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“Revue de la Littérature – PTI en 2016”

Pr Bernard Bonnotte

- Service de médecine interne et immunologie clinique
- INSERM UMR 1098 « Immunopathologie, Immunorégulation »

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Etiologies et physiopathologie

blood® flashback 1946

This paper, by one of the legends of hematology, William Dameshek, and his colleague Edward Miller, is from the inaugural issue of Blood. *By studying bone marrow specimens from controls, patients with acute or chronic immune thrombocytopenia, or patients with other thrombocytopenic disorders, the authors concluded that, in idiopathic thrombocytopenic purpura (ITP), production of platelets from megakaryocytes is defective, even while marrow megakaryocytes are greatly increased in number. This defect resolved after splenectomy. The authors appropriately credit E. Frank with having proposed defective platelet production from megakaryocytes in ITP in 1915. The idea that platelet production was defective in ITP was superseded or ignored for decades, but it has now been validated by the therapeutic effectiveness of the thrombopoietin mimetics in ITP.*

Dameshek W, Miller EB. The megakaryocytes in idiopathic thrombocytopenic purpura, a form of hypersplenism. *Blood*. 1946;1(1):27-50.

THE MEGAKARYOCYTES IN IDIOPATHIC THROMBOCYTOPENIC PURPURA, A FORM OF HYPERSPLENISM

By William Dameshek, M.D., and Captain Edward B. Miller, A.U.S.

IN his book *Opera omnia*, published in 1775, Paul Gottlieb Werlhof[1] devoted a chapter to "Morbus maculosus haemorrhagicus," which he had first described forty years previously. He wrote:

> An adult girl, robust, without manifest cause, was attacked recently, towards the period of her menses, with a sudden severe hemorrhage from the nose, with bright but foul blood escaping together with a bloody vomiting of a very thick extremely black blood. Immediately there appeared about the neck and on the arms, spots partly black, partly violaceous or purple, such as are often seen in malignant smallpox . . . ; moreover the number of the spots increasing and surrounding completely both of the eyes, the back of the nose and the skin around the mouth and chin, with a livid black color, like marked from bruises.

Since the bleeding began simultaneously with the menses and since there was spontaneous recovery, it is indeed probable, as most authorities have agreed since, that this was an example of idiopathic thrombocytopenic purpura. The reasons for the development of sudden, generalized bleeding from all the mucous membranes and into the skin are almost as obscure today as they were in Werlhof's time. In the present paper, an attempt is made to develop a concept of pathogenesis centering about the failure of platelet growth from the megakaryocytes in the bone marrow, and dependent upon an abnormal inhibitory factor in a distant organ, namely, the spleen.

The great diminution in platelets in Werlhof's disease was first recognized by Krauss[2] in 1883 and by Denys[3] in 1887. Hayem[4] later confirmed and amplified these isolated observations. The relationship of the platelets to the giant cells of the bone marrow—the megakaryocytes—became known with the work of J. H. Wright[5] in 1906 and 1910. In 1915, Frank[6] made accurate studies of "essential thrombopenia" and postulated a marked diminution in platelet production by the megakaryocytes.* In the following year, Kaznelson[7] suggested splenectomy as a therapeutic maneuver in a chronic relapsing case of the disease. He assumed, by analogy with hemolytic anemia, that the spleen might have an unusual thrombolytic function. The results of the first operation were brilliant, but in the next two cases[8] only temporary increases in platelets occurred. Since that time the favorable effect of splenectomy in idiopathic thrombocytopenic purpura has been amply confirmed. The quick recovery following splenectomy of many desperately ill patients bleeding spontaneously from all the orifices is one of the most dramatic events in medicine, and must immediately implicate the spleen as of prime pathogenetic importance in the disease. In confirmation of this, the injection of splenic

From the Blood Laboratory of the Boston Dispensary, and the J. H. Pratt Diagnostic Hospital; aided by grants from the Charlton Fund, Tufts College Medical School, and the Upjohn Company.

* Frank is incorrectly quoted by most observers as having suggested a splenic effect on megakaryocyte platelet growth.

70 1946-2016 Leading the Way

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Abdulsalam *et al. BMC Complementary and Alternative Medicine* (2016) 16:107
DOI 10.1186/s12906-016-1091-3

BMC Complementary and Alternative Medicine

CASE REPORT Open Access

Immune thrombocytopenia after bee venom therapy: a case report

Mohammad Adel Abdulsalam, Bader Esmael Ebrahim and Ahmad Jasem Abdulsalam*

Obermann M, Ruck T, Pfeuffer S, Baum J, Wiendl H, Meuth SG
Simultaneous early onset immune thrombocytopenia and autoimmune thyroid disease following alemtuzumab treatment in relapsing remitting multiple sclerosis.
Mult Scler. 2016 Mar 15.

Case Report

Postinfluenza Vaccination Idiopathic Thrombocytopenic Purpura in Three Elderly Patients

Case Reports in Hematology
Volume 2016, Article ID 7913092, 4 pages

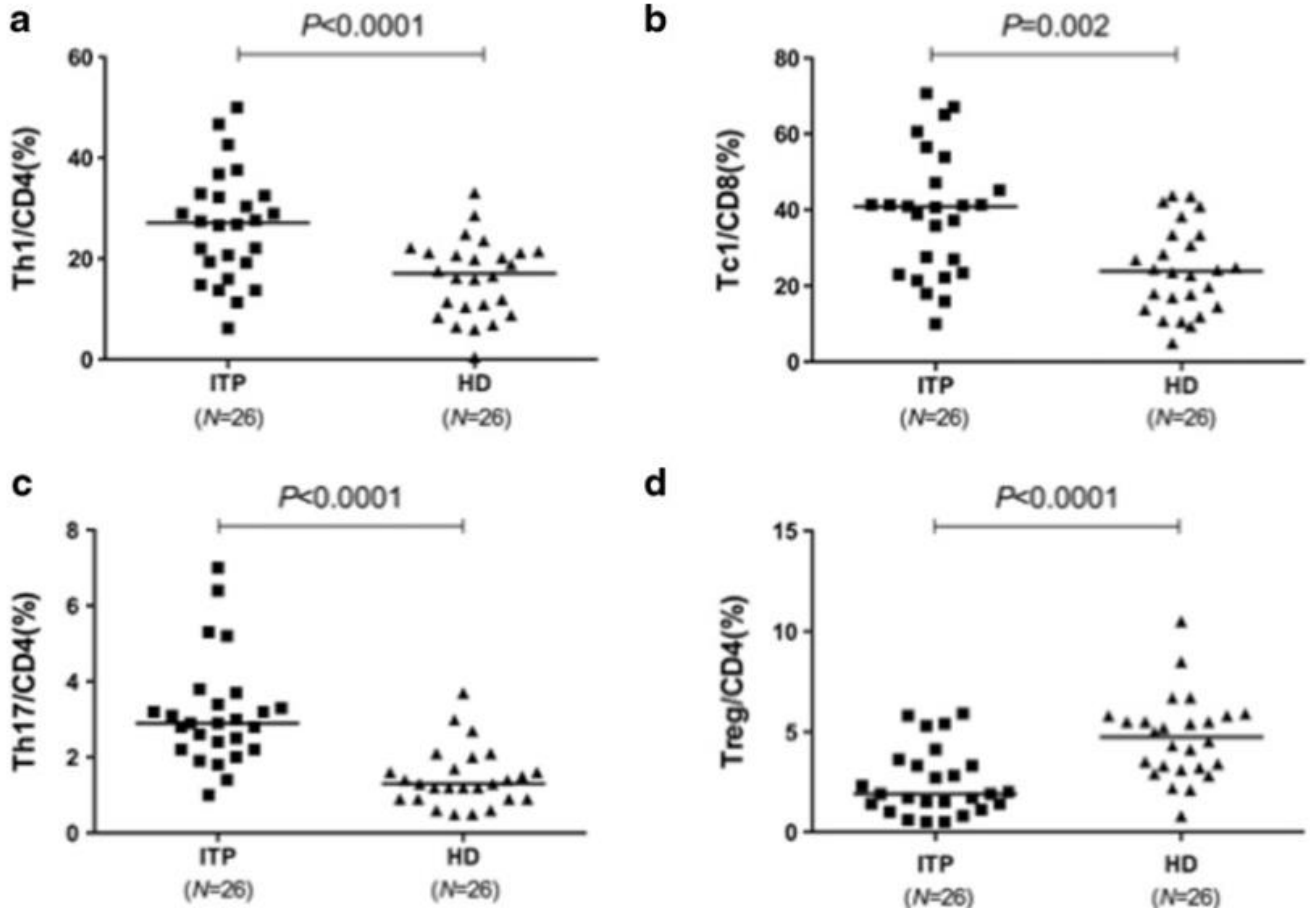
Joji Nagasaki, Masahiro Manabe, Kentaro Ido, Hiroyoshi Ichihara, Yasutaka Aoyama, Tadanobu Ohta, Yoshio Furukawa, and Atsuko Mugitani

Ann Hematol (2016) 95:959–965
DOI 10.1007/s00277-016-2641-y

ORIGINAL ARTICLE

Abnormalities of the bone marrow immune microenvironment in patients with immune thrombocytopenia

