malaise, throat pain	+	−	−	−
Severity of bleeding worse than others with ITP with similar degree of thrombocytopenia	+	+	+	+
HIV testing negative	+	+	+	+
Episodes of intermittent neutropenia	+	−	−	−
Atypical lymphocytes on smear	−	−	+	−

ITP, idiopathic thrombocytopenic purpura; CMV, cytomegalovirus; PCR, polymerase chain réaction; ICH, intracerebral haemorrhage; HIV, human immunodeficiency virus.


(A)
Platelet count
CMV DNA copies/ml detected
IVIG and steroids
Began anti-CMV treatment 04/04/05
Began thrombopoietic agent 05/06/05
Platelet count (x10⁹/l)
CMV DNA copies/ml detected
09/03/05
28/03/05
02/05/05
01/07/05
18/07/05
16/11/05
02/12/06


(C)
Platelet count
CMV antigenemia
Asthma excerbation-
on steroids 15/04/04
CMV IgG/IgM +
Began anti-CMV
Treatment 24/12/03
Platelet count (x10⁹/l)
CMV positive cells per 100,000 detected
12/12/03
22/12/03
03/01/04
16/03/04
27/04/04
28/07/04
16/02/05
10/10/07


(B)
Platelet count
CMV DNA copies/ml detected
Began anti-CMV treatment 15/09/07
Splenectomy
08/02/08
IVIG 10/09/07
IVIG 22/09/07
IVIG 10/10/07
IVIG 26/11/07
Platelet count (x10⁹/l)
CMV DNA copies/ml detected
10/09/07
14/09/07
22/09/07
16/10/07
04/12/07
09/01/08
27/02/08


(D)
Began anti-CMV therapy
19/01/07
Platelet count
CMV DNA copies/ml detected
08/01/07
100mg/day
prednisone
26/01/07
20mg/day
prednisone
Platelet count (x10⁹/l)
CMV DNA copies/ml detected
22/12/06
28/12/06
04/01/07
08/01/07
16/01/07
26/01/07
20/02/07
21/03/07
24/06/08

3. WHICH INITIAL WORKUP IS RECOMMENDED TO LOOK FOR AN UNDERLYING CAUSE/DISEASE ?

Diagnostic Approach in Patients with Suspected ITP

Recommendations for diagnosis of primary ITP in children and adults

1. The diagnosis of ITP is based principally on the exclusion of other causes of isolated thrombocytopenia using patient history, physical examination, blood count and evaluation of the peripheral blood film (to exclude other hematological conditions including hereditary thrombocytopenia and pseudothrombocytopenia). If therapy is administered, platelet count should be closely monitored for response as a diagnostic aid.
2. A complete history, physical examination, full blood count, and an expert analysis of the peripheral blood film should be evaluated at initial diagnosis (Grade C recommendation). Based on the evidence currently available, when there is isolated thrombocytopenia and no abnormal features present on physical examination or examination of the blood smear a bone marrow examination is not required in the initial diagnosis (Grade B recommendation) whether or not treatment is recommended.
3. The **detection of *H. pylori* infection**, with the urea breath test or the stool antigen test, should be included in the initial work-up in appropriate geographical areas (evidence level IIa, Grade B recommendation).
4. The majority of authors routinely test for **HIV and HCV** in all adult patients (evidence level IIb).
5. **Quantitative Ig level testing is indicated** to exclude an immune deficiency syndrome (evidence level IV, Grade C recommendation), or before treatment with intravenous immunoglobulin. In children, Ig level testing may be considered at baseline, and should be measured in those children with persistent or chronic ITP as part of a reassessment evaluation.
6. Bone marrow examination could be appropriate in those relapsing after remission, in patients not responding to initial treatment options, where splenectomy is considered, or if other abnormalities are detected in the blood count or morphology (evidence level III, Grade C recommendation). This examination should ideally include an aspirate, biopsy, flow cytometry, and cytogenetics (evidence level IV, Grade C recommendation).
7. ITP may be **classified as primary or secondary** to other medical conditions present at diagnosis. Furthermore, it may be further classified as newly diagnosed (0–3 months), persistent (>3–12 months), or chronic (>12 months).

Table I. Findings in reported cases of CMV-related ITP*.

