Microangiopatia trombotica dopo trapianto di organi solidi

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Post Transplant Thrombotic Micro Angiopathy TMA

- **D+ HUS** usually does not recur

- **Idiopathic D- HUS or familial HUS**
  - ✓ may recur in 21–28% of children, and in 33 - 56% of adults
  - ✓ an additional recurrence in 16–20% in the absence of full clinical manifestations
  - ✓ in pts with **factor H or factor I mutation, recurrence occurs in about 80–100% of pts**, while pts with **mutation in MCP do not have recurrence after transplantation**

- **De novo TMA**
  - ❖ viral infections
  - ❖ immunosuppressive drugs
  - ❖ immune damage of the graft

De Novo TMA
after Solid Organ Transplantation

- Incidence
- Causes
- Mechanism of action
- Clinical features
- Treatment

De novo TMA after Solid Organ Transplantation

	Liver	Lung	Visceral	Heart	Kidney
Incidence	4.0%	2.3%	?	'Rare'	0.8–14.0%
Onset*	2 weeks	37 weeks	8 weeks	2 years	<3 months
Survival**	73.6%	71.4%	66.7%	40.0%	80% graft recovery
Risk factors***	Stop PI < 1 week post transplantation HLA-sensitization ABO-incompatibility HCV Splenectomy Transplantation for FHF Longer anhepatic phase	History of TMA Female gender CNI + mTORi Concurrent disease	Acute rejection		CMV, parvovirus 19 Deceased donor Anti-phospholipid antibodies

TMA in non-renal solid organ transplantation, Verbiest A. Blood Reviews 28 (2014) 269

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Immunosuppressive drugs + infections + acute rejection

TMA in non-renal solid organ transplantation, Verbiest A. Blood Reviews 28 (2014) 269

TMA after Lung Transplantation

1044 primary LUTX. 864 bi-lateral, 162 unilateral 18 combined heart-lung-transplantations performed between 1999 and 2012 entered the analysis.

TMA occurred in 21 patients (2.0 %) after a median of 264 (4-1759) days post LUTX. All patients received CNI´s + MMF and steroids as primary IS

TMA Therapy consisted of a **modification in IS** in all patients and additionally **plasmapheresis** was performed in 12 patients. **Eculizumab** was applied to 1 pt.

There was **no difference overall survival after LUTX** in patients with and without TMA (logrank 0.221). Kidney function recovered in 12 patients, **43% pts remained on dialysis.**

However **all patients with TMA had a clinical relevant infection shortly prior** to the diagnosis of TMA.

Conclusion: TMA after LUTX is a rare complication and may be triggered by IS and infections.

A. Scheed, 2012 Thoracic Surgery, Medical University of Vienna, Austria

TMA after Liver Transplantation

ADAMTS13 is a disintegrin-like and **metalloproteinase** with thrombospondin type-1 motifs 13 that specifically cleaves unusually-large von Willebrand factor (VWF) multimers under high shear stress, and **down-regulates VWF function to form platelet thrombi**.

Deficiency of plasma ADAMTS13 activity **induces** a life-threatening systemic disease, termed **thrombotic microangiopathy (TMA)**

TMA after Liver Transplantation

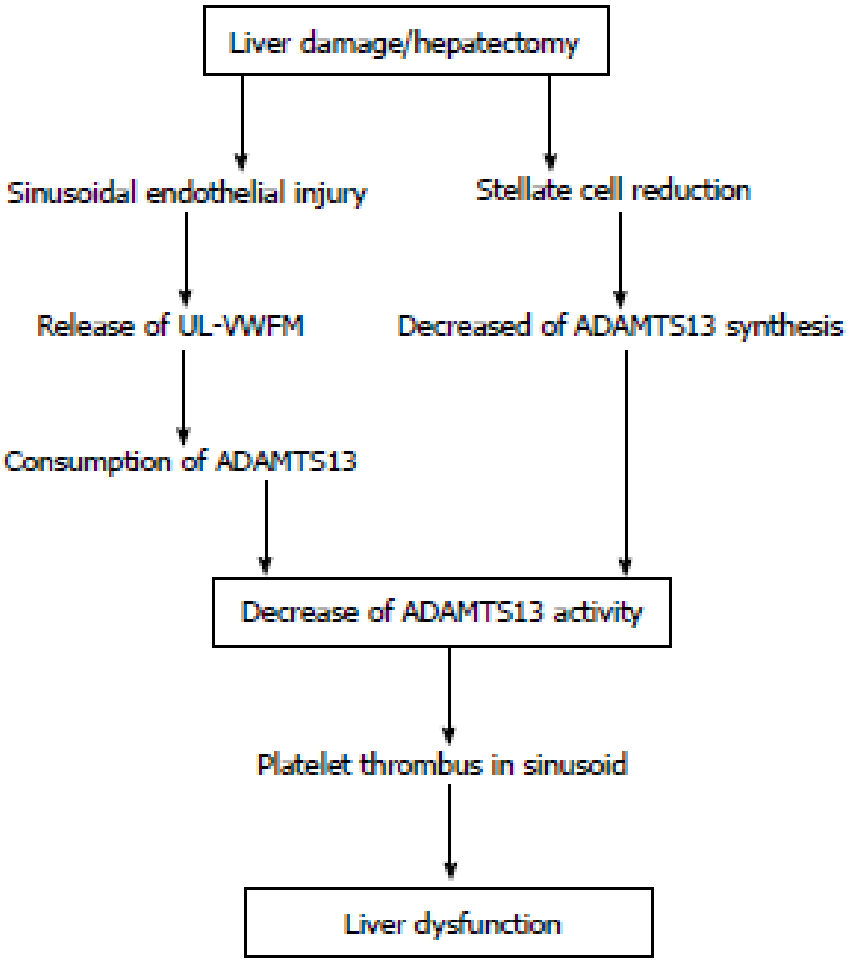
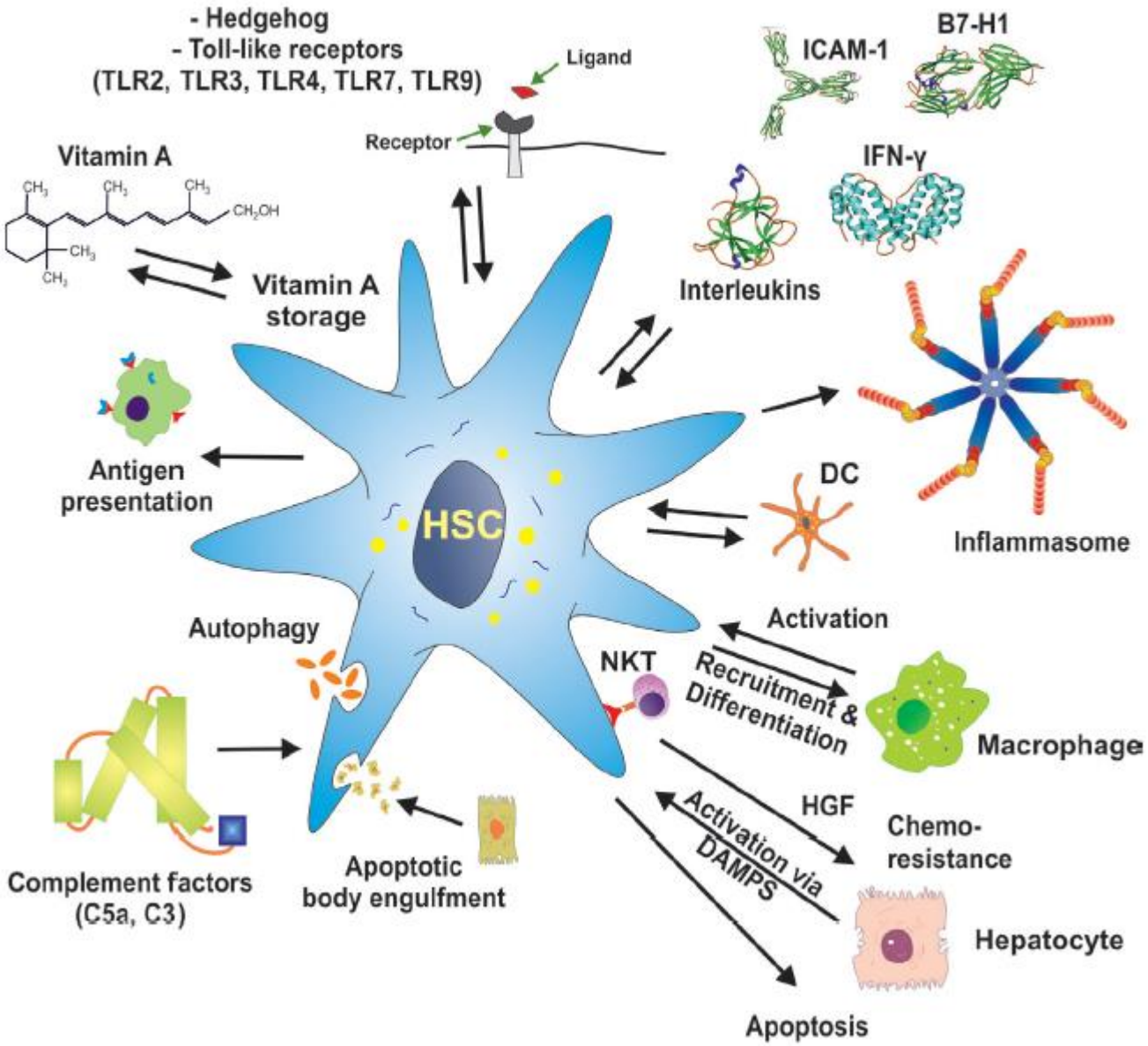
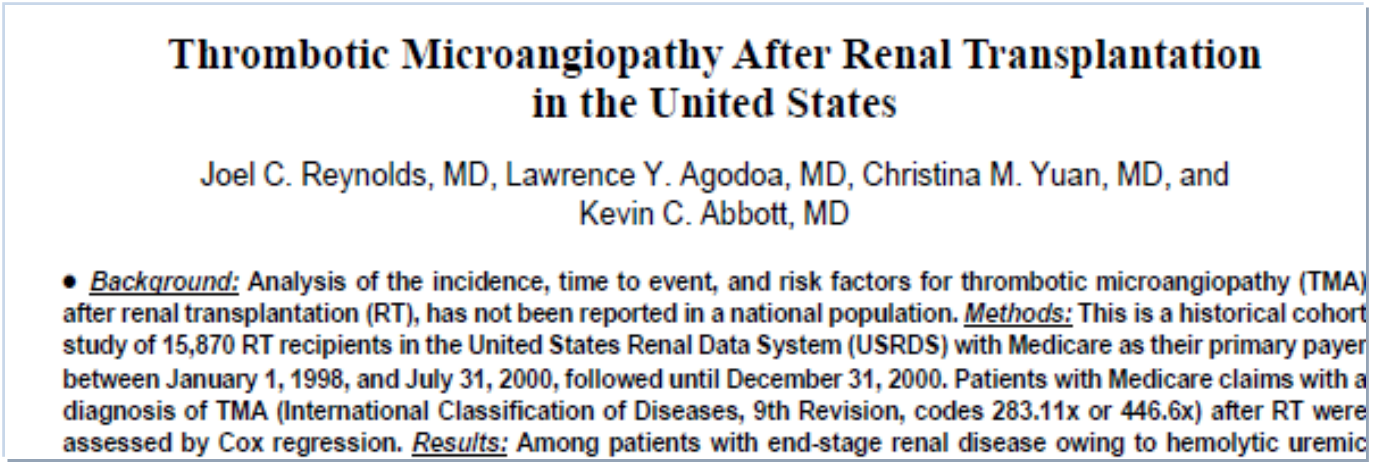