Yang Song[1,2] · Yu-Tong Wang[1] · Xiao-Jun Huang[1,2] · Yuan Kong[1]



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“Revue de la Littérature – PTI en 2016”

Diagnostic

platelets
ISSN: 0953-7104 (print), 1369-1635 (electronic)
Platelets, Early Online: 1–8
 DOI: 10.3109/09537104.2016.1143920
Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

A diagnostic approach that may help to discriminate inherited thrombocytopenia from chronic immune thrombocytopenia in adult patients

Mathieu Fiore[1,2], Xavier Pillois[2], Simon Lorrain[3], Marie-Agnès Bernard[3], Nicholas Moore[3], Pierre Sié[2,4], Jean-François Viallard[5], & Paquita Nurden[2,6]

	ITP	Inherited thrombocytopenia
Patients per group		
Number	9 (17.3%)	23 (44.2%)
Sex		
Male	5 (56%)	5 (22%)
Female	4 (44%)	18 (78%)
Age at inclusion (year)		
Mean (±s.d.)	53.0 (±18)	48.0 (±19)
[p25%–p75%]	[37.5; 66.5]	[32.0; 66.0]
[Min–Max]	[31.0; 85.0]	[18.0; 78.0]
Forms of inherited thrombocytopenia		
MYH9 syndrome	–	12 (52%)
Bernard–Soulier syndrome	–	1 (4%)
Filaminopathy	–	1 (4%)
Familial thrombocytopenia of Unknown etiology	–	9 (39%)

Discriminant criteria	Chronic ITP (n = 9)	IT (n = 23)
Age at discovery <34 y		
Not available	1 (11.1%)	1 (4.3%)
No	6 (66.7%)	7 (30.4%)
Yes	2 (22.2%)	15 (65.2%)
Family history of thrombocytopenia		
Not available	4 (44.4%)	3 (13.0%)
No	5 (55.6%)	1 (4.3%)
Yes	0 (0.0%)	19 (82.6%)
Personal history of bleeding in childhood or at puberty		
Not available	0 (0.0%)	0 (0.0%)
No	9 (100.0%)	9 (39.1%)
Yes	0 (0.0%)	14 (60.9%)
Mean platelet volume >11 fL		
Not available	2 (22.2%)	2 (8.7%)
No	6 (66.7%)	7 (30.4%)
Yes	1 (11.1%)	14 (60.9%)
Giant platelets in peripheral blood smears		
Not available	3 (33.3%)	4 (17.4%)
No	6 (66.7%)	5 (21.7%)
Yes	0 (0.0%)	14 (60.9%)
More than 44% of platelet with an area >4 μm^2 in electron microscopy		
Not available	0 (0.0%)	4 (17.4%)
No	6 (66.7%)	4 (17.4%)
Yes	3 (33.3%)	15 (65.2%)

International Journal of Laboratory Hematology
The Official journal of the International Society for Laboratory Hematology
LETTER TO THE EDITOR
INTERNATIONAL JOURNAL OF LABORATORY HEMATOLOGY

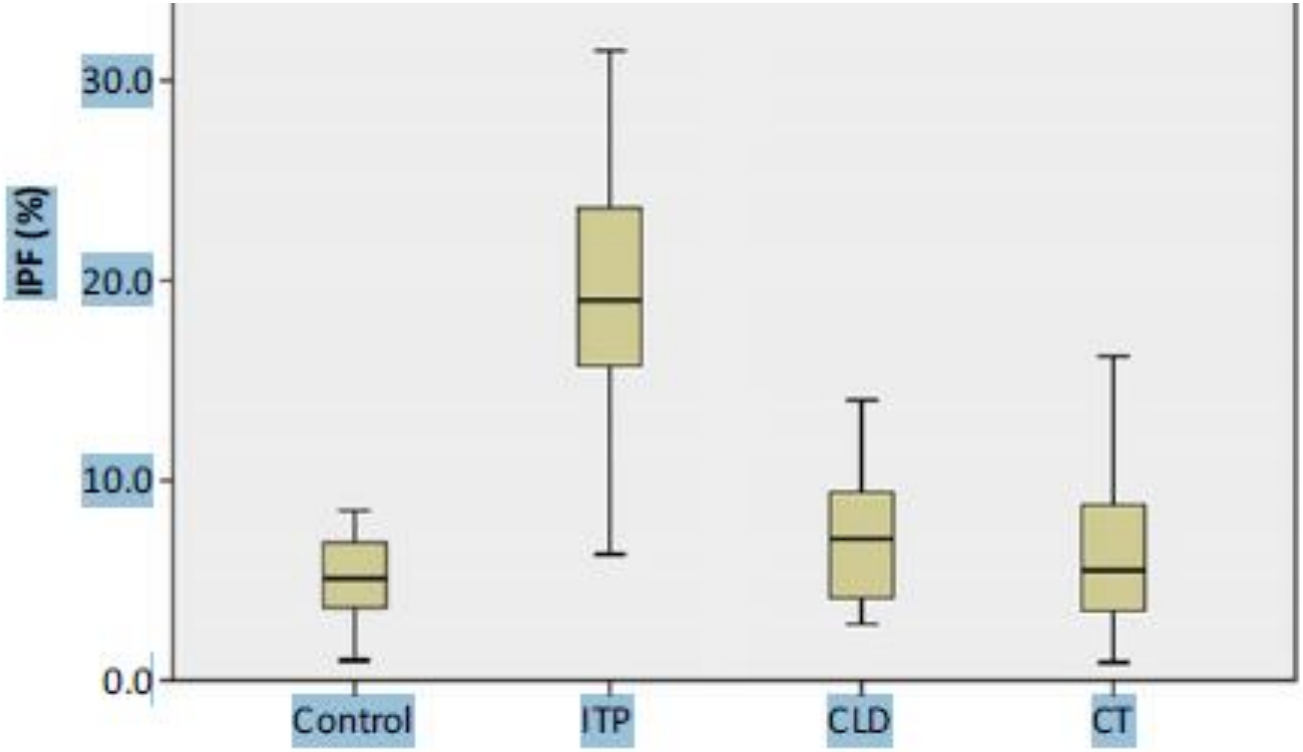
Letter to the Editor

Clinical significance of IPF% measurement in diagnosing thrombocytopenic disorders: distinguishing primary immune thrombocytopenia from other disorders

M. Serrando, A. Marull*, M. Ruiz*, D. Perez del Campo*, I. Puig-Pey*, J. M. Mu~noz†, P. Tejerina*, C. Morales-Indiano‡*
**Clinical Laboratory, University Hospital Dr Josep Trueta, Girona, Spain ‡Haematology Department, Hospital Germans Trias i Pujol, Badalona, Spain*

Immature Platelet fraction

SYSMEX Company



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Traitements

Int J Hematol
DOI 10.1007/s12185-016-1992-4

ORIGINAL ARTICLE

Rituximab salvage therapy in adults with immune thrombocytopenia: retrospective study on efficacy and safety profiles

Emilie Reboursiere[1] · H. Fouques[1] · G. Maigne[2] · H. Johnson[1] · S. Chantepie[1] · A. C. Gac[1] · O. Reman[1] · M. Macro[1] · K. Benabed[1] · X. Troussard[3] · G. Damaj[1] · S. Cheze[1]

- Analyse rétrospective de 35 PTI (en rechute ou réfractaires : 4 splénectomisés)
- Overall response / CR : 47% / 24% à 1 an
- Overall response / CR : 38% / 25% à 2 ans
- 44% mild hypogamma (pas d’infection sévère)

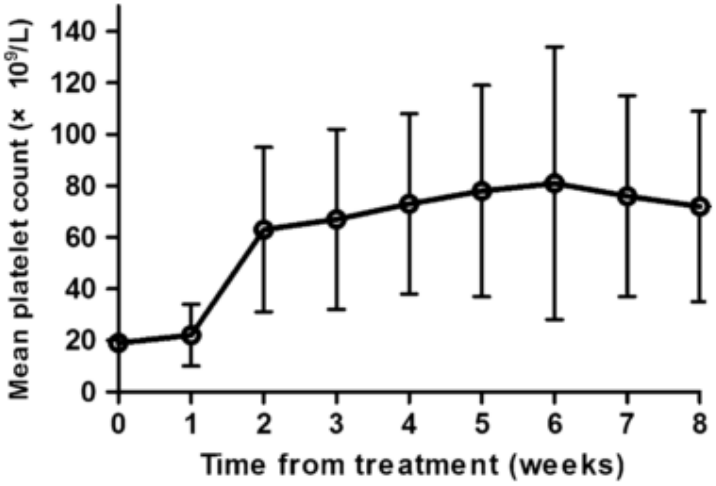
Int J Hematol (2016) 103:180–188
DOI 10.1007/s12185-015-1903-0

