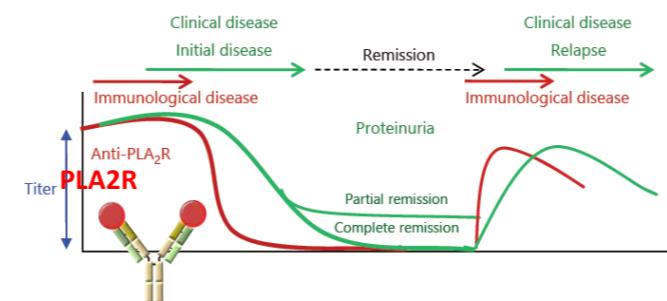


Νέες Προσεγγίσεις στη Νεφρολογία Μεμβρανώδης σπειραματοεφρίτιδα

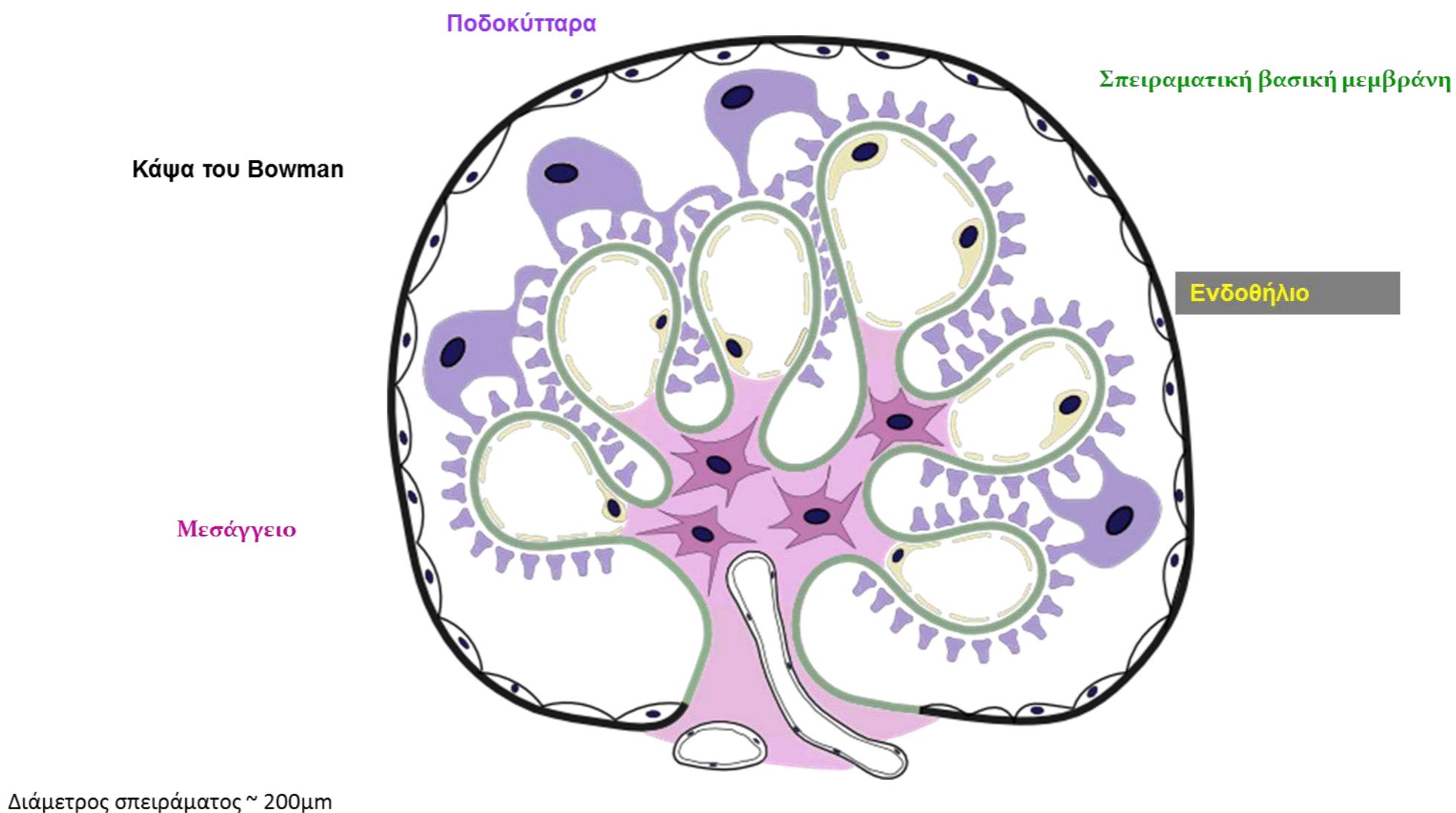


