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“Revue de la Littérature – PTI en 2017”

Pr Bernard Bonnotte

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

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“Revue de la Littérature – PTI en 2017”

Revues

Review Series

blood

CLINICAL PLATELET DISORDERS

Clinical updates in adult immune thrombocytopenia

Michele P. Lambert[1] and Terry B. Gernsheimer[2]

[1]Division of Hematology, The Children's Hospital of Philadelphia, Philadelphia, PA; and [2]Division of Hematology, University of Washington School of Medicine, Seattle, WA

« Recent data suggest that < 25%of patients with ITP undergo splenectomy,[64] despite 5-year response rates of 60% to 70%".

bjh review

State of the art – how I manage immune thrombocytopenia

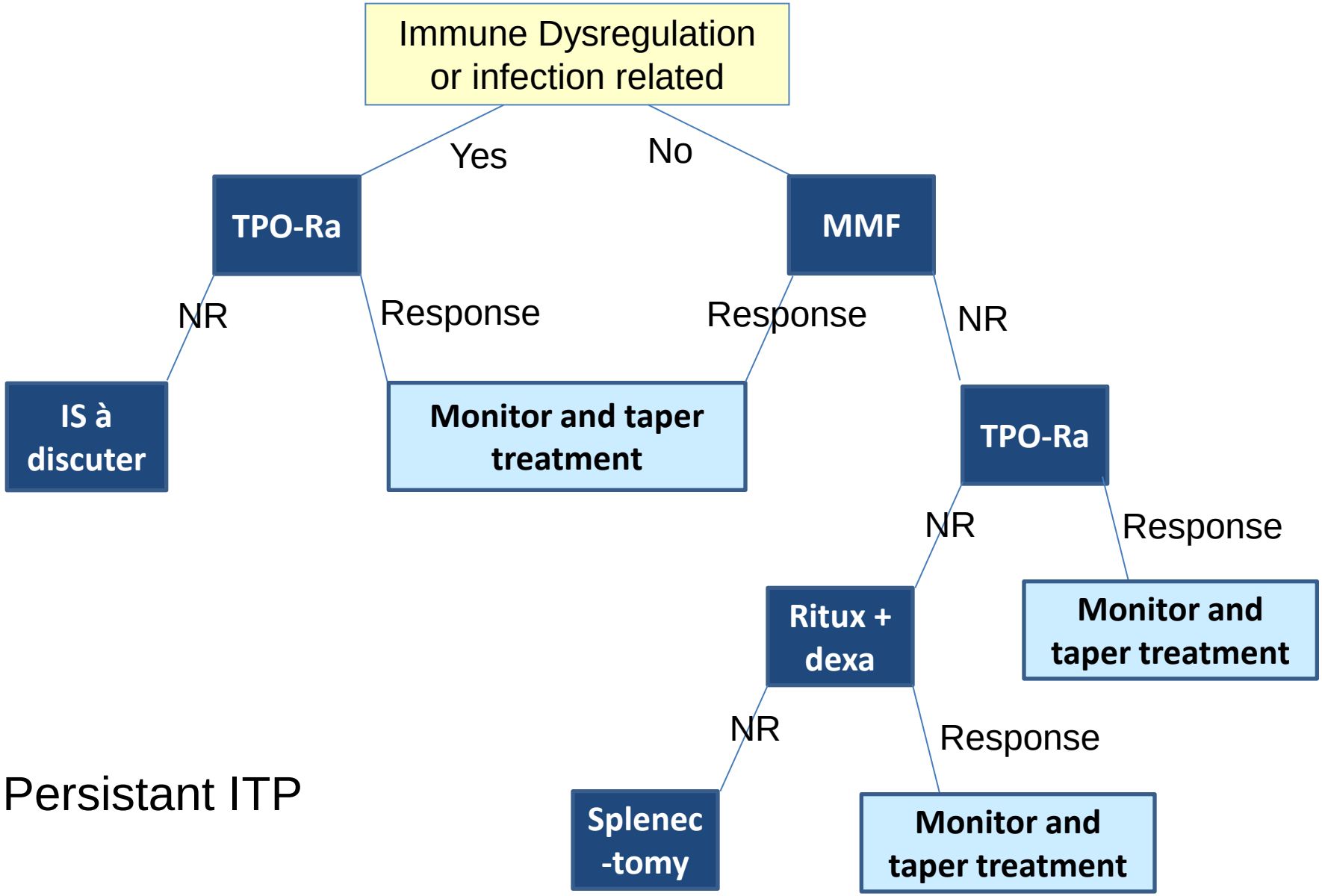
Nichola Cooper

Hammersmith Hospital, Imperial College, London, UK

“We usually recommend treatment for ITP with less than 10 G/L”

Decision to treat between 10 and 30 G/L depends on Age / activity, psychological impact of low platelets / fatigue, bleeding and bruising symptoms, other comorbidity

Anti-D remains a useful agent



Persistant ITP

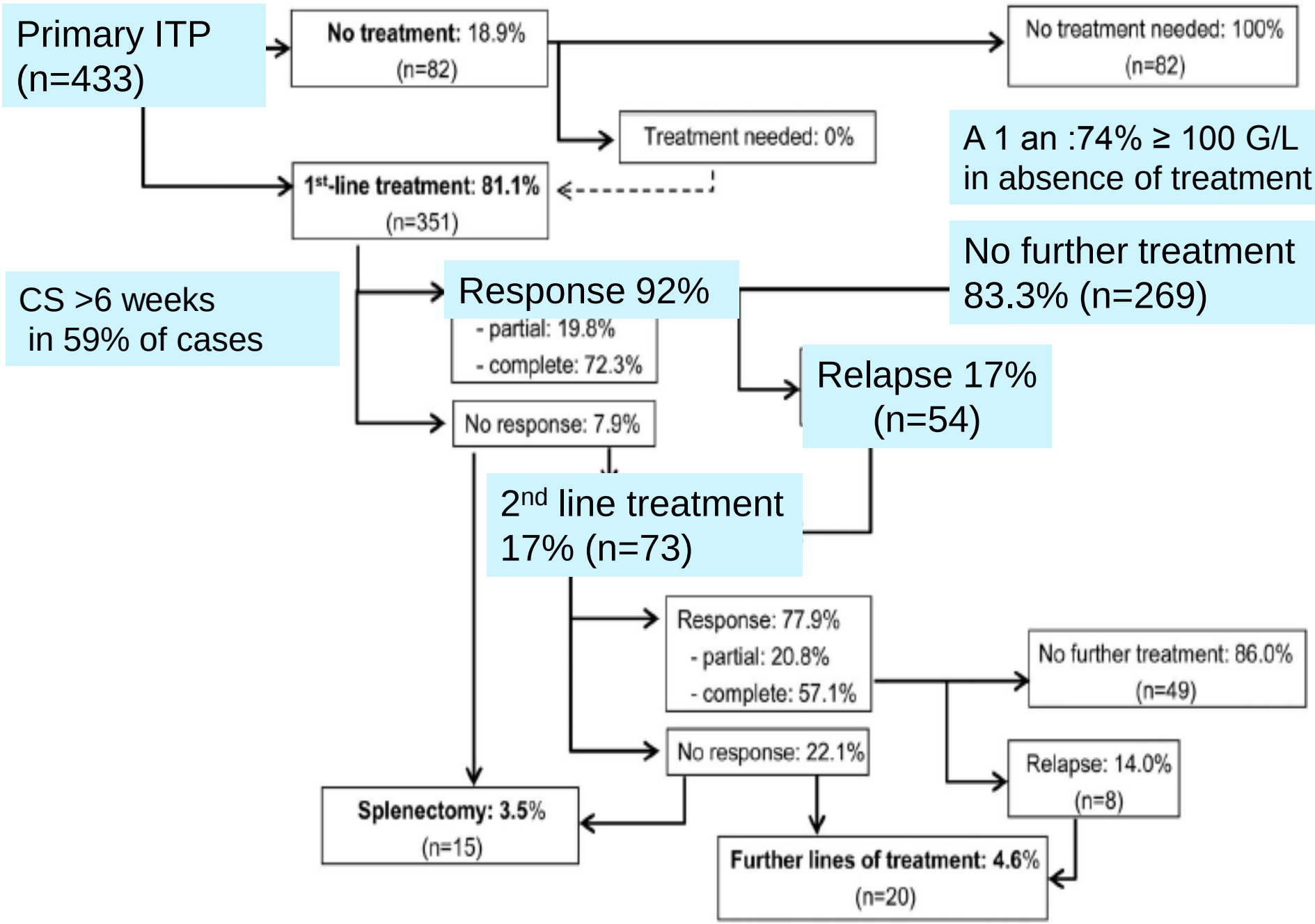
HEMATOLOGY, 2017
http://dx.doi.org/10.1080/10245332.2017.1311442