Figure 6 Hypothesis about mechanism of liver dysfunction *via* the local thrombotic thrombocytopenic purpura like mechanism. UL-VWFM: Unusually large von Willebrand factor multimers; ADAMTS13: A disintegrin-like and metalloproteinase with thrombospondin type-1 motifs 13.

Hepatic stellate cells



Vol 3, No 6 (December 2014): Hepatobiliary Surgery and Nutrition



Thrombotic Microangiopathy After Renal Transplantation in the United States

Joel C. Reynolds, MD, Lawrence Y. Agodoa, MD, Christina M. Yuan, MD, and Kevin C. Abbott, MD

• *Background:* Analysis of the incidence, time to event, and risk factors for thrombotic microangiopathy (TMA) after renal transplantation (RT), has not been reported in a national population. *Methods:* This is a historical cohort study of 15,870 RT recipients in the United States Renal Data System (USRDS) with Medicare as their primary payer between January 1, 1998, and July 31, 2000, followed until December 31, 2000. Patients with Medicare claims with a diagnosis of TMA (International Classification of Diseases, 9th Revision, codes 283.11x or 446.6x) after RT were assessed by Cox regression. *Results:* Among patients with end-stage renal disease owing to hemolytic uremic

- ***historical cohort*** **study of 15,870 RTx recipients in the United States Renal Data System (USRDS) with Medicare as their primary payer 1998 – 2000**

- **149 casi post Tx – TMA**

- **in *ESRD due to hemolytic uremic* syndrome (HUS) post KTx TMA was 28.5 % (14/49 pts)**

- **in ESRD owing to other causes risk of de novo TMA was 0.8% (112 pts)**

- **The risk of TMA was highest for the first 3 months after transplant.**

***American Journal of Kidney Diseases,* Vol 42, No 5, 2003: pp 1058-1068**

Thrombotic Microangiopathy After Renal Transplantation in the United States

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Table 3. Cox Regression Analysis of Factors Independently Associated With Time to HUS and TTP

	P value	AHR	95% CI
Entire cohort			
ESRD owing to HUS (*v* all other causes of ESRD)	<0.001	31.75	14.98, 67.32
Sirolimus use at discharge*	<0.001	2.71	1.32, 5.55
Male recipient (*v* female)	0.038	0.62	0.39, 0.98
Recipient age (<35 *v* > 57)	<0.001	5.40	2.37, 12.35
Donor age (>48.3 *v* < 24.1)	<0.001	2.20	1.12, 4.32
No. in final model	11,671		
No. in final model with imputed values	13,991		
Excluding recipients with ESRD owing to HUS (de novo HUS)†			
Sirolimus use at discharge*	0.007	2.69	1.31, 5.52
Male recipient (*v* female)	0.005	0.50	0.31, 0.81
Recipient age (<35 *v* > 57 y)	<0.001	5.80	2.38, 14.16
Donor age (>48.3 *v* < 24.1 y)	0.006	3.14	1.39, 7.09
No. in final model	11,636		
No. in final model with imputed values	13,948		
Time to TTP			
Sirolimus use at discharge*	<0.001	7.24	2.86, 18.31
No. in final model with imputed values	13,992		

NOTE. Cox regression analysis was not performed for recurrent TMA because of insufficient numbers of cases for analysis.

Abbreviations: AHR, adjusted hazard ratios; CI, confidence interval.

*Versus all other medications.

†TTP was not available as a cause of ESRD.

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	P value	AHR	95% CI

- **Risk factors for de novo TMA included**
  - **younger recipient age**
  - **older donor age**
  - **female recipient**
  - **initial use of sirolimus.**

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Thrombotic Microangiopathy After Renal Transplantation in the United States