Π. Πατεινάκης
Επ Α' Νεφρολόγος
Νεφρολογικό Τμήμα
ΓΝΘ Πατσγεωργίου

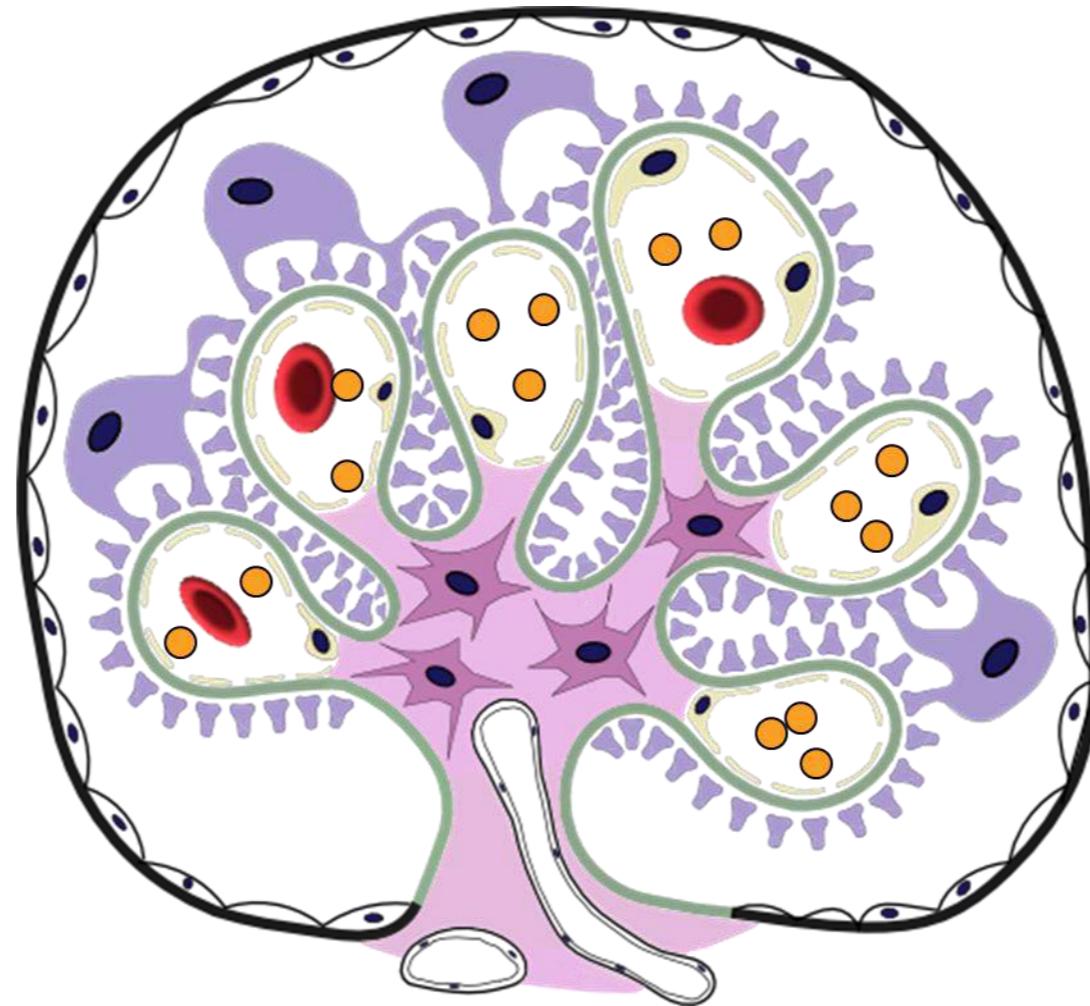
Νεφρός – Νεφρώνας - Σπείραμα



Το σπείραμα



Το σπείραμα



