

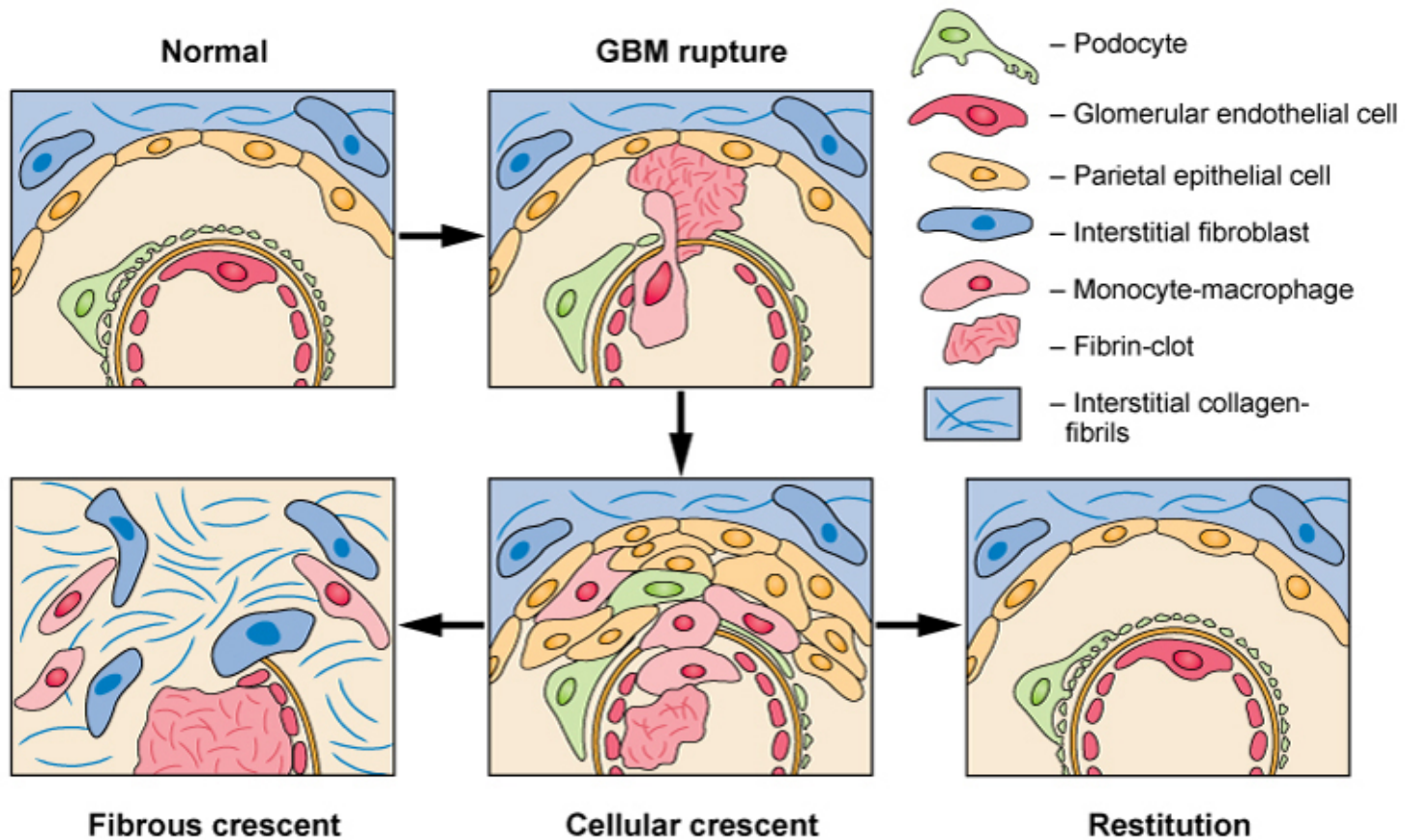
ANCA ilişkili Hızlı İlerleyen Glomerülonefrit – Goodpasture sendromu

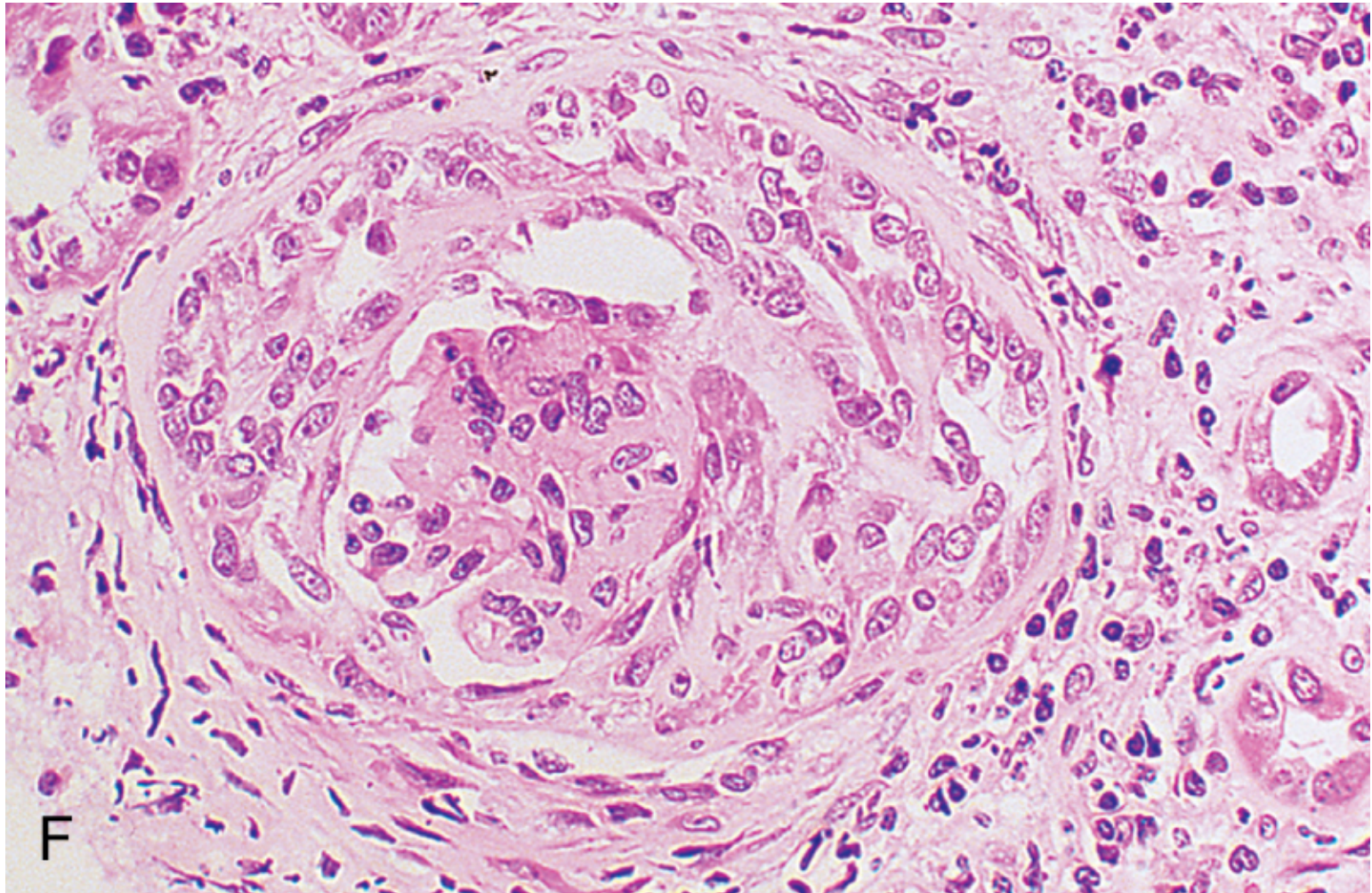
Doç. Dr. Sinan Trabulus
Cerrahpaşa Tıp Fakültesi
Nefroloji Bilim Dalı