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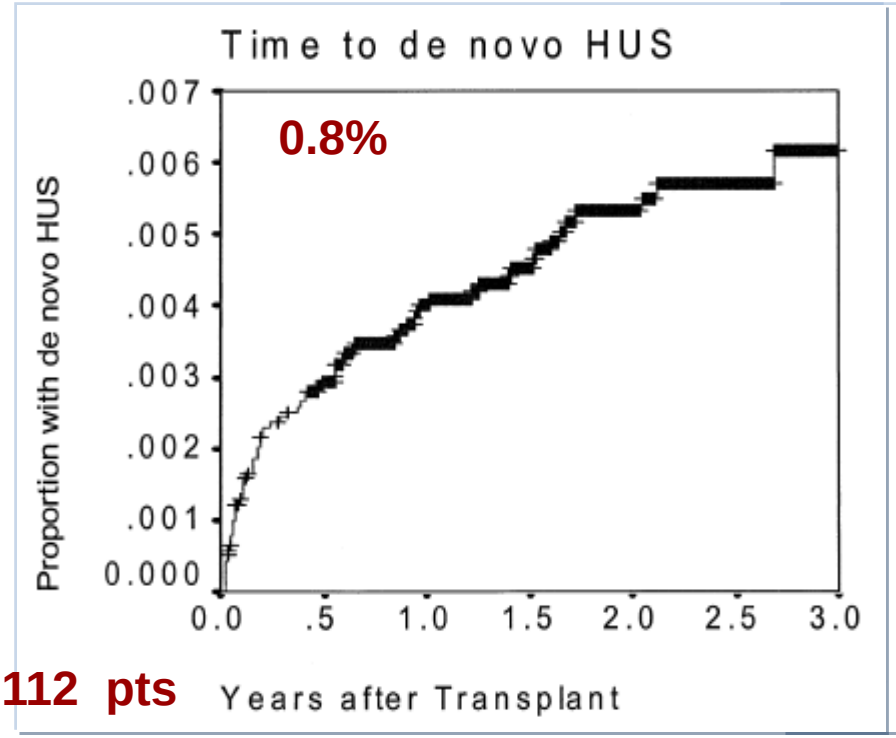
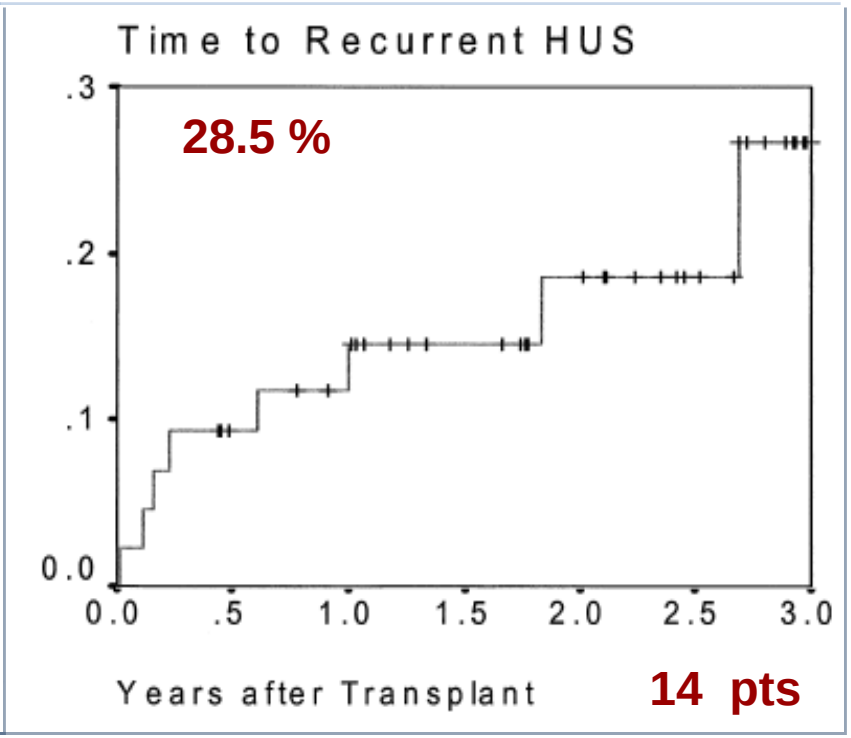
16.257 Medicare transplant pts 1998 - 2000



112 pts



14 pts

single-centre studies reported an incidence ranging between 4% and 14%

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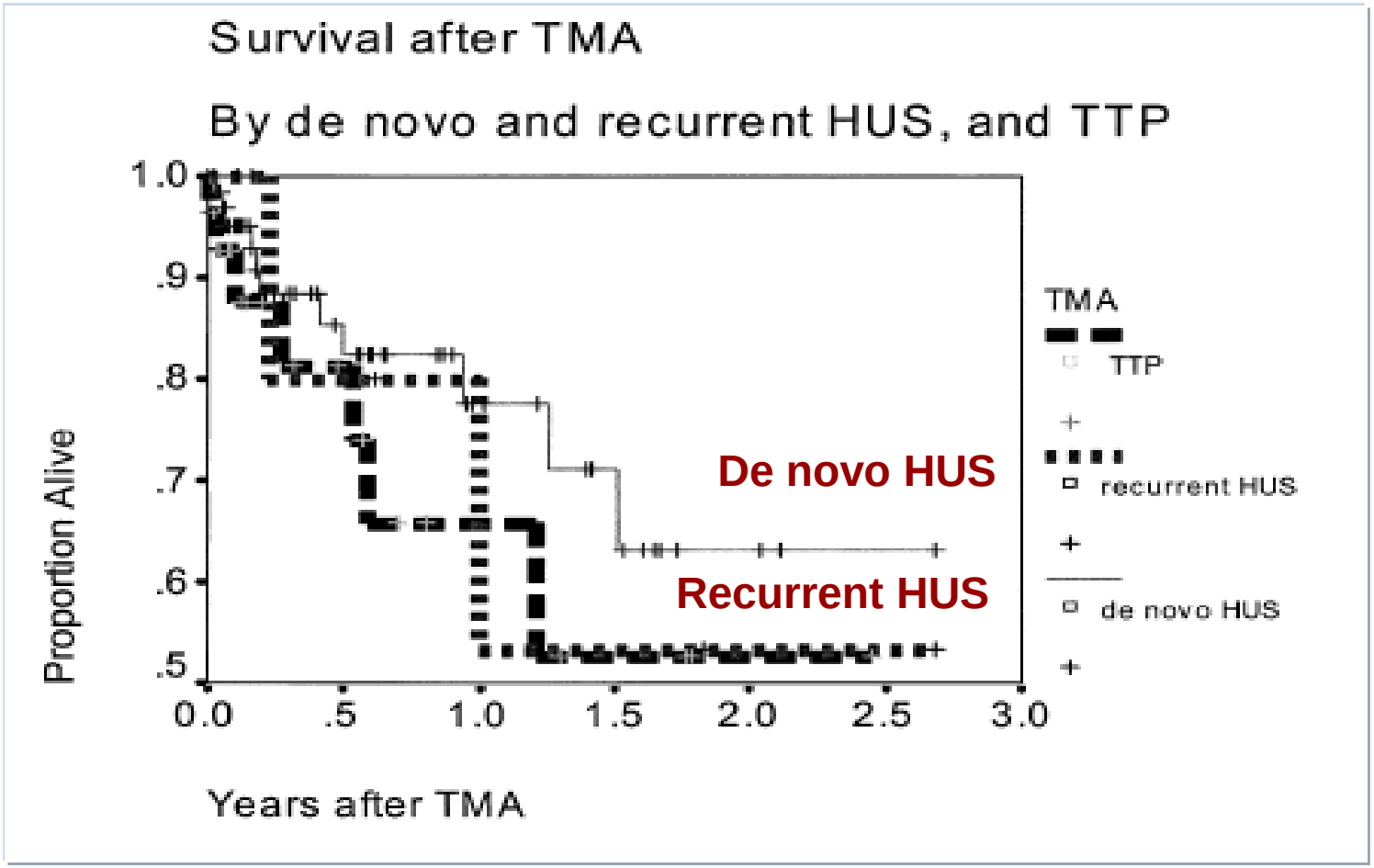

American Journal of Kidney Diseases, Vol 42, No 5 2003: pp 1058-1068

TMA after Solid Organ Transplant

- Incidence
- Causes
- Mechanism of action
- Clinical features
- Treatment

De novo post-transplant TMA

- **the risk of developing a TMA in tx kidneys**.
  - **marginal kidneys**
  - **cytomegalovirus infection**
  - **parvovirus B 19 infection**
  - **BK polyoma virus nephritis**
  - **antiphospholipid antibodies**
  - **Anticardiolipin antibodies in HCV-positive patients**
  - **Malignancy**
  - **Drugs**

TMA after Solid Organ Transplant

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TMA after Solid Organ Transplant

Hypothesis of pathogenesis

- **CNIs: CsA and Tacrolimus are directly toxic to microvascular endothelial cells and can induce microvascular constriction, endothelial lesions and platelet aggregation.**
- **mTOR inhibitors : Sirolimus and Everolimus induce downregulation of Vascular Endothelial Growth Factor, which is required for repairing endothelial injury**
- **Viral Infections (CMV, HIV, And PVB19)**
- **Renal Ischemia Reperfusion Injury**
- **Antibody Mediated Acute Humoral Rejection**

↓

Microvascular endothelial injury and platelet aggregation

Intravascular thrombi

TMA

G. Remuzzi, 2010)

De novo post-transplant TMA

ELSEVIER

Prospective Analysis of Thrombotic Microangiopathy After Renal Transplantation: Comparison Between Cyclosporine and Tacrolimus Immunosuppression

K. Tanabe, T. Tokumoto, H. Ishida, H. Shimmura, K. Omoto, K. Makiyama, F. Toda, and H. Toma

THROMBOTIC microangiopathy (TMA), the so-called hemolytic uremic syndrome (HUS) is a dangerous disorder characterized by microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure.[1]

HUS is a well-recognized serious complication of bone marrow transplantation.[2] Graft-versus-host disease, cytomegalovirus infection, anticancer drug therapy, and total

Table 1. Incidence of TMA

	CyA	FK
ABO incompatible	3/11 (27%)	5/23 (22%)
ABO compatible	1/58 (1.7%)	2/140 (1.4%)

Transplantation Proceedings, 34, 1819–1820 (2002)

TMA after Solid Organ Transplant

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Risk of recurrent post-renal transplant TMA

Table 1. Risk of recurrence of the different forms of thrombotic microangiopathy (TMA) after renal transplantation.