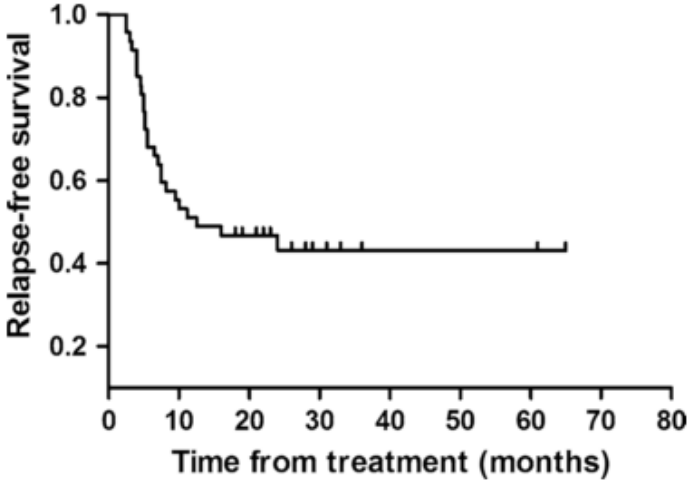
ORIGINAL ARTICLE

Clinical efficacy and tolerability of vincristine in splenectomized patients with refractory or relapsed immune thrombocytopenia: a retrospective single-center study

Young Hoon Park[1] · Hyeon Gyu Yi[1] · Moon Hee Lee[1] · Chul Soo Kim[1] · Joo Han Lim[1]

62 patients :
- 75% (n=47) de réponse à 2 mois (CR:16%/ PR:60%)
- 39% (n=24) de réponse à 1 an
- 22% (n=14) de réponse 2 ans





Contents lists available at ScienceDirect

Thrombosis Research

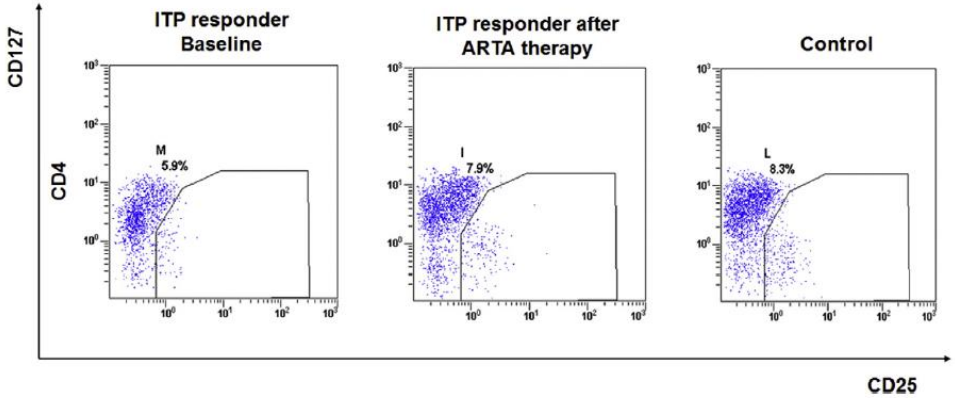
journal homepage: www.elsevier.com/locate/thromres

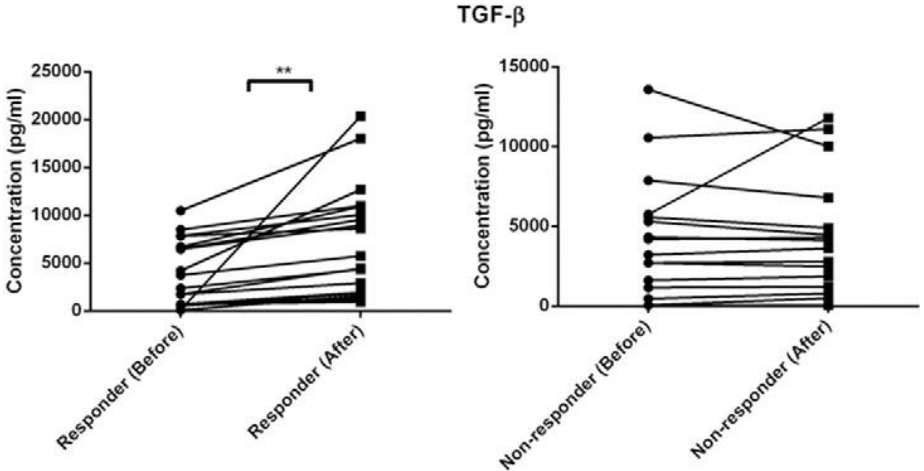
Efficacy of immunomodulatory therapy with all-*trans* retinoid acid in adult patients with chronic immune thrombocytopenia☆

Lan Dai [1], Ri Zhang [1], Zhaoyue Wang *, Yang He *, Xia Bai, Mingqing Zhu, Ziqiang Yu, Chang-geng Ruan

MOH Key Lab of Thrombosis and Hemostasis, Jiangsu Institute of Hematology, the First Affiliated Hospital of Soochow University, 188 Shizi Street, Suzhou 215006, China; Collaborative Innovation Center of Hematology, Soochow University, 1 Shizi Street, Suzhou 215006, China

- 35 Chronic ITP (3 splénectomies/ 19 IS)
- ATRA (10 mg x3 / D)
- Daily with prednisone (10 mg, x2/D)
- Mean treatment duration: 3 months
- Overall response : 54.3% (CR:28,6%)
- Mean follow-up time : 14 ± 7 months
- Relapse : 2 patients





Analyses avant TT
et après un mois

The Effect of Danazol in Primary Immune Thrombocytopenia:An Analysis of a Large Cohort From a Single Center in China.

Clin Appl Thromb Hemost. 2015 Dec 16.

Liu W, Gu X, Fu R, Li Y, Lv M, Sun T, Lv C, Liu X, Xue F, Zhang L, Yang R.

•Analyse rétrospective de 319 persistants ou chroniques ITP traités par Danazol seul (n=103) ou avec CS
•Réponse globale : 65.0%
•Réponse avec Danazol seul = 63.1%
•21.1% = effets secondaires mais seulement 1,2% arrêt

Original Paper

Acta Haematologica

Acta Haematol 2016;135:162–171
DOI: 10.1159/000442703

Received: June 25, 2015
Accepted after revision: November 22, 2015
Published online: January 16, 2016

Clinical Outcome and Predictive Factors in the Response to Splenectomy in Elderly Patients with Primary Immune Thrombocytopenia: A Multicenter Retrospective Study

Young Hoon Park[a] Hyeon Gyu Yi[a] Chul Soo Kim[a] Junshik Hong[b] Jinny Park[b] Jae Hoon Lee[b] Ho Young Kim[c] Hyo Jung Kim[c] Dae Young Zang[c] Se Hyung Kim[d] Seong Kyu Park[d] Dae Sik Hong[d] Guk Jin Lee[e] Jong-Youl Jin[e] on behalf of Gyeonggi/Incheon Branch, The Korean Society of Hematology

184 patients with primary ITP
- elderly group ≥ 60 years, n = 52
- younger group <60 years, n = 132

Table 3. Response after splenectomy

	Overall (n = 184)	Younger group (n = 132)	Elderly group (n = 52)	p
CR	124 (67.4)	92 (69.7)	32 (61.5)	0.288
R	24 (13.0)	14 (10.6)	10 (19.2)	
NR	33 (17.9)	24 (18.2)	9 (17.3)	
Not available	3 (1.6)	2 (1.5)	1 (1.9)	
Overall response (CR+R)	144 (80.4)	106 (80.3)	42 (80.7)	0.466
5-year relapse-free survival		76%	51%	

Values are n (%).

Original Paper

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Table 4. Postoperative complications according to age group

	Overall (n = 184)	Younger group (n = 132)	Elderly group (n = 52)	p
Early complications (within POD 30)	19 (10.3)	9 (6.9)	10 (19.2)	0.013
Bleeding	14 (7.6)	7 (5.3)	7 (13.5)	0.060
Infection	3 (1.6)	1 (0.8)	2 (3.8)	0.036
Cardiovascular event	2 (1.1)	1 (0.8)	1 (1.9)	0.492
Mortality within POD 30	1 (0.5)	0 (0.0)	1 (1.9)	0.110
Late complications (POD 31–100)	16 (8.7)	6 (4.5)	10 (19.2)	0.001
Thrombosis	8 (4.3)	2 (1.5)	6 (11.5)	0.001
Infection	6 (3.3)	4 (3.0)	2 (3.8)	0.382
Bleeding	2 (1.1)	0 (0.0)	2 (3.8)	0.005
RBC transfusions	0 (0–15)	0 (0–15)	0 (0–10)	0.160
Postoperative stay, days	8 (4–60)	7 (4–60)	9.5 (4–52)	0.019

Values are medians (range) or n (%). RBC = Red blood cell.

AJH

Thrombopoietin receptor agonists for preparing adult patients with immune thrombocytopenia to splenectomy: results of a retrospective, observational GIMEMA study

Francesco Zaja,[1*] Wilma Barcellini,[2] Silvia Cantoni,[3] Monica Carpenedo,[4] Giuseppe Caparrotti,[5] Valentina Carrai,[6] Nicola Di Renzo,[7] Cristina Santoro,[8] Massimo Di Nicola,[9] Dino Veneri,[10] Federico Simonetti,[11] Anna M. Liberati,[12] Valeria Ferla,[2] Francesca Paoloni,[13] Enrico Crea,[13] Stefano Volpetti,[1] Enrica Tuniz,[1] and Renato Fanin[1]

TABLE I. Patients' Characteristics.

