Grupo Cooperativo Latinoamericano de Hemostasia y Trombosis

UNICAMP

Púrpura Trombocitopênica Trombótica Adquirida (PTTa)

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Declaração de Potencial Conflito de Interesse

Categoria de Potencial Conflito de Interesse	Indústria
Patrocínio de Transporte ou Hospedagem em Congresso	não
Patrocínio em Estudos Subvencionados pela Indústria	não
Conferencista ou Palestrante em Eventos Patrocinados pela Indústria	Sanofi
Apoio Institucional da Indústria	não
Preparo de Textos Científicos em Periódicos Patrocinados pela Industria	não
Ter Ações da Indústria	não

Apresentação Geral e Diagnóstico

ORIGINAL ARTICLE

The incidence of thrombotic thrombocytopenic purpura-hemolytic uremic syndrome: all patients, idiopathic patients, and patients with severe ADAMTS-13 deficiency

Incidência anual para cada 1.000.000 de habitantes (dados do registro de PTT de Oklahoma)

Diagnóstico	Taxa de incidência (95% IC)
Microangiopatia Trombotica (suspeita de PTT)	11.29 (9.70–12.88)
PTT (def. ADAMTS 13)	**1.74 (1.06–2.41)**

Terrel et al. J Thromb Haemost 2005; 3: 1432–6

Epidemiology and pathophysiology of adulthood-onset thrombotic microangiopathy with severe ADAMTS13 deficiency (thrombotic thrombocytopenic purpura): a cross-sectional analysis of the French national registry for thrombotic microangiopathy

939 pts com PTT (AD <10%) em 14 anos

Diagnóstico	Prevalência
PTT (def. ADAMTS 13)	**13 casos por milhão de habitantes (em 14 anos)**
PTT autoimune	75%
PTT hereditária	3%

Mariotte et al.Lancet Haematol 2016; 3: e237–45

Apresentação clínica (pêntade de clássica)

1. Anemia hemolítica microangiopática
2. Plaquetopenia
3. Alterações neurológicas
4. Insuficiência renal
5. Febre

George JN et al. Semin Hematol 2004; 41: 60–7.

Apresentação clínica (pêntade de clássica)

1. Anemia hemolítica microangiopática
2. Plaquetopenia
3. Alterações neurológicas **(72%)**
4. Insuficiência renal **(45%)**
5. Febre **(22%)**

*Apenas 8% dos casos apresentam todos os 5 sintomas

George JN et al. Semin Hematol 2004; 41: 60–7.

Apresentação clínica e suspeita diagnóstica

Clínica

- Anemia (hemolítica)
- Plaquetopenia < 150 x10^3/ L
- Sinais de isquemia de órgãos alvo (**neurológico**, renal, hepático, cardíaco)
- Sem outra explicação (sepses, CID)

Laboratório

- Provas de hemólise positivas (↑retic., ↑LDH, ↑BI elevada)
- Sinais de destruição mecânica das hemácias (esquizócitos)
- Coombs direto negativo

Moake J. . N Engl J Med 2012, n. 8: 589-600

Critérios diagnósticos

Clínica

- Anemia (hemolítica)
- Plaquetopenia < 150 x10^3/ L
- Sinais de isquemia de órgãos alvo (**neurológico**, renal, hepático, cardíaco)
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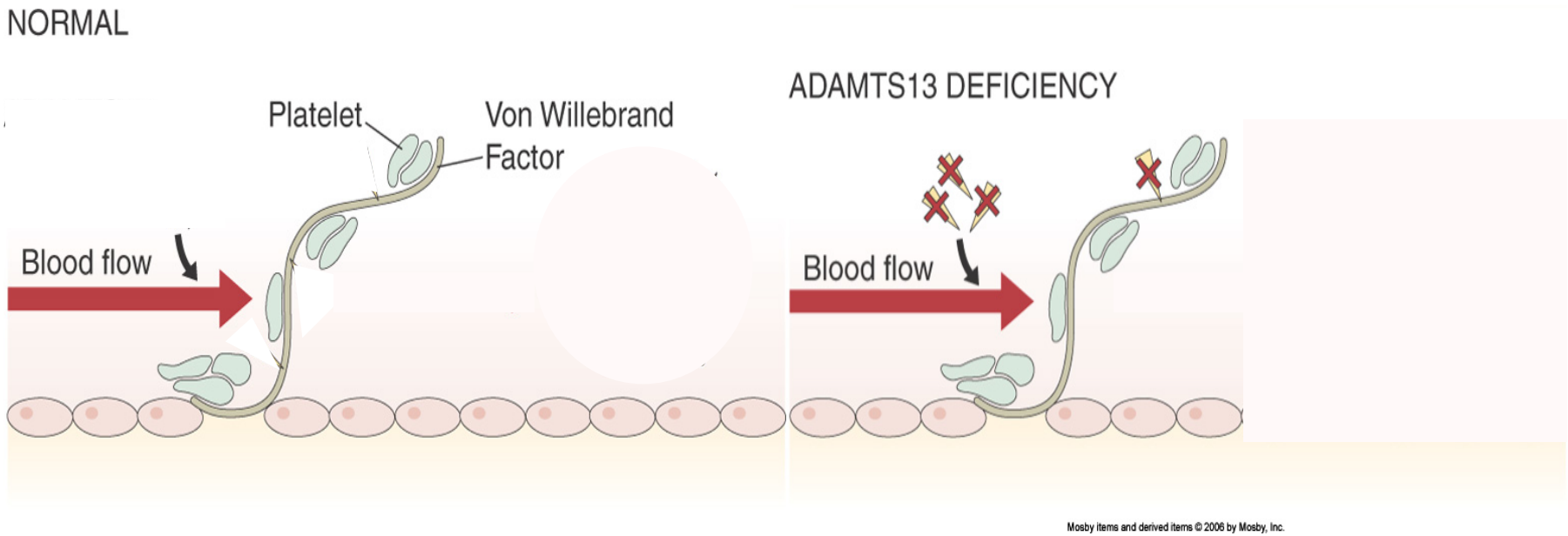
- Coombs direto negativo

Moake J. . N Engl J Med 202, n. 8: 589-600

Confirmação Laboratorial da PTTa

PTT é causada pela deficiência de ADAMTS13



Anticorpos anti-ADAMTS 13 causam a deficiência da enzima

Atividade diminuída da ADAMTS 13 (<10%) **confirma PTT**

X. Long Zheng et al. Blood. 2004;103:4043-4049

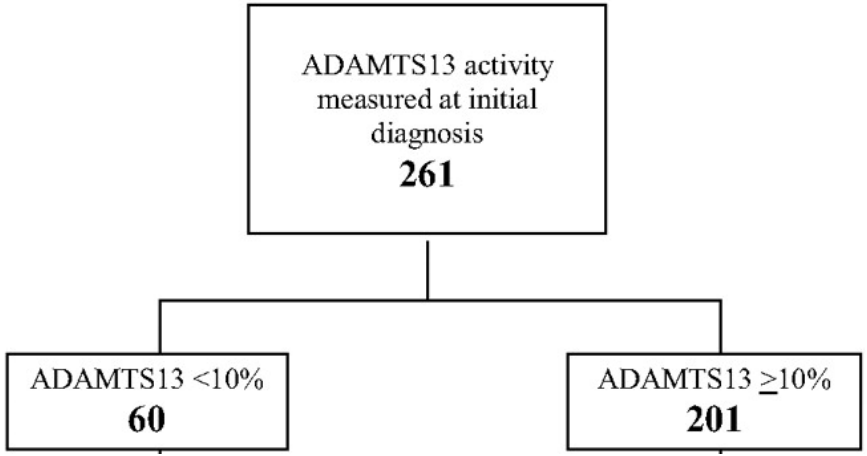
blood
2010 115: 1500-1511
doi:10.1182/blood-2009-09-243790 originally publish
online December 23, 2009

Survival and relapse in patients with thrombotic thrombocytopenic purpura

Johanna A. Kremer Hovinga, Sara K. Vesely, Deirdra R. Terrell, Bernhard Lämmle and James I
George

Pacientes com deficiencia de ADAMTS 13 (PTT confirmada) tem melhor resposta ao tratamento

