Leiden University Medical Center

IVIG therapy in Immune ThrombocytoPenia and FNAIT

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ITP: the problem

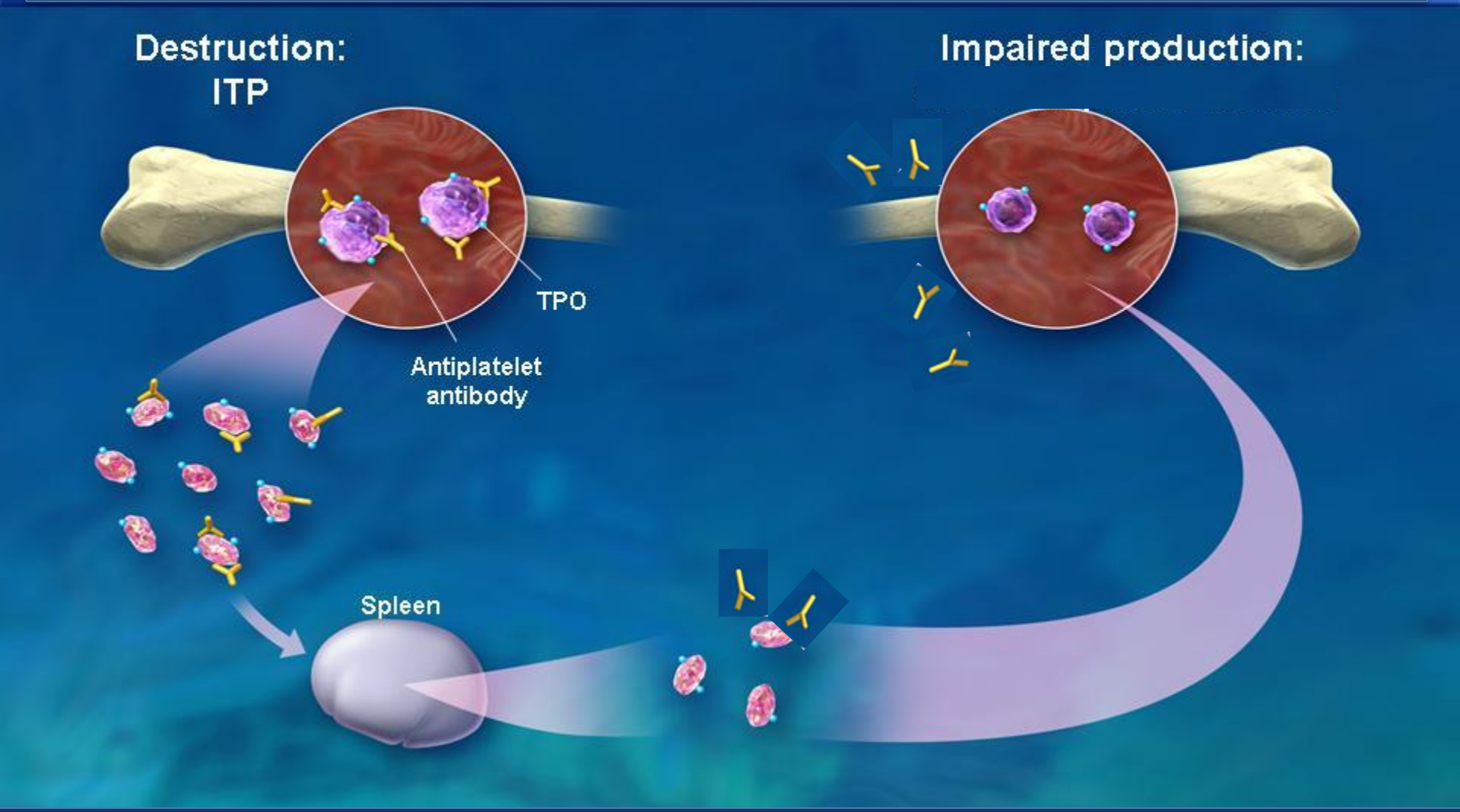
Adults:

- incidence : ± 4 per 100.000 patiënt years
- prevalence: 3,6 - 5,3 per 150.000 inhabitants
- at debut bleeding symptoms and mostly < QoL

Children:

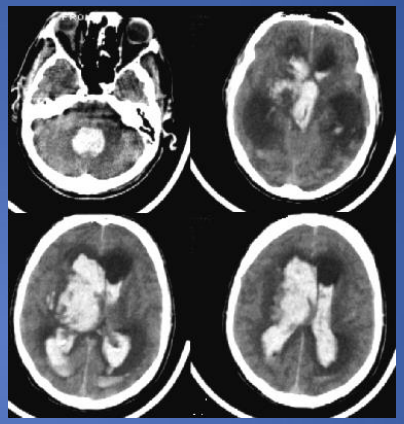
- mostly following infections
- 80-90 % recover within 3 to 12 months
- chronic course 10-25%