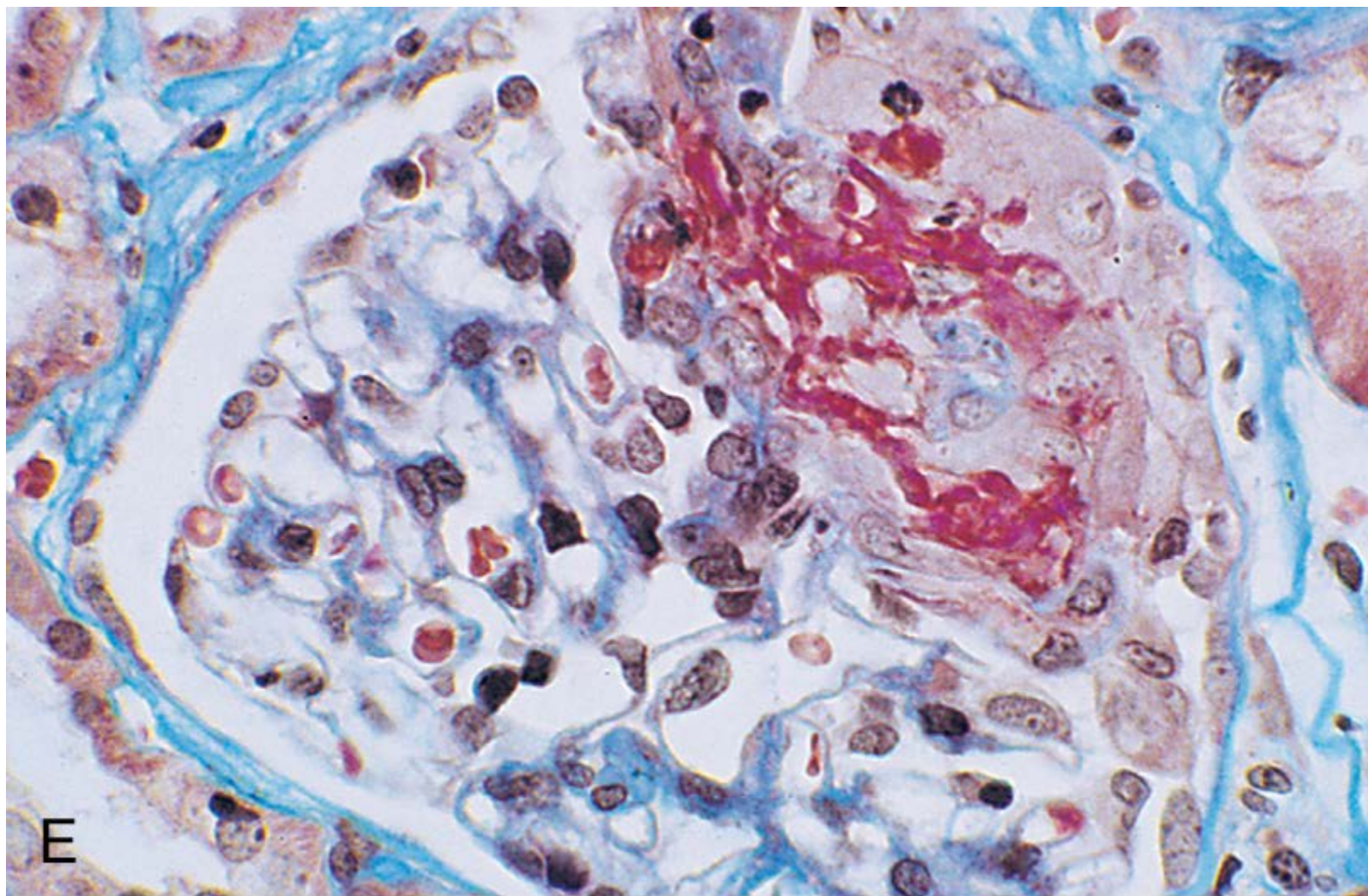
Hızlı İlerleyen Glomerülonefrit

- Günler - haftalar içinde renal fonksiyonun akut ve ciddi şekilde bozulmasına neden olan glomerüler hasar
- Yaygın crescent oluşumu
- Üremik acil
- Nefritik sendrom
- Sistemik immün hastalığın parçası
- Fokal segmental nekrotizan glomerülonefrit (vaskülit sendromları)

Crescent Formation





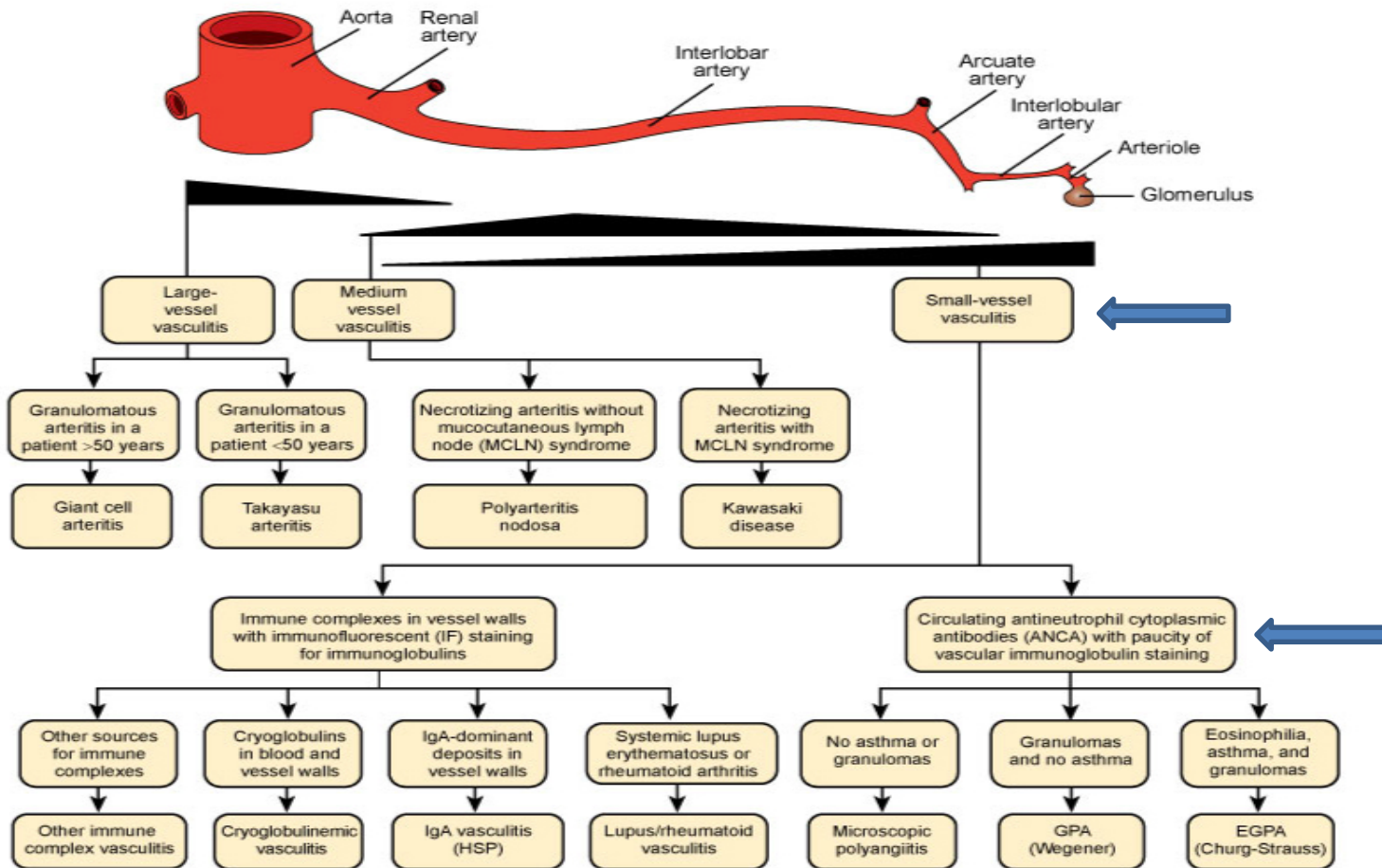


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Etiyoloji

- Goodpasture sendromu
- Vaskülitler
 - Granülomatöz polianjitis (Wegener granülomatozu)
 - Mikroskopik polianjitis
 - Pauci-immun kresentik glomerülonefrit
- İmmun kompleks hastalığı
 - Sistemik lupus eritematozus
 - Poststreptokokkal glomerulonefrit
 - IgA nefropatisi
 - IgA vaskülit (Henoch-Schönlein purpurası)
- Endokardit

Renal Vascular Involvement in Vasculitides



Modified from reference 3.

Fig. 25-1. **Renal vasculitis.** Predominant distribution of renal vascular involvement by a variety of vasculitides. The heights of the trapezoids represent the relative frequency of involvement of different portions of the renal vasculature by the three major categories of vasculitis. *EGPA*, Eosinophilic granulomatous polyangiitis; *GPA*, granulomatous polyangiitis; *HSP*, Henoch-Schönlein purpura.

Pauci-immun Küçük Damar Vaskülitleri (ANCA İlişkili Vaskülitler)

- **Mikroskopik polianjitis (MPA)**
 - nekrotizan vaskülit (granülomatöz inflamasyon yok)
 - *nekrotizan glomerülonefrit*
 - pulmoner kapillaritis
- **Granülomatöz polianjitis (Wegener) (GPA)**
 - nekrotizan granülomatöz inflamasyon
 - en sık solunum sistemi (alt ve üst)
 - *nekrotizan glomerülonefrit*
- **Eozinofilik granülomatöz polianjitis (Churg-Strauss) (EGPA)**
 - astma, eozinofili, nekrotizan granülomatöz inflamasyon