Taylor & Francis
Taylor & Francis Group

Characteristics and management of primary and other immune thrombocytopenias: Spanish registry study

Javier Palau[a], Esther Sancho[b], Magdalena Herrera[c], Sol Sánchez[d], María Eva Mingot[e], Rosa Isabel Upegui[f], Mª José Rodríguez Salazar[g], Fátima de la Cruz[h], Mª Cristina Fernández[i], Tomás José González López[j], José Julio Hernández[k], Eduardo Ríos[l], Mª Fernanda López-Fernández[m], Marta García[n], José-Ángel Hernández[o] and Miguel A. Sanz[a,p]

Observational registry in Spain 2009-2011 : ITP diagnosed within the last 6 months
484 patients : 87.6% adults, 56% women, 10.5% secondary ITP
Median platelet count :12 × 109/L
72% bleeding symptoms


Primary ITP
(n=433)
No treatment: 18.9%
(n=82)
No treatment needed: 100%
(n=82)
Treatment needed: 0%
A 1 an :74% ≥ 100 G/L
in absence of treatment
1st-line treatment: 81.1%
(n=351)
CS >6 weeks
in 59% of cases
Response 92%
- partial: 19.8%
- complete: 72.3%
No further treatment
83.3% (n=269)
Relapse 17%
(n=54)
No response: 7.9%
2nd line treatment
17% (n=73)
Response: 77.9%
- partial: 20.8%
- complete: 57.1%
No further treatment: 86.0%
(n=49)
No response: 22.1%
Relapse: 14.0%
(n=8)
Splenectomy: 3.5%
(n=15)
Further lines of treatment: 4.6%
(n=20)

Received: 13 December 2016 | Revised: 21 February 2017 | Accepted: 21 February 2017

DOI 10.1002/ajh.24702

RESEARCH ARTICLE

WILEY AJH

Newly diagnosed immune thrombocytopenia adults: Clinical epidemiology, exposure to treatments, and evolution. Results of the CARMEN multicenter prospective cohort

Guillaume Moulis[1,2,3] | Johanne Germain[3] | Thibault Comont[4] | Natacha Brun[5] | Claire Dingremont[6] | Brice Castel[7] | Sophie Arista[8] | Laurent Sailler[1,2,3] | Maryse Lapeyre-Mestre[2,3,9] | Odile Beyne-Rauzy[4] | Bertrand Godeau[10] | Daniel Adoue[4] | The CARMEN Investigators Group†

BJOG 2017 – British Journal of Obstetrics & Gynaecology.

Severe Primary Autoimmune Thrombocytopenia (ITP) in Pregnancy: a National Cohort Study

Care, A[1], Pavord, S[2], Knight, M[3], Alfirevic Z[1].

[1]Centre for Women and Children's Health Research, University of Liverpool, Liverpool Women's Hospital, Crown Street, L8 7SS

[2]Oxford University Hospitals, Old Road, Headington, Oxford, OX3 7LE

[3]National Perinatal Epidemiology Unit (NPEU), Nuffield Department of Population Health, University of Oxford, Old Road Campus, Headington, Oxford, OX3 7LF

Pop : Women with severe ITP <50 x 109/l in pregnancy *or* before 2013- 2015 from all UK Consultant led obstetric units.

Results

- Incidence of severe ITP in pregnancy = 0.83 per 10,000 maternities (n=107)
- 22 pregnant women : No therapy during pregnancy
- 85 had therapy. IVIG : 20% / CS + IVIG : 32% / CS : 45%
- 35% reported some symptoms of ITP in their pregnancy
- Postpartum haemorrhage (51%) : + frequent /general pregnant pop (5-10%).
- No neonates required treatment for thrombocytopenia
- No cases of neonatal intracranial bleeding.

Conclusion = Management of severe ITP in pregnancy = **exceptionally** low morbidity and mortality for the neonate.

Table 3. Maternal Outcomes of 105 Women with Severe ITP in the UK					
	No Rx (n=22)	Steroids (n = 38)	IVIG (n = 17)	Steroids + IVIG (n = 28)	Total (n = 105)
Epidural Haematoma, n (%)	0	0	0	0	0
Perineal Haematoma, n (%)	0	0	0	0	0
CS Wound Haematoma, n (%)	0	0	0	0	0
Estimated Blood Loss, median (range), *ml*	500 (150–2000)	400 (100 – 2500)	500 (200 – 2200)	500 (100 – 3000)	500 (100 – 3000)
Postpartum Haemorrhage, n (%)	10 (45)	17 (45)	9 (53)	18 (64)	54 (51)
ITU Admission **	0	0	0	0	0
Hysterectomy due to PPH, n (%)**	0	0	0	0	0
Psychotic post-partum depression, n (%)	0	1 (3)	0	0	1 (1)
Death, n, (0%)	0	0	0	0	0

Table 4. Neonatal Outcomes for 108 infants (106 livebirths) of 105 women* with severe maternal ITP