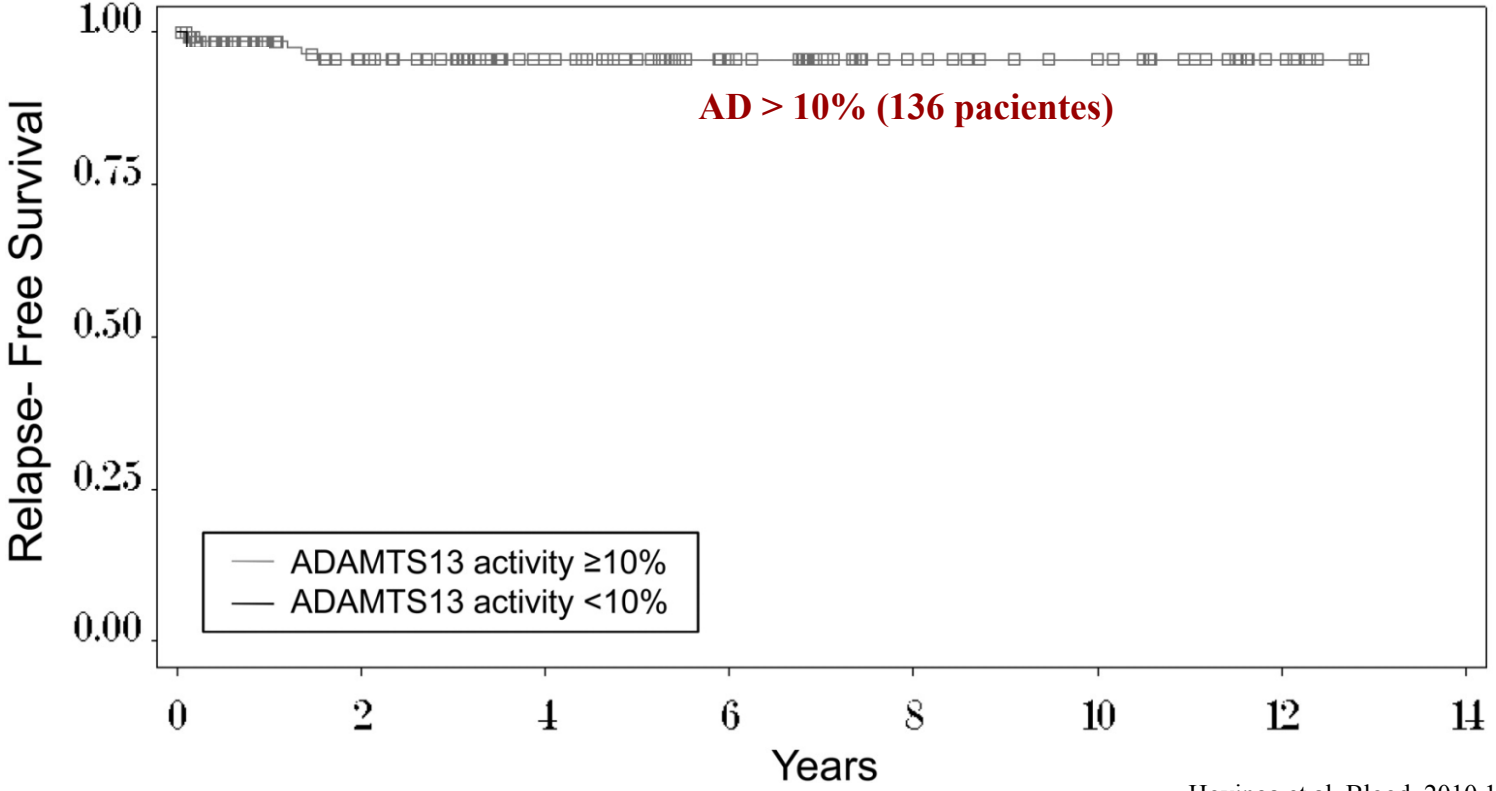
B



Hovinga et al. Blood. 2010 115: 1500-1511

blood
2010 115: 1500-1511
doi:10.1182/blood-2009-09-243790 originally published online December 23, 2009

Survival and relapse in patients with thrombotic thrombocytopenic purpura



Hovinga et al. Blood. 2010 115: 1500-1511

Diagnóstico de Púrpura Trombocitopênica Trombótica

Dosagem da atividade da enzima ADAMTS 13

Atividade extremamente diminuída (<10%)

- **Confirma PTT**
- Define prognóstico
- Detecção do anticorpo anti-ADAMTS 13 -> PTT adquirida

Entretanto o **exame não** está prontamente **disponível** na maioria dos serviços de saúde e o **tempo para liberação** do resultado é longo

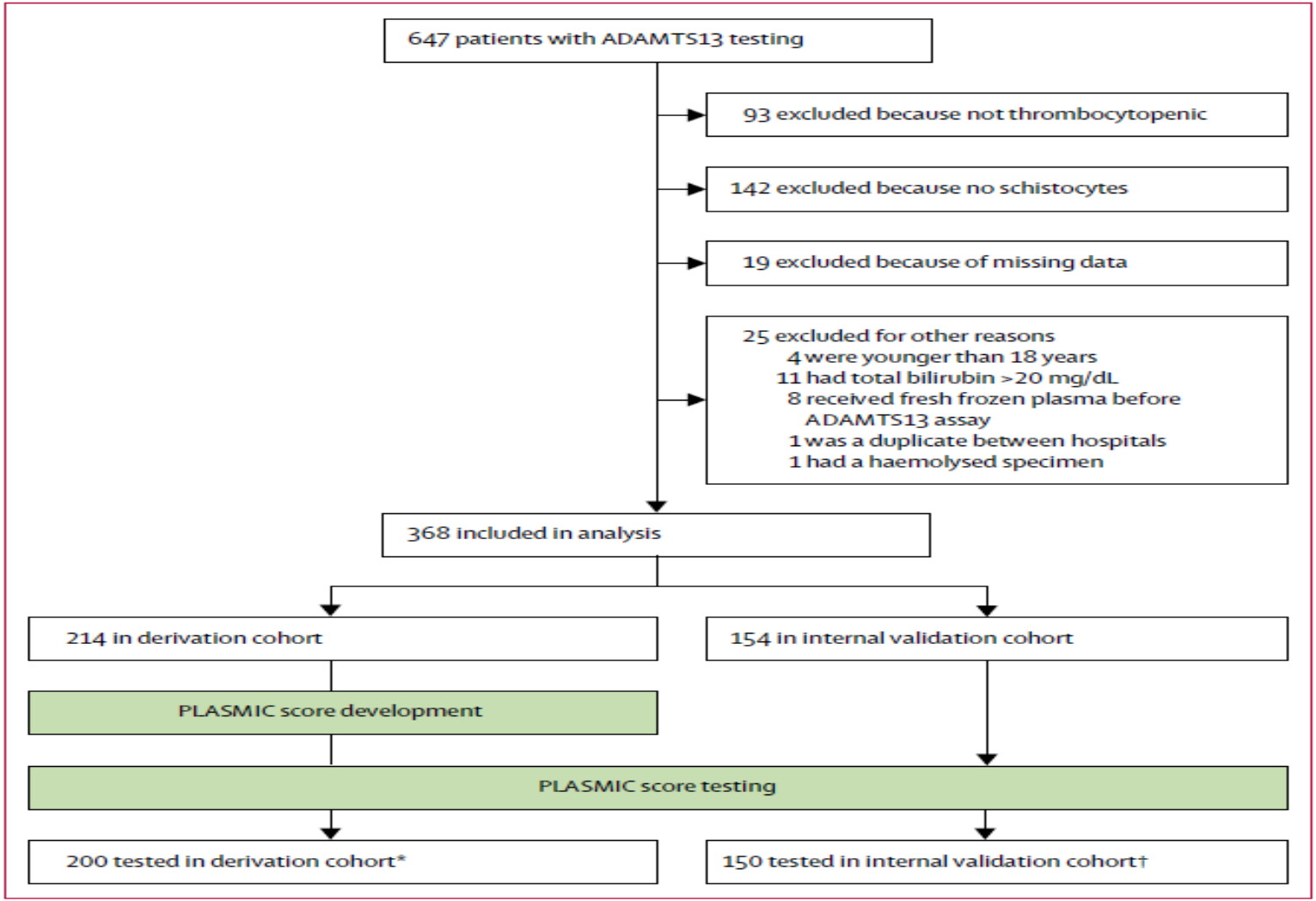
George J. Blood 2010;116:4060-69
Scully et al. J Thromb Haemost 2017; 15: 312–22

Derivation and extern
rapid assessment of ac
microangiopathies: a c

Pavan K Bendapudi, Shelley Hurwitz, Ashley Fry, Mari
Andrew M Brunner, John M Gansner, Srinivas Viswan

Summary

Background Among the syndromes chara
purpura is distinguished by a severe defici

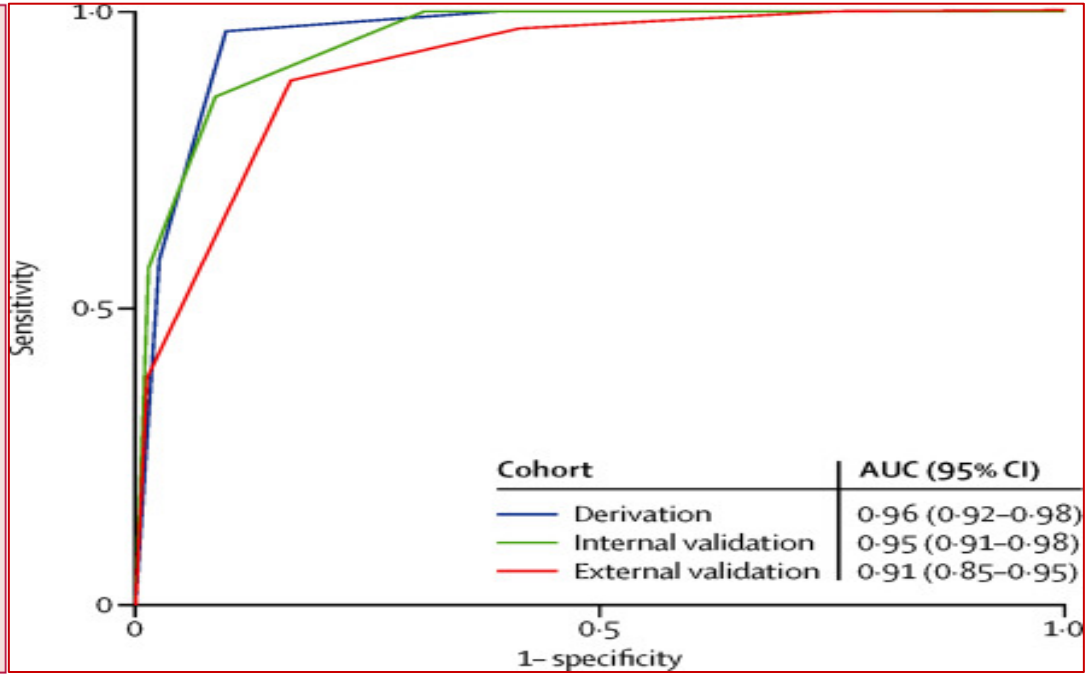


Derivation and external validation of the PLASMIC score for rapid assessment of adults with thrombotic microangiopathies: a cohort study

	Points*
Platelet count <30 × 10^9 per L	1
Haemolysis variable†	1
No active cancer	1
No history of solid-organ or stem-cell transplant	1
MCV <90 fL‡	1
INR <1·5	1
Creatinine <2·0 mg/dL	1

INR=international normalised ratio. MCV=mean corpuscular volume. *Score of 0–4 denotes low risk for severe ADAMTS13 deficiency; score of 5 denotes intermediate risk; score of 6 or 7 denotes high risk. †Reticulocyte count >2·5%, or haptoglobin undetectable, or indirect bilirubin >2·0 mg/dL. ‡<9·0 × 10^{-14} L.