Traditional concepts of ITP



Bleeding = treatment indication

Acute bleeding treatment



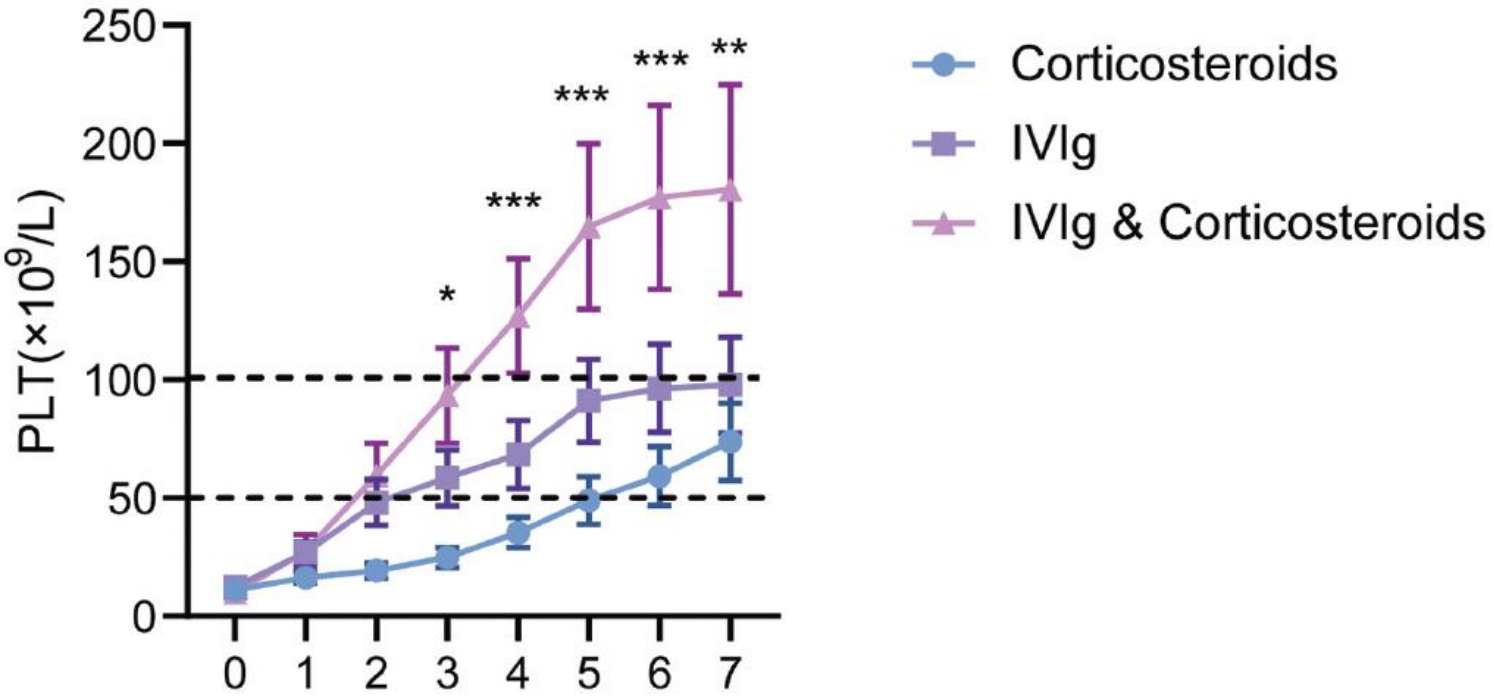
High dose corticosteroids: 50% relapsing

IVIG: max 2 weeks effect)

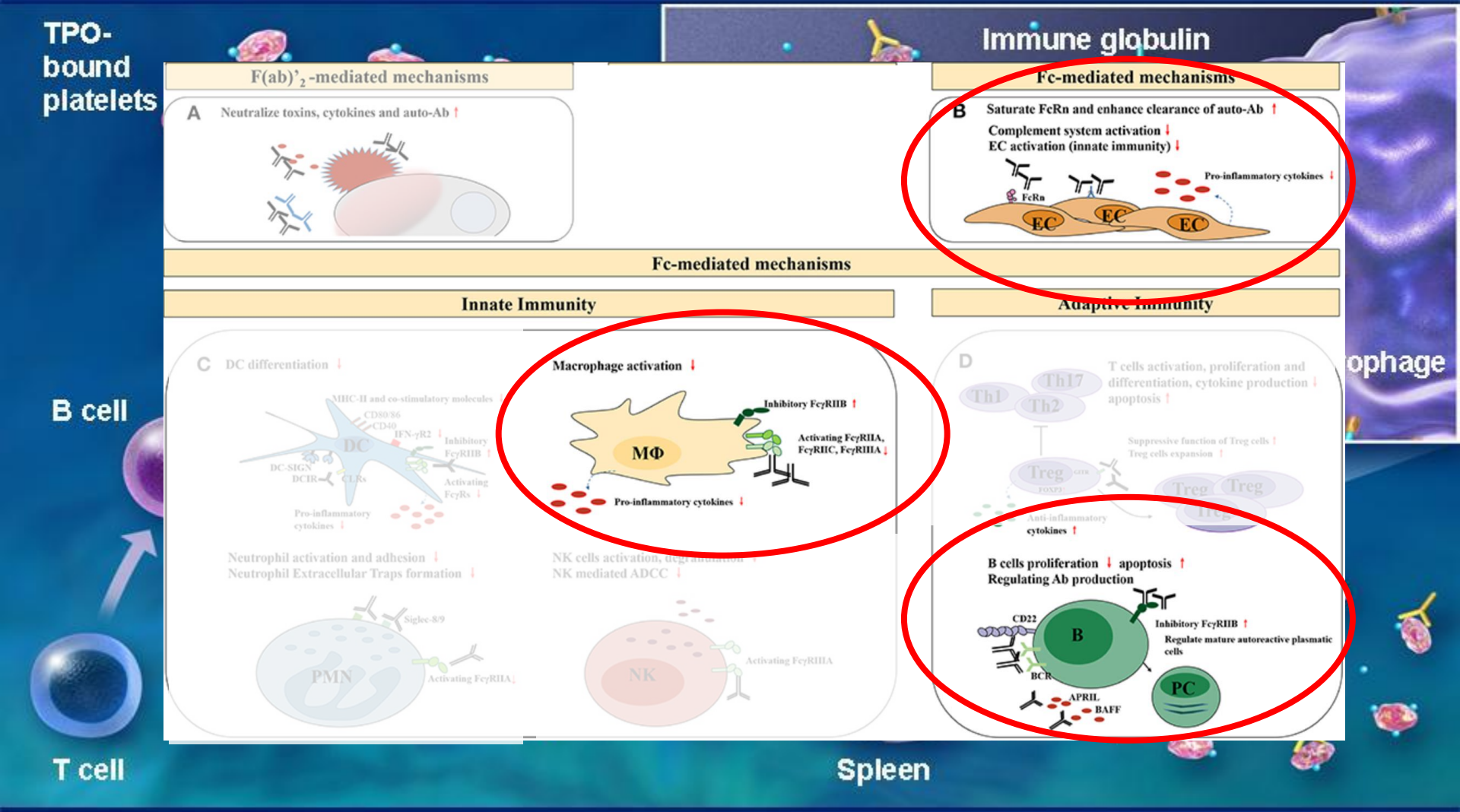
1. Bussel JB. Hematol Oncol Clin North Am 1990; 4:179-191
2. Schipperus et al. Ned Tijdschr Hematol 2013;10:122-131