	No Rx (n=22)	Steroids (n=39)	IVIg (n=19)	Steroids + IVIG (n=28)	Total (n = 108)
Miscarriage, n (%)	1 (4)	0	0	0	1 (1)
Stillbirth, n (%)	1 (4)	0	0	0	1 (1)
Birthweight (g)[a]	3123 (790 – 4900)	3340 (2360-5020)	3250 (1860 – 4135)	3230 (2035– 3990)	3233 (790– 5020)
Cord Platelet count x 10^9/l[a]	174 (59 – 350)	212 (76 – 342)	245 (79 – 326)	193 (88 – 373)	193 (59 – 373)
Recorded	9 (38)	23 (58)	9 (47)	17 (61)	58 (54)
Not taken/No result	15 (62)	16 (42)	10 (53)	11 (39)	52 (48)
Neonatal Thrombocytopenia within First Week, n, (%)					
Yes	6 (27)	7 (18)	2 (11)	8 (29)	20 (19)
No	9 (41)	21 (54)	13 (68)	12 (43)	58 (54)
Unknown / Not recorded	7 (32)	11 (28)	4 (21)	8 (29)	30 (28)
Platelet Nadir					
<20 x 10^9/l	0	0	0	0	0
20-50 x 10^9/l	0	0	0	3 (11)	3 (3)
51 – 100 x 10^9/l	4 (18)	2 (5)	1 (5)	2 (7)	9 (8)
150 – 100 x 10^9/l	2 (9)	5 (13)	1 (5)	3 (11)	11 (10)
Neonatal sepsis or other cause of thrombocytopenia, n, (%)	0	1 (3)	0	1 (4)	2 (2)
Evidence of spontaneous recovery prior to discharge, n (%)	6 (100)	7 (100)	2 (100)	1**	16 (100)
Admissions to NICU, n (%)	0	2 (5)	1(5)	4 (15)	7 (7)
Transcranial USS, n (%)	1 (5)	1 (3)	0	0	2 (2)
Intracranial Haemorrhage, n (%)	0	0	0	0	0
Death, n (%)	0	0	0	0	0

Received: 4 October 2016 | Revised: 27 February 2017 | Accepted: 18 March 2017
DOI: 10.1002/pbc.26598

RESEARCH ARTICLE

WILEY Pediatric Blood & Cancer aspho

Clinical outcome of childhood chronic immune thrombocytopenia: A 38-year experience from a single tertiary center in Thailand

Thirachit Chotsampancharoen[1] | Pornpun Sripornsawan[1] | Sarapee Duangchoo[1] | Malai Wongchanchailert[1] | Edward McNeil[2]

Aim : to determine clinical outcomes and factors influencing remission in childhood chronic ITP.

38-year rétrospective study : 113 chronic ITP aged 0–15 years

Results:

- Traitement reçus : - Oral prednisolone : n=86 (76.2%)
  - IVIG : n=17 (15%)
  - Abstention :10 (8.8%).
  - Splenectomy : 7(6%) patients
- Spontaneous complete remission rates at 3, 5, 10, and 20 years =25, 43, 60, and 75%
- Factors influencing remission :
  - Platelets >60 G/L at the onset of chronic ITP (HR]: 7.24, 95% CI: 3.0–17.5)
  - Treatment with IVIG (HR: 0.37, 95% CI:0.16–0.84).
  - Age, gender, bleeding manifestations, history of preceding infection and vaccination = not predictive of remission.

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Traitements

EXPERIMENTAL AND THERAPEUTIC MEDICINE 13: 519-522, 2017

Analysis of clinical effects and mechanism of recombinant human interleukin-11 with glucocorticoids for treatment of idiopathic thrombocytopenic purpura

XIFENG WU[1], LIJUAN WANG[1], LIN SUN[1], TANTAN LI[1] and XUEHONG RAN[2]

[1]Department of Hematology, Laiwu City People's Hospital, Laiwu, Shandong 271100;
[2]Department of Hematology, Weifang People's Hospital, Weifang, Shandong 261041, P.R. China

80 ITP randomisés en CS ou CS + r human interleukin-11 (IL-11)

Groups	Case	Marked effectiveness	Effectiveness	Ineffectiveness	Effective rate
Control	40	7 (17.5)	16 (40.0)	17 (42.5)	23 (57.5)
Observation	40	15 (37.5)	17 (42.5)	8 (20.0)	32 (80.0)
χ^2			6.179		
P-value			0.046		

Table II. Comparison of onset time, platelet recovery level, platelet antibody positive rate.

Groups	Case	Onset time (days)	Platelet recovery level ($x10^9/l$)	Platelet antibody positive rate [case (%)]
Control	40	4.2±0.6	78.5±14.2	11 (27.5)
Observation	40	3.5±0.7	92.6±13.5	4 (10.0)
t (χ^2)		5.632	5.867	4.021
P-value		0.034	0.030	0.045

Diminution des CD4+CD25+ regulatory T cells dans les 2 groupes mais plus importante dans le groupe IL-11 ($P<0.05$).

bjh research paper

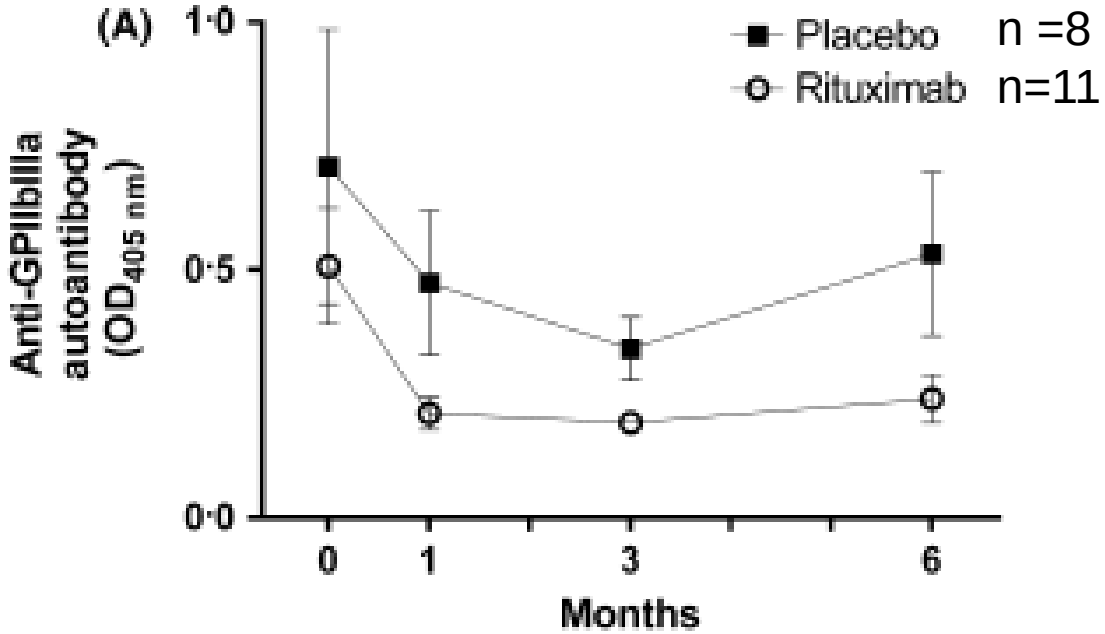
The effect of rituximab on anti-platelet autoantibody levels in patients with immune thrombocytopenia

Donald M. Arnold,[1,2,3]
John R. Vrbensky,[1] Nadia Karim,[1]
James W. Smith,[1] Yang Liu,[1,2]
Nikola Ivetic,[4] John G. Kelton[1,2] and
Ishac Nazy[1,2]