Table 3: The PLASMIC score for prediction of thrombotic microangiopathy associated with severe ADAMTS13 deficiency



Bendapudi et al. Lancet Haematol 2017; 4: e157–64

Derivation and external validation of the PLASMIC score for rapid assessment of adults with thrombotic microangiopathies: a cohort study

	Points*
Platelet count < 30×10^9 per L	1
Haemolysis variable†	1
No active cancer	1
No history of solid-organ or stem-cell transplant	1
MCV <90 fL‡	1
INR <1·5	1
Creatinine <2·0 mg/dL	1

INR=international normalised ratio. MCV=mean corpuscular volume. *Score of 0–4 denotes low risk for severe ADAMTS13 deficiency; score of 5 denotes intermediate risk; score of 6 or 7 denotes high risk. †Reticulocyte count >2·5%, or haptoglobin undetectable, or indirect bilirubin >2·0 mg/dL. ‡<$9{\cdot}0 \times 10^{-14}$ L.

Table 3: **The PLASMIC score for prediction of thrombotic microangiopathy associated with severe ADAMTS13 deficiency**

	Derivation cohort (n=200)	Internal validation cohort (n=150)	External validation cohort (n=146)
0–4	0/84 (0%)	0/89 (0%)	2/47 (4%)
5	2/44 (5%)	3/32 (9%)	6/25 (24%)
6 or 7	58/72 (81%)	18/29 (62%)	61/74 (82%)

Data are number of individuals with ADAMTS13 activity of 10% or less/total number of individuals with that score (%).

Table 4: **Validation of the PLASMIC score**

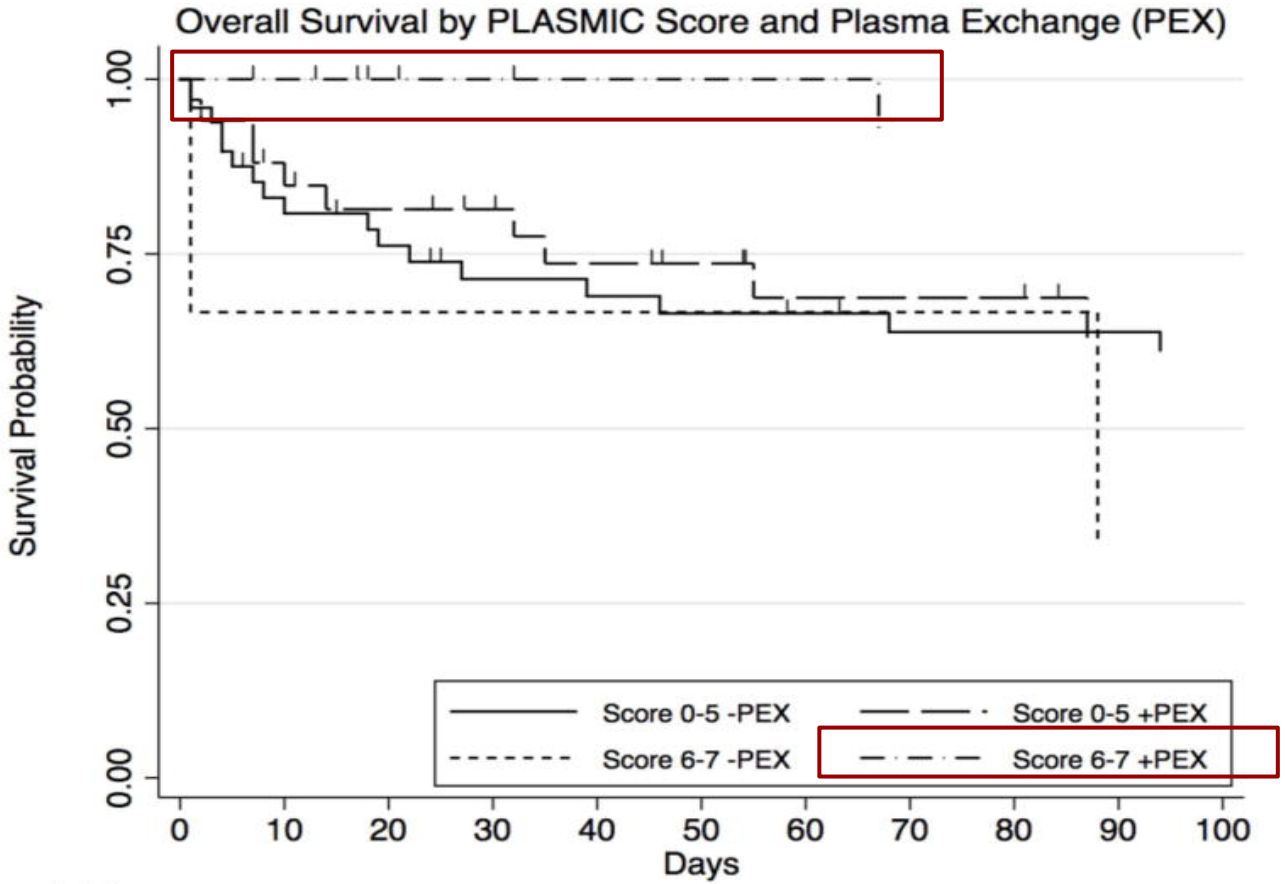
Bendapudi et al. Lancet Haematol 2017; 4: e157–64

DOI: 10.1111/jth.13882

Journal of Thrombosis and Haemostasis, 16: 164–169

BRIEF REPORT

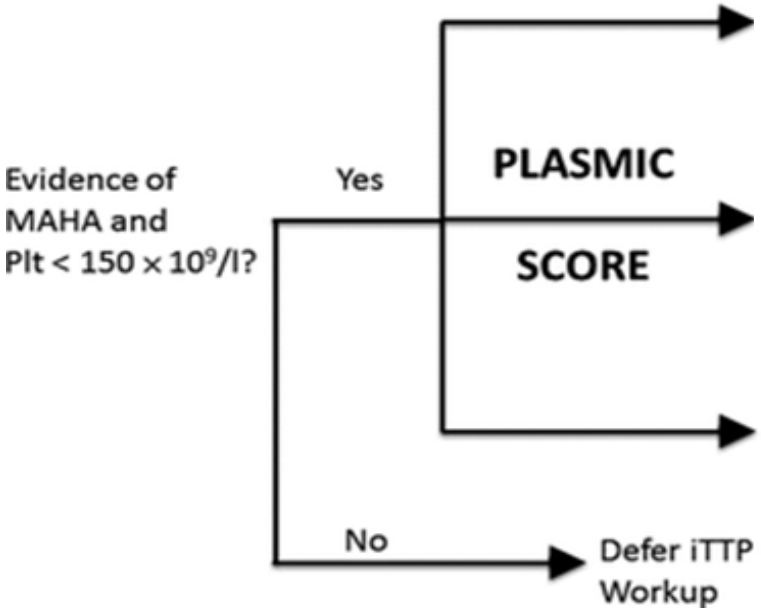
External validation of the PLASMIC score: a clinical prediction tool for thrombotic thrombocytopenic purpura diagnosis and treatment



Li et al. J Thromb Haemost 2018; 16: 164–9.

bjh research paper

Utilizing a PLASMIC score-based approach in the management of suspected immune thrombotic thrombocytopenic purpura: a cost minimization analysis within the Harvard TMA Research Collaborative



Upadhyay et. al. British Journal of Haematology, 2019, 186, 490–498

Tratamento da PTTa. Evolução e Onde Estamos

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Comparison of Plasma Exchange with Plasma Infusion in the Treatment of Thrombotic Thrombocytopenic Purpura

Gail A. Rock, Ph.D., M.D., Kenneth H. Shumak, M.D., Noel A. Buskard, M.D., Victor S. Blanchette, M.D., John G. Kelton, M.D., Rama C. Nair, Ph.D., Robert A. Spasoff, M.D., and the Canadian Apheresis Study Group* et al.

PE: 1,5x volemia plasmatica em 3 sessoes e depois 1,0x
PFC: 30mL/Kg em 24 e depois 15mL/Kg ao dia

Table 1. Demographic Characteristics of the Study Patients at Entry.*

Characteristic	Plasma Exchange (N = 51)	Plasma Infusion (N = 51)
Age (yr)	39.1±13.5	41.9±15.1
Height (cm)	161.5±24.8	160.6±24.1
Weight (kg)	68.5±21.4	67.2±16.7
Sex (no. female)	32	35
Fluctuating neurologic abnormalities (no.)	32	32
History of thrombocytopenic purpura (no.)	5	6

*Plus–minus values are means ±SD.

Table 3. Results at the End of the First Cycle.

Outcome	Plasma Exchange (N = 51)	Plasma Infusion (N = 51)
	number (percent)	
Response*		
Success	24 (47)	13 (25)
Failure	27 (53)	38 (75)
Survival†		
Survived	49 (96)	43 (84)
Died	2 (4)	8 (16)

*P = 0.025 by two-tailed exact binomial test for all comparisons between groups. The difference in the percentages with a successful response was 22 percent (95 percent confidence interval, 4 to 40 percent).

†The difference in the percentages of patients who survived was 12 percent (95 percent confidence interval, 2 to 23 percent).

N Engl J Med 1991; 325; 393-397

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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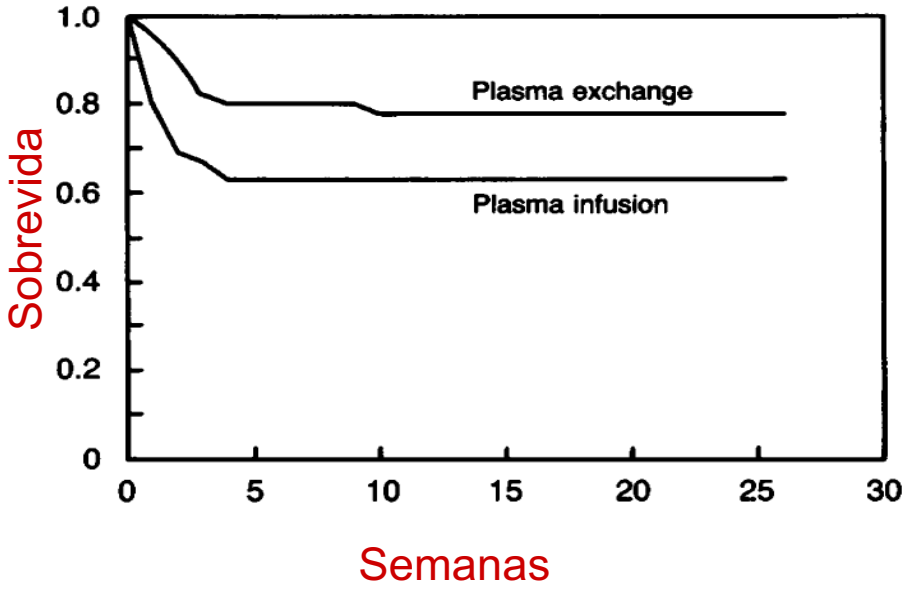


Table 4. Results after Six Months.