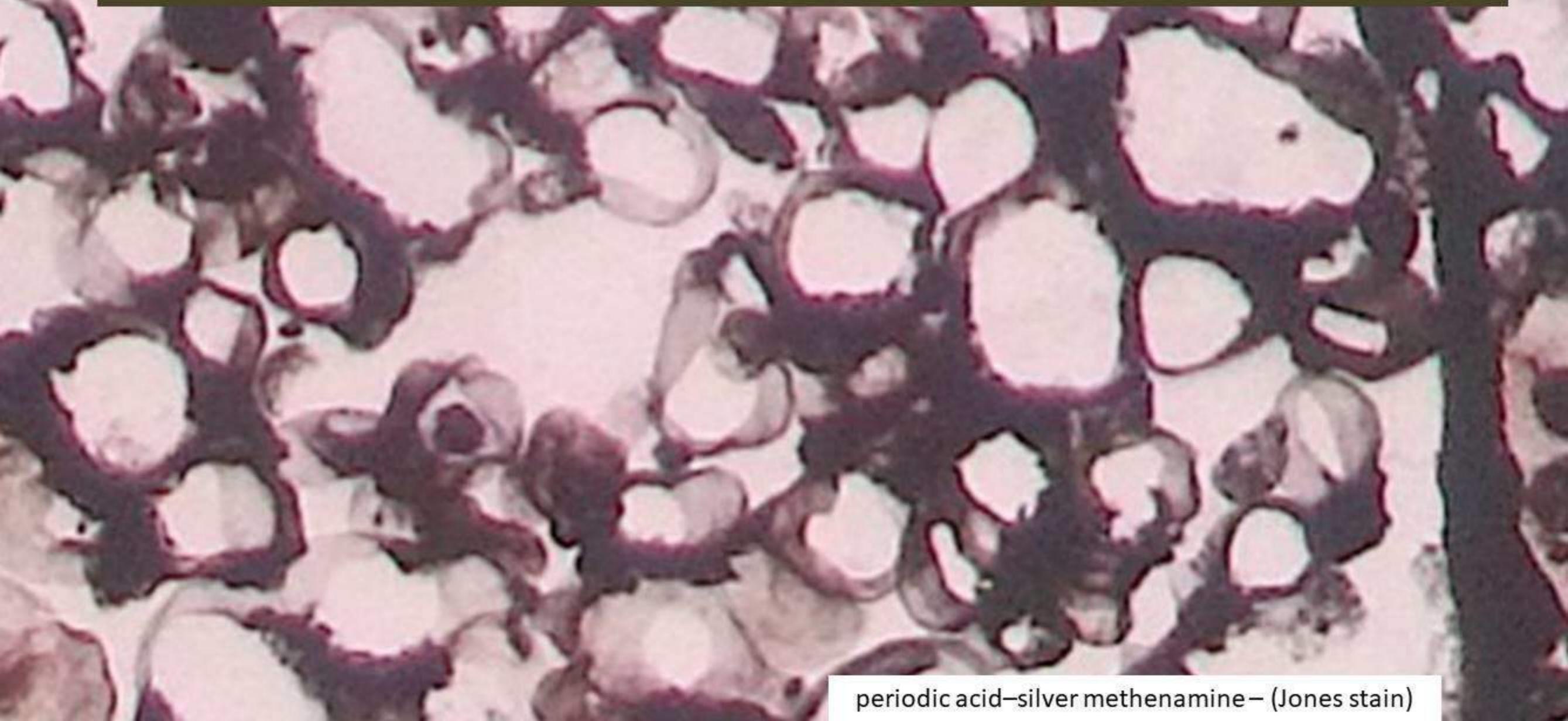
● λεύκωμα

Σπείραμα



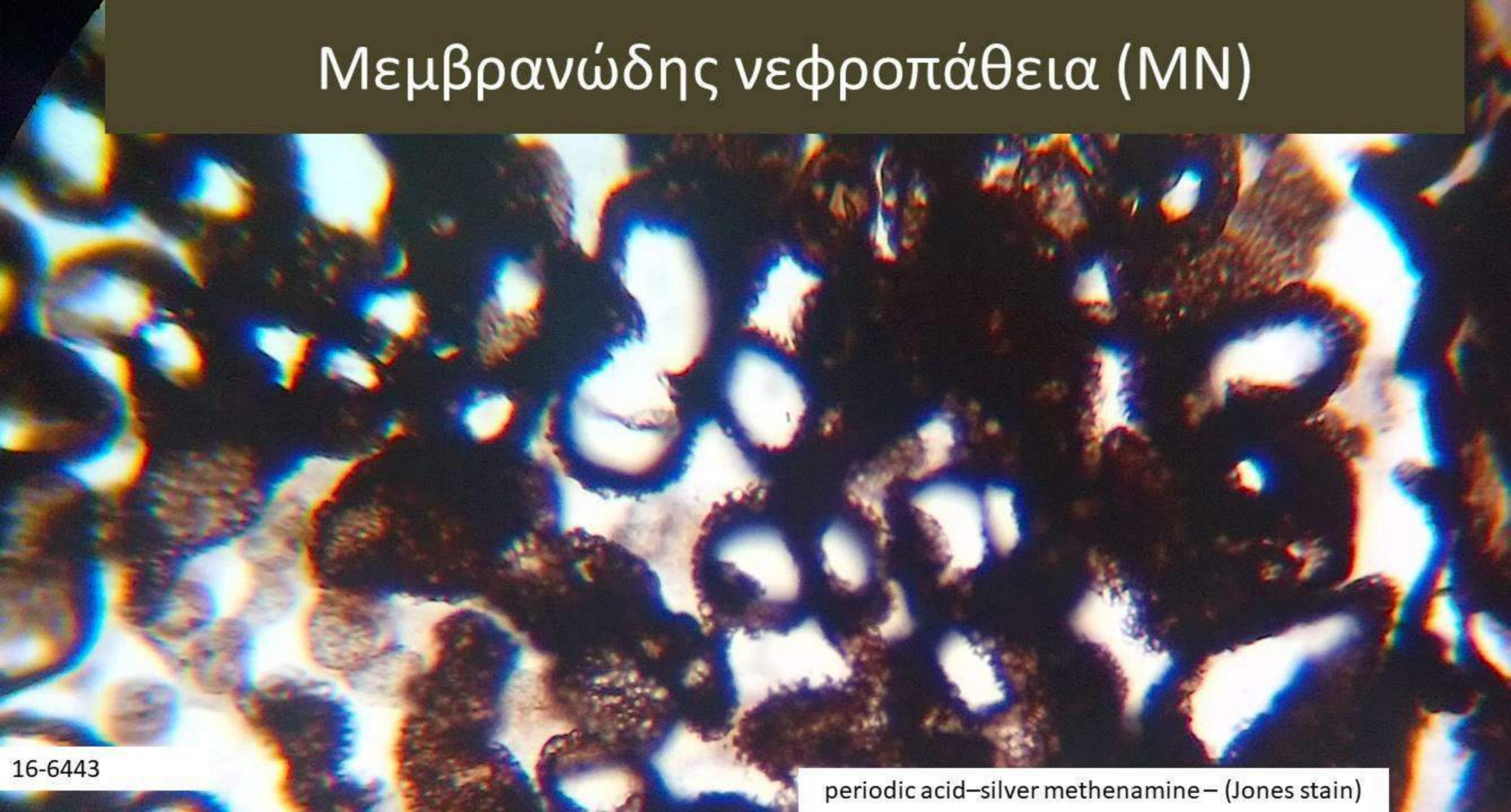
periodic acid–silver methenamine (Jones stain)