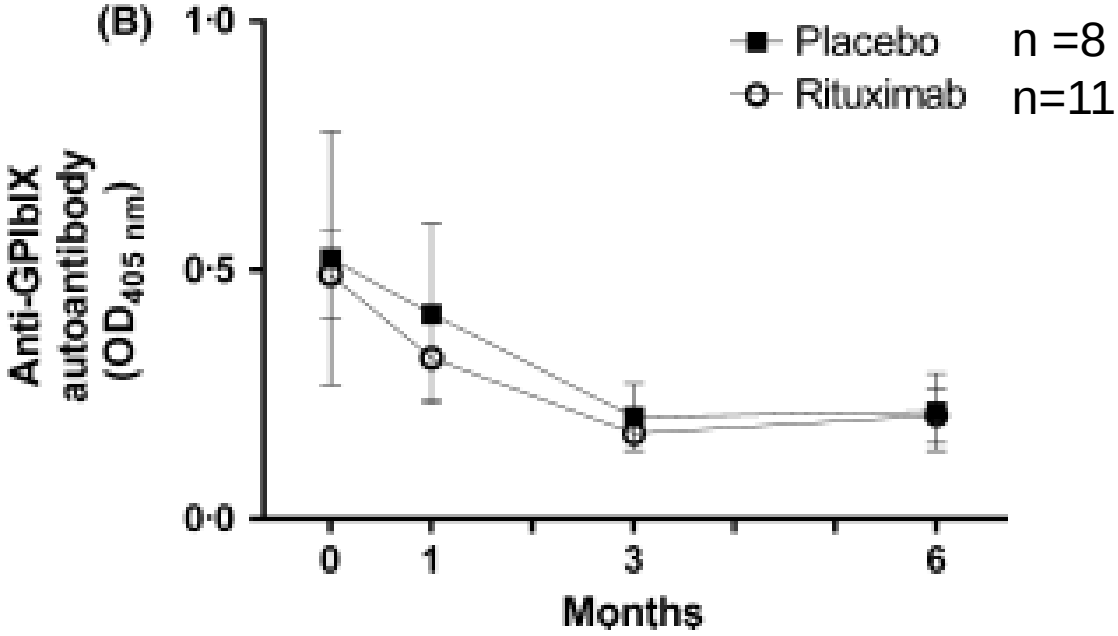
- RTX associé à une diminution des taux d'Ac anti-GP IIbIIIa and anti-GPIbIX ?
- La diminution des Ac corrélée à la réponse ?

A case-control study nested within a previous randomized controlled trial of standard therapy plus adjuvant rituximab or placebo.

55 patients avec recherche des Ac at baseline

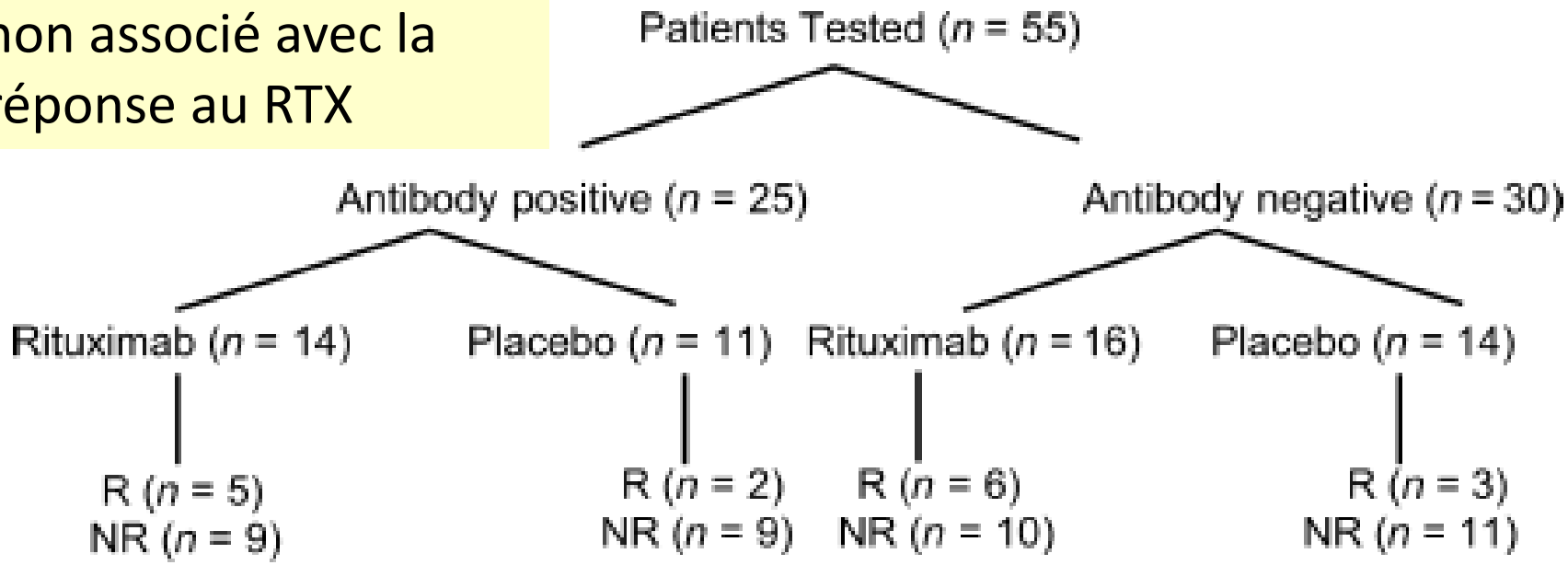


Baisse des Anti-GPIIbIIIa sous RTX

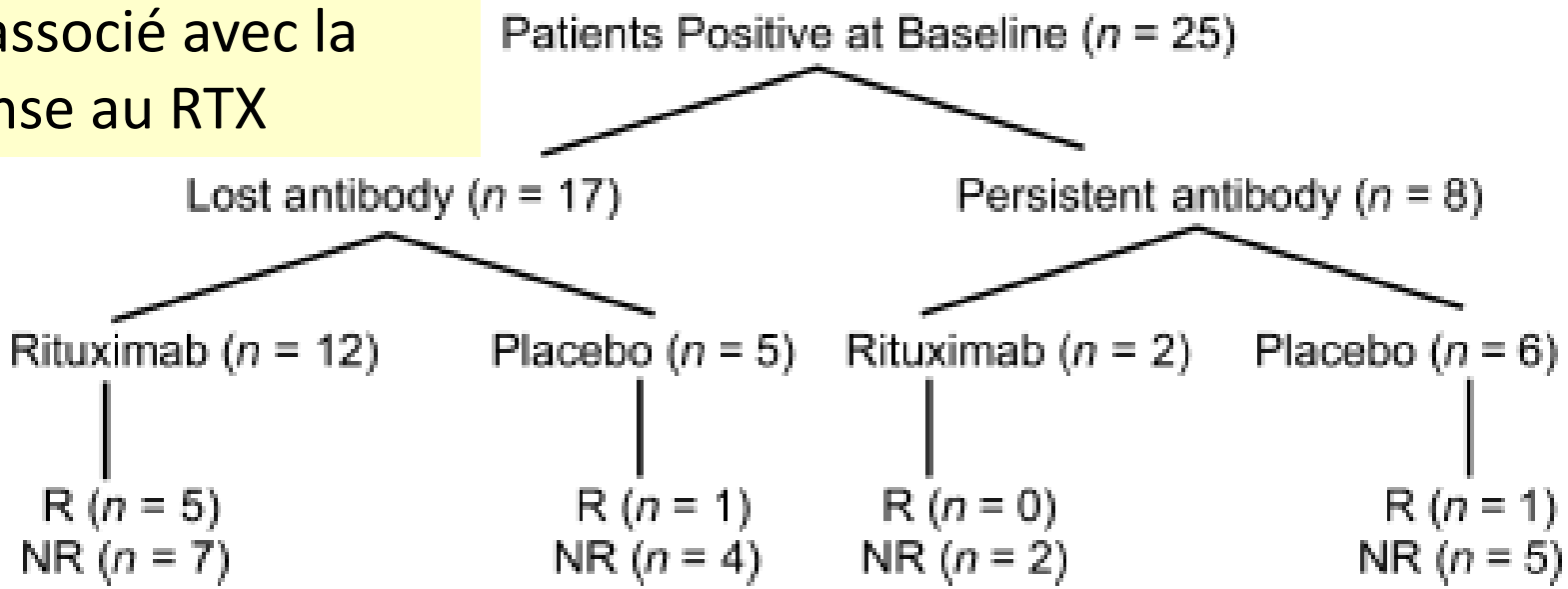


Pas de baisse des Anti-GPIbIX sous RTX

Présence d'un Ac = non associé avec la réponse au RTX



Perte de l'Ac = non associé avec la réponse au RTX



blood®
Prepublished online May 3, 2017;
doi:10.1182/blood-2016-11-751719

PIFT and MAIPA full concordance
7 pts (4 NR and 3 PR) negative
23 pts (3 NR, 3 MR, 7 PR, 10 CR) positive