Patients	31
Median age, years (range)	50.0 (19.3–80.9)
Male/Females	14/17
Primary ITP	30
ITP in previous history of HCV hepatitis	1
Number of previous therapies:	
1	2
2	10
3	11
≥ 4	8
Previous treatment with:	
Rituximab	11
Azathioprine and/or Cyclosporin-A	7
Response to last therapy before TPO-RAs:	
Response (%)	9 (29.0)
Complete response	7 (22.0)
No response (%)	22 (71.0)
Last effective treatments before TPO-Ras	
Intravenous immunoglobulins	3
Rituximab	6
Last ineffective treatments before TPO-RAs:	
Intravenous immunoglobulins	8
Rituximab	2
Cyclosporin-a	5
Prednisone	2
Dexamethasone	2
Dapsone	2
Azathioprine	1
Median platelet count before TPO-RAs ($\times 10^9$/L)	11
Treatment with Romiplostim (%)	24 (77.4)
Treatment with Eltrombopag (%)	7 (22.6)

RESEARCH ARTICLE

AJH

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TABLE II. Response to Thrombopoietin Receptor Agonists Treatment

	All	Romiplostim	Eltrombopag	*P*-value
Patients	31	24	7	
Median duration of treatment (days)	86.5	87.0	84	0.6768
Response (%)	24 (77.4)	19 (79.2)	5 (71.4)	0.6417
Concomitant therapy (corticosteroid/IVIG)	19 (61.3)	17 (70.8)	2 (28.6)	0.0434
Median platelet count before splenectomy ($\times 10^9$/L)	114	114	133.5	0.1484

- Réponse au TPORa : 24 Pts sur 31 (77%)
- Mais CS + IVIG nécessaire pour 19 pts
- 29 splénectomies (2 ont refusé)
- Post-splenectomy complications :1 portal vein thrombosis and 1 pulmonary embolism) avec plq= 260 et 167 X 10^9/L

Mediterranean Journal of Hematology and Infectious Diseases

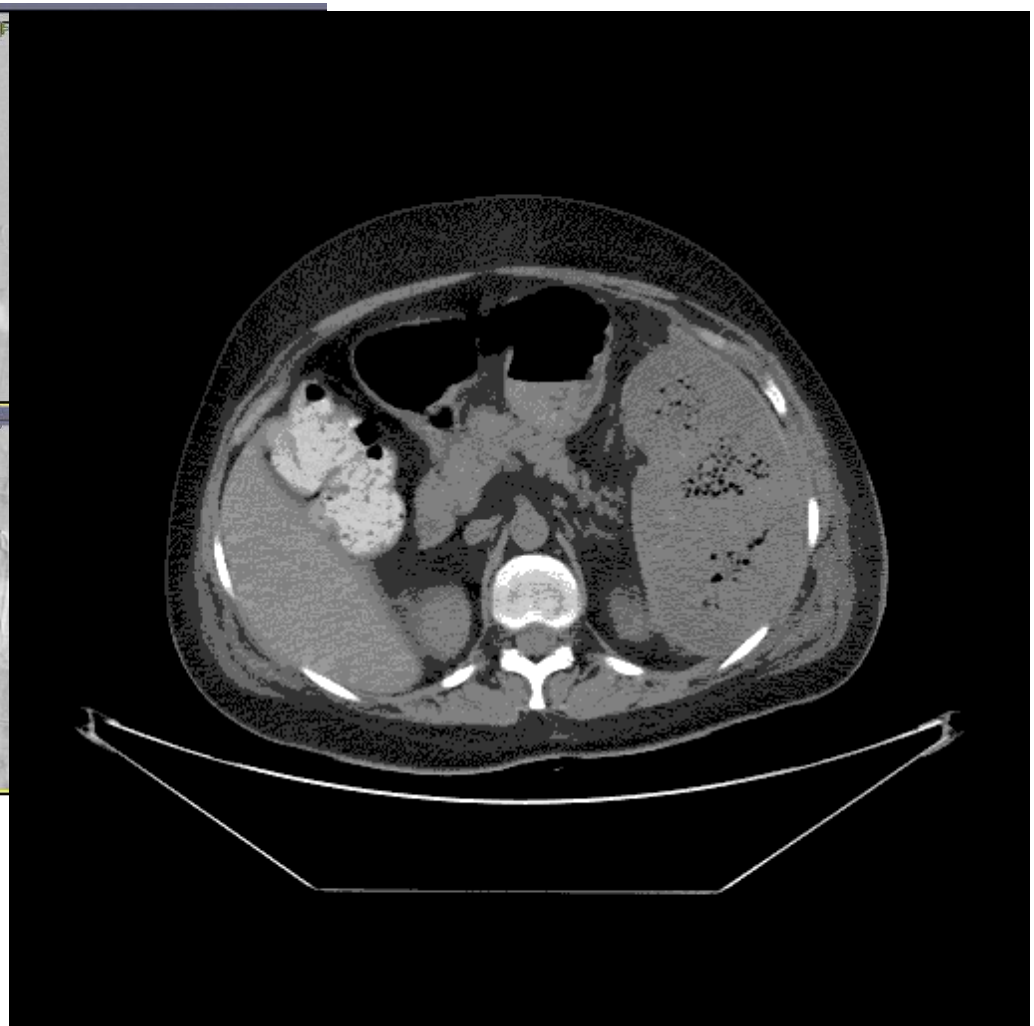
Case Report

Life-Threatening Autoimmune Hemolytic Anemia and Idhiopatic Thrombocytopenic Purpura. Successful Selective Splenic Artery Embolization

Matteo Molica[1], Fulvio Massaro[1], Giorgia Annechini[1], Erminia Baldacci[1], Gianna Maria D'Elia[1], Riccardo Rosati[2], Silvia Maria Trisolini[1], Paola Volpicelli[1], Robin Foà[1] and Saveria Capria[1]

[1] Department of Cellular Biotechnologies and Hematology, Sapienza University, Rome, Italy.
[2] Department of Radiological Sciences, Vascular and Interventional Unit, "Sapienza" University of Rome, Rome, Italy.

Figure 1. SSAE of the inferior branches of the splenic artery.



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Complications des traitements

European Journal of Haematology

European Journal of Haematology

CASE REPORT

Response loss and development of neutralizing antibodies during long-term treatment with romiplostim in patients with immune thrombocytopenia: a case series

Monica Carpenedo[1], Silvia Cantoni[2], Veronica Coccini[1], Enrico Maria Pogliani[3], Roberto Cairoli[2]

[1]Hematology and Transplant Unit, San Gerardo Hospital and University of Milano Bicocca, Monza; [2]Hematology and Oncology Department, Ospedale Niguarda Cà Granda, Milano; [3]Dipartimento di Scienze della Salute University of Milan Bicocca, Monza, Italy

- 28 ITP traités par romiplostim
- patients : perte de réponse (3/8 progressive, 5/8 rapide)
- Neutralizing antibody testés sur 4 patients et + chez 3/4
- Pas de cross réaction avec TPO endogène
- Disparition des Ac après 7 et 9 mois (2 patients)
- Ac neutralisants : fréquence ? Difficulté de réaliser les tests

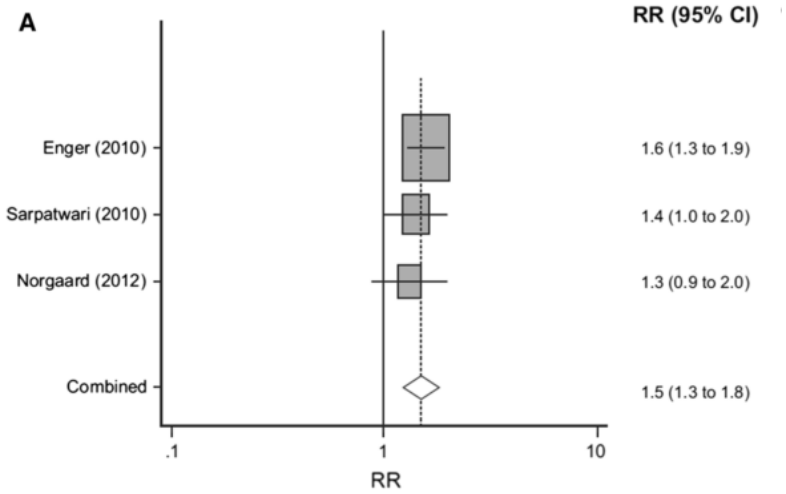
Int J Hematol
DOI 10.1007/s12185-016-1974-6