Patogenez

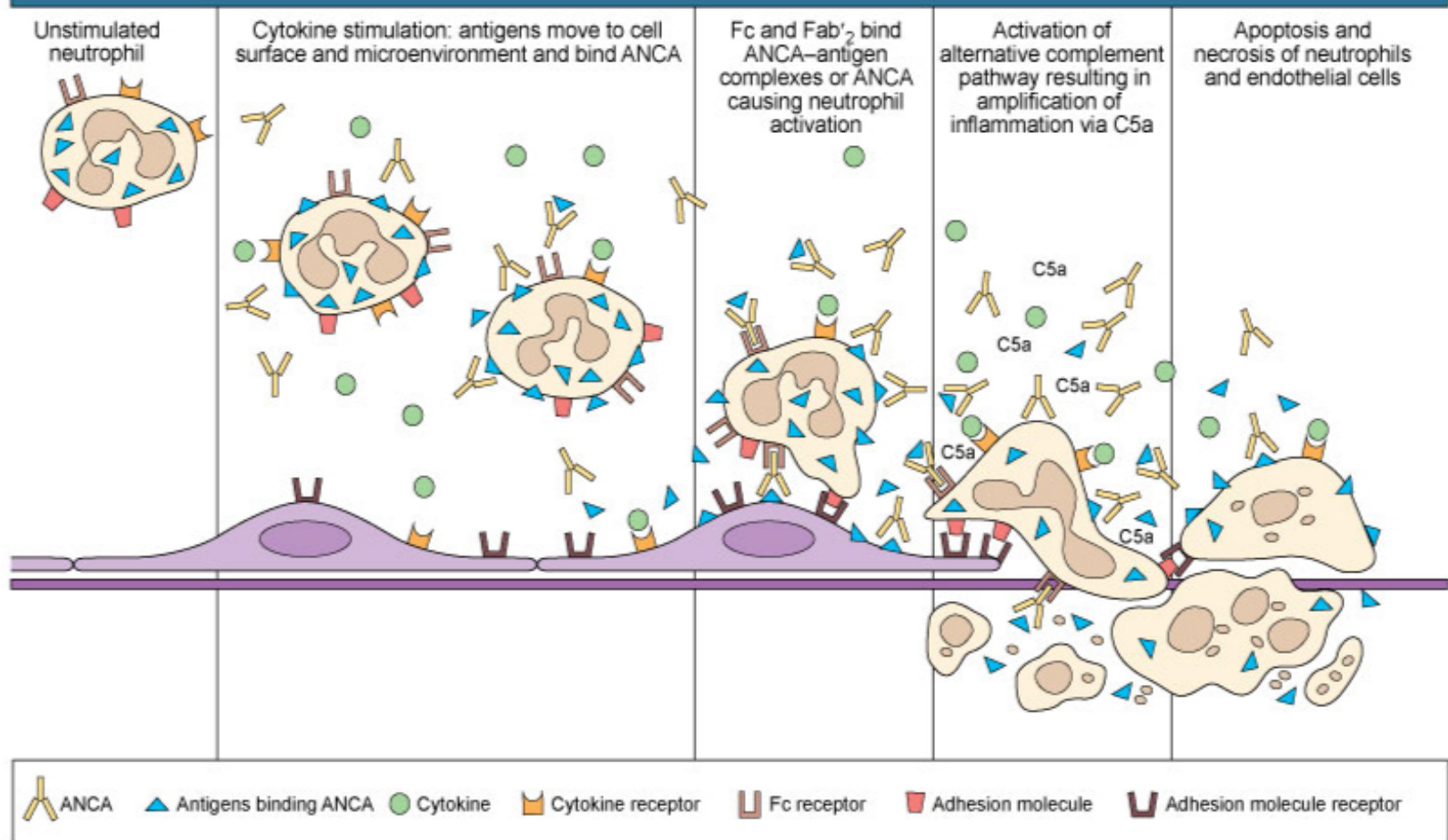
- **Antinötrofil sitoplazmik antikorlar (ANCA)**
 - proteinaz 3 (PR3)
 - miyeloperoksidaz (MPO)
- **Lizozom ilişkili membran proteini 2 (LAMP-2)' ye karşı gelişen otoantikorlar**
 - LAMP-2, bakteriyel adhezin FimH' ye benzer
 - fimbriyalı gram negatif bakteriler
 - moleküler taklit

Kain R. Molecular mimicry in pauci-immune focal necrotizing glomerulonephritis. Nat Med, 2008

Roth AJ. Anti-LAMP-2 antibodies are not prevalent in patients with antineutrophil cytoplasmic autoantibody glomerulonephritis. J Am Soc Nephrol, 2012

- **İlaçlar**
 - Propiltiyoürasil, hidralazin, penisillamin
 - Levamizol katkılı kokain (Levamisole-induced vasculitis)
- **Sitokinler tarafından nötrofillerin uyarılması (viral enfeksiyon)**
 - Alternatif kompleman yolunun aktivasyonu
 - C3a, C5a ve solubl C5b-9 düzeylerinde artış

ANCA-Induced Vasculitis: A Possible Pathogenetic Path



Modified from reference 22.

Fig. 25-3. **Vasculitis induced by antineutrophil cytoplasmic antibody (ANCA).** Hypothetical sequence of pathogenetic events.

- PR3 → endotelyal hücrelerde apoptoz
- MPO → endotelyal hücrelerde intrasellüler oksidanların üretimi
Yang JJ. Internalization of proteinase 3 is concomitant with endothelial cell apoptosis and internalization of myeloperoxidase with generation of intracellular oxidants. Am J Pathol, 2001
- PR3-AAV → **anti-anjiyojenik faktör sFlt1** (sVEGFR-1) ' de artma

sFlt1' in esas kaynağı monositler

C5a, monositlerden sFlt1 salınımında major etken

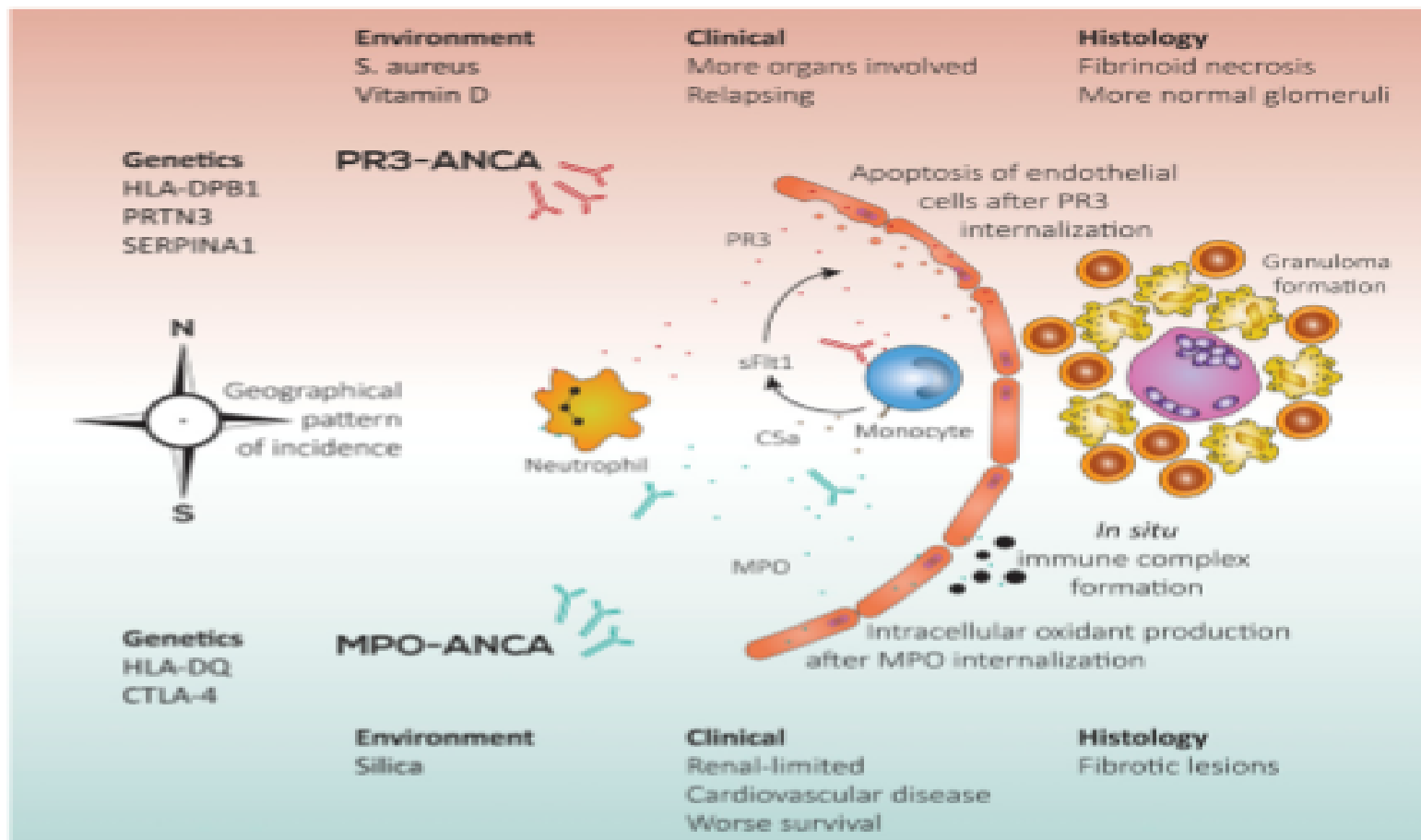


Figure 2. Pathogenic model highlighting the differences between PR3-ANCA and MPO-ANCA vasculitis. PR3-AAV is more common in the northern parts of the world whereas MPO-AAV is more common in the southern parts. Different genetic backgrounds have been found and different etiologic factors are considered. Clinically and histologically both vasculitides differ. On the cellular level, PR3 and MPO exert different effects on endothelial cells. These differences possibly point out separate pathogenic pathways.