Efficacy and Safety Analysis of Combination Therapy Consisting of Intravenous Immunoglobulin and Corticosteroids versus Respective Monotherapies in the Treatment of Relapsed ITP in Adults

Lijun Fang et al. *Glob Med Genet 2023;10:87–96*



Immune Thrombocytopenic Purpura Current Treatment Options: Immune Globulin

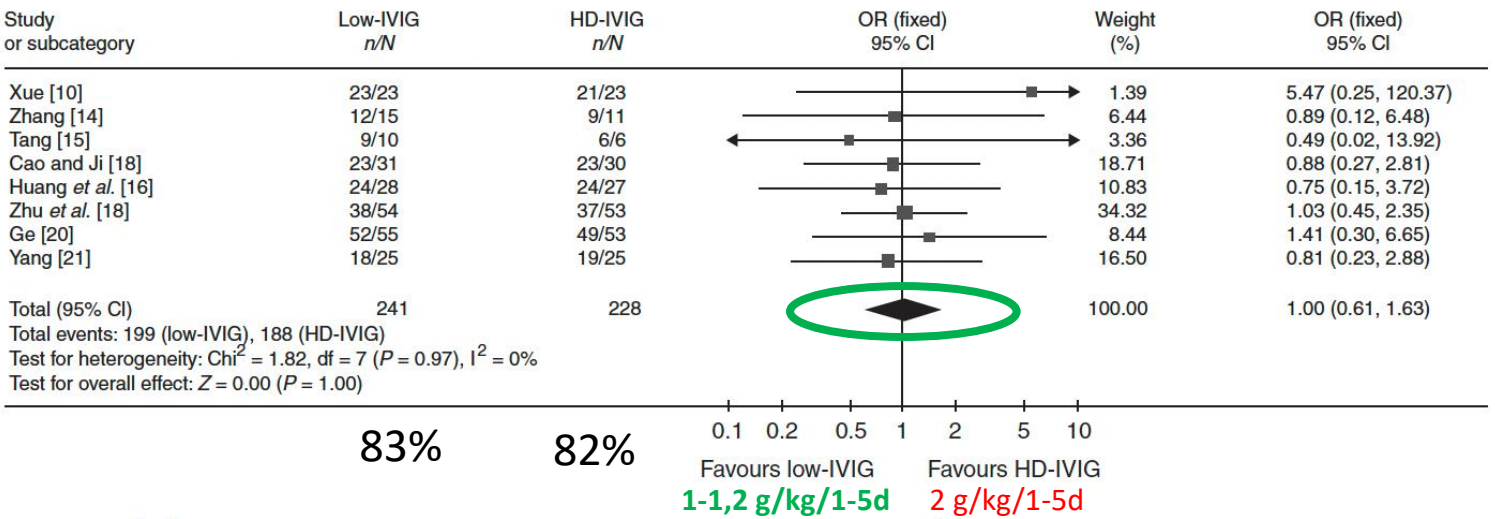


Swab et al. Nat Rev Immunol. 2013;13(3):176-89

Liu et al. Front. Immunol.2020;11:1660-

The efficacy of different dose intravenous immunoglobulin in treating acute idiopathic thrombocytopenic purpura: a meta-analysis of 13 randomized controlled trials

Y-H Qin et al. Blood Coagulation and Fibrinolysis 2010, 21:713–721



83% 82%

Effective rate. Chi^2, χ^2-test; CI, confidence interval; df, degree of freedom; HD, high dose; I^2, heterogeneity index; IVIG, intravenous immunoglobulin; OR, odds ratio.