Lack of detectable platelet autoantibodies is correlated with non-responsiveness to rituximab treatment in ITP patients

direct platelet immunofluorescence test

	detectable platelet-associated antibodies at baseline		
	Positive	Negative	total
CR	16 (20%)	1 (5%)	17
PR	19 (24%)	3 (15%)	22
MR	8 (10%)	0 (0%)	8
NR	36 (46%)	16 (80%)	52
total	79	20	99

***

European Journal of Haematology

European Journal of Haematology 98 (371–377)

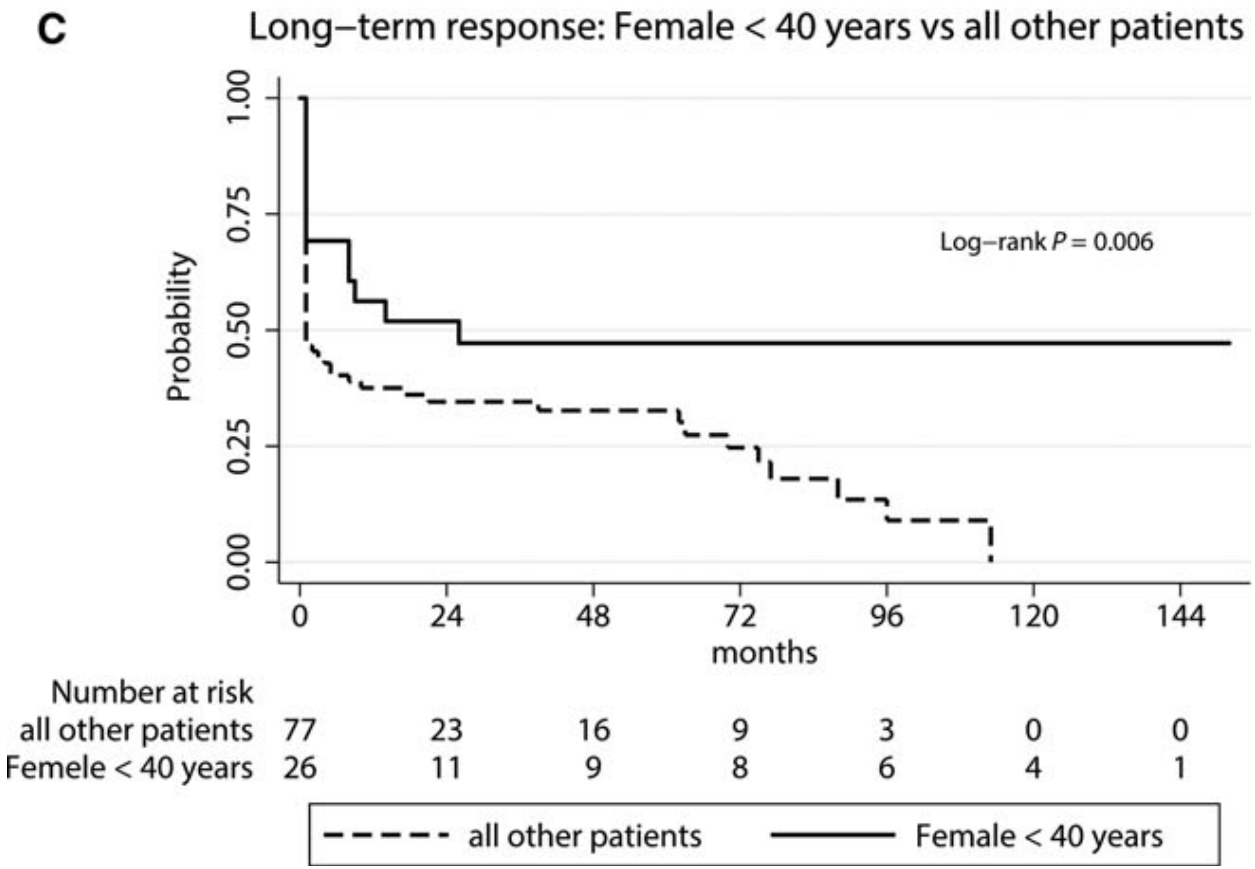
ORIGINAL ARTICLE

Rituximab in immune thrombocytopenia: gender, age, and response as predictors of long-term response

Miriam Marangon[1], Nicola Vianelli[1], Francesca Palandri[1], Maria Gabriella Mazzucconi[2], Cristina Santoro[2], Wilma Barcellini[3], Bruno Fattizzo[3], Stefano Volpetti[4], Elisa Lucchini[4], Nicola Polverelli[1], Monica Carpenedo[5], Miriam Isola[6], Renato Fanin[4], Francesco Zaja[4]

Evaluable patients	103
Age	
Median age, years [range]	46 [15–82]
Patients younger than 40 yr	38 (37%)
Sex	
Male	42 (41%)
Female	61 (59%)
TP duration	
Median interval, months [range]	20 [1–403]
Number of previous therapies	
1 line of therapy	49 (48%)
2 lines of therapy	37 (36%)
≥3 lines of therapy	17 (16%)
Previous TPO receptor agonists	4 (4%)
Splenectomy	
No	92 (89%)
Yes	11 (11%)
Platelet count	
Median platelet count before rituximab (x 10^9/L)	15 [1–217]

median period of observation = 5 ans



- Patients < 40 yr = higher probability to achieve CR
- Women < 40 yr = higher probability to achieve R and CR
- Estimated LTR rate = 36% and 31% after 48 and 72 months, respectively
- Efficiency of RTX higher in younger women, with LTR rate possibly approaching that of splenectomy

Hematology Reports 2017; volume 9:703

The efficacy of colchicine and dapsone combination therapy in relapsed immune thrombocytopenia

Thanawat Rattanathammethee, Wasan Theerajangkhaphichai, Ekarat Rattarittamrong, Sasinee Hantrakool, Chatree Chai-Adisaksopha, Lalita Norasetthada, Adisak Tantiworawit

Division of Hematology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

Colchicine + dapsone for relapsed and refractory ITP

- Retrospective study of 64 ITP patients
- Relapsed ITP : 65.6%
- Platelet 22.6×109/L
- Response rate : 82.8% (75.0% = CR)
- Median time to response 8 weeks.
- Stop steroid treatment in 30 patients (50%)
- Side effect :12.5%