Outcome	Plasma Exchange	Plasma Infusion		
		No Crossover	Crossover	Total
Response*				
No. of patients	51 (100)	32 (100)	19 (100)	51 (100)
Success	40 (78)	10 (31)	15 (79)	25 (49)
Failure	11 (22)	22 (69)	4 (21)	26 (51)
Survival†				
No. of patients	51 (100)	20 (100)	31 (100)	51 (100)
Success	40 (78)	10 (50)	22 (71)	32 (63)
Failure	11 (22)	10 (50)	9 (29)	19 (37)

*P = 0.002 by two-tailed exact binomial test for all comparisons between groups. The difference between the plasma-exchange and plasma-infusion groups in the percentage with a successful response was 29 percent (95 percent confidence interval, 11 to 47 percent).

†The difference between the plasma-exchange and plasma-infusion groups in the percentage who survived was 15 percent (95 percent confidence interval, −2.5 to +32.5 percent).

N Engl J Med 1991; 325; 393-397

Uso de corticosteróides

- Caráter autoimune da PTT adquirida justifica o uso de corticosteróides, assim como de outros imunossupressores
- CE em altas doses são utilizados há mais de 30 anos

Ann Hematol (2010) 89:591–596
DOI 10.1007/s00277-009-0877-5

ORIGINAL ARTICLE

High versus standard dose methylprednisolone in the acute phase of idiopathic thrombotic thrombocytopenic purpura: a randomized study

Table 2 High-dose versus standard-dose methylprednisolone treatment in patients with idiopathic TTP; comparison of treatment outcomes

	Standard-dose methylprednisolone (n=30) Number of patients (%)	High-dose methylpred nisolone (n=30)	Difference (95% CI)	P value
Failure to achieve good response at day 9[a]	13 (43.4)	7 (23.4)	−20 (−43 to +3)	0.17
Failure to achieve complete remission at day 23[b]	16 (53.4)	7 (23.4)	−30 (−53 to −6)	0.03
Death	4 (13.3)	1 (3.3)	−10 (−23 to +3)	0.35

[a] Platelet count more than 100×10^9/L for two consecutive days without deterioration in the neurological status

[b] Increase of platelets to more than 150×10^9/L, normalisation of LDH value and improvement in neurological status

Tratamento padrão da PTT

- Plasmaférese diária
  - Iniciar o mais breve possível
  - Troca 1 a 1,5x volemia diariamente
  - Cessar após plaquetas > 150x109/L
- CE em altas doses durante toda a internação

ORIGINAL ARTICLE

Consensus on the standardization of terminology in thrombotic thrombocytopenic purpura and related thrombotic microangiopathies

Resposta Clínica
Normalizacao das plaquetas (> 150x 109 L-1) e LDH (< 1,5x acima do limite) após cessação a plasmaférese

Remissão Clínica
Manutenção da resposta clínica > 30 dias após cessação da plasmaférese

Exacerbação
Redução da contagem plaquetária (< 150x 109 L-1), aumento da LDH e necessidade de reiniciar plasmaférese dentro de 30 dias após a resposta clínica

Recaída
Redução da contagem plaquetária (< 150x 109 L-1), mesmo assintomática, > 30 dias após cessação da plasmaférese

PTT refratária
Plaquetopenia (< 50x109 L-1) e aumento de LDH persistentes (> 1,5x) após 5 sessões de plasmaférese e corticosteróides

Scully et al. J Thromb Haemost 2017; 15: 312–22

Outros imunossupressores: Rituximab

Table 1
Reports involving 10 or more patients treated with rituximab in the acute phase of autoimmune TTP.

Series (year)	N	Age (yr) median (range)	% F	% R	Number of rituximab infusions, median (range)	CR (%)	Days to CR median (range)
Scully et al. (2007 [9]	25	43 (17–67)	76	44	4 (2–8)	100	11
Jasti et al. (2008) [5]	12	43 (19–59)	83	8	(1–13)	83	18 (14–41)
Ling et al. (2009) [6]	13	42 (23–71)	69	54	NA	92	NA
de la Rubia et al. (2010) [7]	24	(24–72)	71	42	4 (1–8)	87.5	14 (7–35)
Scully et al. (2011) [12]*	40	42 (21–76)	65	15	4 (2–8)	82.5	12
Froissart et al. (2012) [10]	22	36.8 ± 11	67	14	4	82	12 ± 6.7
Page et al. (2016) [8]	16	41 (20–79)	75	0	4 (1–4)	100	21 (5–76)[a]
Benhamou et al. (2016) [11]	24	39.3 (30–47)	75	12.5	2 (14 patients) or 3 (10 patients)	95	14 (IQR, 12–22)[a]

N: number of patients, F: female, R: relapsing patients, CR: complete remission, NA: data not available
* 1a linha

Vários estudos não randomizados reportaram o uso de RTX em pacientes sem resposta clínica, com exacerbação ou recaída da PTT e mostraram boa taxa de remissão (82 -100%)

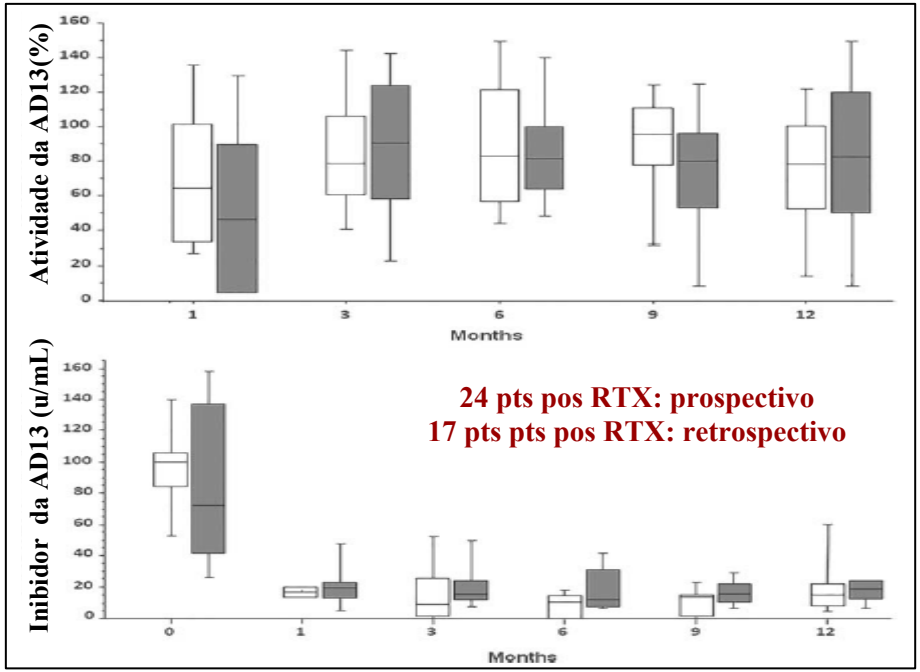
Entretanto a resposta ao RTX em geral é tardia (entre 11 - 21 dias)

Coppo, French Reference Center for Thrombotic Microangiopathies. Transfusion and Apheresis Science 56 (2017) 52–56

RESEARCH ARTICLE

AJH

Efficacy of a rituximab regimen based on B cell depletion in thrombotic thrombocytopenic purpura with suboptimal response to standard treatment: Results of a phase II, multicenter noncomparative study



Benhamou et a. Am J Hematol 2016;91:1246–51.

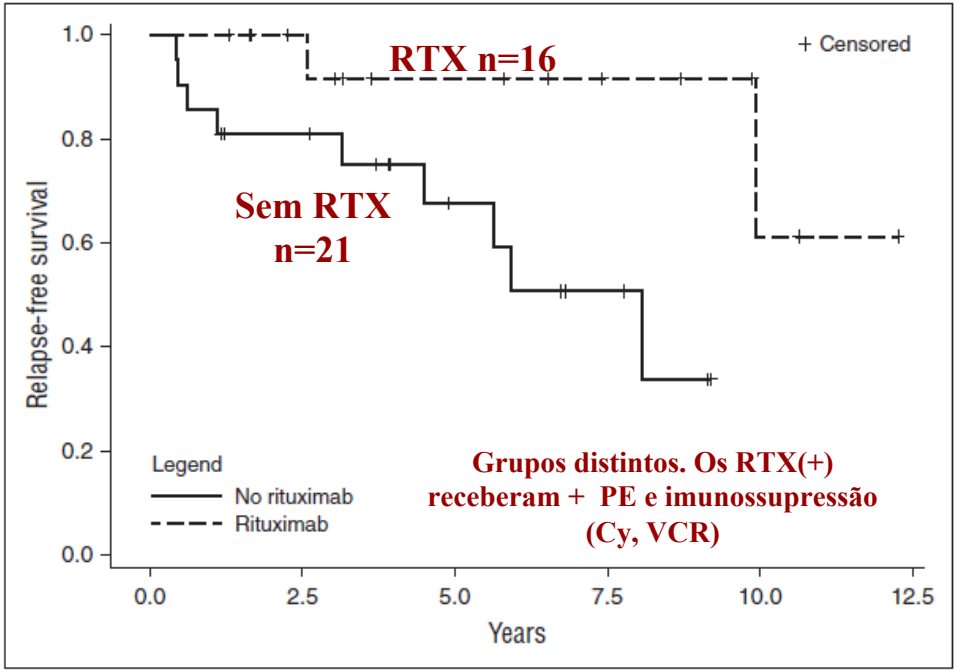
Letters to *Blood*

blood

To the editor:

Rituximab reduces risk for relapse in patients with thrombotic thrombocytopenic purpura

Evaren E. Page,[1,2] Johanna A. Kremer Hovinga,[3] Deirdra R. Terrell,[1] Sara K. Vesely,[1] and James N. George[1,2]