Σπρειραματικά τριχοειδή



periodic acid–silver methenamine – (Jones stain)

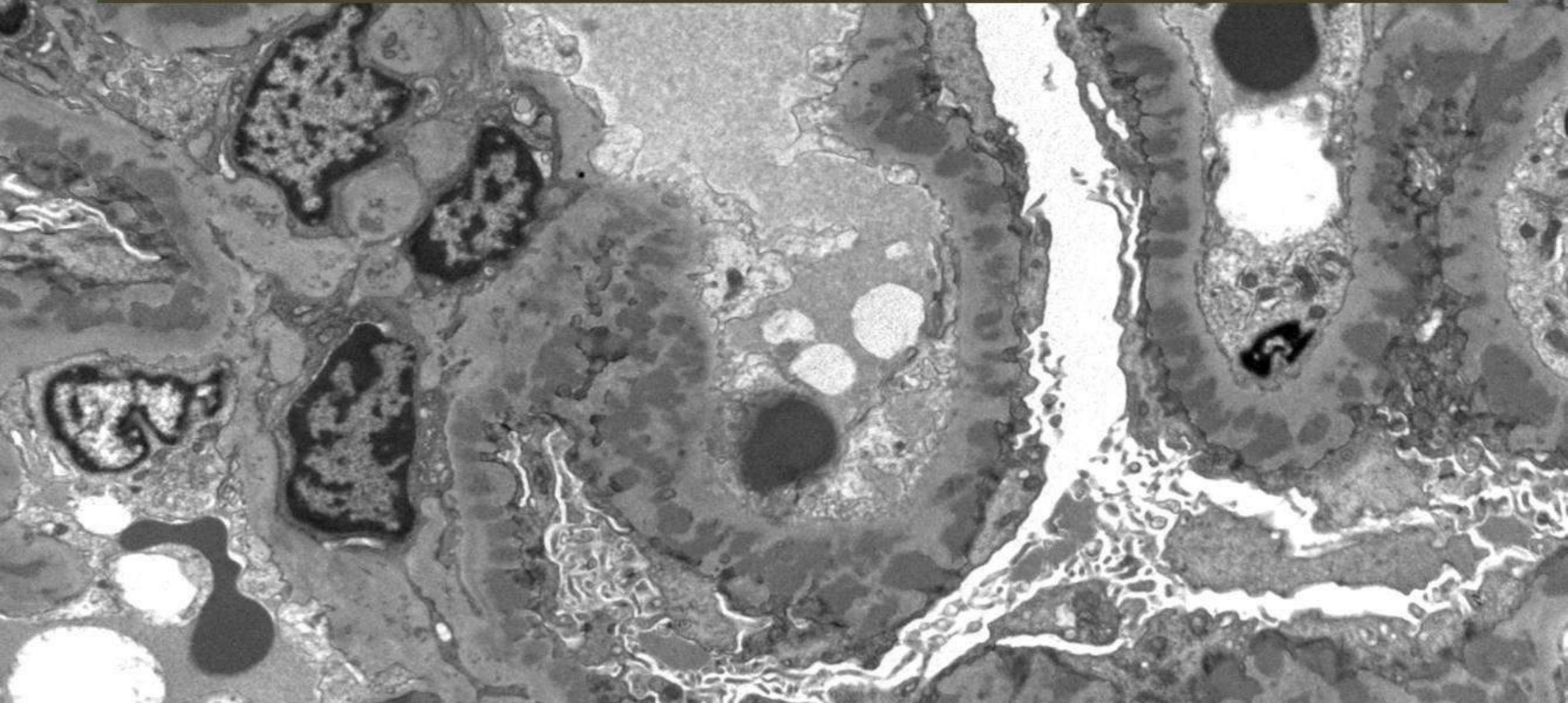
Μεμβρανώδης νεφροπάθεια (MN)