KDIGO Clinical Practice Guideline for Glomerulonephritis

VOLUME 2 | ISSUE 2 | JUNE 2012

<http://www.kidney-international.org>

13.1: Initial treatment of pauci-immune focal and segmental necrotizing GN

- 13.1.1: We recommend that cyclophosphamide and corticosteroids be used as initial treatment. (1A)
- 13.1.2: We recommend that rituximab and corticosteroids be used as an alternative initial treatment in patients without severe disease or in whom cyclophosphamide is contraindicated. (1B)

13.2: Special patient populations

- 13.2.1: We recommend the addition of plasmapheresis for patients requiring dialysis or with rapidly increasing SCr. (1C)
- 13.2.2: We suggest the addition of plasmapheresis for patients with diffuse pulmonary hemorrhage. (2C)
- 13.2.3: We suggest the addition of plasmapheresis for patients with overlap syndrome of ANCA vasculitis and anti-GBM GN, according to proposed criteria and regimen for anti-GBM GN (see Chapter 14). (2D)
- 13.2.4: We suggest discontinuing cyclophosphamide therapy after 3 months in patients who remain dialysis-dependent and who do not have any extrarenal manifestations of disease. (2C)

Plazma Değişimi

- Hastalığa yol açan anormal proteinlerin (immunoglobulinler) uzaklaştırılması
- Ciddi aktif renal hastalık
 - böbrek fonksiyonunda hızlı bozulma
 - ciddi böbrek fonksiyon bozukluğu
(serum kreatinin > 4 mg/dl)
 - başvuruda hemodiyalize bağımlı böbrek yetmezliği
- Eşzamanlı anti-GBM hastalığı
- Pulmoner hemoraji

Plasma exchange in focal necrotizing glomerulonephritis without anti-GBM antibodies

**CHARLES D. PUSEY, ANDREW J. REES, DAVID J. EVANS, D. KEITH PETERS,
and C. MARTIN LOCKWOOD**

*Departments of Medicine and Histopathology, Royal Postgraduate Medical School, Hammersmith Hospital, London, England,
United Kingdom*

Tedavi grupları:

- Tedavi grubu 25 hasta (PD, Pred, Cyc, AZA)
- Kontrol grubu 23 hasta (sadece immunsupresif tedavi)

Başlangıçtaki renal fonksiyon

- Diyalize bağımlı olmayan gruplarda renal outcome farklı değil
 - kreatinin < 500 $\mu\text{mol/L}$ (n=17)
 - kreatinin > 500 $\mu\text{mol/L}$ (n=12)
- Diyaliz bağımlı grupta (n=19) renal outcome daha iyi (p=0.041)
- PD diyaliz bağımlı grupta immunsupresif tedaviye ilave fayda sağlar.

Table 3. Improvement in renal function at one month

	Treatment (25)	Control (23)
Creatinine <500 $\mu\text{mol/liter}$	9/9	7/8
Creatinine >500 $\mu\text{mol/liter}$	5/5	7/7
Dialysis-dependent ^a	10/11	3/8

^a $P = 0.041$, Fisher's exact test

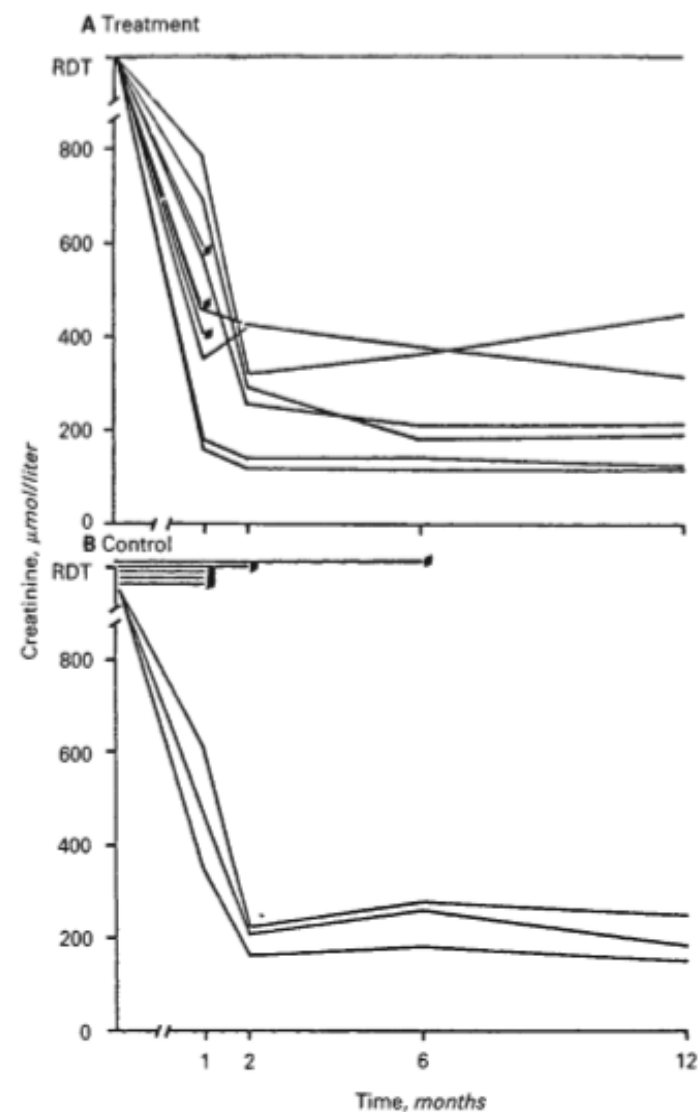


Fig. 3. Serial serum creatinine in patients who were dialysis-dependent. ϕ = died.

Table 1. Completed clinical trials in ANCA-associated vasculitis

Name	Treatment Studied	Patients	Primary Outcomes
CYCAZAREM ¹⁶⁸	Azathioprine versus cyclophosphamide in remission maintenance	GPA and MPA	Azathioprine is as effective as cyclophosphamide and reduces cumulative cyclophosphamide doses for maintenance of remission
CYCLOPS ¹⁶⁹	IV cyclophosphamide versus oral cyclophosphamide in remission induction	GPA, MPA and RLV	IV cyclophosphamide is as effective as oral cyclophosphamide and reduces cumulative cyclophosphamide doses for induction therapy
IMPROVE ¹⁷⁰	Mycophenolate mofetil versus azathioprine in remission maintenance	GPA and MPA	Mycophenolate mofetil is less effective than azathioprine for maintenance of remission
MAINRITSAN ¹⁵⁴	Rituximab versus azathioprine in remission maintenance	GPA and MPA	Rituximab is more effective to prevent relapse compared with azathioprine whereas adverse events are similarly frequent
MEPEX ¹⁷¹	Plasma exchange versus methylprednisolone in remission induction	GPA and MPA	Renal outcome is better when plasma exchange was performed in patients with severe renal disease but patient survival is similar
MTX versus LEF ¹⁷²	Oral methotrexate versus leflunomide for remission maintenance	GPA	Less relapses occur with leflunomide as compared with methotrexate for remission maintenance but more adverse events occur with leflunomide
NORAM ¹⁷³	Methotrexate versus cyclophosphamide for remission induction	GPA and MPA	Methotrexate is less effective than cyclophosphamide in patients with non-renal AAV for disease control
RAVE ^{135,153}	Rituximab versus cyclophosphamide in remission induction	GPA and MPA	A single course of rituximab is as effective and as safe as treatment with cyclophosphamide followed by azathioprine
RITUXVAS ¹⁵²	Rituximab with cyclophosphamide versus cyclophosphamide in remission induction	GPA and MPA	In patients with severe renal disease, rituximab in combination with two pulses of cyclophosphamide is as effective and as safe for remission induction as cyclophosphamide pulse therapy
WEGENT ¹⁷⁴	Methotrexate versus azathioprine in remission maintenance	GPA and MPA	Methotrexate is as effective and as safe for remission maintenance as azathioprine
WGET ¹⁷⁵	Etanercept with standard therapy versus standard therapy in remission induction and maintenance	GPA	Etanercept is not effective for maintenance of remission and when combined with standard therapy results in a high rate of treatment related complications (e.g., malignancies)

IV, intravenous; RLV, renal-limited vasculitis.