Page et al.Blood

Outros tratamentos imunossupressores

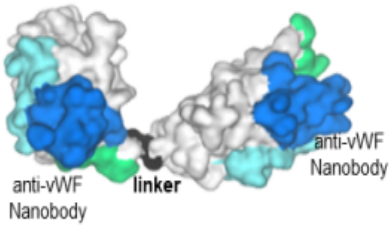
- Vincristina
- Ciclosporina
- Esplenectomia
- Bortezomib

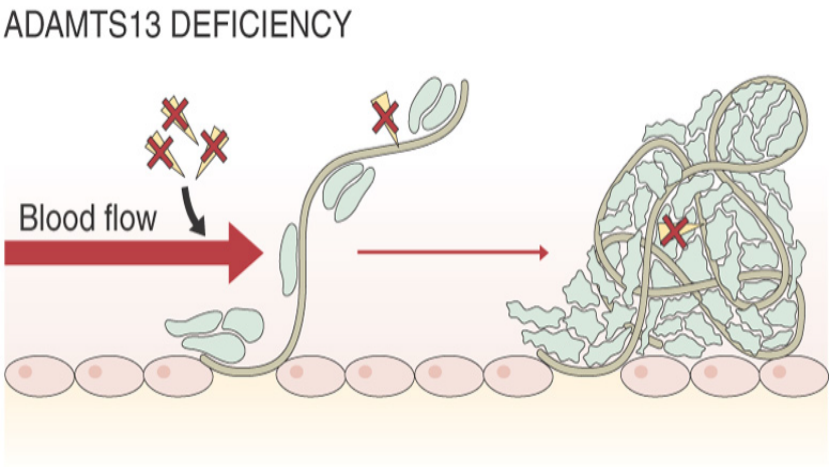
Não imunossupressor: N-acetilcisteína

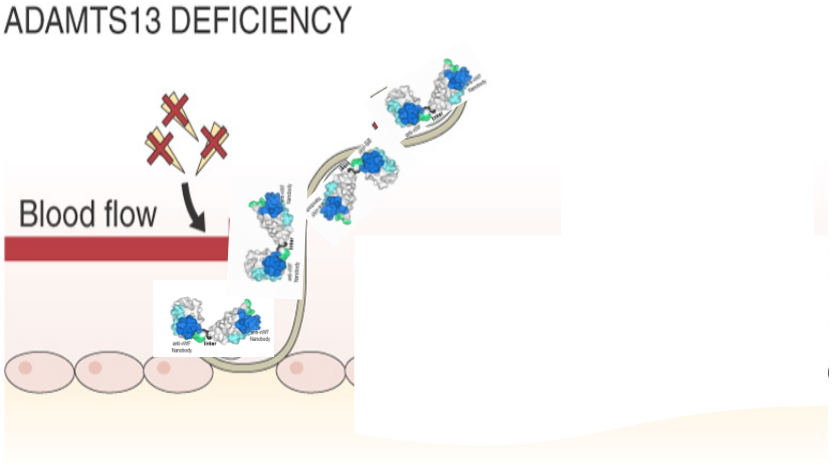
Coppo, French Reference Center for Thrombotic Microangiopathies. Transfusion and Apheresis Science 56 (2017) 52–56

Mudança de paradigma no tratamento da PTT
Caplacizumab

Imunoglobulina humanizada anti–FVW (Nanobody, Ablynx), que se liga ao domínio A1 do FVW e previne sua interação com a GP Ib-IX-V das plaquetas







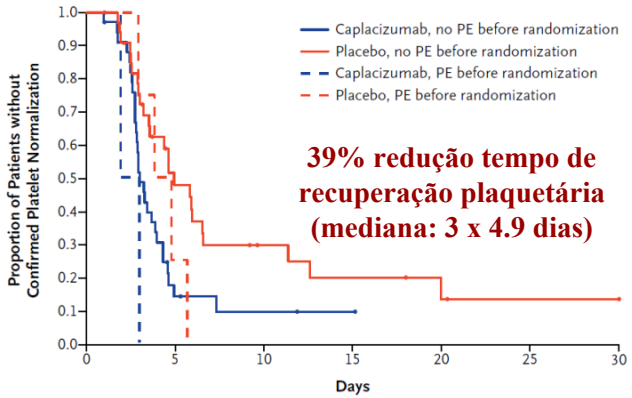
Callewaert et al. Blood 2012; 120: 3603-10.

The NEW ENGLAND JOURNAL of MEDICINE
FEBRUARY 11, 2016 VOL. 374 NO. 6

Caplacizumab for Acquired Thrombotic Thrombocytopenic Purpura

75 pacientes randomizados para caplacizumab (36) ou placebo (39) durante PE + 30 dias

Desfecho Primario



39% redução tempo de recuperação plaquetária (mediana: 3 x 4.9 dias)

No. at Risk							
Caplacizumab, no PE before randomization	34	4	2	1	0	0	0
Placebo, no PE before randomization	35	13	6	4	2	1	1
Caplacizumab, PE before randomization	2	0	0	0	0	0	0
Placebo, PE before randomization	4	1	0	0	0	0	0

Figure 1. Time to Confirmed Normalization of Platelet Count in the Intention-to-Treat Population.
Censored observations are represented by dots. Data for any patient still at risk at 30 days were censored at 30 days. PE denotes plasma exchange.

Desfecho Secundário

Table 2. Primary and Secondary Efficacy End Points in the Intention-to-Treat Population.

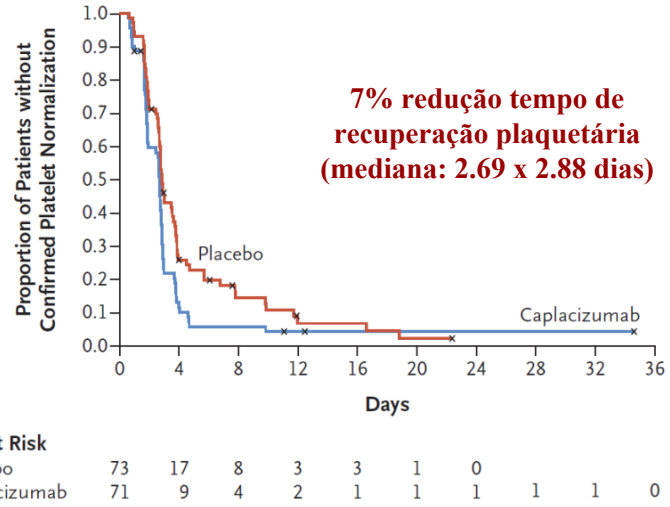
End Point	Caplacizumab (N=36)	Placebo (N=39)
Secondary end points		
Exacerbation of TTP — no. (%)‡	3 (8)	11 (28)
Relapse — no. (%)		
During 1-mo follow-up period	8 (22)	0
During 12-mo follow-up period§	11 (31)	3 (8)
Complete remission after initial daily PE — no. (%)¶	29 (81)	18 (46)
Mean no. of PE days (range)		
During daily PE period	5.9 (3–15)	7.9 (2–35)
During overall study-drug treatment period	7.7 (3–21)	11.7 (2–43)
During the first 30 days of follow-up	10.2 (4–29)	11.7 (2–43)

Peyvandi et. al N Engl J Med 2016;374:511-22

The NEW ENGLAND JOURNAL of MEDICINE

Caplacizumab Treatment for Acquired Thrombotic Thrombocytopenic Purpura

145 pacientes randomizados para caplacizumab (72) ou placebo (73) durante PE + 30 dias + 28 dias caso AD < 10%



7% redução tempo de recuperação plaquetária (mediana: 2.69 x 2.88 dias)

Figure 1. Time to Confirmed Normalization of the Platelet Count in the Intention-to-Treat Population.
Symbols indicate censored data.

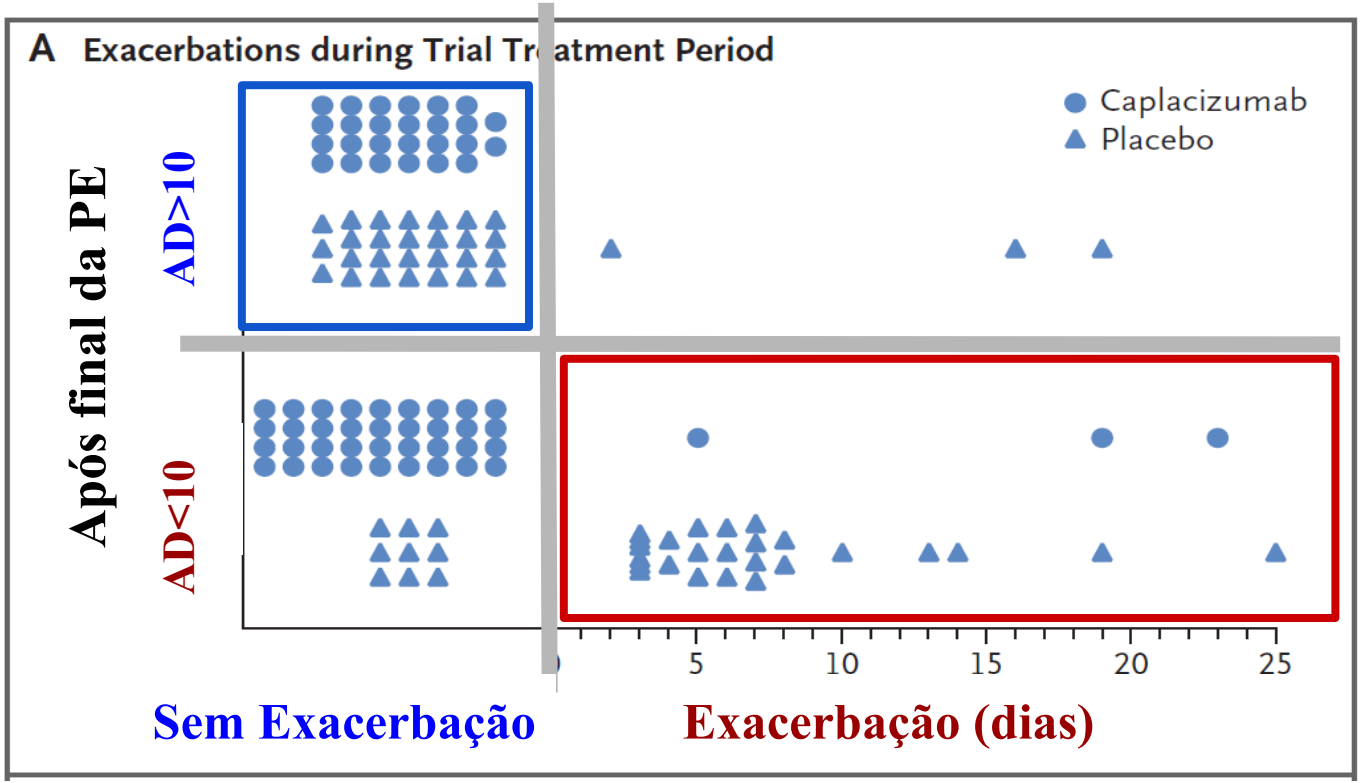
Table 2. Primary and Secondary Efficacy Outcomes in the Intention-to-Treat Population.