ORIGINAL ARTICLE

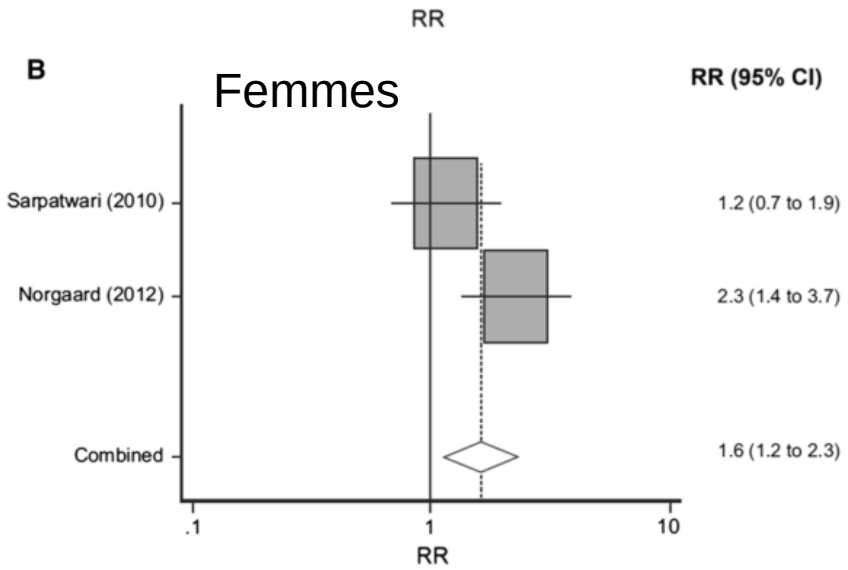
Thromboembolism in patients with immune thrombocytopenia (ITP): a meta-analysis of observational studies

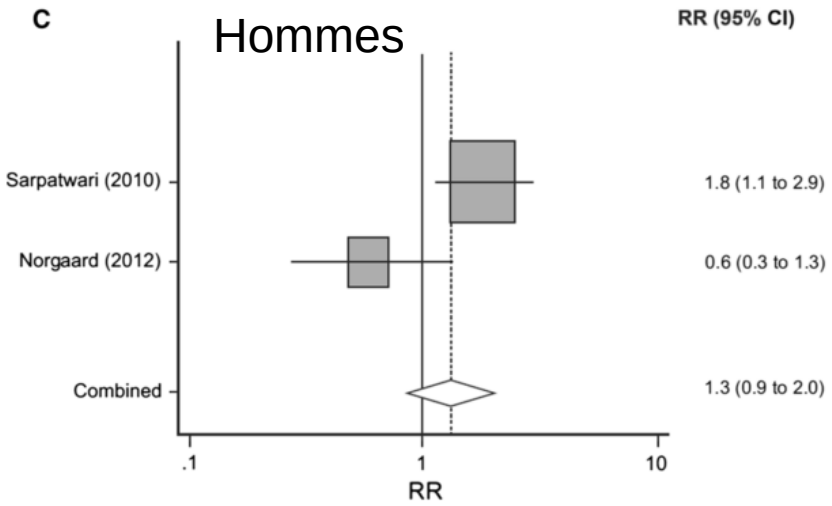
Wendy J. Langeberg[1] · W. Marieke Schoonen[2] · Melissa Eisen[1] · Laurence Gamelin[1] · Scott Stryker[3]

Pop générale



Risque de thrombose artérielle





Int J Hematol
DOI 10.1007/s12185-016-1974-6

CrossMark

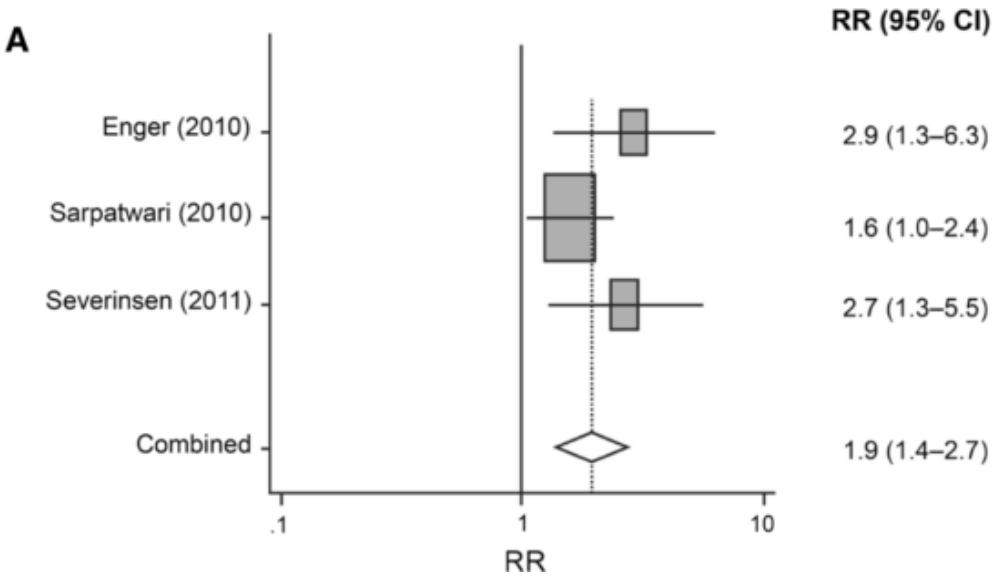
ORIGINAL ARTICLE

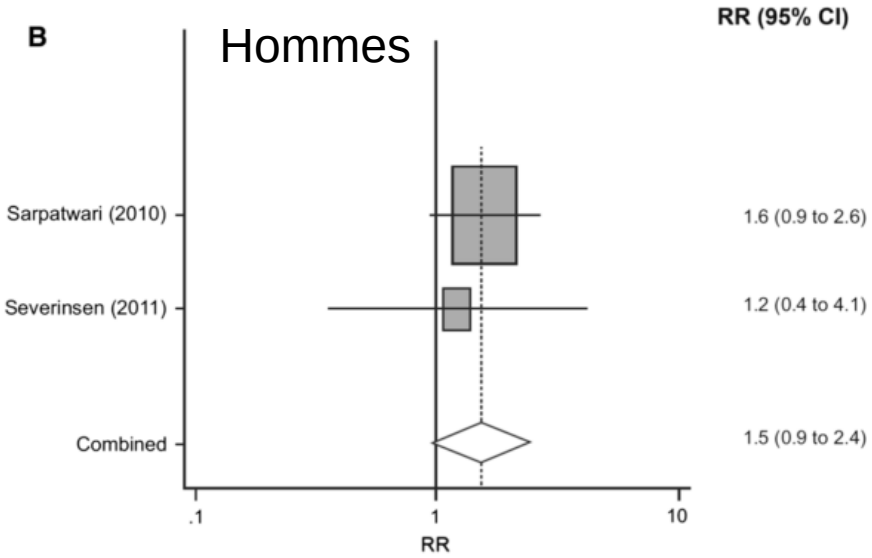
Thromboembolism in patients with immune thı (ITP): a meta-analysis of observational studies

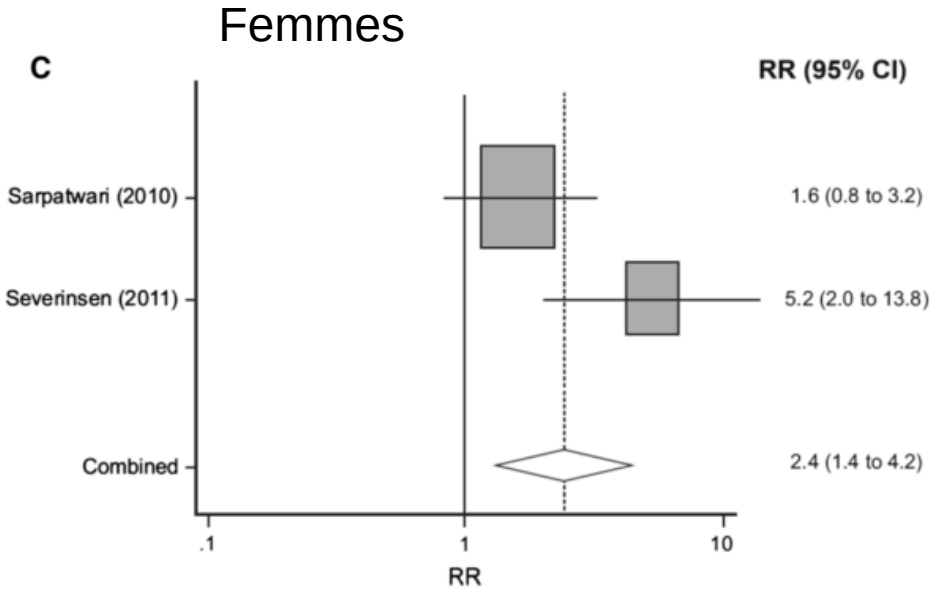
Wendy J. Langeberg[1] · W. Marieke Schoonen[2] · Melissa Eisen[1] · Laurence G
Scott Stryker[3]