16-6443

periodic acid–silver methenamine – (Jones stain)

MN - Ηλεκτρονικό μικροσκόπιο



Νεφρωσικό σύνδρομο



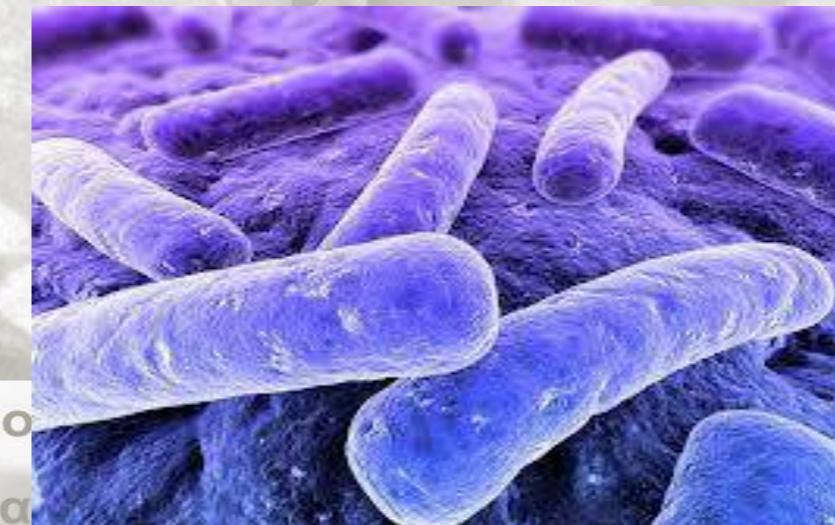
Αλβουμίνη ορού $<3,5\text{g/dL}$
Υπερλιπιδιαιμία



Νεφρωσικό σύνδρομο

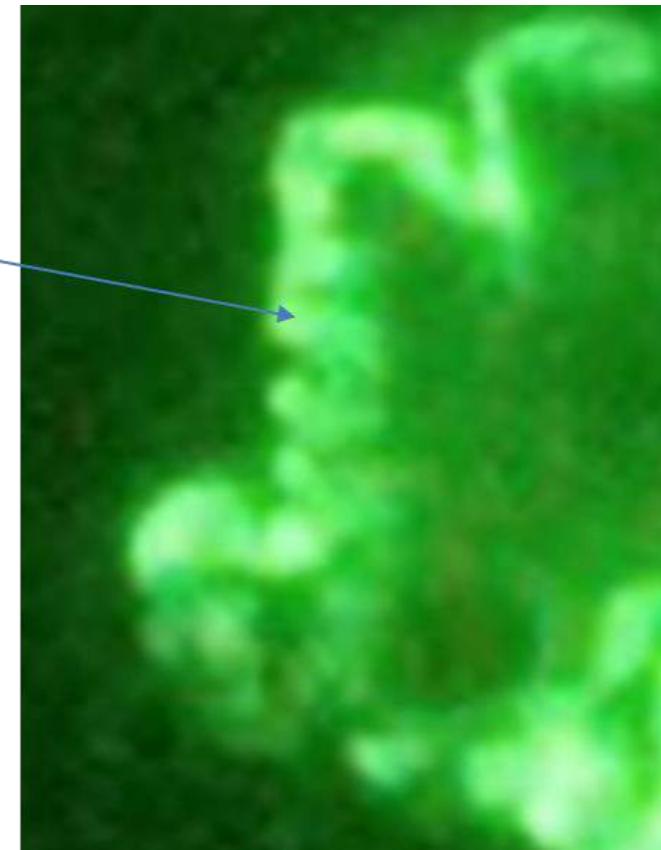
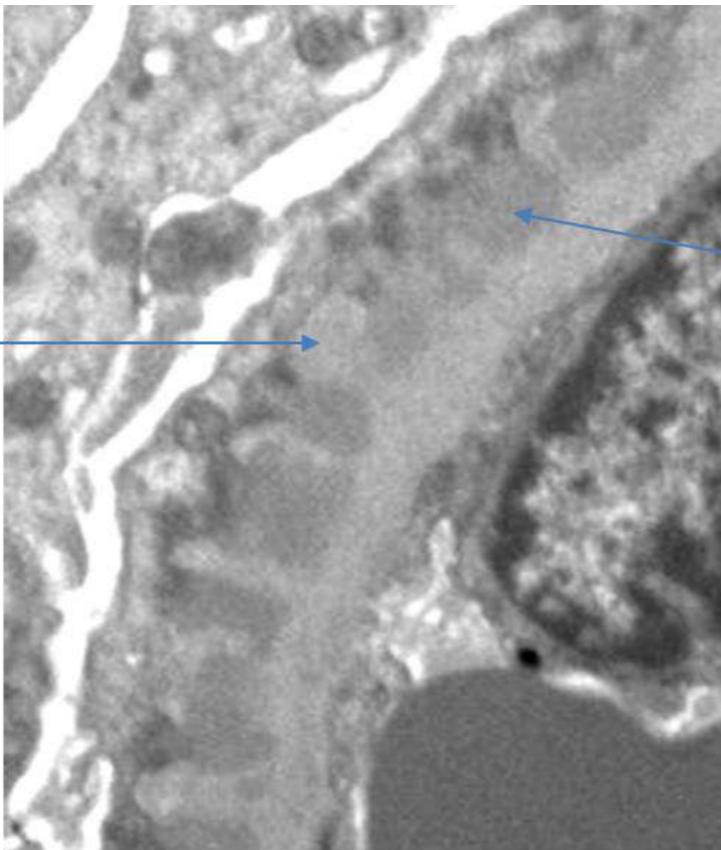
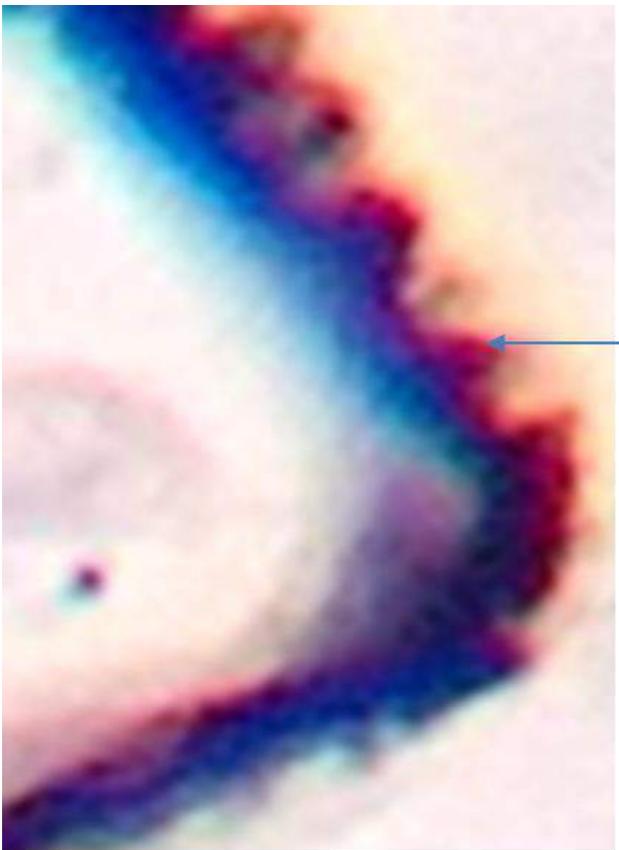