Outcome	Caplacizumab (N=72)	Placebo (N=73)	P Value
Key secondary outcomes			
Composite of TTP-related death, recurrence of TTP, or major thromboembolic event during the double-blind treatment period — no. (%)	9 (12)	36 (49)	<0.001
TTP-related death	0	3 (4)	
Recurrence of TTP: exacerbation†	3 (4)	28 (38)	
Major thromboembolic event	6 (8)	6 (8)	
Recurrence of TTP at any time during the trial — no. (%)†	9 (12)	28 (38)	<0.001
During the double-blind treatment period: exacerbation	3 (4)	28 (38)	
During the follow-up period: relapse‡	6 (8)	0	
Refractory TTP — no. (%)§	0	3 (4)	0.06
Median time to normalization of organ-damage markers (95% CI) — days	2.86 (1.93–3.86)	3.36 (1.88–7.71)	

Scully et. al N Engl J Med 2019;380:335-46

The NEW ENGLAND JOURNAL of MEDICINE

Caplacizumab Treatment for Acquired Thrombotic Thrombocytopenic Purpura



Scully et. al N Engl J Med 2019;380:335-46

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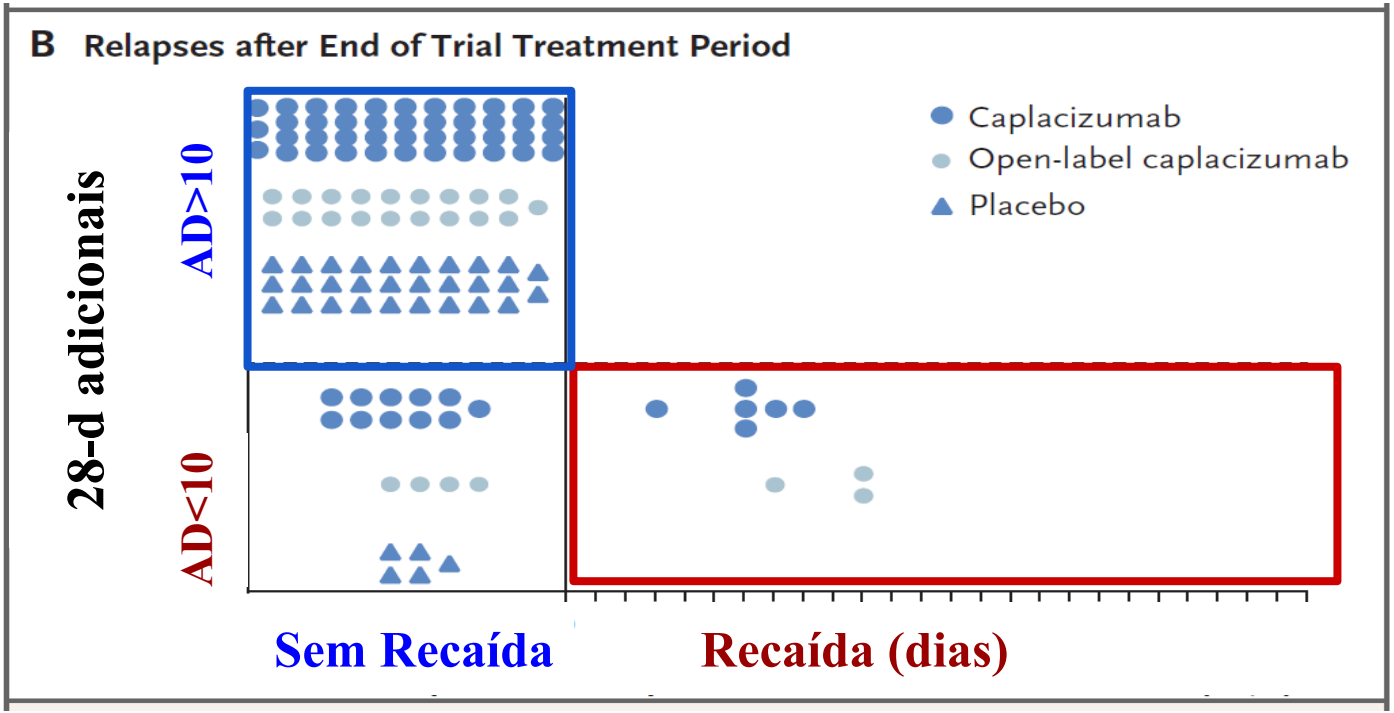
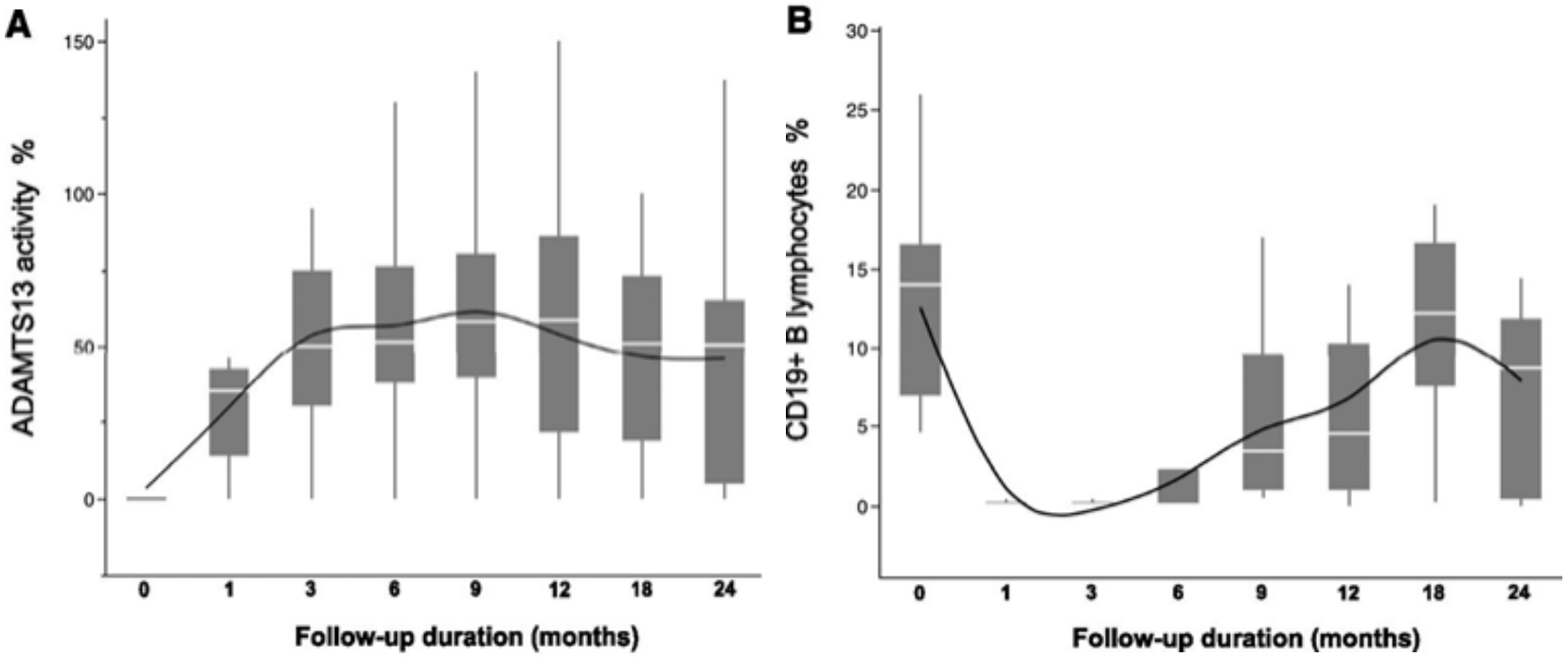