Forms of TMA in native kidneys	Risk of recurrence in transplanted kidneys
Postdiarrhoeal (D+)	Negligible
Nonpostdiarrhoeal (D–).	
Sporadic or familial forms	
Mutation in factor H	80%
Mutation in factor I	80–100%
Mutation in membrane cofactor protein	0%
Idiopathic	33–56%
Secondary to pregnancy, drugs, etc.	Negligible

C. Ponticelli Transplant International 2006 (19) 789

TMA after Solid Organ Transplantation

Clinical presentation

The clinical presentation of TMA is variable:

a) SYSTEMIC signs of hemolytic uremic syndrome (HUS)

- **Findings of hemolytic - anemia Hb < 8 g/dl**
- **Thrombocytopenia, platelet count ≤ 10 × 10^4/mm^3**
- **Progressive deterioration of renal function**
- **Elevated serum lactate dehydrogenase [LDH]) level**
- **Reduced serum haptoglobin level**
- **peripheral fragmented erythrocytes schistocytes**

b) LOCALIZED TMA only into the allograft do not present systemic manifestation of HUS. 29-38% of TMA in SOT

De novo post-transplant HUS vs localized TMA

De Novo Thrombotic Microangiopathy in Renal Transplant Recipients: A Comparison of Hemolytic Uremic Syndrome With Localized Renal Thrombotic Microangiopathy

Joshua Schwimmer, MD, Tibor A. Nadasdy, MD, PhD, Patrice F. Spitalnik, MD, Karen L. Kaplan, MD, and Martin S. Zand, MD, PhD

American Journal of Kidney Diseases, Vol 41, No 2 (February), 2003: pp 471-479

De novo post-transplant TMA

Table 2. Patient Data

Patient	Age (y)	Sex	Race	End-Stage Renal Disease Diagnosis	Type of Transplant	No. of Transplants	Loss From TMA	Follow-Up (mon)	Local *v* Systemic	Cause
1	47	M	C	Type 1 diabetes	CAD	1	No	55	L	TAC
2	24	F	C	Type 1 diabetes	SKP	1	No	84	L	TAC
3	33	M	AA	Chronic glomerulonephritis	CAD	1	No	94	L	CSA
4	57	M	AA	Type 2 diabetes	LD	1	No	32	L	TAC
5	40	M	C	Type 1 diabetes	CAD	1	No	26	L	TAC
6	42	M	AA	Hypertensive nephrosclerosis	CAD	1	No	70	L	CSA
7	46	M	C	Renal cell carcinoma	CAD	1	No	75	L	CSA
8	47	F	C	Polycystic	LD	1	No	29	L	Unknown
9	38	F	C	Polycystic	CAD	1	Yes	68	S	CSA
10	30	F	C	Reflux nephropathy	CAD	1	No	26	S	TAC
11	28	M	C	Pauci-immune glomerulonephritis	CAD	1	Yes	15	S	Unknown
12	49	M	C	Type 1 diabetes	CAD	1	Yes	44	S	TAC
13	49	M	AA	Hypertensive nephrosclerosis	CAD	1	Yes	27	S	TAC
14	56	F	H	Chronic glomerulonephritis	CAD	1	No	137	S	CSA
15	43	F	C	Interstitial nephritis	CAD	1	No	93	S	CSA
16	46	M	C	Chronic glomerulonephritis	CAD	1	No	27	S	TAC
17	35	F	C	Renal cell carcinoma	CAD	2	No	156	S	CSA
18	50	F	C	Polycystic	LD	1	No	35	S	TAC
19	42	F	C	ImmunoglobulinA nephropathy	CAD	1	No	23	S	TAC
20	31	F	C	Type 1 diabetes	CAD	1	Yes	11	S	CSA
21	40	M	C	Chronic glomerulonephritis	CAD	1	Yes	39	S	CSA

Abbreviations: C, Caucasian; AA, African American; H, Hispanic; CAD, cadaveric transplant; LD, living donor; SKP, simultaneous kidney pancreas transplant; L, local; S, systemic.

American Journal of Kidney Diseases, Vol 41, No 2 (February), 2003: pp 471-479

De novo post-tx systemic vs localized TMA

Table 2. Patient Data

Patient	Age (y)	Sex	Race	End-Stage Renal Disease Diagnosis	Type of Transplant	No. of Transplants	Loss From TMA	Follow-Up (mon)	Local *v* Systemic	Cause
1	4						No	55	L	TAC
2	2						No	84	L	TAC
3	3						No	94	L	CSA
4	5						No	32	L	TAC
5	4						No	26	L	TAC
6	4						No	70	L	CSA
7	4						No	75	L	CSA
8	4						No	29	L	Unknown
9	3						Yes	68	S	CSA
10	3						No	26	S	TAC
11	2						Yes	15	S	Unknown
12	4						Yes	44	S	TAC
13	4						Yes	27	S	TAC
14	5						No	137	S	CSA
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20	3						Yes	11	S	CSA
21	40	M	C	Chronic glomerulonephritis	CAD	1	Yes	39	S	CSA

Localized TMA

Graft loss 0 / 8 0%

Systemic TMA

Graft loss 6 /13 46%

Abbreviations: C, Caucasian; AA, African American; H, Hispanic; CAD, cadaveric transplant; LD, living donor; SKP, simultaneous kidney pancreas transplant; L, local; S, systemic.

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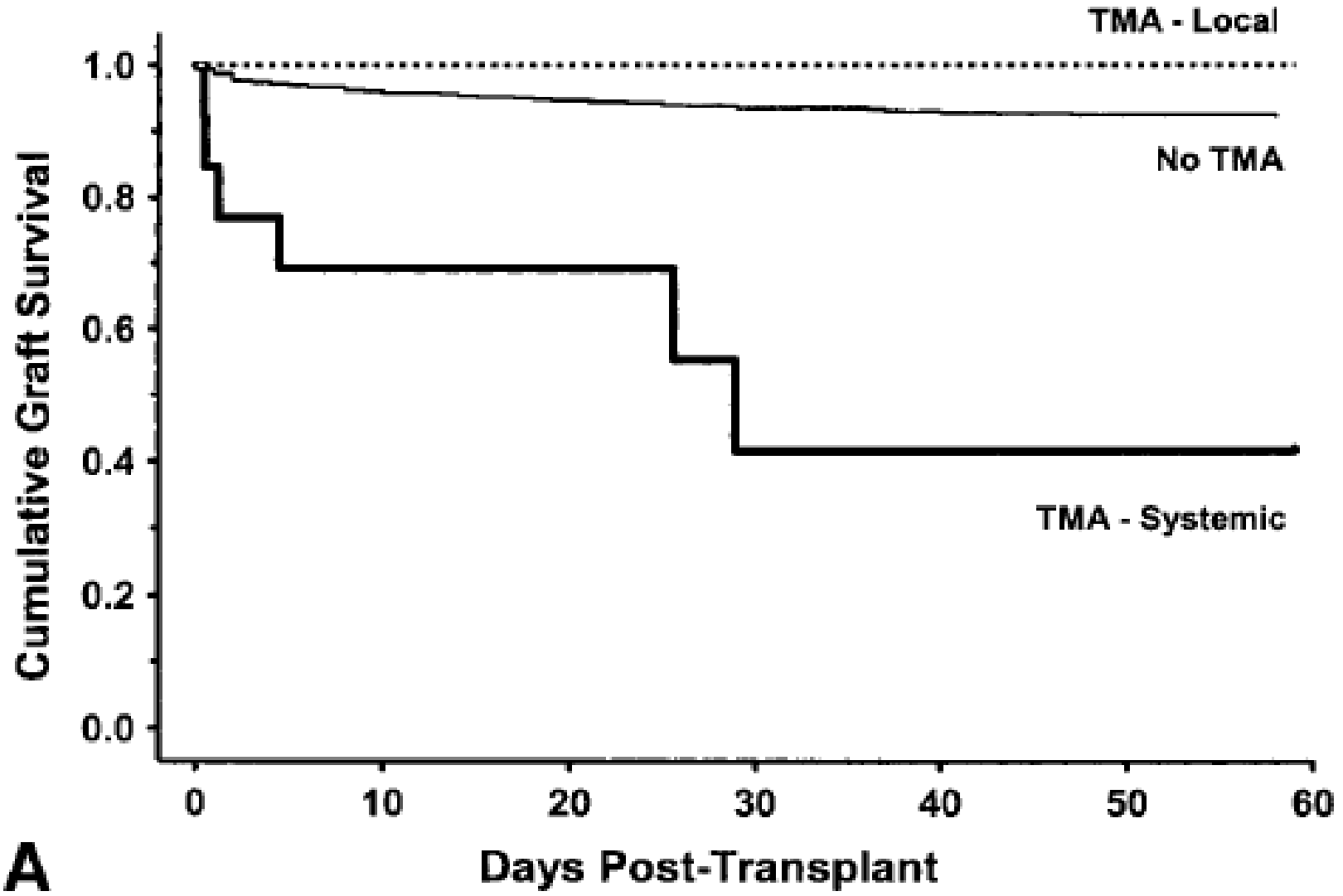
5y Graft Survival Systemic vs localized TMA