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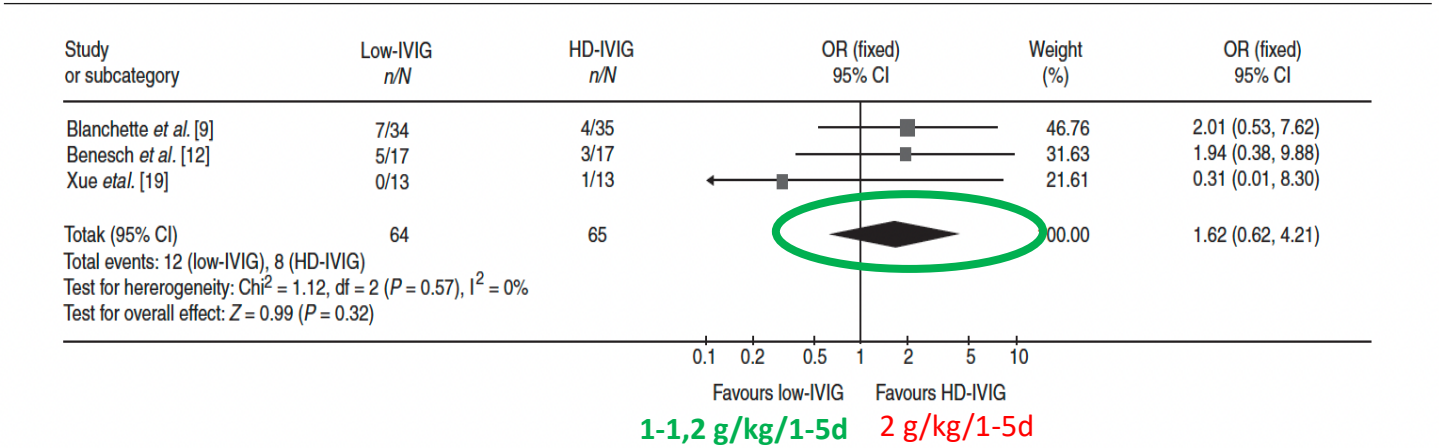
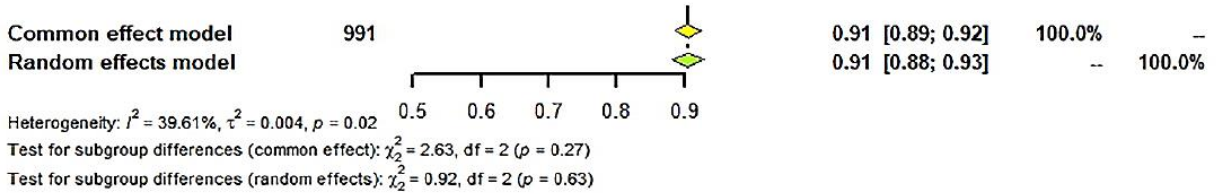


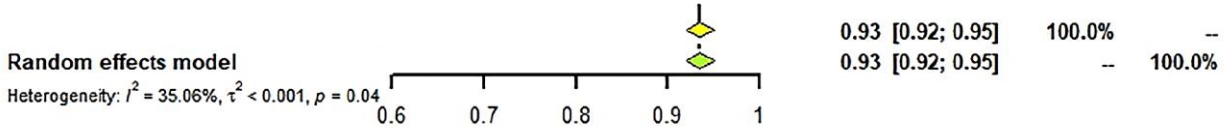
Rate of developing into chronic idiopathic thrombocytopenic purpura. Chi^2, χ^2-test; CI, confidence interval; df, degree of freedom; HD, high dose; I^2, heterogeneity index; IVIG, intravenous immunoglobulin; OR, odds ratio.

Can low-dose intravenous immunoglobulin be an alternative to high-dose intravenous immunoglobulin in the treatment of **children** with newly diagnosed immune thrombocytopenia: a systematic review and meta-analysis (of 25 trials)
Ren X et al. *BMC Pediatrics* (2024) 24:199

Effectivity rate **0,6-1g/kg/1-5d**



Effectivity rate 2 g/kg/5d



TIKI trial: observation (n=100) versus IVIg (0.8 g/kg, single dose; n=100)

blood®

ISSUES FIRST EDITION ABSTRACTS COLLECTIONS

CLINICAL TRIALS AND OBSERVATIONS | AUGUST 30, 2018

Intravenous immunoglobulin vs observation in childhood immune thrombocytopenia: a randomized controlled trial

Clinical Trials & Observations

Katja M. J. Heitink-Pollé, for the TIKI Investigators Cuno S. P. M. Uiterwaal, for the TIKI Investigators
Leendert Porcelijn, for the TIKI Investigators Rienk Y. J. Tamminga, for the TIKI Investigators
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Gestur Vidarsson, for the TIKI Investigators Annemieke G. Laarhoven, for the TIKI Investigators
Masja de Haas, for the TIKI Investigators Marrie C. A. Bruin for the TIKI Investigators

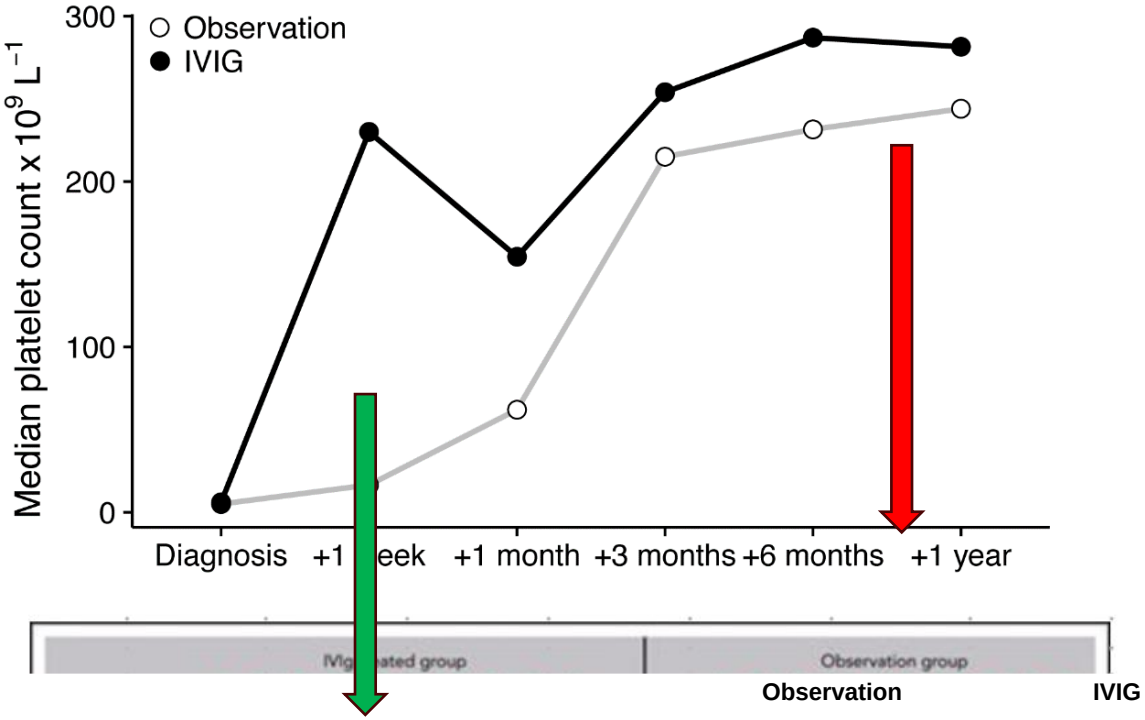
Blood (2018) 132 (9): 883–891.