Exacerbação e recaída associadas a persistência da deficiência da ADAMTS 13

Scully et. al N Engl J Med 2019;380:335-46

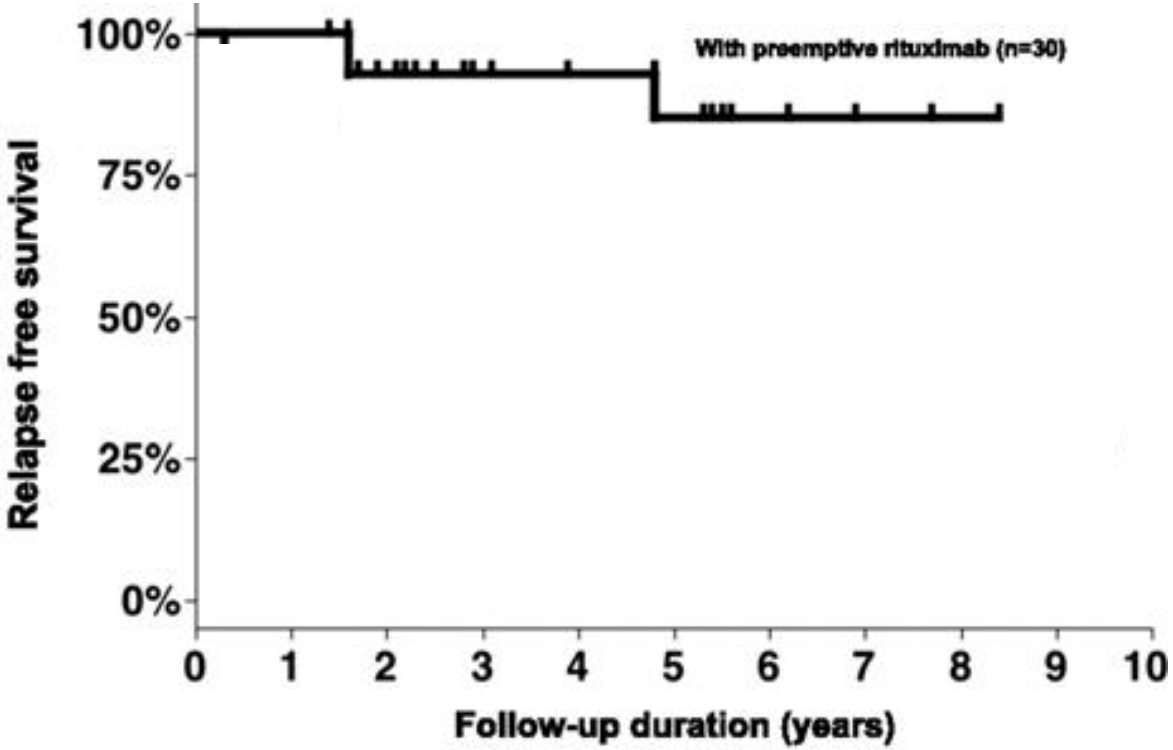
Uso preemptivo de Rituximab

Pacientes com PTT que tenham deficiência persistente da ADAMTS13 após remissão, tem 74% de risco de terem recaída durante o seguimento clínico



Hie et al. Blood (2014) 124 (2): 204–210
Jestin et al. Blood (2018) 132 (20): 2143–2153

Uso preemptivo de Rituximab



Numbers at risk										
Rituximab	30	30	24	15	13	12	7	3	2	1
No rituximab	18	17	11	9	9	8	8	5	5	3

Rituximab preemptivo pode reduzir em 85% o risco de recaída da PTT em pacientes com deficiência persistente da ADAMTS 13

Hie et al. Blood (2014) 124 (2): 204–210
Jestin et al. Blood (2018) 132 (20): 2143–2153

Em resumo

- PTT adquirida doença autoimune causada pela ação de anticorpos anti-ADAMTS13 e acúmulo de multímeros de alto peso molecular do FVW
- Deficiência da ADAMTS13 confirma o diagnóstico de PTT adquirida
- PLASMIC score tem valor preditivo negativo para def. ADAMTS13
- Tratamento inicial: plasmaférese diária + corticosteróides +/- rituximab
- Tratamento complementar (novo paradigma): caplacizumab
- Persistência de ADAMTS13 < 10% configura pior prognóstico

ISTH Guidelines for Diagnosis of Thrombotic Thrombocytopenic Purpura*

Suspeita clínica+alta probabilidade pré-teste de PTTa

Coletar ADAMTS 13
Iniciar plasmaférese + corticóides

ADAMTS 13 > 20%	ADAMTS 13: 10 - 20%	ADAMTS 13 < 10%
Considerar outros diagnósticos	Avaliar clinicamente se manutençao do tratamento Considerar outros diagnósticos	Manter tratamento Considerar adicionar Rituximab; Caplacizumab

*Apresentado no congresso virtual do ISTH em julho de 2020, não publicado

ISTH Guidelines for Treatment of Thrombotic Thrombocytopenic Purpura

PRIMEIRO EVENTO OU RECIDIVA

1. **Recomenda** tratamento com corticosteróides + plasmaférese (recomendação forte, evidência fraca)
2. **Sugere** adição de rituximab ao tratamento inicial (recomendação condicional, evidência muito fraca)
3. **Sugere** uso de caplacizumab no tratamento inicial (recomendação condicional, evidência moderada)

REMISSÃO CLÍNICA MAS ADAMTS 13 DEFICIENTE

1. **Sugere** a uso de rituximabe para profilaxia. (recomendação condicional, evidência muito fraca)
2. Em **gestantes recomenda** tratamento profilático. (recomendação forte, evidência muito fraca)

Zheng, X.L. J Thromb Haemost. Accepted Author Manuscript. doi:10.1111/jth.15010

Casos Clínicos

Caso Clínico 1

platelets

http://informahealthcare.com/plt
ISSN: 0953-7104 (print), 1369-1635 (electronic)

Platelets, Early Online: 1–4
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informa healthcare

CASE REPORT

Acquired thrombotic thrombocytopenic purpura due to antibody-mediated ADAMTS13 deficiency precipitated by a localized Castleman's disease: A case report

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Abstract

Acquired ADAMTS13 inhibitor causing thrombotic thrombocytopenic purpura (TTP) may be precipitated by some infections, inflammatory diseases or neoplasia. We reported a case of refractory TTP precipitated by a newly diagnosed localized Castleman's disease (CD). TTP was initially treated with plasma exchange and immunosuppressive therapy with corticosteroids; however the treatment failed to promote sustained response. During hospitalization, an abdominal tumor was diagnosed and resected; the histological analysis revealed a CD of hyaline-vascular variant rich stroma. After tumor removal, the patient achieved a long-lasting clinical remission and normalized ADAMTS13 activity. This clinical case describes a novel association of acquired ADAMTS13 inhibitor and CD. The antibody to ADAMTS13 developed along with the systemic manifestation of CD and promptly disappeared after the resection of the tumor. There are reports of neoplasia-associated thrombotic microangiopathy however direct evidence of CD-dependent ADAMTS13 inhibitor had not yet been reported.

Keywords

ADAMTS13, antibody, castleman's disease, lymphoproliferative disorder, thrombotic microangiopathy, thrombotic thrombocytopenic purpura

History

Received 11 January 2014
Revised 6 March 2014
Accepted 11 March 2014
Published online 22 May 2014

Caso Clínico 1

- Masculino, 40 anos
- Quadro de adinamia, febre, icterícia, dor abdominal e cefaléia de início há 30 dias
- Diagnóstico inicial: Leptospirose
- Tratamento: antibioticoterapia e suporte

Benevides, Orsi. Platelets. 2015;26(3):263–6

Caso Clínico 1

- Após 15 dias teve piora clínica
  - Ataque isquêmico transitório, plaquetopenia grave e insuficiência renal (5 sessões de diálise)
- Hemograma:
  - Hb= 5,5 g/dL (anemia)
  - Reticulócitos= 8% (reticulocitose)
  - Plaquetas 5000/uL (plaquetopenia)
  - Esquizócitos no sangue periférico
- Coombos direto negativo

Benevides, Orsi. Platelets. 2015;26(3):263–6

Caso Clínico 1

- Outras provas de hemólise
  - BI=2,5
  - LDH=950
  - Haptoglobina sérica < 7g/dL
- Função renal
  - U=62 Cr=2,3
- CT de crânio
  - Pequenas áreas sugestivas de isquemia

Benevides, Orsi. Platelets. 2015;26(3):263–6

Caso Clínico 1

- Preenche critérios para microangiopatia trombótica
  - Anemia hemolítica, esquizócitos, plaquetopenia
- PLASMIC score
  - https://harvardtma.partners.org/PLASMIC/
  - 6 pontos (60 - 80% de chance de AD < 10% / PTT)
    - (+) plaquetopenia, hemolise, ausencia de neoplasia ou transplante, coagulograma e VCM normais
    - (-) creatinina maior que 2,0 mg/dL

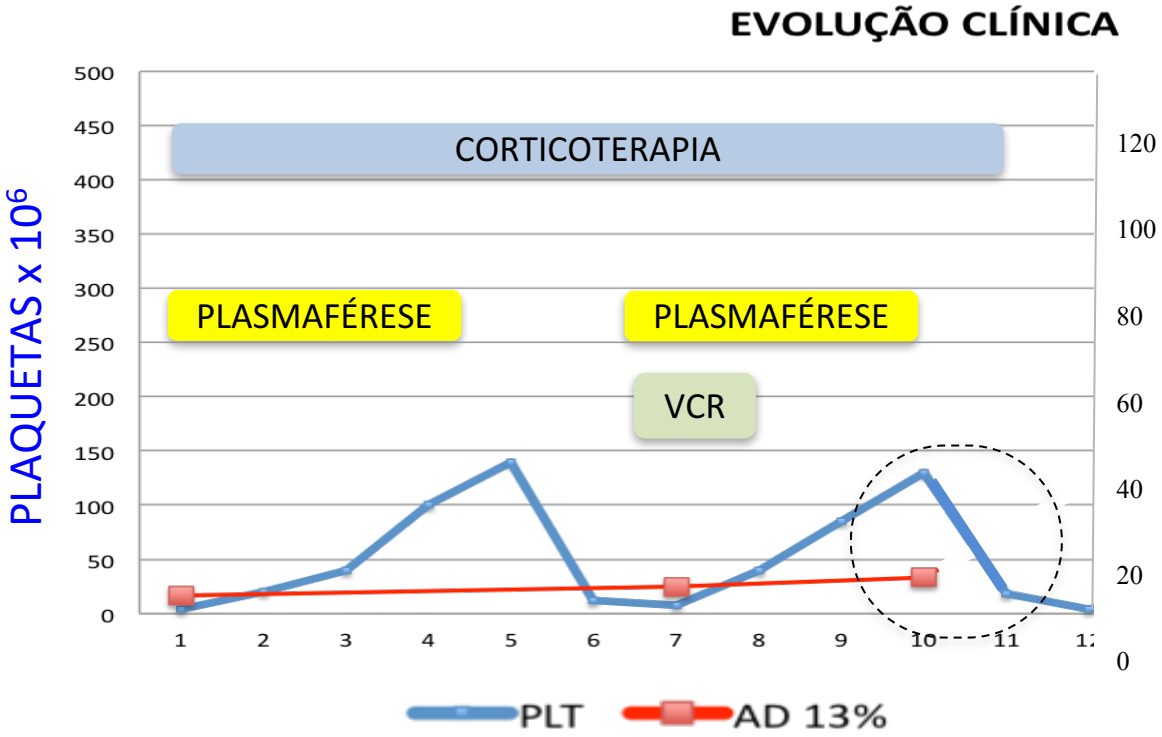
Benevides, Orsi. Platelets. 2015;26(3):263–6