Randomized Trial of Plasma Exchange or High-Dosage Methylprednisolone as Adjunctive Therapy for Severe Renal Vasculitis

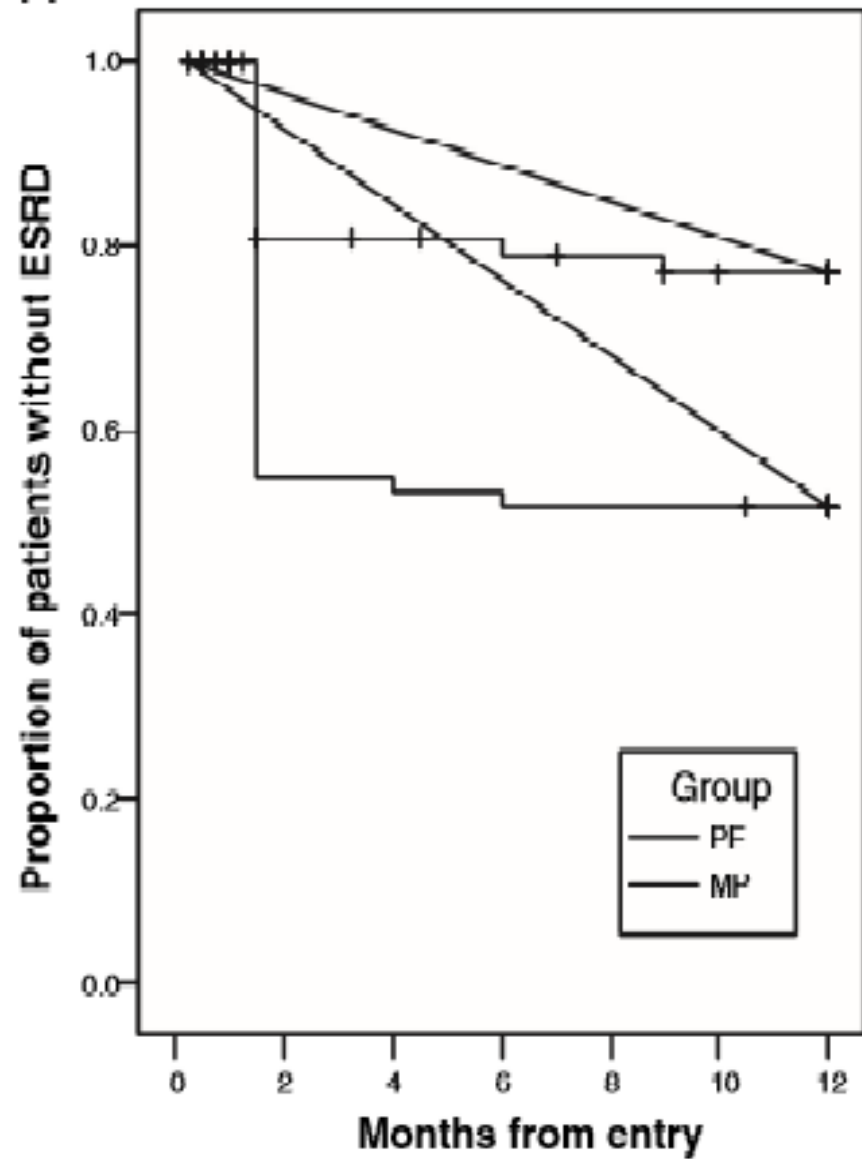
David R.W. Jayne,^{*} Gill Gaskin,[†] Niels Rasmussen,[†] Daniel Abramowicz,[§] Franco Ferrario,^{||} Loïc Guillevin,[¶] Eduardo Mirapeix,^{**} Caroline O.S. Savage,^{††} Renato A. Sinico,^{||} Coen A. Stegeman,^{‡‡} Kerstin W. Westman,^{§§} Fokko J. van der Woude,^{||||} Robert A.F. de Lind van Wijngaarden,^{¶¶} and Charles D. Pusey; on behalf of the European Vasculitis Study Group[†]

J Am Soc Nephrol 18: 2180–2188, 2007.

MEPEX çalışması

- Yeni tanı koyulmuş ANCA ilişkili sistemik vaskülitli 137 hasta
- Kreatinin > 5.8 mg/dl
- 7 seans PD (n=70) veya 3000 mg İV MP (n=67)
- Her iki grup oral Cyc ve prednisolon
- 3. ayda PD grubunda MP grubuna göre hasta ve renal sürvi daha iyi (%69' a karşılık %49) (p=0.02).
- PD ile 1. yılda ESRD' e ilerleme riskinde %24 azalma
- 1. yılda hasta sürvisi PD grubunda %73, MP grubunda %76 (fark yok)
- Advers olay oranı PD grubunda %50, MP grubunda %48 (fark yok)

A



$p = 0.008$

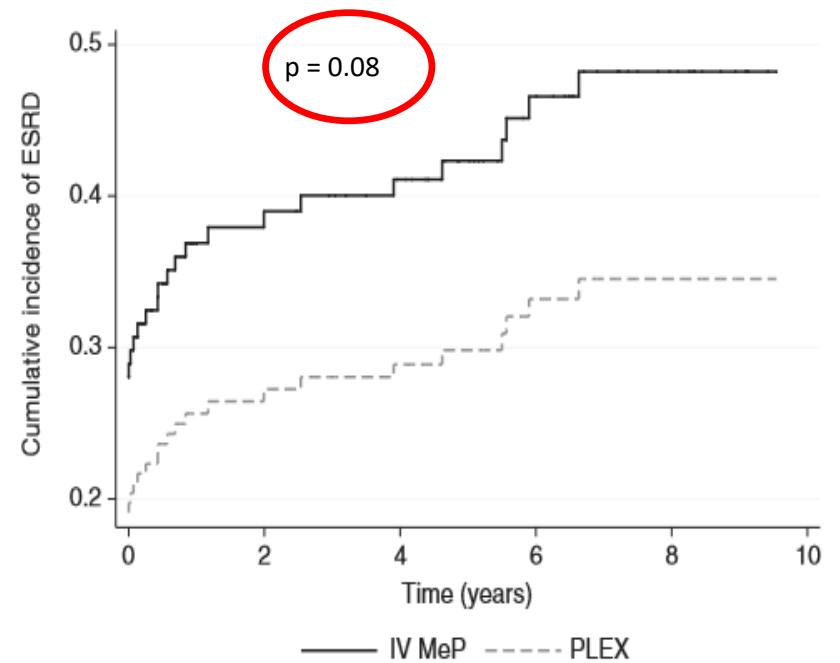
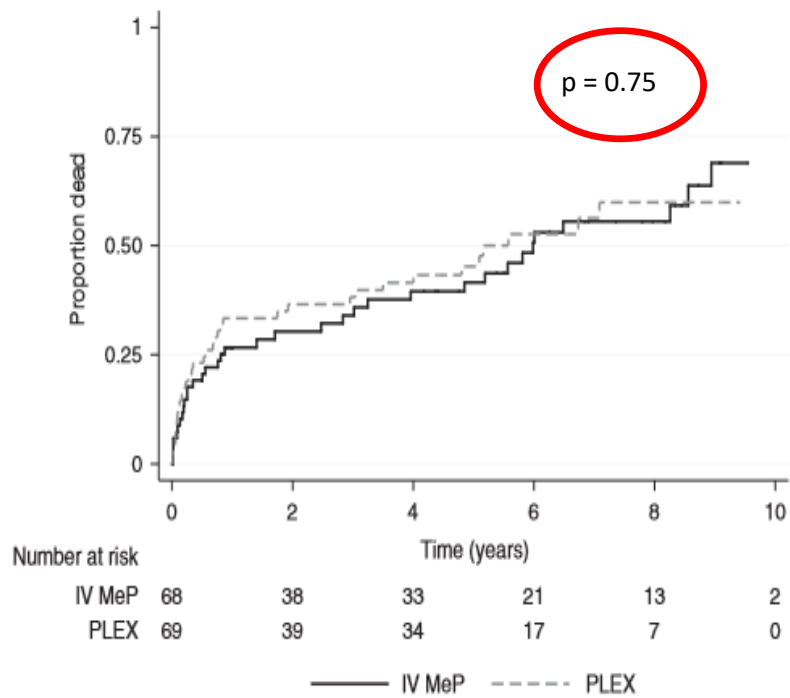
Long-term follow-up of patients with severe ANCA-associated vasculitis comparing plasma exchange to intravenous methylprednisolone treatment is unclear

Michael Walsh¹, Alina Casian², Oliver Flossmann³, Kerstin Westman⁴, Peter Höglund⁵, Charles Pusey⁶ and David R.W. Jayne² on behalf of the European Vasculitis Study Group (EUVAS)

- Yeni tanı koyulmuş ANCA ilişkili sistemik vaskülitli 137 hasta
- Kreatinin > 5.8 mg/dl veya diyaliz gerektiren
- PD (n=69) veya MP (n=68)
- Her iki grup oral Cyc ve prednisolon
- Median takip süresi 3.95 yıl
- Her grupta da 35 ölüm (p=0.75)
- PD grubunda 23 hastada, MP grubunda 33 hastada ESRD (p=0.08)

Table 3 | Long-term primary and secondary outcomes by treatment group

Outcome	IV MeP, <i>n</i> = 68 (%)	PLEX, <i>n</i> = 69 (%)	HR (95% CI)	<i>P</i> -value
Death or ESRD	46 (68)	40 (58)	0.81 (0.53–1.23)	0.32
Death	35 (51)	35 (51)	1.08 (0.67–1.73)	0.75
ESRD ^a	33 (49)	23 (33)	0.64 (0.40–1.05)	0.08
Relapse ^a	16 (21)	10 (14)	0.56 (0.26–1.21)	0.14



Guidelines on the Use of Therapeutic Apheresis in Clinical Practice—Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Seventh Special Issue

Joseph Schwartz,¹ Anand Padmanabhan,² Nicole Aqui,³ Rasheed A. Balogun,⁴
Laura Connelly-Smith,⁵ Meghan Delaney,⁶ Nancy M. Dunbar,⁷ Volker Witt,⁸
Yanyun Wu,⁹ and Beth H. Shaz^{1,10,11*}

ANCA-ASSOCIATED RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS (GRANULOMATOSIS WITH POLYANGIITIS AND MICROSCOPIC POLYANGIITIS)

Incidence: 8.5/1,000,000/yr	Indication	Procedure	Recommendation	Category
	Dialysis dependence ^a	TPE	Grade 1A	I
	DAH	TPE	Grade 1C	I
	Dialysis independence ^a	TPE	Grade 2C	III
No. of reported patients: > 300	RCT	CT	CS	CR
	8(296)	1(26)	22(347)	NA

^aAt presentation, defined as Cr >6 mg/dL. DAH = diffuse alveolar hemorrhage.