Προδιάθεση για

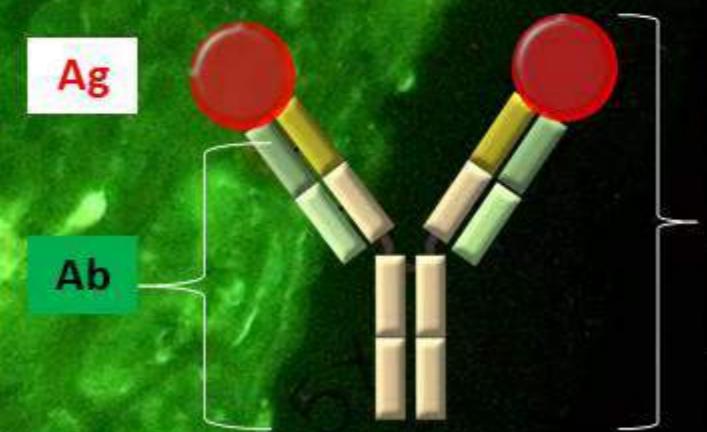
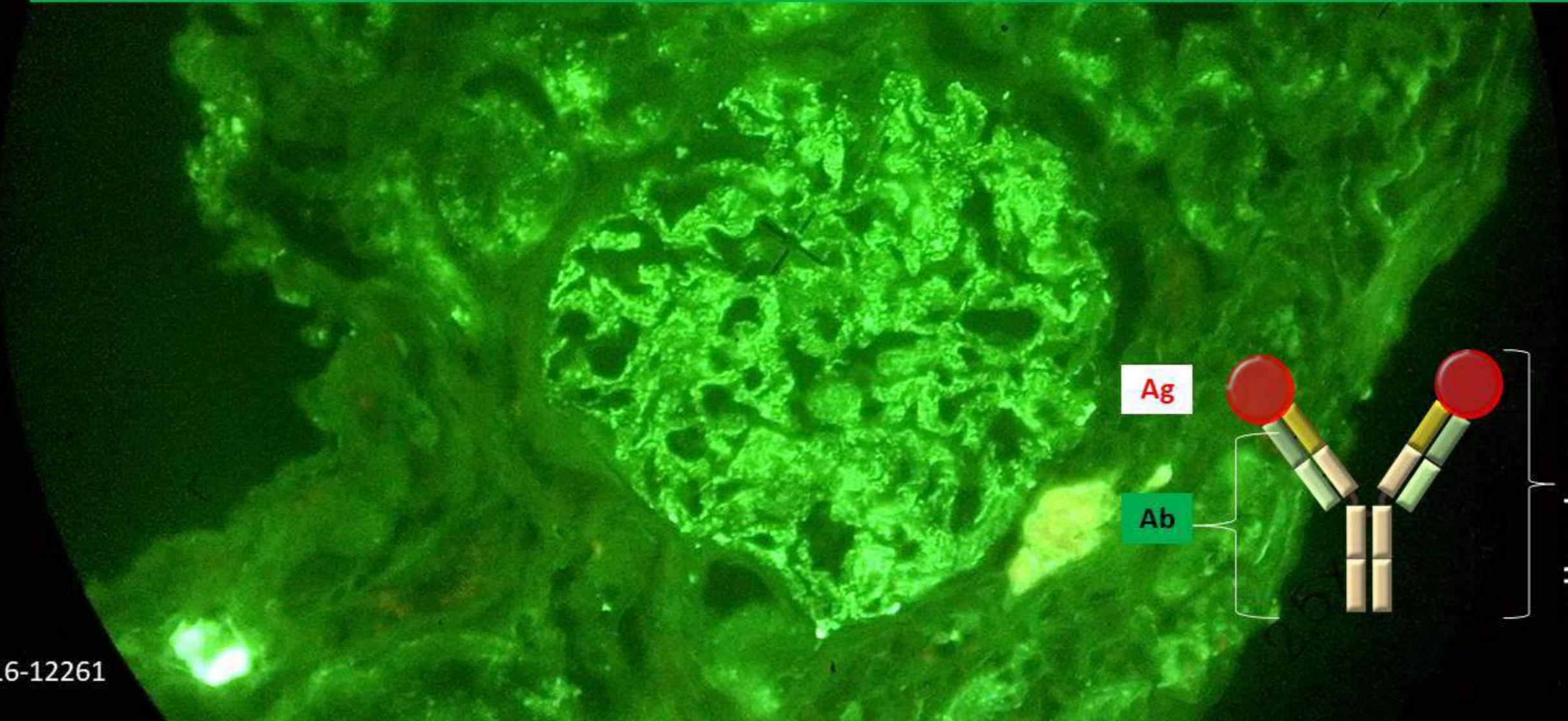