https://doi.org/10.1182/blood-2018-02-830844

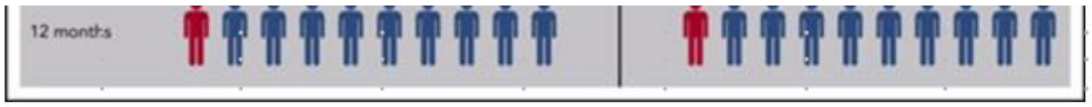
Article history

Childhood ITP: Dutch Workbook Pediatric Haematology; version 2024; E. Huisman et al., MD

Buchanan Score	Bleeding	Symptoms	Management
0	No	No new symptoms	Watchful waiting*
1	Mild	< 100 petechiae; < 5 small hematoma (< 3cm). No mucosal bleeding	Watchful waiting*
2	Moderate	>100 petechiae; >5 large hematoma (< 3cm). No mucosal bleeding	Watchful waiting*
3	Severe	Mild mucosal bleeding (epistaxis, gum-; oropharyngealgastrointestinal, hematuria, menorrhagia, without necessity of interference	**Consult paediatrician-hematologist** Watchful waiting or 7-10 days TXA or if hematuria: IVIG
4		Severe mucosal bleeding, suspicion internal bleeding for which interference is necessary (for example: Hb loss > 1 mmol/l) i.o.m. kinderarts-hematoloog IVIg en Prednison z.n. trombocyten of een erytrocytentransfusie.	**Consult paeditrician-hematologist** and start IVIG with or without Prednison, if necessary platelet and or RBC transfusion



Bleeding		
Grade 2/3, observation	6	0
Grade 3, treatment	3	1
Grade 4/5	9	1



Heitink-Pollé *et al., BLOOD 2018*

Is dosing of therapeutic immunoglobulins optimal? A review of a three-decade long debate in Europe *Jacqueline Kerr et al. Frontiers in immunology 2014*

WITH relevant

Primary immune thrombocytopenia (ITP), in patients at
bleeding or prior to surgery to correct the platelet count.

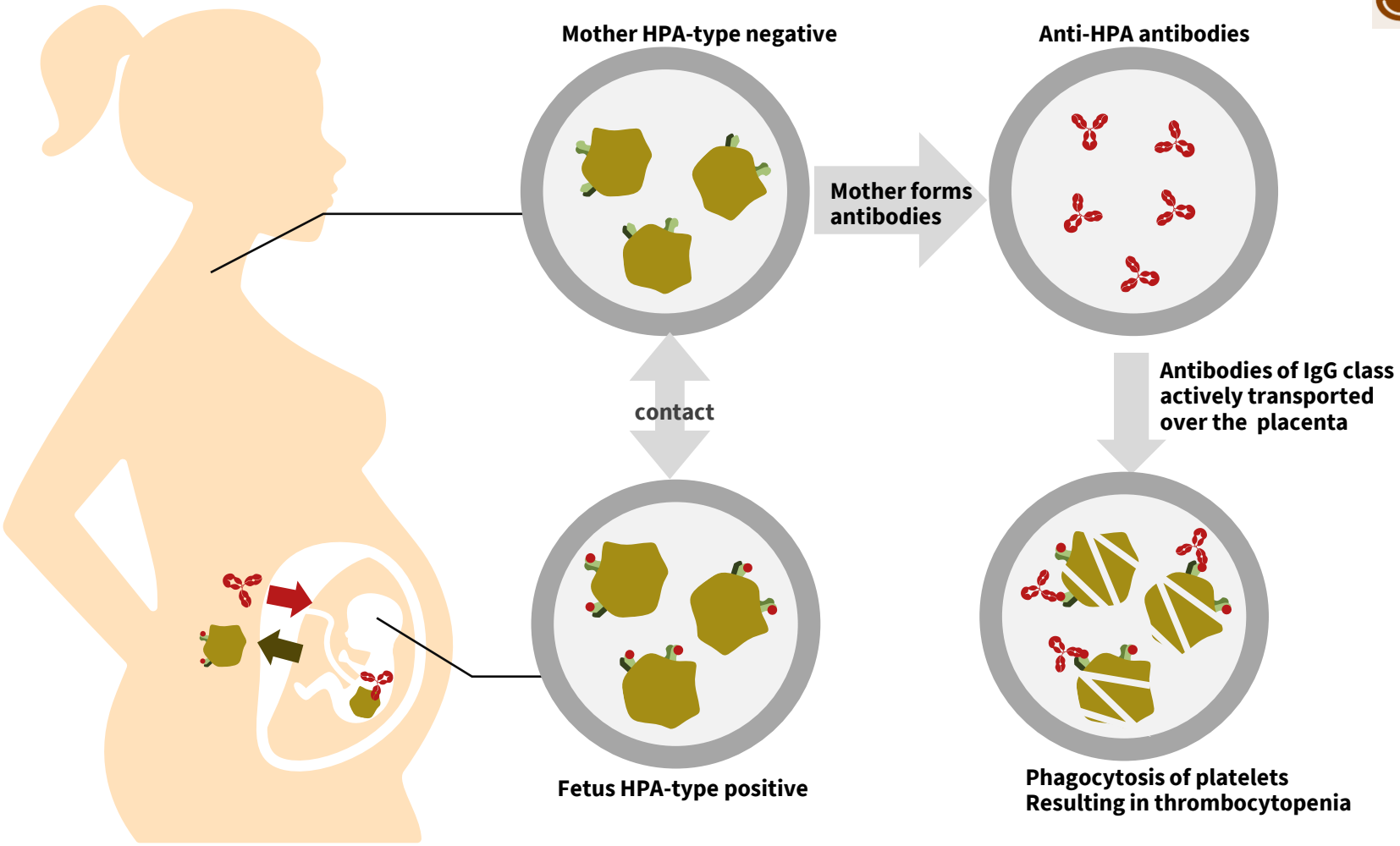
There are two alternative treatment schedules:

0.8–1 g/kg given on day one; this dose may be repeated once within 3 days

0.4 g/kg given daily for 2–5 days.

Rodeghiero F et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. *Blood* (2009) **113**(11):2386–93.

Fetal Neonatal Alloimmune Thrombocytopenia (FNAIT)



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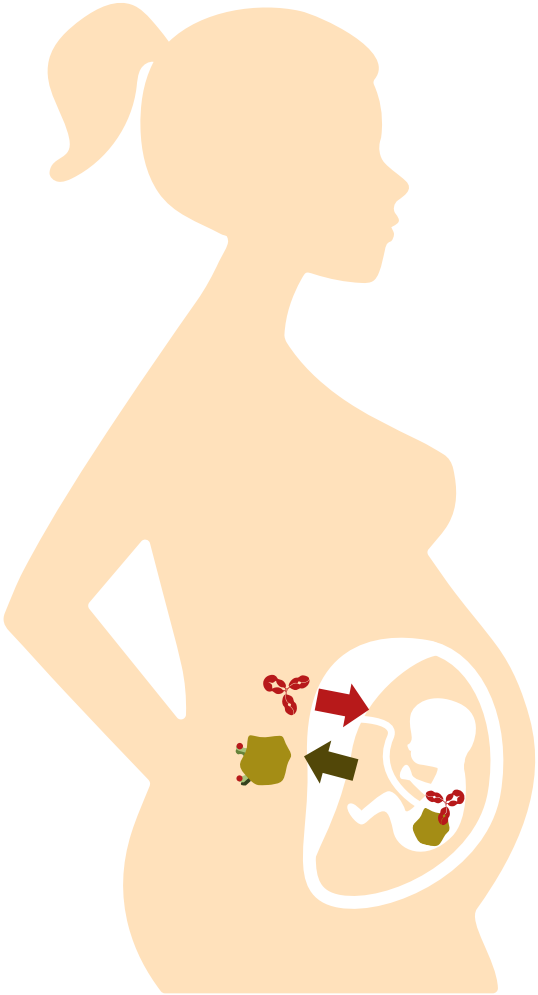
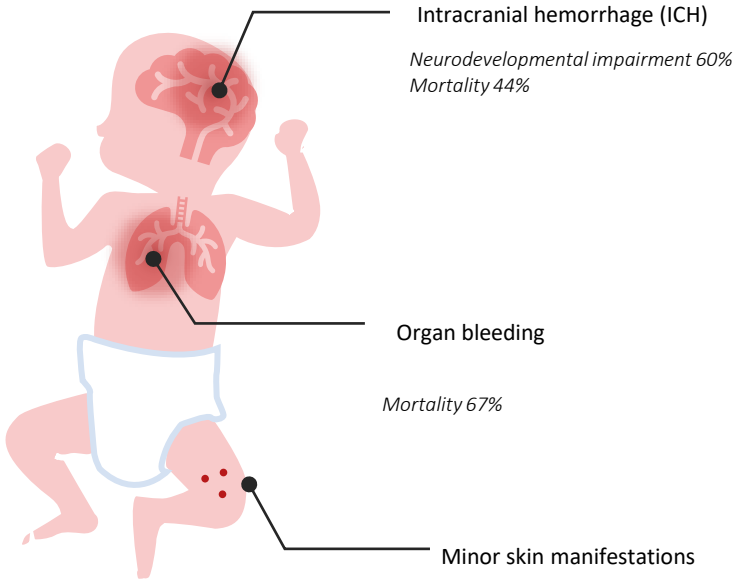




HPA-1a immunisation causes severe bleeding in 11 in 10,000 pregnancies of HPA-1a negative women.

Human Platelet Antigens: distribution worldwide

System	Phenotype	White ancestry (%)	Black ancestry (%)	Asian ancestry (%)
HPA-1	HPA-1b1b	2-3	<1	<1
HPA-4	HPA-4a4a	>99.9	100	99.5
HPA-5	HPA-5a5a	88	82	99
CD36	CD36-negative	<0.4	8	3-11

Example: if of HPA-1b1b type means 'HPA-1a negative' and you may produce anti-HPA-1a