Technical notes

In patients with DAH, replacement with plasma is recommended to avoid dilutional coagulopathy.

Volume treated: 1–1.5 TPV

Frequency: Daily or every other day

Replacement fluid: Albumin; plasma when DAH present

Duration and discontinuation/number of procedures

Consider daily procedures in fulminant cases or with DAH then every 2–3 days for total of 6–9 procedures.

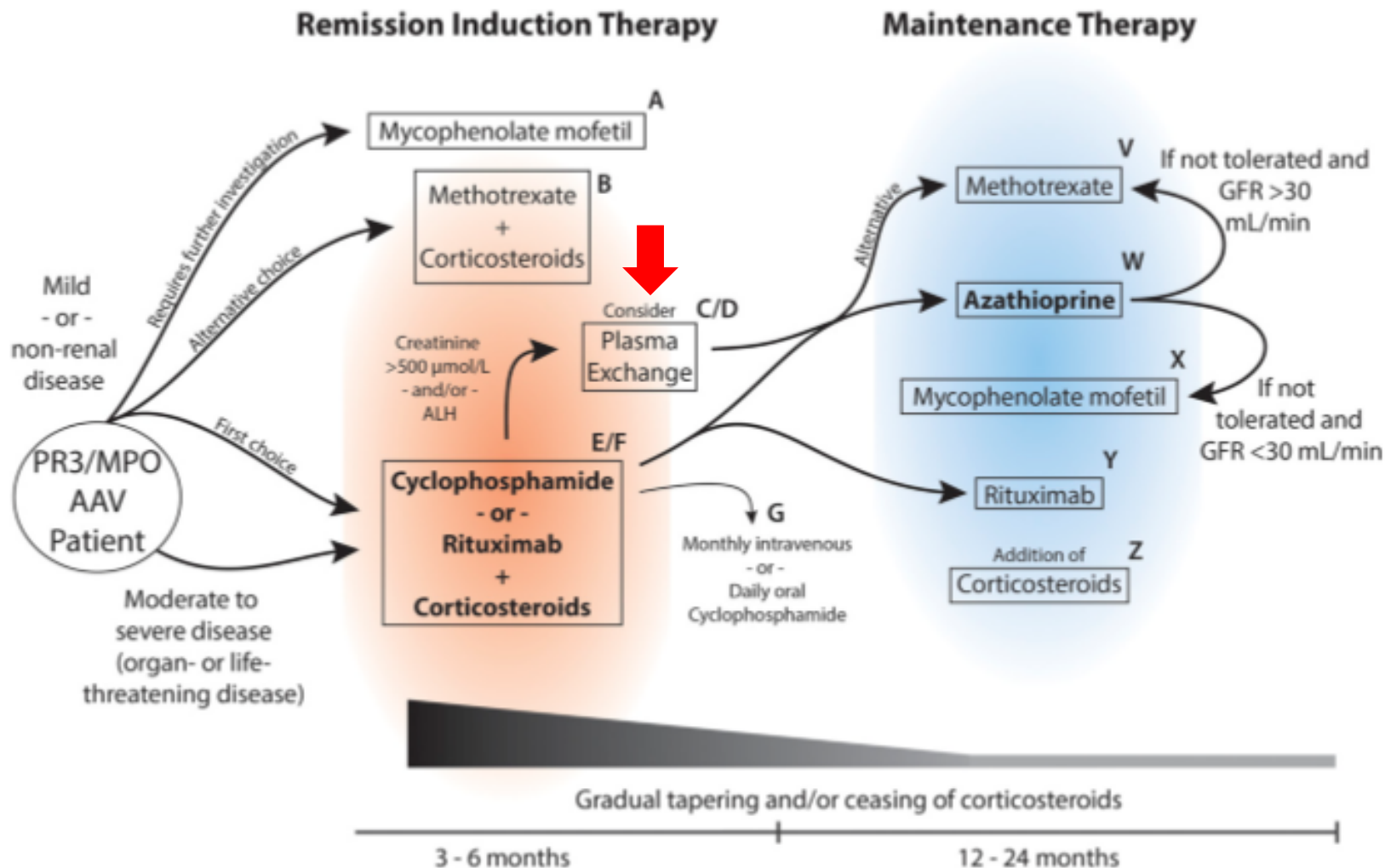


Figure 3. Flow diagram for treatment in AAV. Evidence for every step is given as follows, linked to the symbols in the diagram. (A) Silva *et al.*¹⁷⁶ and Stassen *et al.*¹⁶⁰ (B) NORAM trial¹⁷³; (C) MEPEX trial¹⁷¹; (D) PEXIVAS trial (table 2); (E) RAVE trial¹⁵³ and RITUXVAS trial¹³⁵; (F) LoVAS trial and RAVELOS study (table 2); (G) CYCLOPS trial¹⁶⁹; (V) WEGENT trial¹⁷⁴; (W) CYCAZAREM trial¹⁶⁸; (X) IMPROVE trial¹⁷⁰; (Y) MAINRITSAN¹⁵⁴ (table 1), RITAZAREM and SCOUT trials (table 2); (Z) TAPIR trial (table 2).

Table 2. Currently planned or ongoing clinical trials in ANCA-associated vasculitis

Name	Treatment Studied	Status	Patients	Primary Outcomes	Clinical Trial no.
ABROGATE	Abatacept (CTLA-4 immunoglobulin)	Not yet recruiting	GPA	Treatment failure after 12 months of treatment	NCT02108860
Evaluate the efficacy of achieving glucocorticoid-free remission in patients with relapsing non-severe GPA					
ALEVIAE	Alemtuzumab (monoclonal anti-CD52)	Unknown	GPA and MPA	Complete or partial remission after 6 months; adverse event	NCT01405807
Evaluating whether alemtuzumab induces sustained remission in refractory patients					
BIANCA-SC	Blisibimod (selective antagonist of BAFF)	Not yet recruiting	GPA and MPA	Induction of clinical remission	NCT01598857
Evaluate efficacy of blisibimod when taken with methotrexate to induce remission					
BREVAS	Belimumab (human monoclonal anti-BAFF)	Recruiting	GPA and MPA	Time to first relapse	NCT01663623
Assessing efficacy of belimumab in maintenance of remission following a standard induction regimen					
CLASSIC	CCX168 (C5a inhibitor)	Recruiting	GPA and MPA	Safety and efficacy of two-dose regimen	NCT02222155
Studying the safety and efficacy of CCX168 for induction therapy (low versus high dose) with conventional therapy					
CLEAR	CCX168 (C5a inhibitor)	Recruiting	GPA and MPA	Safety (adverse events) and efficacy (BVAS)	NCT01363388
Studying the safety and efficacy of CCX168 versus placebo for induction therapy on a background of conventional therapy					
LoVAS	Rituximab with glucocorticoids	Recruiting	GPA and MPA	Remission induction	NCT02198248
Comparing rituximab with low-dose glucocorticoids versus rituximab with high-dose glucocorticoids					
MAINRITSAN-2	Rituximab (two strategies)	Active, not recruiting	GPA and MPA	Number of minor and major relapses	NCT01731561
PEXIVAS	Plasma exchange	Recruiting	GPA and MPA	All-cause mortality; end-stage renal disease	NCT00987389
Assess efficacy of a rituximab regimen based on rate of ANCA and CD19 lymphocytes for maintenance of remission					
Determining whether plasma exchange with immunosuppressive therapy are effective in reducing death and ESRD					
RAVELOS	Rituximab (chimeric monoclonal anti-CD20)	Recruiting by invitation	GPA and MPA	Long-term safety and effects of rituximab	NCT01586858
Following the patients included in the RAVE study to study long-term outcome after rituximab treatment					
RITAZAREM	Rituximab	Recruiting	GPA and MPA	Time to first relapse	NCT01697267
Evaluating whether repeated rituximab will maintain remission					
SCOUT	Glucocorticoids and rituximab	Recruiting	GPA and MPA	Complete remission	NCT02169219
Studying whether an 8-week course of glucocorticoids with rituximab is effective as remission induction					
TAPIR	Glucocorticoids	Recruiting	GPA	Increase of the glucocorticoid dose for disease relapse	NCT01933724– NCT01940094
Evaluating the effects of low-dose glucocorticoids (5 mg/day) versus stopping completely in GPA in remission					

PEXIVAS çalışması

- Çok merkezli, prospektif, randomize kontrollü
- 2010 – 2018 yılları
- ≥ 15 yaş
- Devam etmekte, fakat hasta alımı tamamlandı
- ANCA ilişkili vaskülitin tedavisinde, PD ve glukokortikoidler