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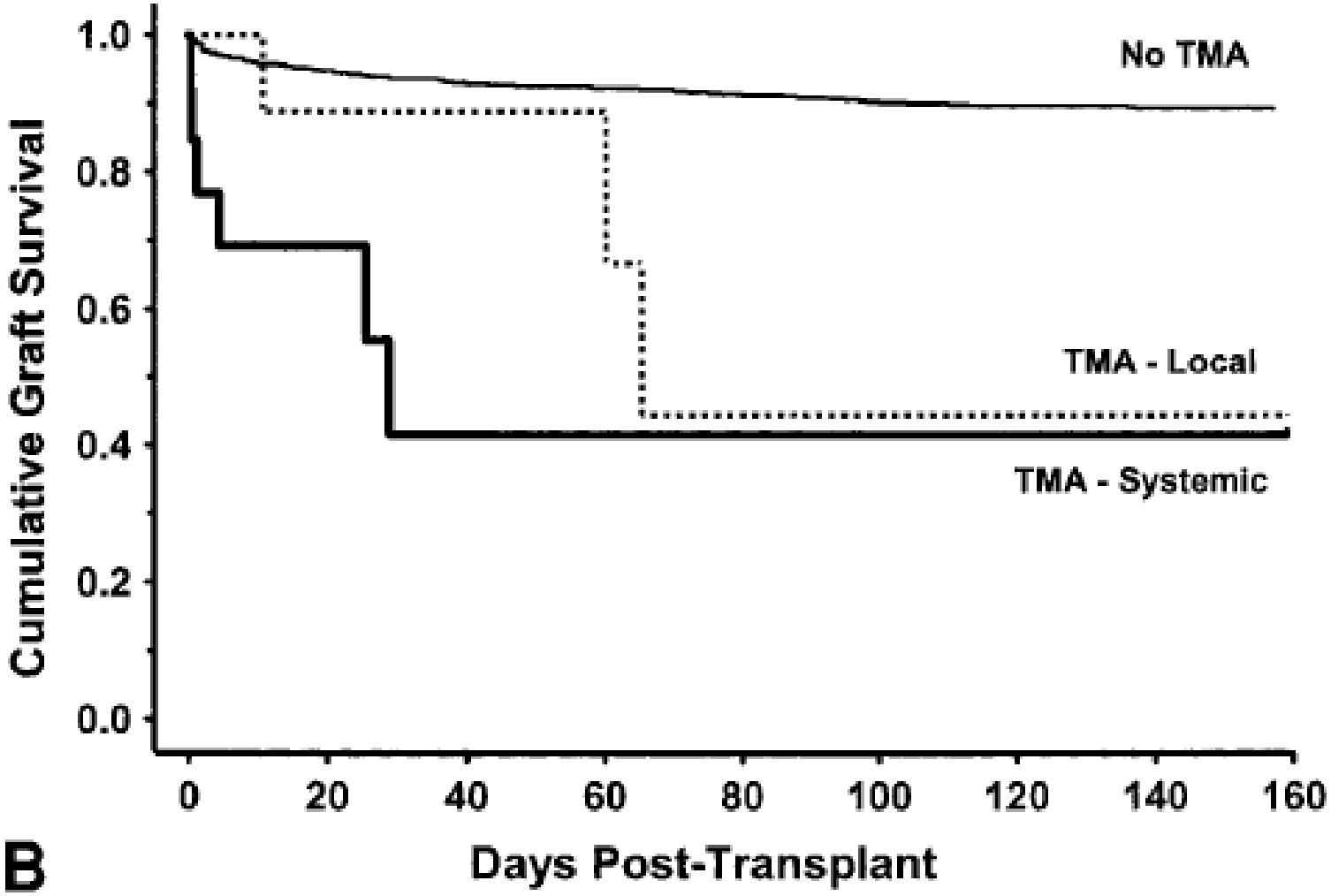
American Journal of Kidney Diseases, Vol 41, No 2 (February), 2003: pp 471-479

13y Graft Survival Systemic vs localized TMA



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De novo post-tx systemic vs localized TMA

Table 4. Comparison of Local and Systemic Posttransplantation TMA

	Local (n = 8)	Systemic (n = 13)	*P*
Diagnosis (days posttransplantation)	106.6 ± 104.2	21.5 ± 19.0	0.0034*
Pretransplant diabetic nephropathy (%)	50	15	0.0961
Hematocrit (relative % decrease)	14.3 ± 10.7	34.3 ± 11.2	0.0007*
Change in creatinine from nadir (mg/dL)	0.66 ± 0.28	0.60 ± 0.24	0.5960
Platelet count nadir (× 1,000/mL)	224 ± 113	66 ± 30	0.0001*
Lactate dehydrogenase peak (U/L)	659 ± 578	1169 ± 870	0.1834
Total bilirubin peak (mg/dL)	0.49 ± 0.16	1.16 ± 0.44	0.0006*
Haptoglobin nadir (mg/dL)	271 ± 185	42.1 ± 75.9	0.0237*
Schistocytes (%)	13	62	0.0247*
Acute rejection on biopsy (%)	50	31	0.3898
Required dialysis (%)	0	54	0.0131*
TMA-related graft loss (%)	0	39	0.0499*
Plasma exhange (%)	13	38	0.3363
Systolic blood pressure (mm Hg)	141 ± 14	149 ± 13	0.1368
Diastolic blood pressure (mm Hg)	76 ± 10	79 ± 8	0.2539

NOTE. Numeric values expressed as mean ± SD, and percentages for categorical values expressed with respect to number in either local or systemic TMA categories. To convert to SI units: creatinine (1 mg/dL = 88.4 μmol/L), bilirubin (1 mg/dL = 17.1 μmol/L), haptoglobin (1 mg/dL = 0.01 g/L).

*Statistically significant, $P < 0.05$.