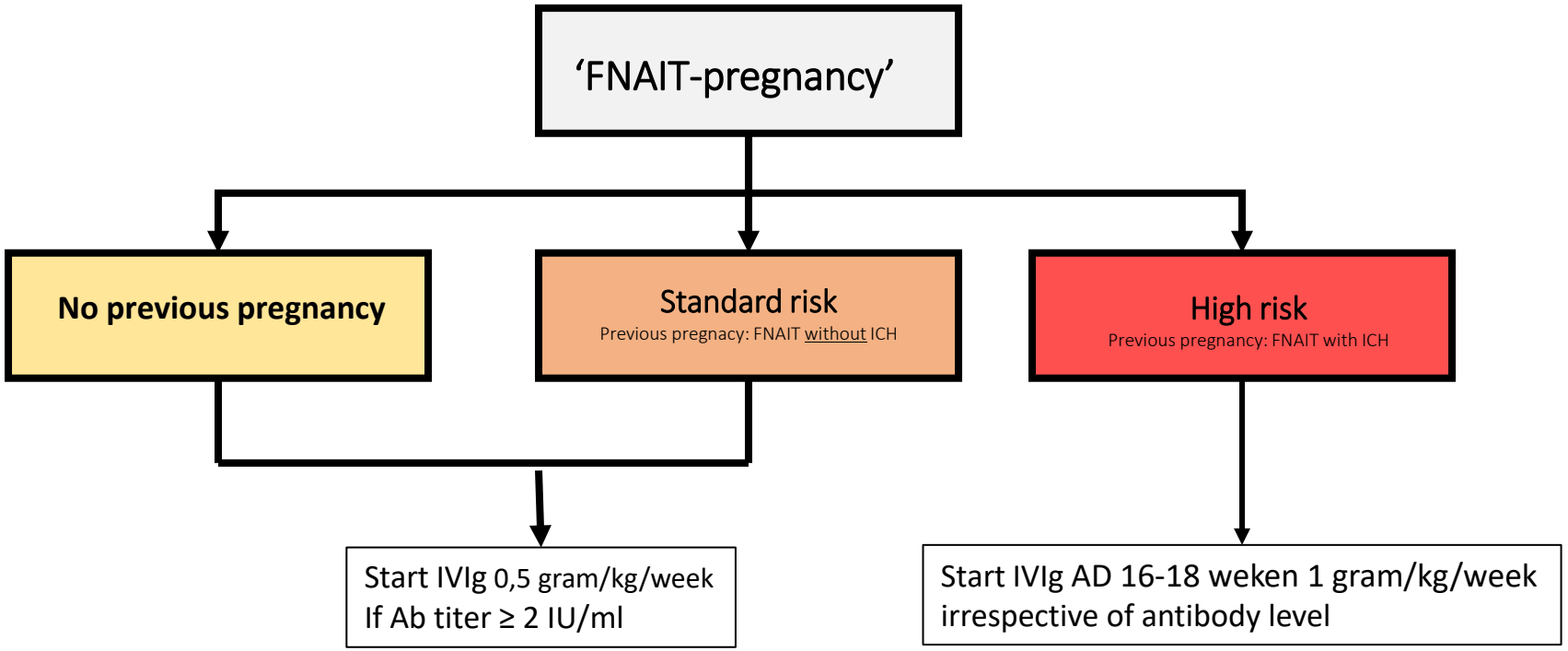
ISBT Working Party: Human Platelet Antigen Database (www.versiti.org)

FNAIT: is risk stratification possible?

-information outcome previous pregnancy
-antibody titers

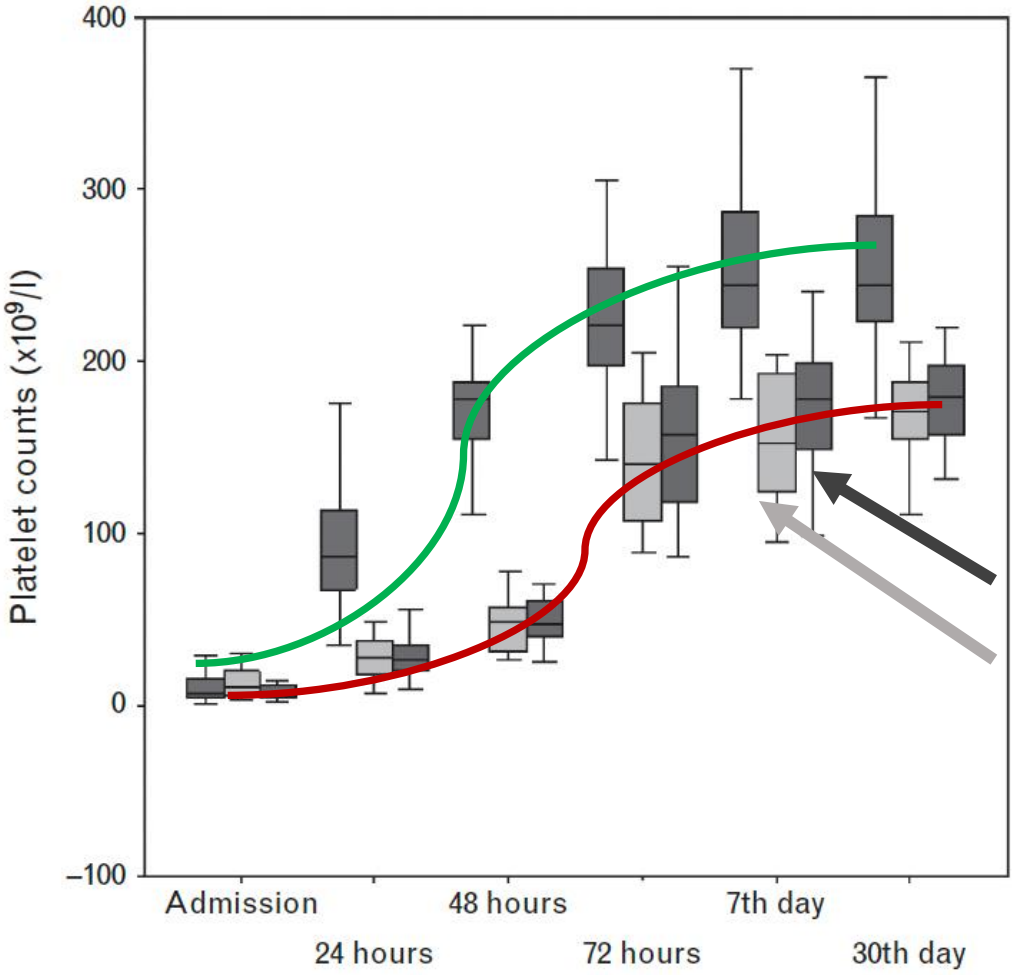
BLOOD, 16 MARCH 2017 • VOLUME 129, NUMBER 11