AJH WILEY E79

Received: 8 February 2017 | Revised: 17 February 2017 | Accepted: 20 February 2017

DOI 10.1002/ajh.24698

Evaluation of the efficiency of hydroxychloroquine in treating children with immune thrombocytopenia (ITP)

CEREVANCE

46 enfants : 30 filles /16 garçons
6 aigus / 13 persistants / 27 chroniques
ANA + : 24 (55%)
Traitement de seconde ligne : 37 (80%)
35% de RC (dont 75% ANA+)
60% (R ou CR) à 12 mois

E80 WILEY AJH

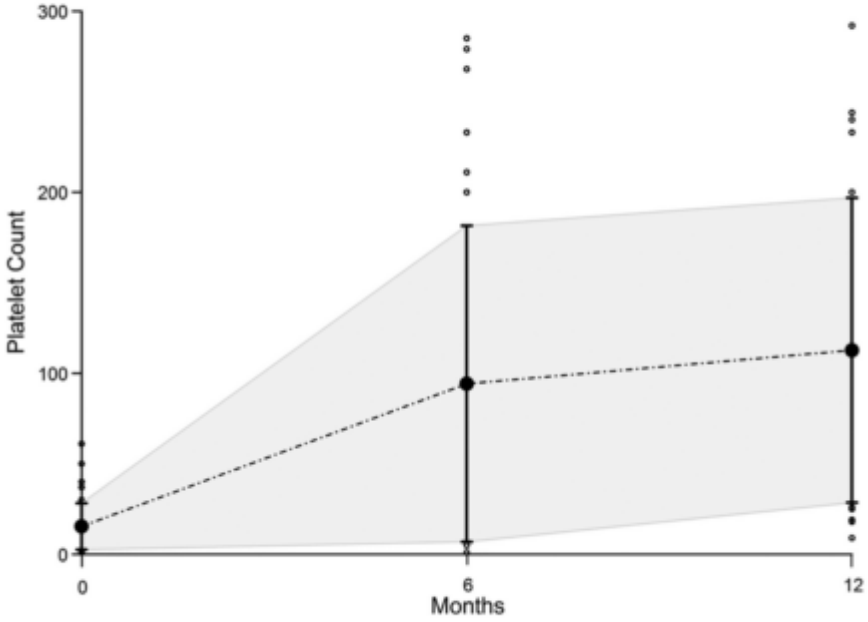


FIGURE 1 Response to hydroxychloroquine and platelets counts

Medicine (Baltimore). 2016 Nov;

Observational Study

Medicine®

OPEN

Long-term complications of splenectomy in adult immune thrombocytopenia

Lan-Huong Thai[a], Matthieu Mahévas[a,*], Françoise Roudot-Thoraval[b], Nicolas Limal[a], Laetitia Languille[a], Guillaume Dumas[a], Mehdi Khellaf[a], Philippe Bierling[a], Marc Michel[a], Bertrand Godeau[a]

Etude rétrospective :

83 ITP splénectomisés suivis pdt 10 ans ou + versus 83 ITP non splénectomisés

Caractéristiques des ITP patients

	Splénectomie	Pas de Splénectomie	
Male/female, no.	23/60	23/60	
Age at ITP diagnosis, years, median (range)	37 (3–92)	38 (3–93)	0.765
Duration of follow-up after splenectomy, months, median (range) or duration of follow-up after theoretical date of splenectomy	192 (1–528)	192 (2–528)	—
Severe hemorrhagic event (visceral hemorrhage),* no. (%)	22 (26)	7 (8)	0.004
No. of ITP treatments,* median (range)	4 (1–17)	2 (1–6)	<0.001
Medical treatment,* no. (%)			0.008
Immunosuppressive treatments	29 (35)	5 (6)	
Rituximab	11 (13)	11 (13)	
TPO receptor agonists	8 (23)	7 (8)	
Ongoing treatment at the last visit in living patients, no. (%)	10/66 (15)	16/74 (21)	0.387
Platelet count at the last follow-up in living patients, no. (%)	/66	/74	
$>100 \times 10^9$/L	46 (70)	52 (70)	0.941
$\geq 30 \times 10^9$/L	19 (29)	20 (27)	
$<30 \times 10^9$/L	1 (1)	2 (3)	

Evénements thromboemboliques

	Splenectomized patients, n=83	Controls, n=83	*P*
No. of patients with at least 1 VTE, no. (%)	13 (16)	2 (2)	0.005
Patients presenting at least 1 associated confounding risk factor of VTE,* no. (%)	7 (54)	2 (100)	0.15
Early postoperative	5 (6)		
Portal vein thrombosis	3		
PE±DVT	2		
Late postoperative	10 (12)	2 (2)	0.032
Portal vein thrombosis	1	0	
DVT	4	0	
PE±DVT	5	2	
Recurrence of VTE, no.	4	1	
Postembolic pulmonary arterial hypertension, no.	2	1	

Evénements cardio-vasculaires

No. of patients with at least 1 CV event, no. (%)	10 (12)	4 (5)	0.143
CV risk factors,[†] median (range)	3 (0–6)	4 (1–5)	
Site of CV events, no.			
Myocardial infarction	3	3	
Ischemic stroke, transient ischemic attack	7	2	0.106

Infections

No. of patients with at least 1 bacterial infections, no. (%)	18 (22)	12 (14)	0.335
No. of infections,	26	13	
Site of infection, no. (%)			
Lung	14/26 (54)	6/13 (46)	
Gastrointestinal/urogenital/skin	7/26 (39)	7/13 (54)	
Unknown	5/26 (19)	0	
Microbiology documentation, no. (%)	9/26 (35)	3/13 (23)	
Streptococcus pneumoniae	4	1	
Haemophilus influenzae	1	0	
Neisseria meningitidis	0	0	
Other	5	2	
Infectious events requiring hospitalization, no. (%)	26/26 (100)	8/13 (61.5)	0.002
Severe sepsis or septic shock, no. (%)	5/26 (19)	0 (0)	0.149
Death due to septic shock, no. (%)	3/18 (17)	0 (0)	0.255
OPSI, no.	1	0	

Cancer

No. of patients with at least 1 cancer and/or malignant hemopathy, no. (%)	12 (14)	10 (12)	0.789
Urinary tract (prostate, renal, bladder)	5	2	
Skin	4	3	
Colorectal	2	1	
Gynecological (breast, uterus)	2	3	
Lung	0	1	
Malignant hemopathy	5	2	

Morbi/Mortalité

	Response (n = 43)	Refractory or relapsed disease (n = 40)	Controls (n = 83)
Patients, no. (%)			
VTE	8 (19)	5 (12.5)	2 (2)
CV event	3 (7)	7 (17.5)	4 (5)
Infectious event	8 (19)	10 (25)	12 (14)
Deaths, no. (%)	6 (14)	11 (27.5)	9 (11)
Age at death, years, median (range)	75 (57–95)	62 (21–94)	81 (51–94)
Cause of death, no.			
Hemorrhage	1	5	0
Infection	1	2	0
VTE	0	0	0
CV disease	0	2	1
Cancer, malignant hemopathy	3	1	2
Other	1	1	4
Unknown	0	1	2

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Nouvelles causes de PTI

Shiuan et al. Journal for ImmunoTherapy of Cancer (2017) 5:8
DOI 10.1186/s40425-017-0210-0

Journal for ImmunoTherapy of Cancer

CASE REPORT Open Access

Thrombocytopenia in patients with melanoma receiving immune checkpoint inhibitor therapy