Anti-glomerüler Bazal Membran Hastalığı (Goodpasture Hastalığı)

- Glomerül kapillerleri ve pulmoner kapillerler
- Anti-bazal membran otoantikorlarının bazal membranda birikimi
- Pulmoner hemoraji
- Nekroz ve kresentlerle seyreden GN

Etiyoloji ve Patogenez

- Glomerüler bazal membranın bir komponentine karşı otoimmünite

- Tip IV kollajen zincirinin karboksil terminal, nonkollajenöz alanı [$\alpha 3(\text{IV})\text{NC1}$] (Goodpasture antijeni)

Saus J. Identification of the Goodpasture antigen as the $\alpha 3(\text{IV})$ chain of collagen IV. J Biol Chem, 1988

- Predispozan faktörler

- HLA class II alelleri (DRB1*1501 ve DR4 aleller) ile güçlü ilişki
- Buna karşın DR1 ve DR7 güçlü bir koruma

Phelps RG. The HLA complex in Goodpasture's disease: A model for analyzing susceptibility to autoimmunity. Kidney Int, 1999

Predispozan olaylar

Otoimmün cevabı ve hastalığı indükleyenler

Glomerülü etkileyen sistemik küçük damar vaskülit

Membranöz nefropati

Litotripsi

Üriner obstrüksiyon

Multipl sklerozun alemtuzab ile tedavisi

Pulmoner hemorajiyi presipite edenler

Sigara ve diğer pulmoner irritanlar

Yüksek F_{iO_2} (fraksiyonel inspire edilen oksijen konsantrasyonu)

Hidrokarbon maruziyeti

Pulmoner enfeksiyon (Influenza A)

Sıvı yüklenmesi

Antikoagülan kullanımı (diyaliz veya plazma değişimi)

Trombositopeni ve pıhtılaşma faktörlerinin tüketilmesi (plazma değişimi)

- **Renal hasar mekanizması**

- Biriken antikorlar ön planda IgG1
- T hücreleri hem B hücrelerinin otoantikor üretiminde hem de glomerüler kresentlerin oluşumunda önemli

Ooi JD. Advances in the pathogenesis of Goodpasture's disease: From epitopes to autoantibodies to effector T cells. J Autoimmun, 2008

Ooi JD. The HLA-DRB1*15:01-restricted Goodpasture's T cell epitope induces GN. J Am Soc Nephrol, 2013

- **Pulmoner hemoraji**

- Alveoler kapiller endotelyal hücre bariyeri
- Antikorların glomerüler kapiller endotelyumun diyafram bulunmayan fenestrasyonlarından direkt geçişi



KDIGO Clinical Practice Guideline for Glomerulonephritis

VOLUME 2 | ISSUE 2 | JUNE 2012

<http://www.kidney-international.org>

14.1: Treatment of anti-GBM GN

- 14.1.1: We recommend initiating immunosuppression with cyclophosphamide and corticosteroids plus plasmapheresis (see Table 31) in all patients with anti-GBM GN except those who are dialysis-dependent at presentation and have 100% crescents in an adequate biopsy sample, and do not have pulmonary hemorrhage. (*1B*)
- 14.1.2: Start treatment for anti-GBM GN without delay once the diagnosis is confirmed. If the diagnosis is highly suspected, it would be appropriate to begin high-dose corticosteroids and plasmapheresis (Table 31) while waiting for confirmation. (*Not Graded*)
- 14.1.3: We recommend no maintenance immunosuppressive therapy for anti-GBM GN. (*1D*)
- 14.1.4: Defer kidney transplantation after anti-GBM GN until anti-GBM antibodies have been undetectable for a minimum of 6 months. (*Not Graded*)

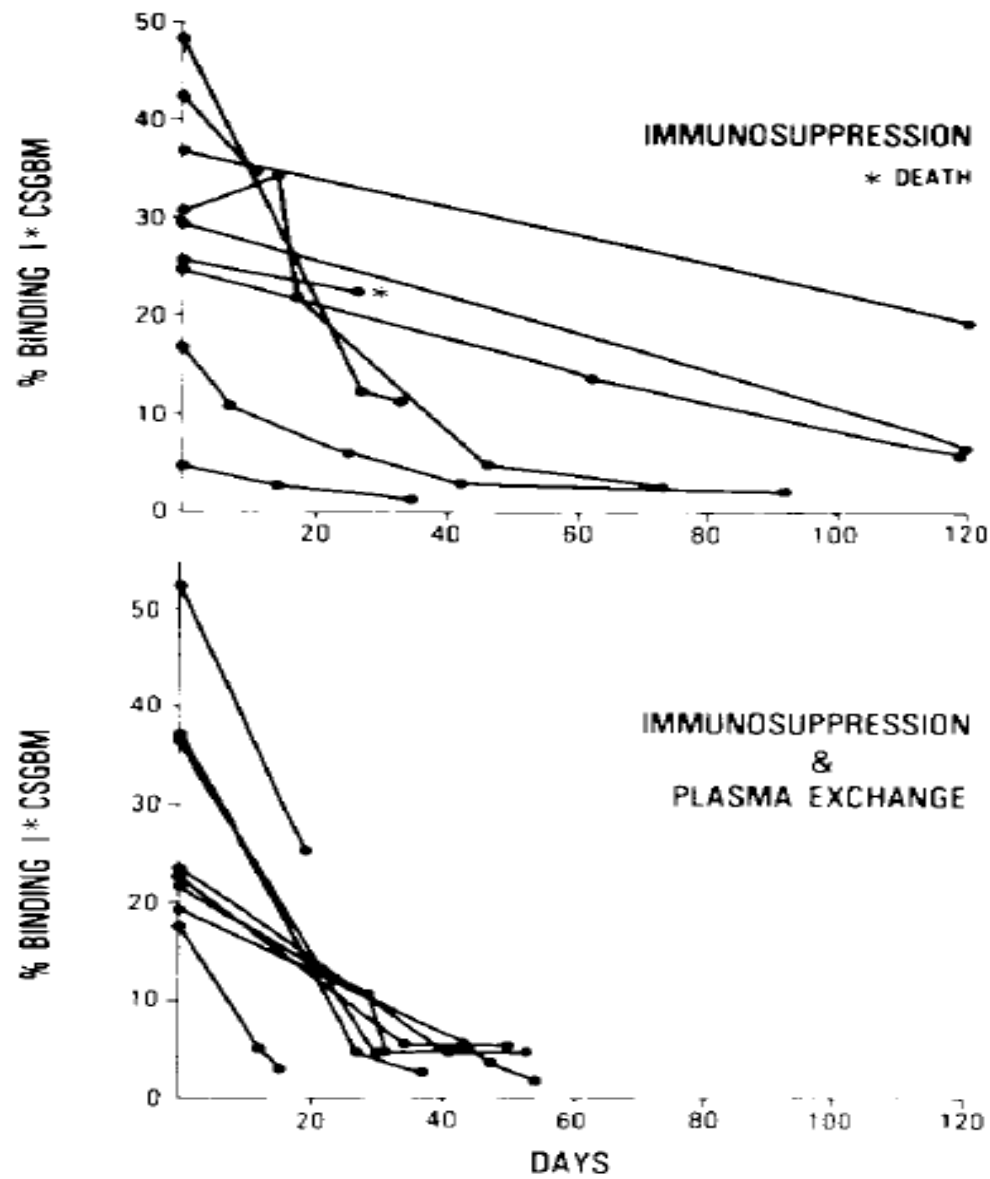
Plazma Değişimi

- Hergün / gūnaşırı 4 L deęişim (replasman sıvısı albūmin)
 - Yeni renal biyopsi yapılmıř veya pulmoner hemorajisi bulunanlarda iřlem sonunda 1 - 2 L TDP
- Bařlangıç PD 2 - 3 hafta
 - Hala hemoptizi varsa veya anti-GBM belirgin supresse olmamıř/negatifleřmemiř ise PD' ne devam
- PD esnasında ciddi enfeksiyon: İV immunglobulin (100 - 400 mg/kg)

Therapy of Anti-Glomerular Basement Membrane Antibody Disease: Analysis of Prognostic Significance of Clinical, Pathologic and Treatment Factors

JOHN P. JOHNSON, M.D., JACK MOORE, JR., M.D., HOWARD A. AUSTIN, III, M.D.,
JAMES E. BALOW, M.D., TATIANA T. ANTONOVYCH, M.D., AND
CURTIS B. WILSON, M.D.¹

- Tek randomize çalışma
- 17 hasta
- PD + Cyc + Pred uygulanan 8 hastanın ikisi diyalize bağımlı
- Tek başına Cyc + Pred verilen 9 hastanın 6' sı diyalize bağımlı
- PD grubunda tedavinin sonunda ort. kreatinin, immunsupresyon grubundakinin yarısı ($p < 0.05$).
- Tedaviden bağımsız olarak başlangıçta kresent yüzdesi $< \%30$ ve kreatinin < 3 mg/dl ise outcome daha iyi
- Ciddi kresentik tutulum ve kreatinin > 4 mg/dl ise outcome daha kötü