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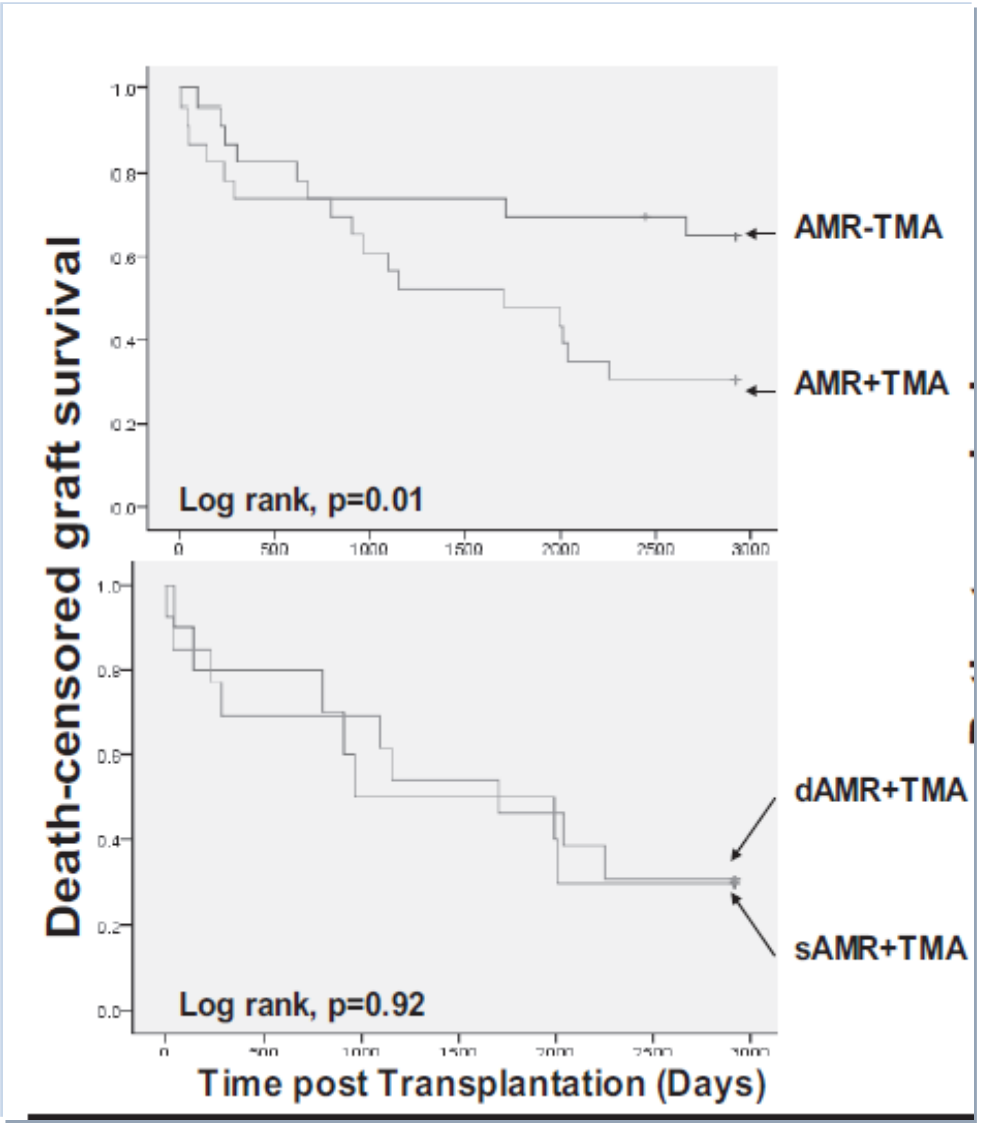
AMR +/-TMA and renal allografts surv



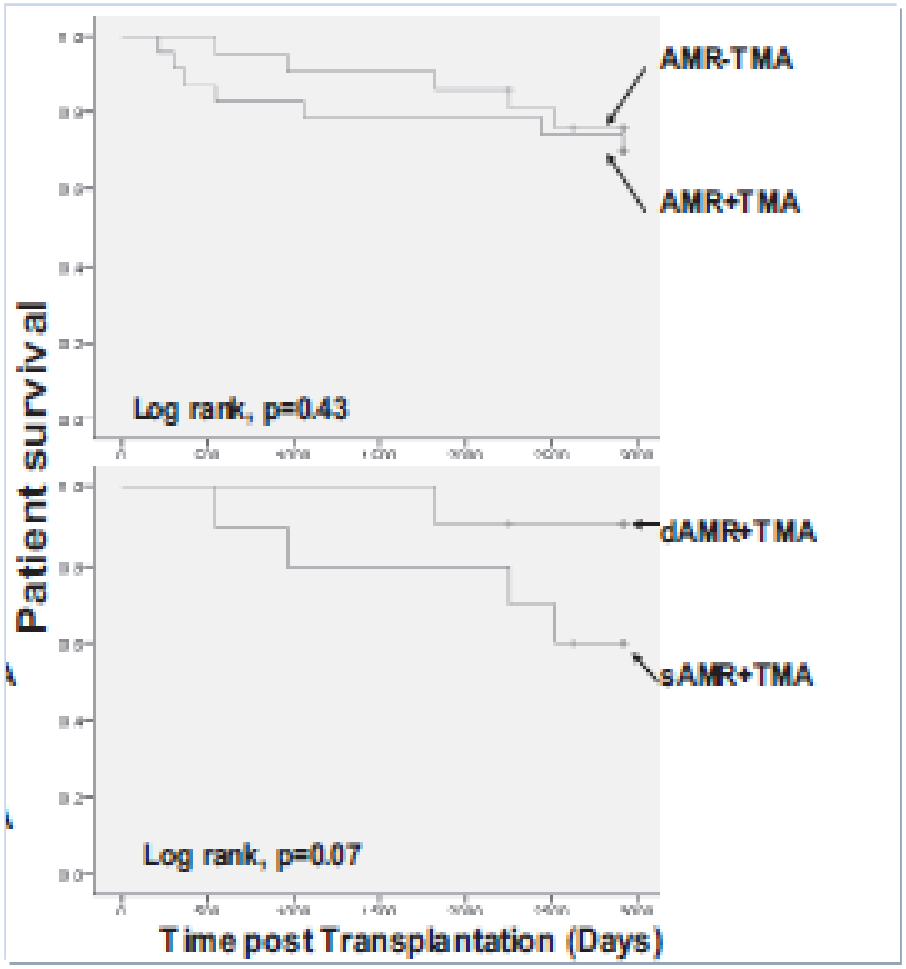
definitive AMR (d-AMR) presents three diagnostic features:

- Morphological tissue injury;
- immunostaining of C4d
- donor-specific anti-HLA ab (DSA).

suspicious AMR (s-AMR) when one of the three features is missing.

Clin Transplant 2016: 30: 105–117 DOI: 10.1111/ctr.12645

AMR +/-TMA in renal allografts PT surv



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De novo post-transplant TMA historical treatment

- Complete **withdrawal of the offending CNIs and mTORi** is essential [61], although not all patients respond [62].

- **Plasma exchange** in addition to CNI withdrawal resulted in a graft salvage rate of 80% in two series [30,56] and in other anecdotal cases [18,65].

- The **addition of i.v. immunoglobulins** resulted in a stable remission in a patient with plasmapheresis-resistant HUS after a double liver and kidney transplantation [66].

- In cases with **cytomegalovirus infection, ganciclovir treatment** may resolve TMA in cases resistant to plasmapheresis and CNI withdrawal [67].

- **Reinstitution of the offending CNI** has been successfully made in a number of patients after recovery of graft function [56,60,68].

- It is possible, however, that the aetiological role of CNIs in the latter cases was secondary or even questionable. As we have today a

Thrombotic Micro Angiopathy TMA

Treatment

- **patients at high risk of TMA recurrence should initially avoid those immunosuppressive drugs (CNI, mTOR antagonists and OKT3) that may enhance the development of TMA.**

- **A possible strategy may consist in an induction therapy with an anti-CD25 monoclonal antibody associated with mycophenolic acid and steroids.**

- **In case of recurrence, plasma exchange twice a week and i.v. immunoglobulins (0.4 g/kg body weight) should be administered until remission.**

- **If there is no response, rituximab (375 mg/m2 weekly for 2–4 administrations) may be attempted.**

Pediatr Nephrol (2015) 30:693–697
DOI 10.1007/s00467-014-3036-8

De novo post-transplant TMA

BRIEF REPORT

De novo tacrolimus-induced thrombotic microangiopathy in the early stage after renal transplantation successfully treated with conversion to everolimus

Gerard Cortina · Raphaela Trojer · Siegfried Waldegger · Stefan Schneeberger · Nadezda Gut · Johannes Hofer

Nephro Urol Mon. 2015 May; 7(3): e27073. DOI: 10.5812/numonthly.7(3)2015.27073

Published online 2015 May 23. **Research Article**

Effectiveness of Intravenous Immunoglobulin Plus Plasmapheresis on Antibody-mediated Rejection or Thrombotic Microangiopathy in Iranian Kidney Transplant Recipient

Simin Dashti-Khavidaki [1,*]; Lida Shojaie [2]; Amin Hosni [2]; Mohammad Reza Khatami [1]; Atefeh Jafari [2]

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De novo post-transplant TMA screening

- **HUS:**
  - **hemolytic-anemia, rapid deterioration of renal function, peripheral schistocytes and thrombocytopenia**
  - **deterioration of graft function + LDH increase**

evaluate

- **mutation of genes encoding factor H or I**
- **anticardiolipine antibodies**
- **coagulation genetic alterations in autosomal dominant polycystic kidney disease (ADPKD) with thrombophilia**

De novo post-transplant TMA
current treatment

- prevention of TMA recurrence
- treatment of recurrent or de novo TMA

De novo post-transplant TMA
current treatment

- plasma exchange sessions + IVIg 100 mg/Kg
- conversion to Belatacept

De novo post-transplant TMA

American Journal of Transplantation 2009; 9: 424–427
Wiley Periodicals Inc.

doi: 10.1111/j.1600-6143.2008.02482.x

Case Report

Belatacept as Maintenance Immunosuppression for Postrenal Transplant *de novo* Drug-Induced Thrombotic Microangiopathy

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curs most frequently in renal transplantation. This is in part because the hemolytic uremic syndrome (HUS) is a not infrequent cause of end stage renal disease, and familial forms in particular have a high rate of recurrence within renal allografts. TMA is described as *de novo* if the disorder arises after transplantantion in patients with no prior history of TMA.