Eileen Shiuan[1,2†], Kathryn E. Beckermann[3*†], Alpaslan Ozgun[4], Ciara Kelly[5], Meredith McKean[6], Jennifer McQuade[7], Mary Ann Thompson[11], Igor Puzanov[12], John P. Greer[3], Suthee Rapisuwon[8], Michael Postow[9,10], Michael A. Davies[7], Zeynep Eroglu[4] and Douglas Johnson[3]

Idiopathic thrombocytopenic purpura and autoimmune neutropenia induced by prolonged use of Nivolumab in Hodgkin's Lymphoma

A. Bulbul1,2*, **A. Mustafa3**, **S. Chouial1**, **S.Rashad4**
Department of Hematology/Oncology, Kymera Independent Physicians, Carlsbad, NM, USA

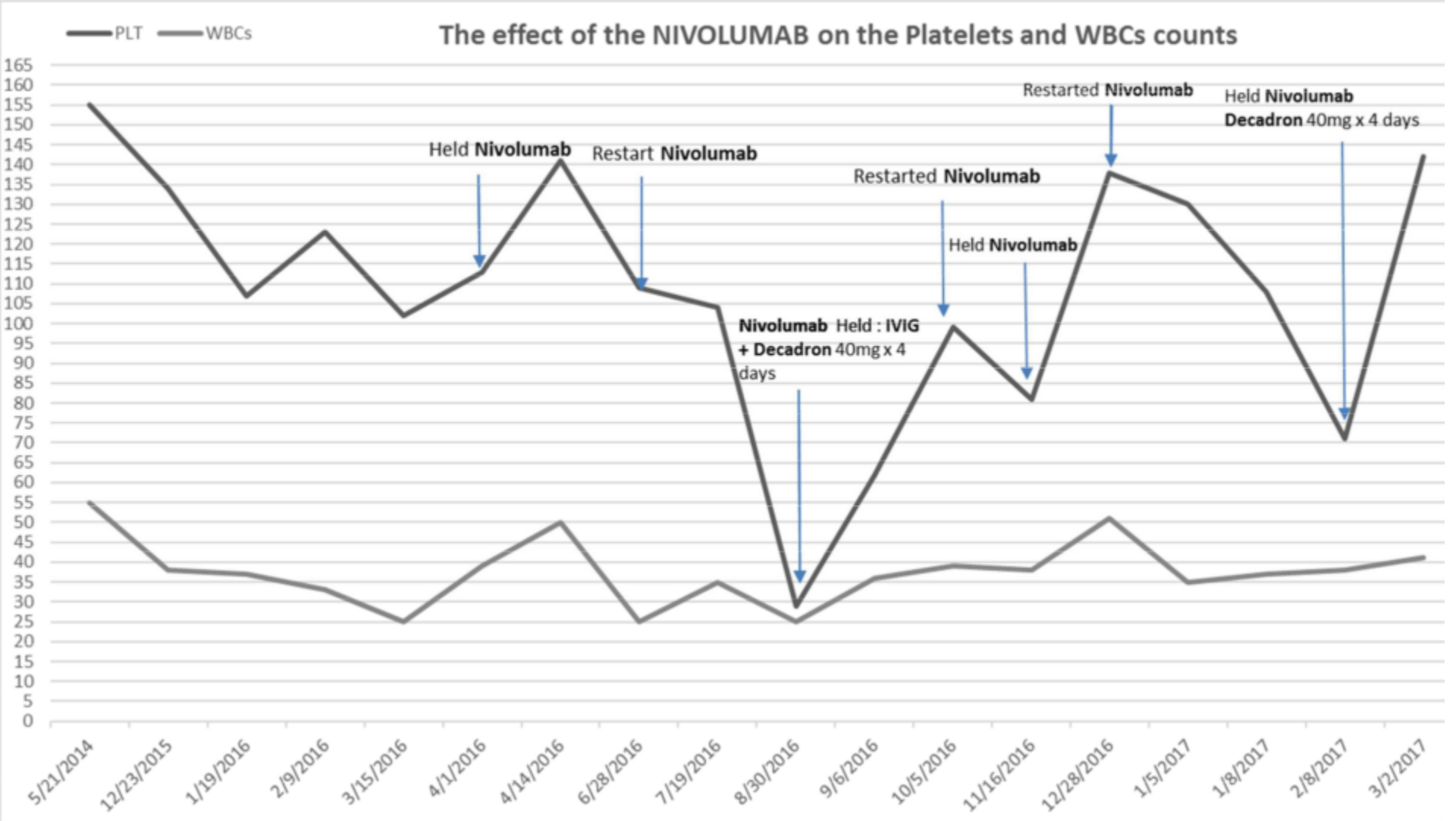
2 cas sévères avec nécessité d'IgIV et de ritux

< 1% sur 2500 mélanomes métastatiques traités
Plusieurs cas chez des Hodgkin

TT : CS avec arrêt temporaire des checkpoint inhibitors

Idiopathic thrombocytopenic purpura and autoimmune neutropenia induced by prolonged use of Nivolumab in Hodgkin's Lymphoma

A. Bulbul[1,2*], A. Mustafa[3], S. Chouial[1], S.Rashad[4]



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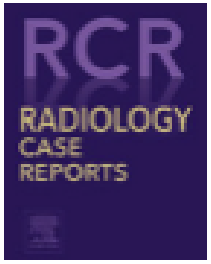
Complication rare

Radiology Case Reports 12 (2017) 278–280

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://Elsevier.com/locate/radcr



Case Report

Submucosal esophageal hematoma precipitated by chronic idiopathic thrombocytopenic purpura