J. Clin. Med. **2023**, *12*, 5492. https://doi.org/10.3390/jcm12175492



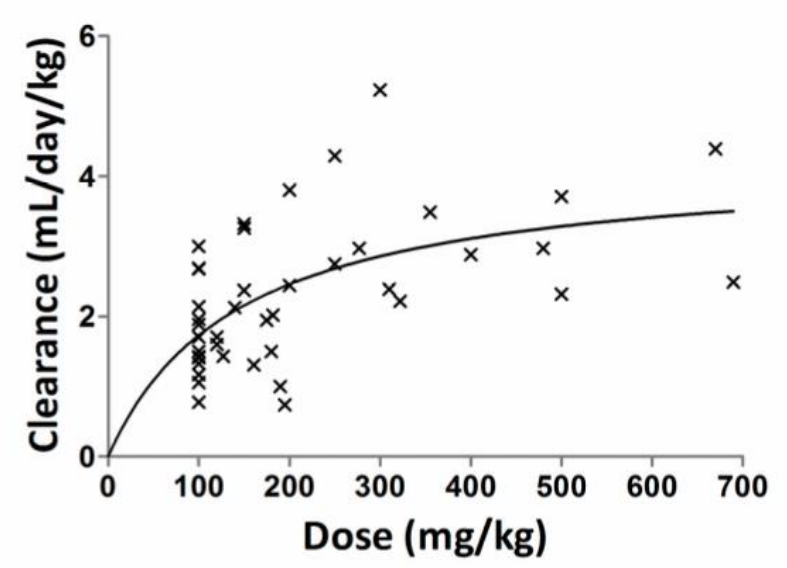
A comparison of intravenous immunoglobulin (2 g/kg totally) and single doses of anti-D immunoglobulin at 50 mg/kg,75 mg/kg in newly diagnosed children with idiopathic thrombocytopenic purpura: Ankara hospital experience

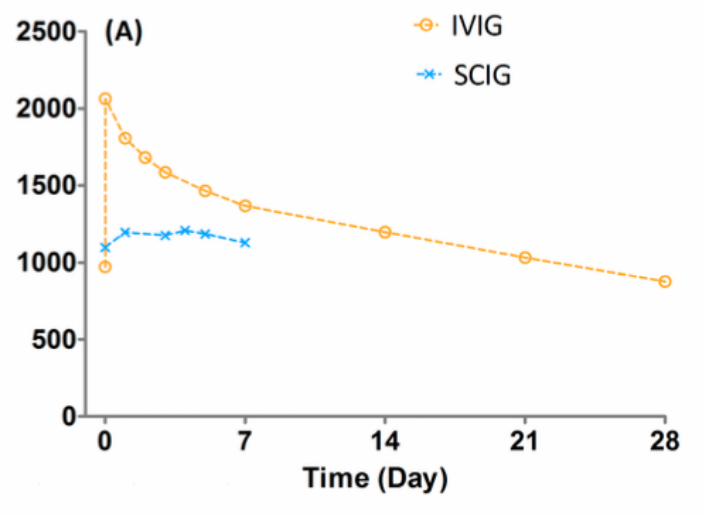
Alioglua B, et al. Blood Coagul Fibrinolysis 24:505– 509 ß 2013



Considerations for Optimizing Dosing of Immunoglobulins Based on Pharmacokinetic Evidence

Mahmood I et al Antibodies 2020, 9, 24;





Comparative study between two bleeding grading systems of immune thrombocytopenia purpura

Chena Q, et al. 2021 Hematology, 26:1, 769-774

Table 2. IBLS scoring criteria.

Site	Bleeding grade 0	1	2
Skin (physical examination, PE)	None	1–5 bruises and/or scattered petechiae	> 5 bruises with size > 2 cm and/or diffuse petechiae
Oral (PE)	None	1 blood blister or > 5	
Petechiae or gum bleeding that clears easily with rinsing	Multiple blood blisters and/or gum bleeding		
Skin (Hx)	None	1–5 bruises and/or scattered petechiae	> 5 bruises with size > 2 cm and/or diffuse petechiae
Oral (Hx)	None	1 blood blister or > 5 petechiae and/or gun bleeding < 5 minutes	Multiple blood blisters and/or gum bleeding > 5 minutes
Epistaxis	None	Blood when blowing nose and/or epistaxis < 5 minutes (per episode)	Bleeding > 5 minutes (per episode)
Gastrointestinal	None	Occult blood	Gross blood
Urinary	None	Microscopic (+ve dipstick)	Macroscopic
Gynecological	None (normal period)	Spotting not at time of normal period	Bleeding > spotting not at time of period or very heavy period
Pulmonary	None	N/A	Yes
Intracranial hemorrhage	None	N/A	Yes
Subconjunctival hemorrhage	None	Yes	N/A

Page et al. 2007 Blackwell Publishing Ltd, British Journal of Haematology, 138, 245–248

Table 3. ITP-2016 scoring criteria.

Score	Age (years)		Skin		Mucous		Organ				
								Visceral			
	≥ 65	≥ 75	Head and face	Other	Accidental	Multiple	With anemia	Anemia	No anemia	Life-threatening	Central system
1	√			√							
2		√	√		√						
3						√		√			
5							√		√		
8										√	√