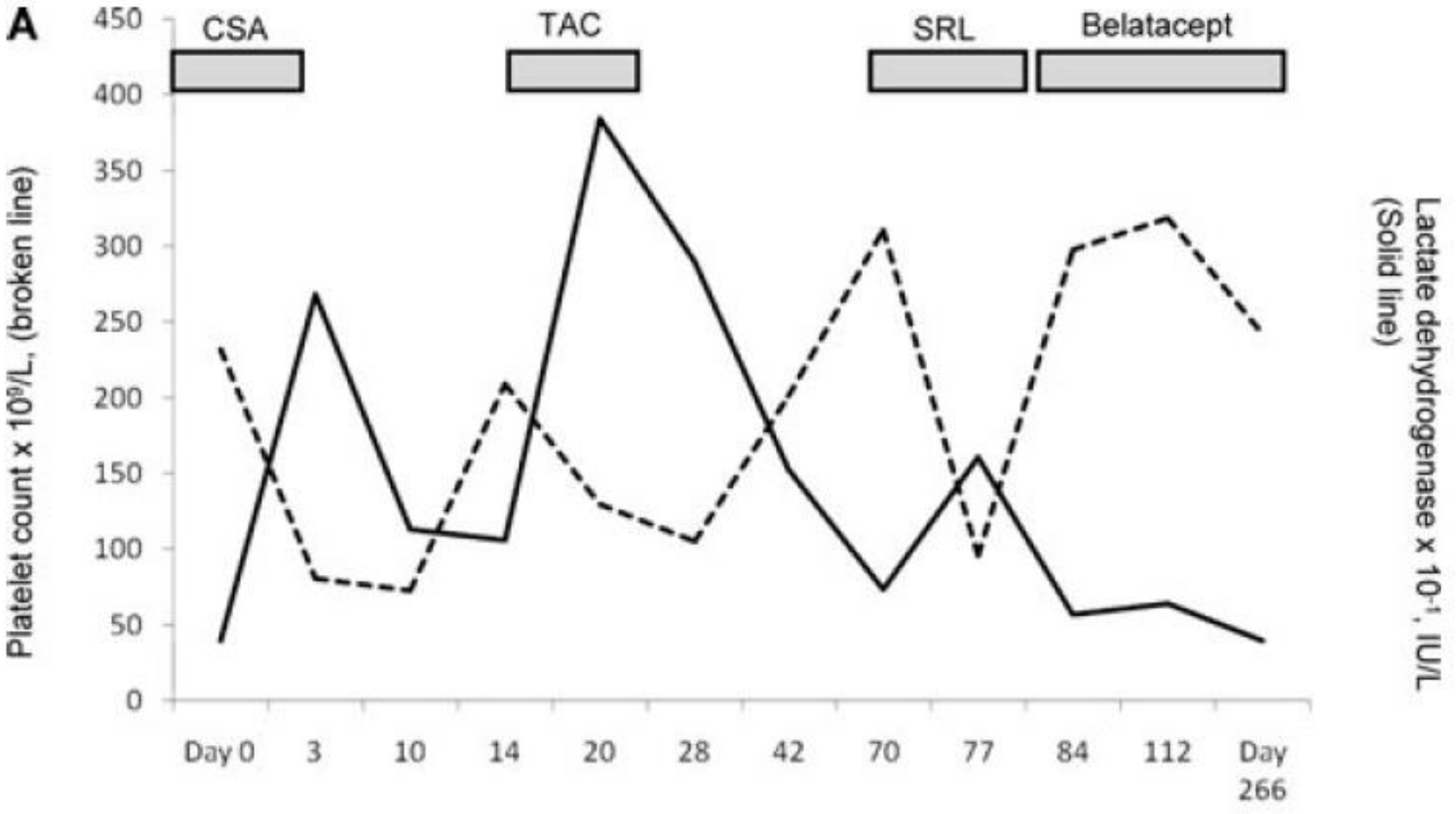
In the latter group, immunosuppressants are usually im-

De novo post-transplant TMA

changes in PTL and LDH

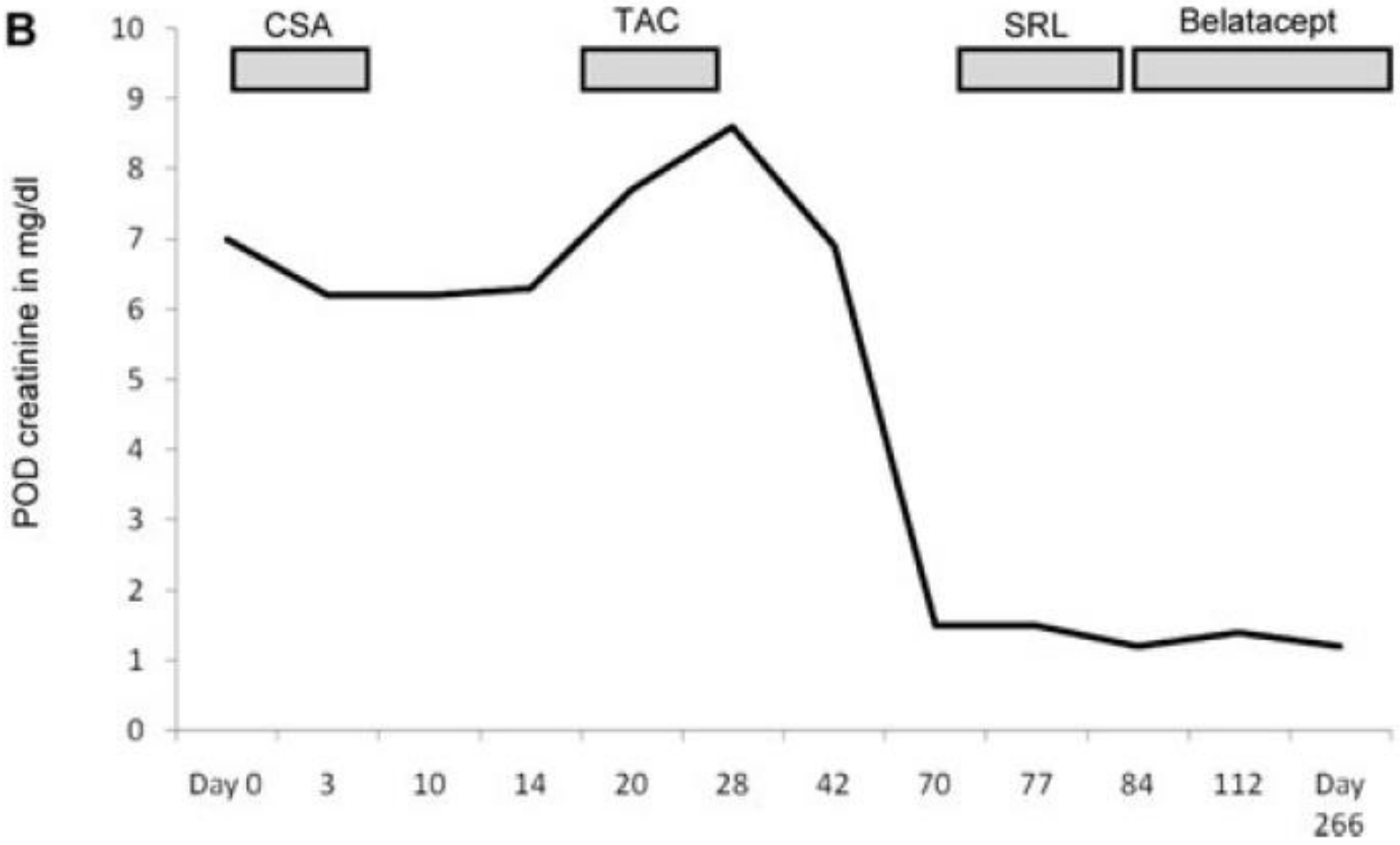
with different immunosuppressive agents

Ashman et al.