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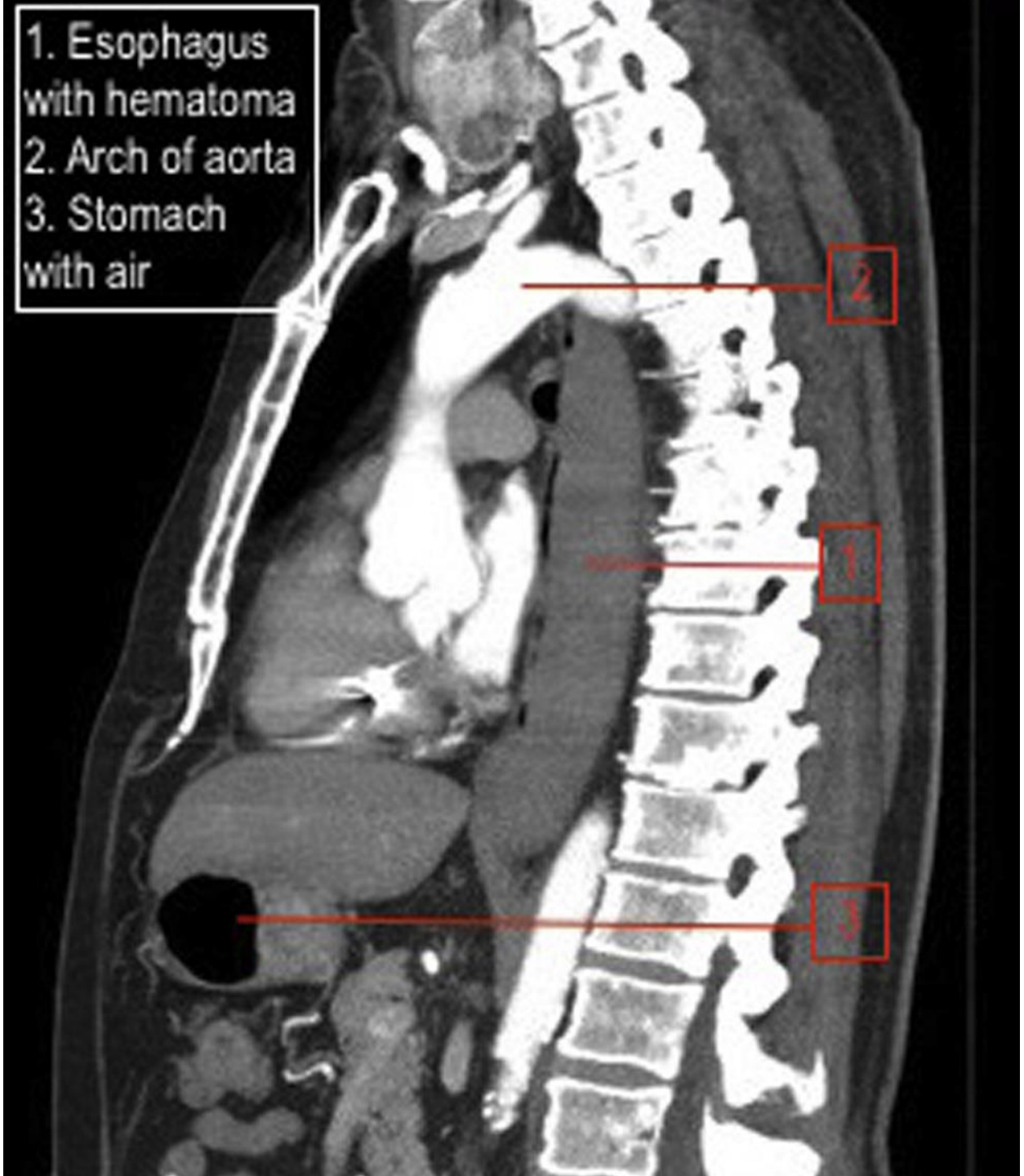
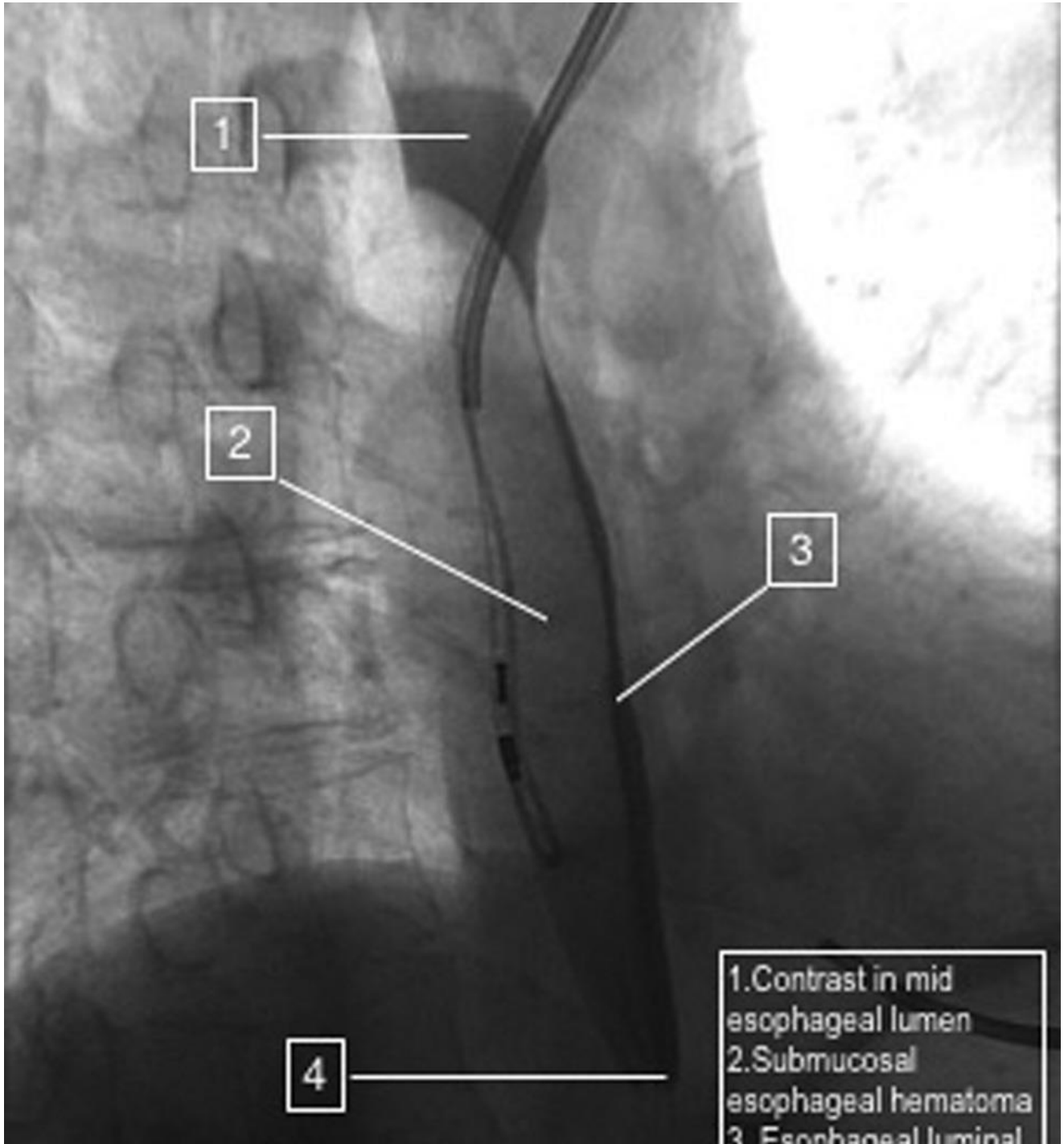
- An 81-year-old male presented to the Emergency with chief
- complaints of chest pain and dysphagia that radiated to the upper abdomen
- illness revealed the chest pain was precipitated suddenly while eating lunch


1. Esophagus
with hematoma
2. Arch of aorta
3. Stomach
with air
2
1
3


1
2
3
4
1.Contrast in mid esophageal lumen
2.Submucosal esophageal hematoma
3. Esophageal luminal

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Traitements

Case Reports of Idiopathic Thrombocytopenia Unresponsive to First-Line Therapies Treated With Traditional Herbal Medicines Based on Syndrome Differentiation

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Table 1. Ingredients and Doses of the Modified *Jigolpieum* Water Extract

Pharmaceutical Name	Total Daily Dose (g/d)
Lycii radicis cortex	15
Moutan cortex	15
Ginseng radix	12
Zingiberis rhizoma siccus	12
Cinnamomi cortex spissus	12
Glycyrrhizae radix	6
Angelicae gigantis radix	6
Cnidii rhizoma	6
Paeoniae radix rubra	6
Rehmanniae radix	6
Poria (Hoelen)	12
Alismatis rhizoma	12

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RESEARCH ARTICLE Open Access

Gonadectomy effects on the risk of immune disorders in the dog: a retrospective study

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TAKE HOME MESSAGE : Conserver vos testicules