Pop générale

Risque de thrombose veineuse







Contents lists available at ScienceDirect

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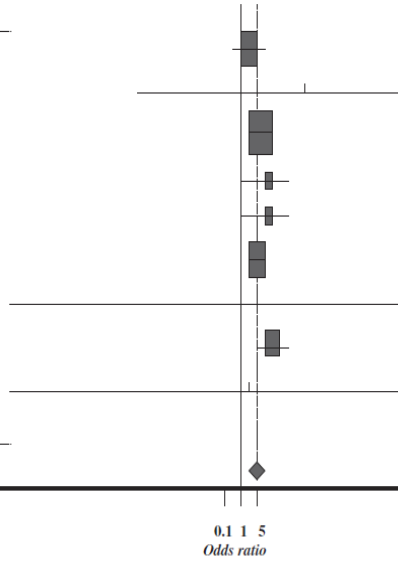
journal homepage: www.elsevier.com/locate/autrev

Review

Risk of thrombosis in patients with primary immune thrombocytopenia and antiphospholipid antibodies: A systematic review and meta-analysis

Guillaume Moulis [a,*], Alexandra Audemard-Verger [b], Laurent Arnaud [c], Cécile Luxembourger [d], François Montastruc [e], Amelia Maria Gaman [f], Elisabet Svenungsson [g], Marco Ruggeri [h], Matthieu Mahévas [i], Mathieu Gerfaud-Valentin [j], Andres Brainsky [k], Marc Michel [i], Bertrand Godeau [i], Maryse Lapeyre-Mestre [e], Laurent Sailler [a]

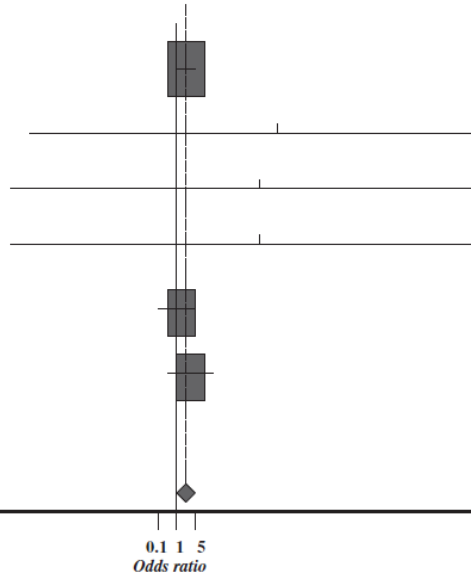
Study	Thromboses LA pos.	Thromboses LA neg.	OR (95% CI)
Ruggeri	3/39	19/525	2.22 (0.63-7.85)
Wong	6/43	0/124	-
Kim	13/48	8/117	5.06 (1.94-13.21)
Yang	1/5	1/65	16.00 (0.84-305.74)
Moulis	1/6	1/87	17.20 (0.93-317.35)
Pierrot-Deseilligny	4/16	10/199	6.30 (1.72-23.07)
Dash	0/11	0/29	-
Diz-Küççükkaya	10/20	2/62	30.00 (5.71-157.66)
Stasi	0/54	0/95	-
Total	**38/242**	**41/1303**	**6.11 (3.40-10.99)**



Test for overall effect: p<0.001
Heterogeneity: I^2=0%

Lupus anticoagulant

Study	Thromboses aCL pos.	Thromboses aCL neg.	OR (95% CI)
Kim	8/39	13/126	2.24 (0.85-5.90)
Gaman	2/4	0/25	-
Yang	2/17	0/53	-
Moulis	2/20	0/73	-
Pierrot-Deseilligny	4/54	10/161	1.21 (0.36-4.02)
Diz-Küççükkaya	5/22	5/67	3.65 (0.94-14.08)
Total	**23/156**	**27/505**	**2.14 (1.11-4.12)**



Test for overall effect: p=0.023
Heterogeneity: I^2=0%

Anticardiolipin antibodies

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UNIVERSITÉ BOURGOGNE FRANCHE-COMTÉ

Inserm
U1098 « Immunorégulation, immunopathologie »

CHU
Centre Hospitalier Universitaire Dijon

“Revue de la Littérature – PTI en 2016”

Real Life – Grossesse – Vieillesse, …

Ann Hematol
DOI 10.1007/s00277-016-2665-3

ORIGINAL ARTICLE

Real-life management of primary immune thrombocytopenia (ITP) in adult patients and adherence to practice guidelines

María Luisa Lozano[1] · N. Revilla[1,2] · T. J. Gonzalez-Lopez[3] · S. Novelli[4] · J. R. González-Porras[5] · B. Sánchez-Gonzalez[6] · N. Bermejo[7] · S. Pérez[8] · F. J. Lucas[9] · M. T. Álvarez[10] · M. J. Arilla[11] · M. Perera[12] · J. do Nascimento[13] · R. M. Campos[14] · L. F. Casado[15] · V. Vicente[1]

Table 3 Percentage of first-line treatments used and responses to different therapies

	First-line treatment	Response to treatment		
	N (%)	No response $<30 \times 10^9$/L *N* (%)	Response $30–100 \times 10^9$/L *N* (%)	Complete response $>100 \times 10^9$/L *N* (%)
Steroids (83.1 % response)	65 (64.3 %)	11 (16.9)	17 (26.2)	37 (56.9)
Prednisone/methylprednisolone	59 (58.4 %)	9 (15.3)	14 (23.7)	36 (61.0)
Dexamethasone	6 (5.9 %)	2 (33.3)	3 (50.0)	1 (16.7)
Immunoglobulins +/− steroids (83.9 % response)	31 (30.7 %)	5 (16.1)	7 (22.6)	19 (61.3)
Immunoglobulins and steroids	27 (26.7 %)	4 (14.8)	6 (22.2)	17 (63.0)
Immunoglobulins	4 (4.0 %)	1 (25.0)	1 (25.0)	2 (50.0)
Other therapies	5 (5.0 %)	–	3 (60.0)	2 (40.0)
Rituximab	1 (1.0 %)	–	1 (100.0)	–
Eltrombopag	1 (1.0 %)	–	1 (100.0)	–
Prednisone and cyclosporin	1 (1.0 %)	–	1 (100.0)	–
Prednisone and rituximab and immunoglobulins and platelet transfusion	1 (1.0 %)	–	–	1 (100.0)
Prednisone and romiplostim and immunoglobulin	1 (1.0 %)	–	–	1 (100.0)
Total	101 (100 %)	16 (15.8)	27 (26.7)	58 (57.4)

Ann Hematol
DOI 10.1007/s00277-016-2665-3

ORIGINAL ARTICLE

Real-life management of primary immune thrombocytopenia (ITP) in adult patients and adherence to practice guidelines

	Second-line treatment	% of patients receiving second-line treatment according to response to first-line treatment		
	N (%)	No response $<30 \times 10^9$/L *N* (%)	Response $30–100 \times 10^9$/L *N* (%)	Complete response $>100 \times 10^9$/L *N* (%)
Steroids (85.0 % response)	20 (35.7 %)	4 (28.6)	5 (31.2)	11 (42.3)
Prednisone/methylprednisolone	14 (25.0 %)			
Dexamethasone	6 (10.7 %)			
TPO receptors (87.5 % response)	14 (25.0 %)	6 (42.8 %)	4 (25.0)	4 (15.4)
Romiplostim	11 (19.6 %)			
Eltrombopag	3 (5.4 %)			
Immunoglobulins +/− steroids (69.2 % response)	13 (23.2 %)	3 (21.4)	4 (25.0)	6 (23.1)
Other therapies (88.9 % response)	9 (16.1 %)	–		–
Splenectomy	6 (10.7 %)	1 (7.1)	2 (12.5)	3 (11.5)
Rituximab	2 (3.6 %)	–	1 (6.2)	1 (3.8)
Azathioprine	1 (1.8 %)	–	–	1 (3.8)
Total	56 (100 %)	14/16 (87.5)	16/27 (59.2)	26/58 (44.8)

	TPO-ra *N* (%)	Splenectomy *N* (%)
First-line therapy (*N* = 101)	2 (2.0 %)	0 (0.0 %)
Second-line therapy (*N* = 56)	14 (25.0 %)	6 (10.7 %)
Third-line therapy (*N* = 24)	6 (25.0 %)	3 (12.5 %)
Fourth therapy (*N* = 8)	5 (62.5 %)	1 (12.5 %)
Fifth/sixth-line therapy (*N* = 6)	2 (33.3 %)	0 (0 %)
Second or subsequent line therapies (*N* = 94_	27 (28.7 %)	10 (10.6 %)

Research Article

Pregnancy and Birth Outcomes among Women with Idiopathic Thrombocytopenic Purpura

Hindawi Publishing Corporation
Journal of Pregnancy
Volume 2016, Article ID 8297407, 8 pages
http://dx.doi.org/10.1155/2016/8297407

Diego F. Wyszynski,[1] Wendy J. Carman,[2] Alan B. Cantor,[3] John M. Graham Jr.,[4] Liza H. Kunz,[5] Anne M. Slavotinek,[6] Russell S. Kirby,[7] and John Seeger[2,8]

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Harvard Medical School, Boston, MA 02120, USA