Caso Clínico 1

- Diagnóstico: Púrpura Trombocitopênica Trombótica
- Exames complementares: dosagem da atividade de ADAMTS 13 = 0%
- Tratamento: Plasmaférese + corticoterapia

Benevides, Orsi. Platelets. 2015;26(3):263–6

Caso Clínico 1



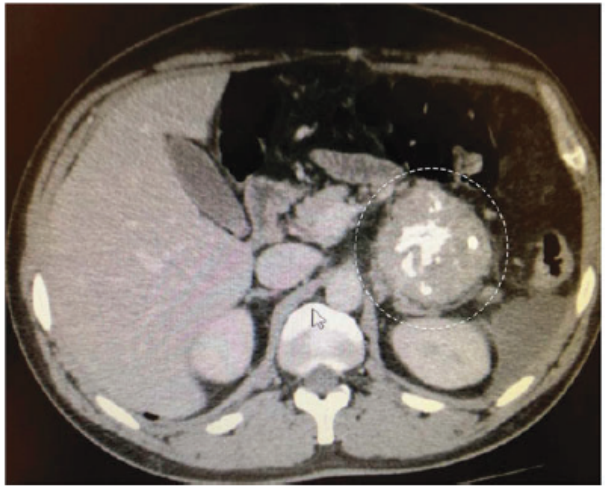


Figure 2. CT scan showing a retroperitoneal tumor located inferior to the tail of the pancreas and anterior to the left kidney, with foci of gross calcification in between, circumscribed, measuring $7.0 \times 6.5 \times 9.0$ cm. The tumor was heterogeneously hypervascular in the arterial phase (shown in the Figure) with homogenization in other phases.

CT de abdomem mostrou tumor vascular de 10 cm de diâmetro

Benevides, Orsi. Platelets. 2015;26(3):263–6

Caso Clínico 1

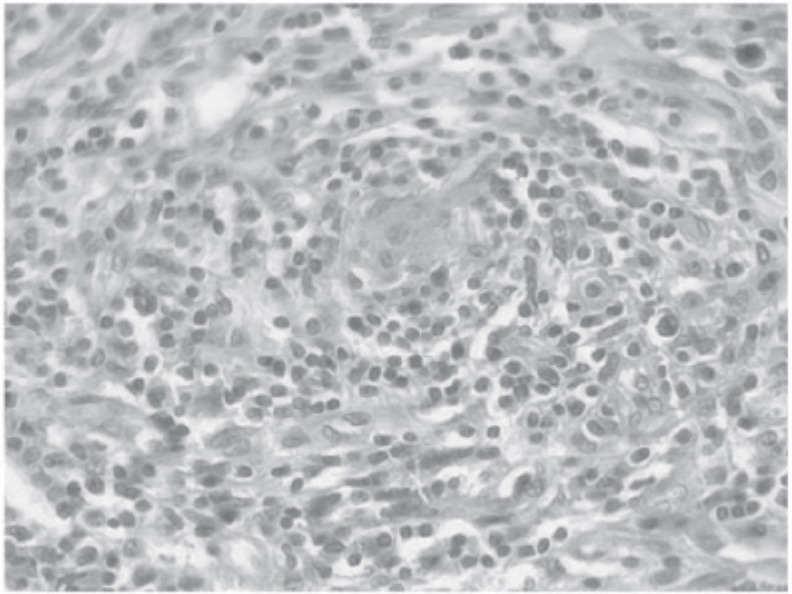


Figure 3. Histology of the tumor: Germinal center surrounded by concentrically arranged lymphocytes, which give the classic ''onion skin'' appearance described in CD.

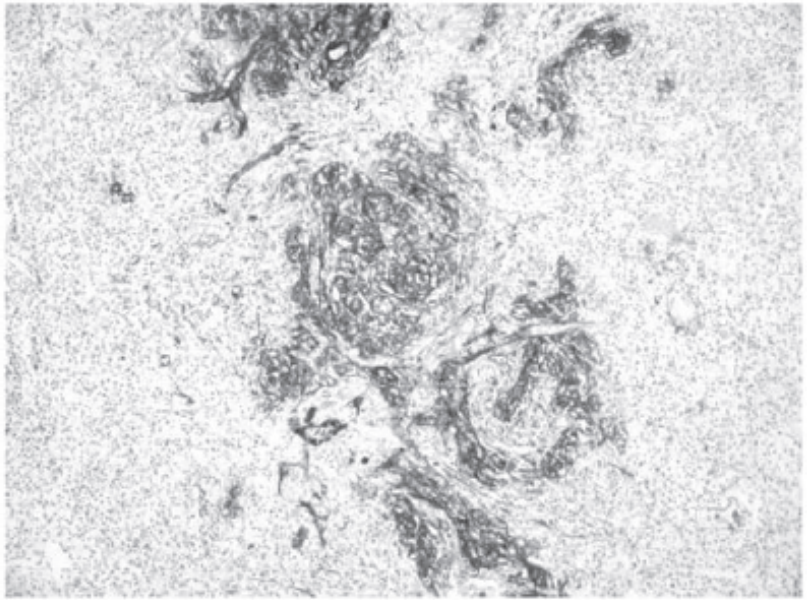


Figure 4. Imunohistochemistry: Germinal center and surrounding lymphocytes show CD23 positivity.

Benevides, Orsi. Platelets. 2015;26(3):263–6

Caso Clínico 1

- PTTa, secundária a doença linfoproliferativa
- Controlada com plasmaférese
- Tratamento definitivo
  - tratamento doença de base
  - normalização da ADAMTS 13

Caso Clínico 2

- Feminina, 34 anos, 30 dias de história
- Após parto: quadro de adinamia, sem febre, sangramento na cicatriz da cesariana. Anemia e plaquetopenia, transfusão de 4 ui CH nos últimos 30 dias.
- Diagnóstico inicial: Falência Medular (AA? SMD? Leucemia Aguda?)
- Conduta: internação para investigação

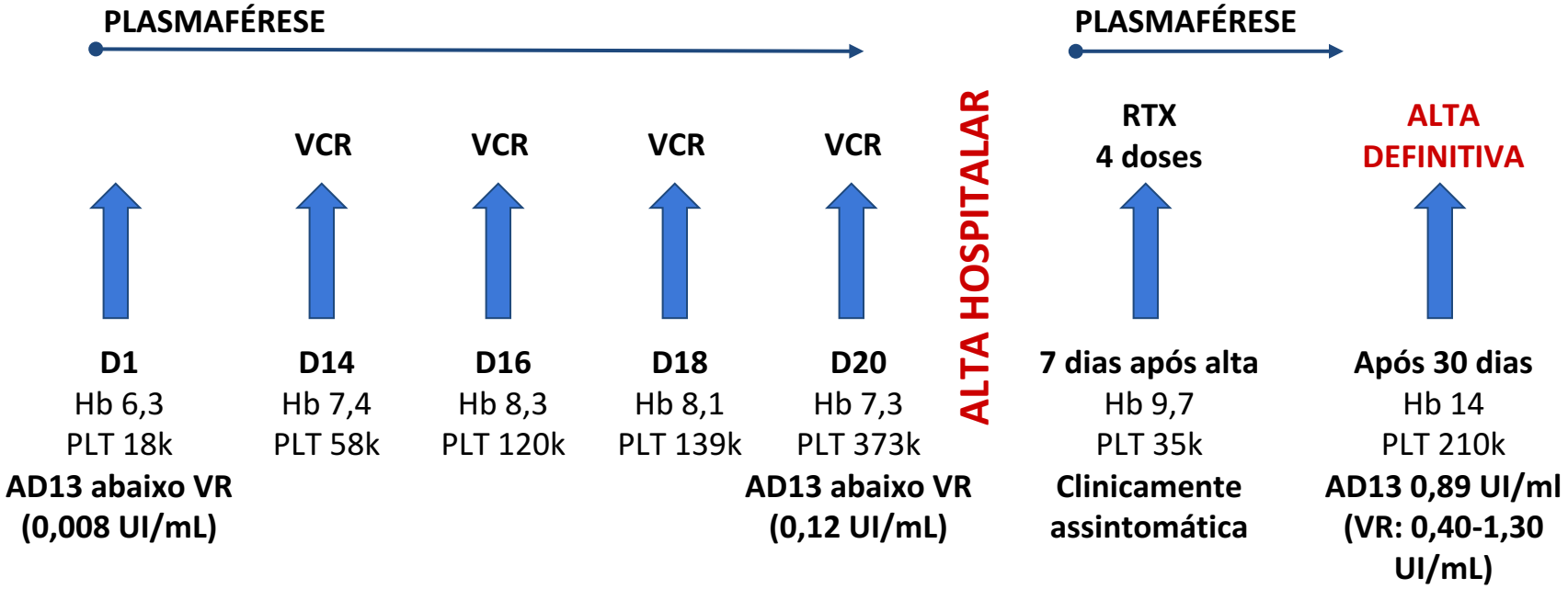
Caso Clínico 2

- Sangue periférico
  - Hb 8,5; VCM 92,5
  - GB 4840 (diferencial normal) LUC: 1,5%
  - Plaq: 22.000
  - Frequentes esquizócitos
- Provas de hemólise
  - BT 2,6 (BI 2,0 BI: 0,6)
  - LDH 2153; Hapto < 7,5
  - CD negativo
- Função renal, hepática, TTPa e TP normais

Caso Clínico 2

- Preenche critérios para microangiopatia trombótica
  - Anemia hemolítica, esquizócitos, plaquetopenia
- PLASMIC score
  - https://harvardtma.partners.org/PLASMIC/
  - 6 pontos (60 - 80% de chance de AD < 10% / PTT)
- ADAMTS 13= 0,118 UI/mL (VR: 0,4 – 1,3)

Caso Clínico 2



1 ano após do episódio agudo de PTTa: assintomatica, hemograma normal, AD13 = 0,23 UI/mL (VR: 0,40-1,30 UI/mL)

Caso Clínico 2

- PTTa, associada a puerpério
- Remissão hematológica mantendo deficiência ADAMTS 13
- Seguimento longo prazo

ferorsi@unicamp.br

Obrigada!