0.78 ± 0.16 vs
 0.31 ± 0.11 , $p < 0.05$

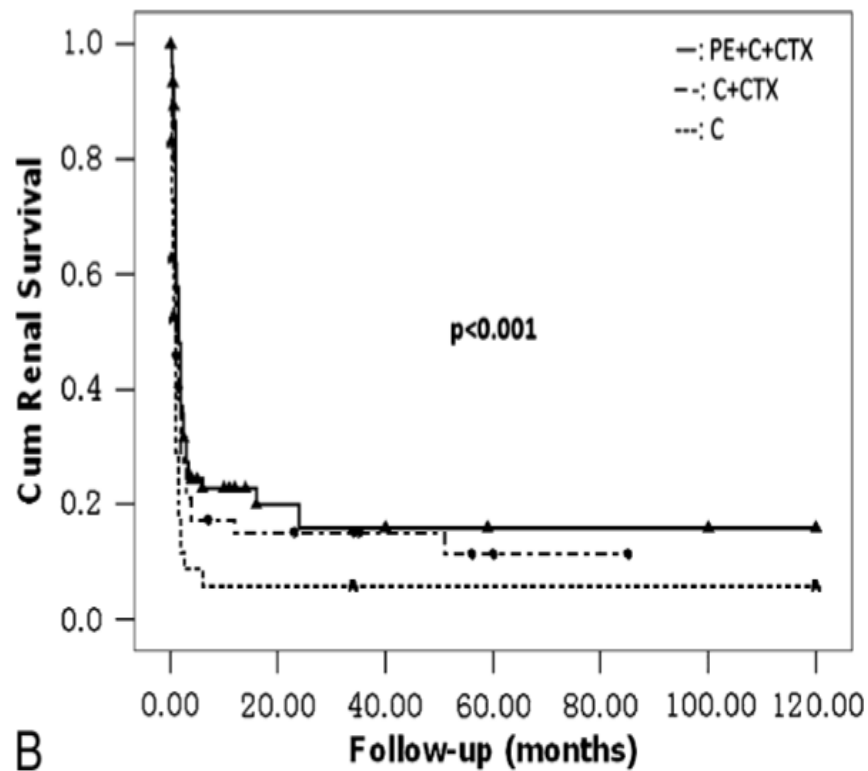
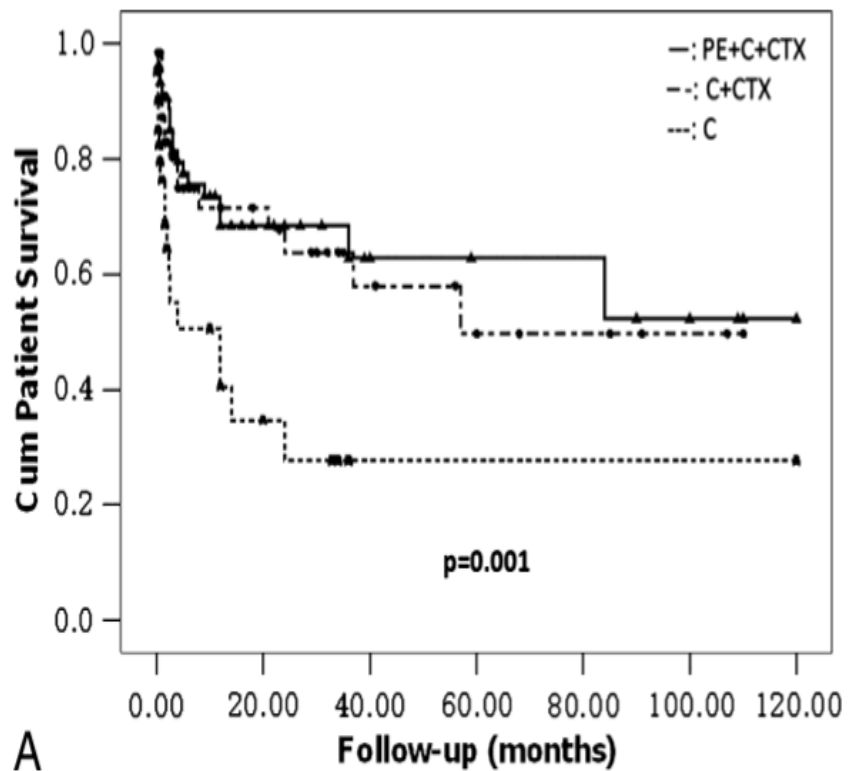
Anti-Glomerular Basement Membrane Disease

Outcomes of Different Therapeutic Regimens in a Large Single-Center Chinese Cohort Study

Zhao Cui, MD, Juan Zhao, MD, Xiao-yu Jia, MB, Sai-nan Zhu, ScM, Qi-zhuang Jin, MB, Xu-yang Cheng, MD, and Ming-hui Zhao, MD, PhD

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- 1998 - 2008 yılları arasında retrospektif
- 1. grup PD + Cyc + steroid (n=76)
- 2. grup Cyc + steroid (n=59)
- 3. grup steroid (n=41)
- Kombinasyon tedavisinde hasta ve renal sürvi daha iyi
- Özellikle pulmoner hemorajisi olanlarda hasta sürvi daha iyi (hasta mortalitesi için HR, 0.29; p = 0.004)
- Ciddi renal hasarda (inisyal kreatinin > 6.8 mg/dl) renal sürvi daha iyi (renal yetmezlik için HR , 0.52; p = 0.014).



Guidelines on the Use of Therapeutic Apheresis in Clinical Practice—Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Seventh Special Issue

Joseph Schwartz,¹ Anand Padmanabhan,² Nicole Aqui,³ Rasheed A. Balogun,⁴
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Yanyun Wu,⁹ and Beth H. Shaz^{1,10,11*}

ANTI-GLOMERULAR BASEMENT MEMBRANE DISEASE (GOODPASTURE'S SYNDROME)

Incidence: 1/1,000,000/yr	Indication	Procedure	Recommendation	Category
	Dialysis-dependence ^a , no DAH	TPE	Grade 2B	III
	DAH	TPE	Grade 1C	I
	Dialysis-independence ^a	TPE	Grade 1B	I
No. of reported patients: > 300	RCT	CT	CS	CR
	1(17)	0	19(468)	21

^aAt presentation, defined as Cr > 6 mg/dL. DAH = diffuse alveolar hemorrhage.

Technical notes

In the setting of DAH, plasma should be used for part or whole of the replacement fluid.

Volume treated: 1–1.5 TPV

Frequency: Daily or every other day

Replacement fluid: Albumin; plasma when DAH present

Duration and discontinuation/number of procedures

In most patients undergoing TPE and immunosuppression, anti-GBM antibodies fall to undetectable levels within 2 weeks; thus, the minimum course of TPE should be 10–20 days. The presence or absence of antibody should not be used to initiate or terminate therapy, because antibody is not demonstrable in a few patients with the disease and may be present in patients without active disease. In those patients with active disease, TPE should continue until resolution of evidence of ongoing glomerular or pulmonary injury.

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It is critical that TPE is implemented early in the course of anti-GBM. Several series have demonstrated that most patients with creatinine less than 6.6 mg/dL recover renal function with treatment. Those with an initial creatinine >6.6 mg/dL or who are dialysis-dependent at the time of initiation of TPE usually will not recover kidney function due to irreversible glomerular injury.

Such patients do not benefit from TPE and it should not be performed unless DAH is present. IA and DFPP have been used in few cases with efficient removal of anti-GBM antibodies. DAH can be rapidly fatal, or may have relatively mild manifestations, and responds to TPE in 90% of affected patients. Therefore, a low threshold for initiating TPE is warranted in the presence of DAH.

Suportif Tedavi

- İlk birkaç gün içinde en sık ölüm nedeni pulmoner hemorajiye bağlı solunum yetmezliği
 - presipite edici faktörlerin elimine edilmesi
- İlk birkaç günden sonra ise en sık enfeksiyon
 - damar yollarının sayısını azaltmak
 - lökopeni $< 3500/\text{mm}^3$ veya nütropeni durumunda siklofosamid kesilmeli
(gerekirse granülosit koloni stimüle eden faktör)

Hastalık Aktivitesi Üzerine Tedavi Etkinliğinin İzlenmesi

- Anti-GBM düzeylerinin takip edilmesi
 - PD tedavileri sırasında her hafta
 - PD' den sonra her iki haftada bir (negatif oluncaya kadar)
 - 6 ay süresince ayda bir
- 8 hafta içinde saptanamaz olmalı

Sonuçlar 1

- Tek başına aferez **yeterli/kalıcı** olmaz, mutlaka hastalığın tedavisi de yapılmalı
- **ANCA ilişkili vaskülit**
 - PD, ciddi aktif renal hastalık, eşzamanlı anti-GBM hastalığı ve pulmoner hemorajide faydalı
 - PD, diyaliz bağımlı grupta immunsupresif tedaviye ilave fayda sağlar.

Sonuçlar 2

- **Goodpasture hastalığı**

- PD' ne erken başlanması
- PD + Cyc + steroid kombinasyon tedavisinde hasta ve renal sürvi daha iyi
- Tedaviden bağımsız olarak başlangıçta kresent yüzdesi $< \%30$ ve kreatinin < 3 mg/dl ise outcome daha iyi
- Başlangıç kreatinin > 6.6 mg/dl veya PD başlandığında diyalize bağımlı olanlarda irreversibl glomerüler hasar