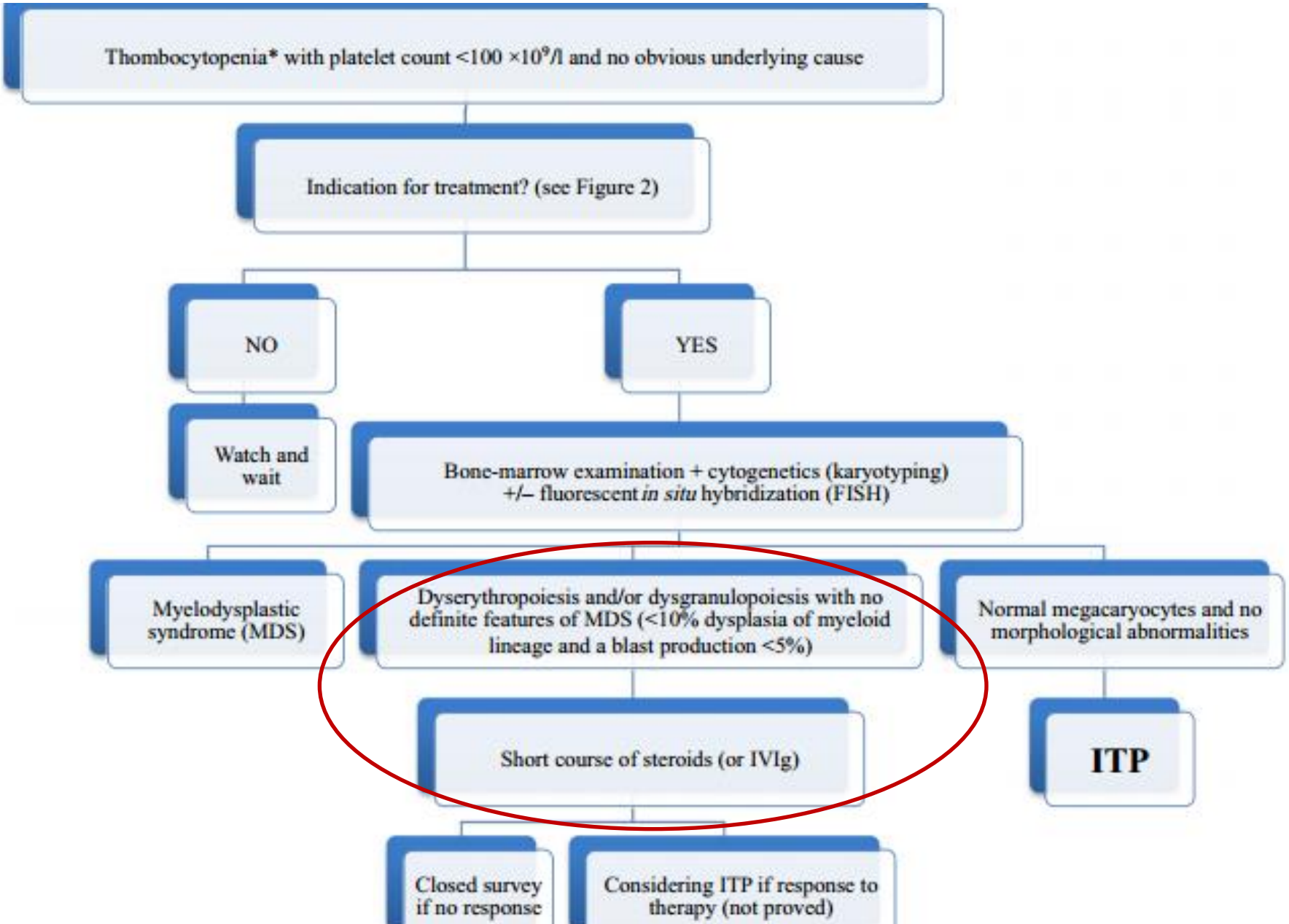
US Health Insurance database
446 pregnancies in women with ITP (1995-2009)

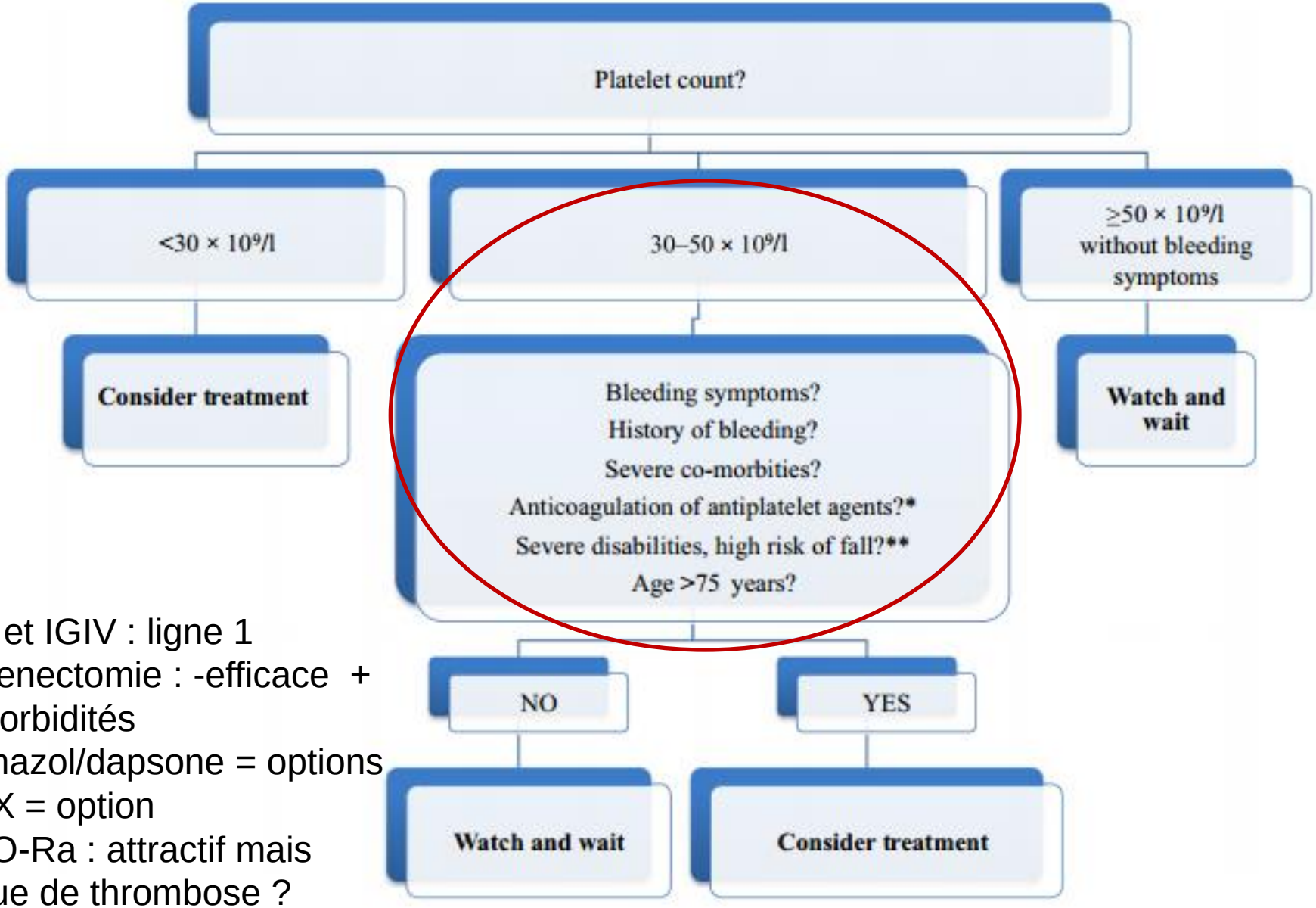
Outcomes	All pregnancies among women with ITP	
	N	%
	446	100
Live birth	346	77.6
Spontaneous or elective termination or stillbirth	24	5.4
Outcome unknown	76	17.0
Premature delivery[1]	38	8.5

Outcomes	All pregnancies among women with cITP	
	N	%
	84	100
Live birth	57	67.9
Spontaneous or elective termination or stillbirth	11	13.1
Outcome unknown	16	19.0
Premature delivery[1]	8	9.5
Low birthweight[1]	1	1.2