Clinical Features/Laboratory Findings	Reference
Paediatrics patients ≤18 years old	Mizutani *et al* (1995); Fiala and Kattlove (1973); Sakata *et al* (1999)
Adult patients	Alliot and Barrios (2005); Ichiche *et al* (2003); Von Spronsen and Breed (1996); Sahud and Bachelor (1978); Wright (1992); Arruda *et al* (1997); Gural *et al* (1998); Swanobori *et al* (1997); Chanarin and Walford (1973); Harris *et al* (1975); Ip and Corner (1973); Eisenberg and Kaplan (1993); Miyahara *et al* (1997); Nomura *et al* (2005); Shimm *et al* (1980)
Increase in platelet count as CMV PCR normalizes	Alliot and Barrios (2005); Arruda *et al* (1997); Harris *et al* (1975)
Steroids result in worsening ITP/no benefit	Alliot and Barrios (2005); Sahud and Bachelor (1978); Arruda *et al* (1997); Gural *et al* (1998); Harris *et al* (1975); Fiala and Kattlove (1973)
Nadir platelet count ≤5×10^9/l	Ichiche *et al* (2003); Von Spronsen and Breed (1996); Wright (1992); Gural *et al* (1998); Chanarin and Walford (1973); Nomura *et al* (2005); Fiala and Kattlove (1973)
Transaminitis	Von Spronsen and Breed (1996); Sahud and Bachelor (1978); Wright (1992); Mizutani *et al* (1995); Gural *et al* (1998); Swanobori *et al* (1997); Eisenberg and Kaplan (1993); Miyahara *et al* (1997)
Improvement in platelet count with ganciclovir/cytogam	Von Spronsen and Breed (1996); Arruda *et al* (1997)
Need for splenectomy	Sahud and Bachelor (1978); Gural *et al* (1998); Fiala and Kattlove (1973)
Presence of ICH	Gural *et al* (1998)
Bone marrow with megakaryocytic hyperplasia	Alliot and Barrios (2005); Sahud and Bachelor (1978); Mizutani *et al* (1995); Arruda *et al* (1997); Gural *et al* (1998); Swanobori *et al* (1997); Chanarin and Walford (1973); Harris *et al* (1975); Fiala and Kattlove (1973); Sakata *et al* (1999)
History of, or presented with CMV-like illness: myalgia, fever, headache, malaise, throat pain	Ichiche *et al* (2003); Von Spronsen and Breed (1996); Arruda *et al* (1997); Gural *et al* (1998); Swanobori *et al* (1997); Chanarin and Walford (1973); Harris *et al* (1975); Ip and Corner (1973); Eisenberg and Kaplan (1993); Miyahara *et al* (1997); Nomura *et al* (2005); Shimm *et al* (1980); Fiala and Kattlove (1973)
Severity of bleeding worse than others with ITP with similar degree of thrombocytopenia	Gural *et al* (1998); Eisenberg and Kaplan (1993)
Episodes of neutropenia	Mizutani *et al* (1995)
Atypical lymphocytes on peripheral smear	Ichiche *et al* (2003); Von Spronsen and Breed (1996); Sahud and Bachelor (1978); Wright (1992); Arruda *et al* (1997); Gural *et al* (1998); Swanobori *et al* (1997); Chanarin and Walford (1973); Ip and Corner (1973); Eisenberg and Kaplan (1993); Miyahara *et al* (1997); Shimm *et al* (1980); Fiala and Kattlove (1973)

Adapted from M. Michel et al.

La Revue de médecine interne 42 2021 50–57

CBC => **Isolated** thrombocytopenia

Normal clinical examination and normal peripheral blood smear

Drug exposure ? Patient' history ?
Proceed with the « standard » minimal workup

- HIV, (HCV) tests
- Quantitative Ig levels, IgG, IgA and IgM
- Antinuclear Abs
- H pylori based on patient's origin and characteristics
- DAT
- TSH

Primary ITP is very likely if all the above are negative or normal

Fever and/or presence of large activated basophilic lymphocytes on the smear +/- transaminitis

EBV and CMV tests (IgG,IgM, PCR)
Parvovirus B19 if arthralgia and/or skin rash

Lymphadenopathy
And/or splenomegaly

EBV test, Ly. Immunophenotyping
CT-Scan (chest + abdomen)

History of thrombosis
And/or recurrent fetal losses
And/or ANA strongly positive

Lupus anticoagulant
Anticardiolipin and anti B2gp1 Abs

Clinical characteristics, management and outcome of Covid-19-associated immune thrombocytopenia. A French multicenter series.

N = 14 patients (50% women)
Median age was **64 years** [range: 53-79] Median follow-up of 60 days [range: 30-63]
Only patients with a plt ct < 30,000 were included
No cases of thrombosis
Good initial response to ITP treatment > 11 RC

Mahévas, BJH 2020

Thrombocytopenia following Pfizer and Moderna SARS-CoV-2 vaccination

Eun-Ju Lee[1] | Douglas B. Cines[2] | Terry Gernsheimer[3] | Craig Kessler[4] | Marc Michel[5] | Michael D. Tarantino[6] | John W. Semple[7] | Donald M. Arnold[8] | Bertrand Godeau[5] | Michele P. Lambert[9,10] | James B. Bussel[11]

- **N = 20 cases** reports of thrombocytopenia following vaccination
- Median age was **41 years** (22-73), 11 females
- 11 received the Moderna vaccine and 9 the Pfizer
- Onset of symptoms (petechia, brusing and/or mucosal bleeding) between Day 1 and Day 22 post vaccination, **median = 5 days**
- **Median nadir of the platelet count = 2 x10^9/L (1-36)**
- 4 out 20 patients had a previous history of mild to moderate thrombocytopenia including 1 case of inherited thrombocytopenia)
- 1 patient died of ICH

Am J Hematol. 2021;1–4.