American Journal of Transplantation 2009; 9: 424–427

De novo post-transplant TMA improved renal function with belatacept



American Journal of Transplantation 2009; 9: 424–427

Kidney Tx with Eculizumab for aHUS

Eculizumab in Hemolytic Uremic Syndrome

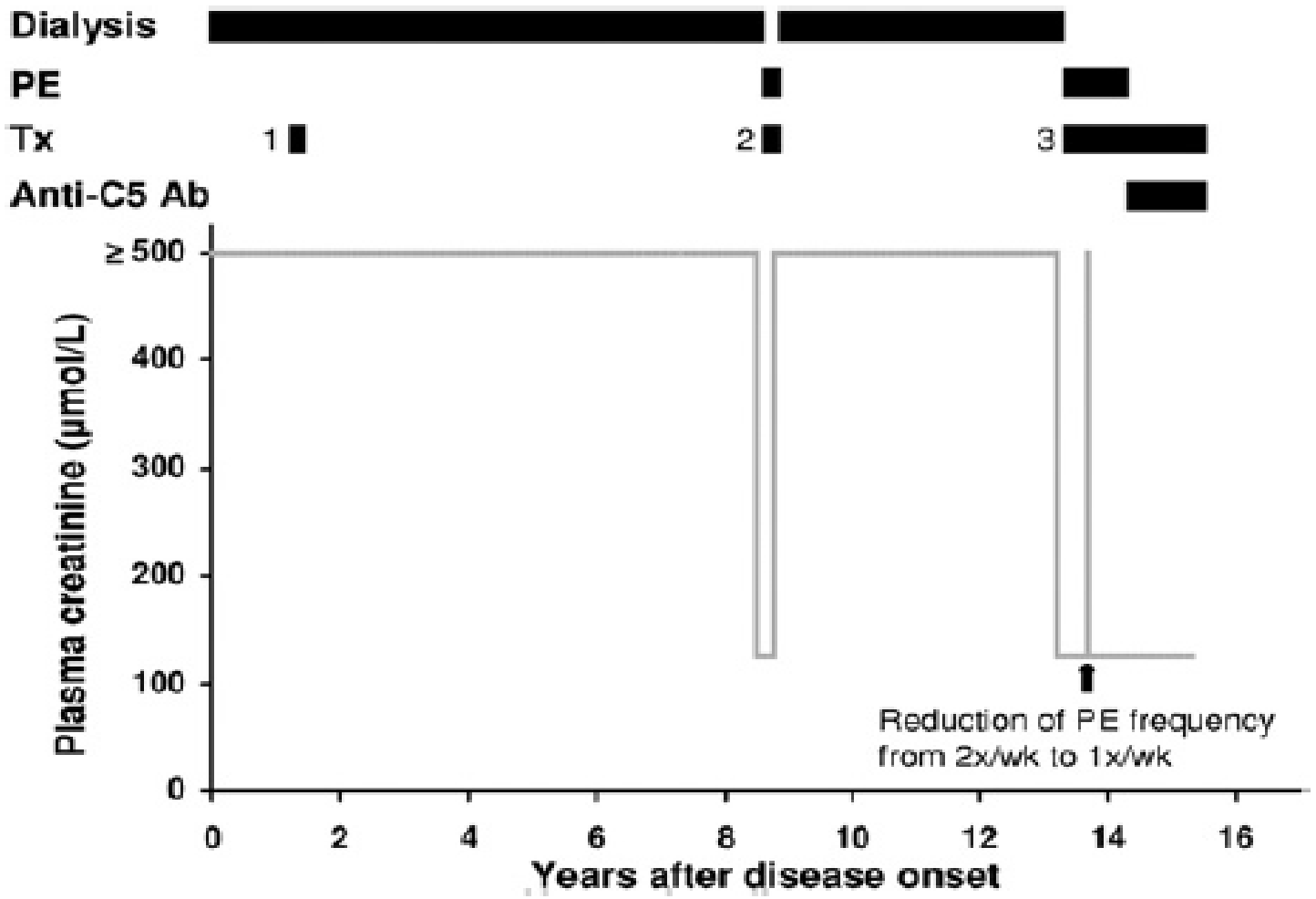


Table 2. Therapies for the Treatment of TMA

Therapy	Status
	Antiplatelet Agents
Aspirin	Anecdotal reports with inconsistent outcome in TTP forms[37-39]
Dipyridamole	Anecdotal reports with inconsistent outcome in TTP forms[37,39]
Dextran 70	Anecdotal reports with inconsistent outcome in TTP forms[40]
Prostacyclin	Anecdotal reports with inconsistent outcome in TTP forms[40,41]
	Antithrombotic Agents
Heparin	Anecdotal reports with inconsistent outcome in HUS[37]
Streptokinase	Anecdotal reports with inconsistent outcome in HUS[42]
	Antioxidant Agents
Vitamin E	Anecdotal reports with inconsistent outcome in HUS[43]
	Immunosuppressive Agents
Eculizumab	FDA and CHMP approved for use in treatment of aHUS
Immunoglobulins	Probably indicated in patients with TTP and anti-ADAMTS13 autoantibodies, aHUS with anti-CFH or anti-C3 autoantibodies, and autoimmune disease[44]
Prednisone/prednisolone	Probably indicated in patients with TTP and anti-ADAMTS13 autoantibodies, aHUS with anti-CFH or anti-C3 autoantibodies, and autoimmune disease[43]
Rituximab	Probably indicated in patients with TTP and anti-ADAMTS13 autoantibodies, aHUS with anti-CFH or anti-C3 autoantibodies, and autoimmune disease[45]
Vincristine	Probably indicated in patients with TTP and anti-ADAMTS13 autoantibodies, aHUS with anti-CFH or anti-C3 autoantibodies, and autoimmune disease[46]
	Fresh Frozen Plasma
Cryosupernatant	Indicated if plasma exchange not possible[47]
Plasma exchange	First-line therapy (except streptococcal disease)[48-50]
Plasma infusion	Indicated if plasma exchange not possible[43,47,49]
Solvent detergent-treated plasma	Indicated if plasma exchange not possible[51]
	Others
Liver transplant	Cure for complement genetic defect (CFH, CFI)[52,55]
Recombinant CFH	Experimental evidence only (laboratory data)[53]

Abbreviations: ADAMTS13, a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13; CFH, complement factor H; CFI, complement factor I; CHMP, European Committee for Medicinal Products for Human Use; FDA, US Food and Drug Administration; HUS, hemolytic uremic syndrome; TMA, thrombotic microangiopathy; TTP, thrombotic thrombocytopenic purpura.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Belatacept and Long-Term Outcomes in Kidney Transplantation

Flavio Vincenti, M.D., Lionel Rostaing, M.D., Ph.D., Joseph Grinyo, M.D., Ph.D., Kim Rice, M.D., Steven Steinberg, M.D., Luis Gaite, M.D., Marie-Christine Moal, M.D., Guillermo A. Mondragon-Ramirez, M.D., Jatin Kothari, M.D., Martin S. Polinsky, M.D., Herwig-Ulf Meier-Kriesche, M.D., Stephane Munier, M.Sc., and Christian P. Larsen, M.D., Ph.D.

7 years follow up

Patient and graft survival and the mean eGFR were significantly higher with belatacept than with CsA

N Engl J Med 2016;374:333-43.
DOI: 10.1056/NEJMoa1506027

Belatacept vs CNIs

Mediana di follow- up 8,4 anni (range 7.5 – 9.3 y)

(# pts)	Belatacept # 14	CNI # 6
eGFR ml/min	60.5 ± 16.8	50.4 ± 16.7
DGF	10 % (2)	5% (2)
Acute Rejection	5% (1)	10% (2)
DSA	0	16% (1)
Drop-out	14.3% (2)	33.3% (2)

Renal Transplantation 2016

- Standard donor
- Old for Old
- Extended Criteria Donors
- Hyperimmunized pts
- Living donation
  - Standard / extended criteria donors
  - ABO incompatible
  - HLA incompatible positive crossmatch
- Deceased Cardiac Death

Immunosoppressione 2016

- ✓ CNIs Cyclosporine / Tacrolimus
- ✓ MMF / MPA / Aza
- ✓ mTORi Everolimus / Sirolimus
- ✓ Basiliximab
- ✓ Thymoglobuline
- ✓ Rituximab
- ✓ Eculizumab / Bortezomib
- ✓ Belatacept

TMA post Solid Organ transplantation

- Seria complicazione del trapianto d'organo
- Probabimente la reale incidenza è sottovalutata
- Screening necessario in pts con storia di TMA
- Tipologia di pazienti trapiantati oggi potrebbe aumentare i casi di de novo TMA
- Esistono possibilità di cura
- Necessari studi clinici