How we manage immune thrombocytopenia in the elderly

Matthieu Mahévas, Marc Michel and Bertrand Godeau



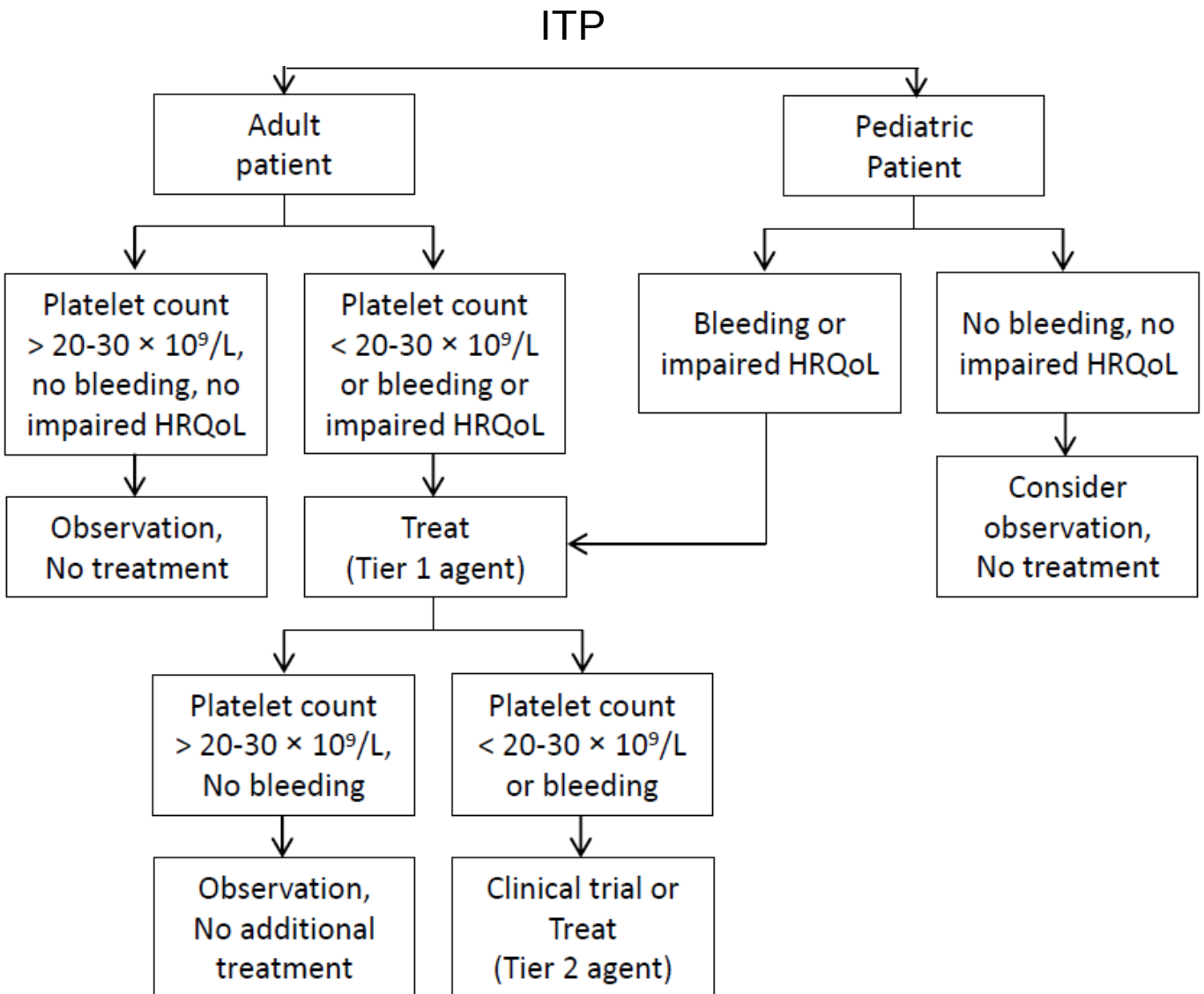


- CS et IGIV : ligne 1
- Splenectomie : -efficace + comorbidités
- Danazol/dapsone = options
- RTX = option
- TPO-Ra : attractif mais risque de thrombose ?

Blood First Edition Paper, prepublished online April 6, 2016;

HOW I TREAT REFRACTORY IMMUNE THROMBOCYTOPENIA

Adam Cuker and Cindy E. Neunert



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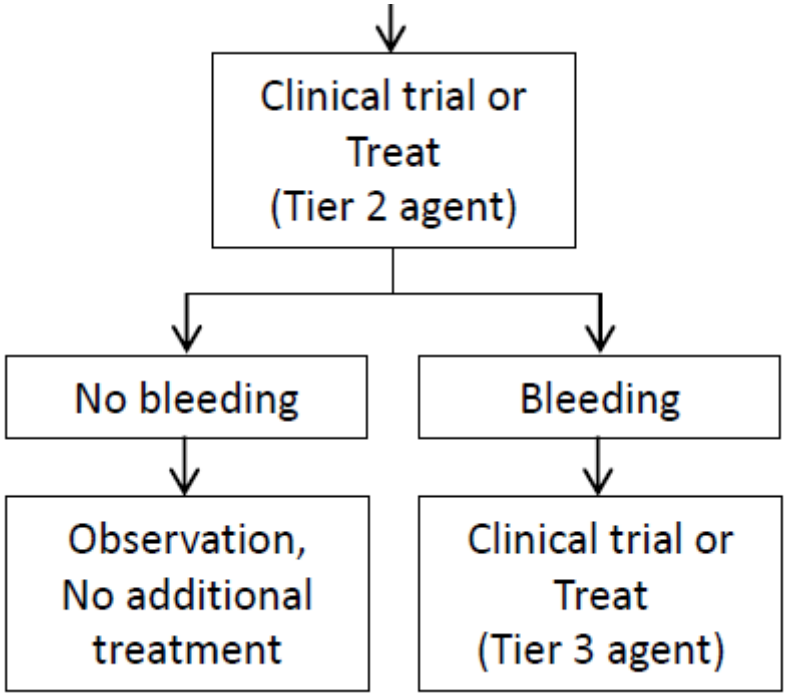

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HOW I TREAT REFRACTORY IMMUNE THROMBOCYTOPENIA

Adam Cuker and Cindy E. Neunert

« Nous épuisons toutes les options niveau 1 avant de passer au niveau 2 »

Table 2. Tier 1 treatment options.

Drug	Dose	Response rate[1]	Time to response	Selected toxicities
Low-dose prednisone	≤ 5 mg PO daily	< 10%	N/A[2]	Weight gain Hyperglycemia Hypertension Osteoporosis Cataracts
Rituximab	375 mg/m^2 IV weekly × 4 (lower doses may be effective)	60% overall 40% complete 20-25% at 5 years	1-8 weeks	Infusion reactions Serum sickness HBV reactivation PML (rare)
Romiplostim	1-10 µg/kg SC weekly	80% overall 40-50% persistent	1-4 weeks	Reticulin fibrosis Rebound thrombocytopenia Thrombosis
Eltrombopag	25-75 mg PO daily	80% overall 40-50% persistent	1-2 weeks	Reticulin fibrosis Rebound thrombocytopenia Thrombosis Hepatotoxicity

Table 3. Tier 2 treatment options.

Drug	Dose	Response rate[1]	Time to response	Selected toxicities
6-mercaptopurine	50-75 mg/m^2 PO QD	83%	Not reported	Hepatotoxcity Neutropenia Infection Pancreatitis
Azathioprine	1-2 mg/kg PO QD (maximum 150 mg/day)	40-60%	3-6 months	Hepatotoxcity Neutropenia Infection Pancreatitis
Cyclosporin A	5-6 mg/kg/day PO divided twice daily (titrate to blood levels of 100-200 ng/mL)	30-60%	3-4 weeks	Nephrotoxicity Hypertension Tremor Parathesias Gingival hyperplasia
Cyclophosphamide	0.3-1.0 g/m2 IV repeated every 2-4 weeks × 1-3 doses 50-200 mg PO daily, once response achieved dose tapered to 50mg	24-85%	1-16 weeks	Neutropenia Nausea/Vomiting Infertility Secondary malignancy
Danazol	50-800 mg/day PO divided 2-4 times daily	10-70%	3-6 months	Hepatotoxcity Virilization Amenorrhea
Dapsone	75-100 mg PO QD	40-75%	3 weeks	Hemolysis (in patients with G6PD deficiency) Rash Nausea Methemoglobinuria
Mycophenolate mofetil	250-1000 mg PO BID	11-80%	4-6 weeks	Headache Diarrhea Nausea Anorexia Infection
Vinca alkaloids	Vincristine: 1-2 mg IV weekly × 3 weeks Vinblastine: 10mg IV weekly × 3 weeks	10-75%	5-7 days	Peripheral neuropathy Vesication at infusion site Constipation Fever Neutropenia

HOW I TREAT REFRACTORY IMMUNE THROMBOCYTOPENIA

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Table 4. Tier 3 treatment options.

Treatment	Dose	Response rate	Selected toxicities
ATRA[86]	10 mg PO TID	29%	Retinoic Acid Syndrome Flu-like Symptoms Musculoskeletal pain Nausea/Vomtiing Peripheral neuropathy
Autologous HSCT[87]	Cyclophosphamide 50 mg/kg IV QD × 4 days (conditioning)	43%	Neutropenic fever Infection
Colchicine[88]	1.2 grams PO QD	21%	Agranulocytosis Neuritis Diarrhea Nausea/Vomiting
Interferon α[89–92]	Various	0-36%	Neutropenia Fever Influenza-like symptoms Hepatotoxicity
Plasma exchange[93-95]	One plasma volume exchange QD × 1-8 days	29-80%	Hypocalcemia Anaphylactoid reactions
Protein A immunoadsorption[96]	Average of 6 treatments (0.25 to 2.0 L plasma per treatment) over 2- 3 weeks	21%	Hyper-sensitivity reactions Pain Nausea/Vomiting Cardiopulmonary complications
Vitamin C[97-100]	2 grams PO QD	0-82%	Dsypepsia Nausea/Vomiting

ATRA, all-trans retinoic acid; HSCT, hematopoietic stem cell transplant