λοιμώξεις

Εναποθέσεις και MN



MN Ανοσοφθορισμός - IgG



16-12261

Altia MN

Conditions and Agents Associated with Membranous Nephropathy		
Groups	Common	Uncommon
Immune diseases	Systemic lupus erythematosus,	Rheumatoid arthritis, Hashimoto's disease, Graves' disease, mixed connective tissue disease, Sjögren's syndrome, primary biliary cirrhosis, bullous pemphigoid, small bowel enteropathy syndrome, dermatitis herpetiformis, ankylosing spondylitis, graft-versus-host disease, Guillain-Barré syndrome, bone marrow and stem cell transplantation, anti-GBM and ANCA-positive crescentic GN
Infectious or parasitic diseases	Hepatitis B	Hepatitis C, syphilis, filariasis, hydatid disease, schistosomiasis, malaria, leprosy
Drugs and toxins	Gold, penicillamine, NSAIDs	Mercury, captopril, formaldehyde, hydrocarbons, bucillamine agents
Miscellaneous	Tumors, renal transplantation	Sarcoidosis, sickle cell disease, Kimura disease, angiofollicular lymph node hyperplasia

"In about two thirds of patients, however, no obvious etiologic agent or condition can be identified"

Comprehensive Clinical Nephrology - 4th Edition 2010

The NEW ENGLAND JOURNAL *of* MEDICINE

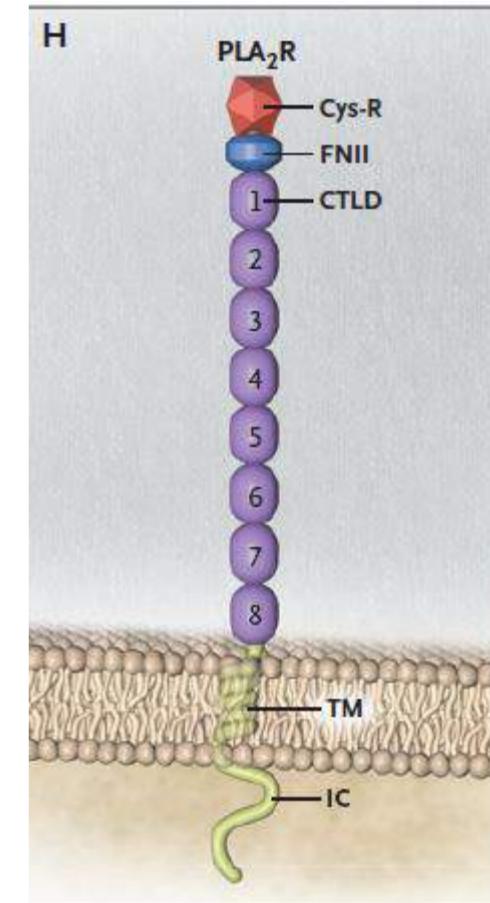
ESTABLISHED IN 1812

JULY 2, 2009

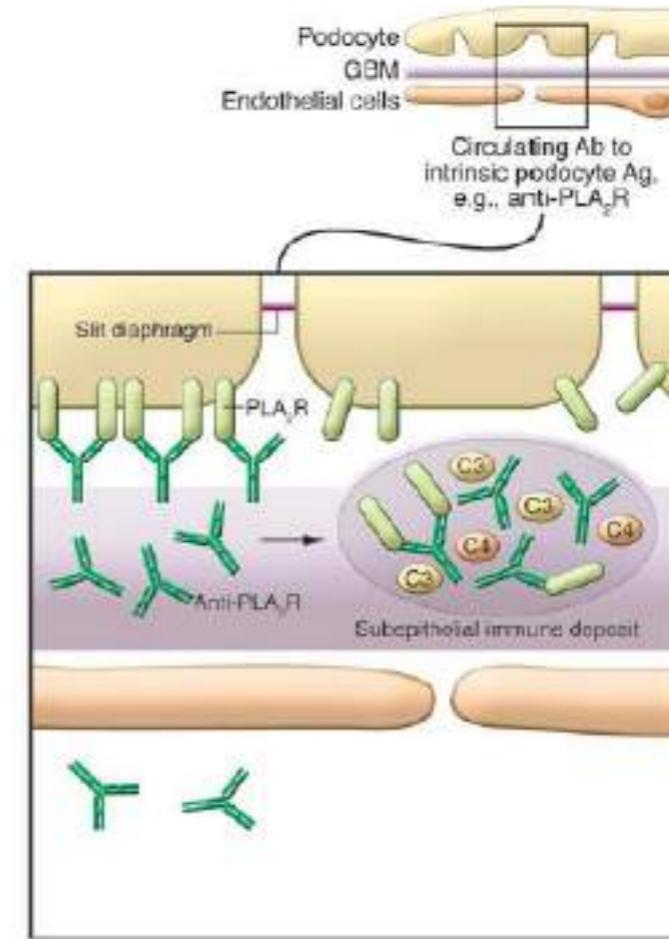
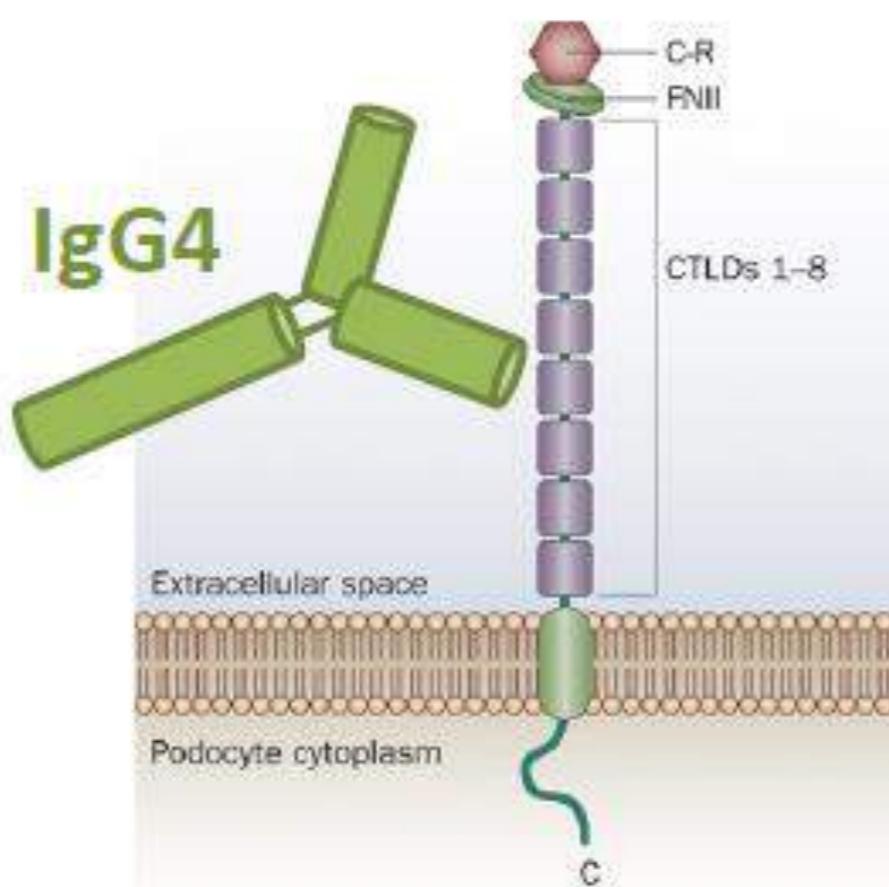
VOL. 361 NO. 1

M-Type Phospholipase A₂ Receptor as Target Antigen in Idiopathic Membranous Nephropathy

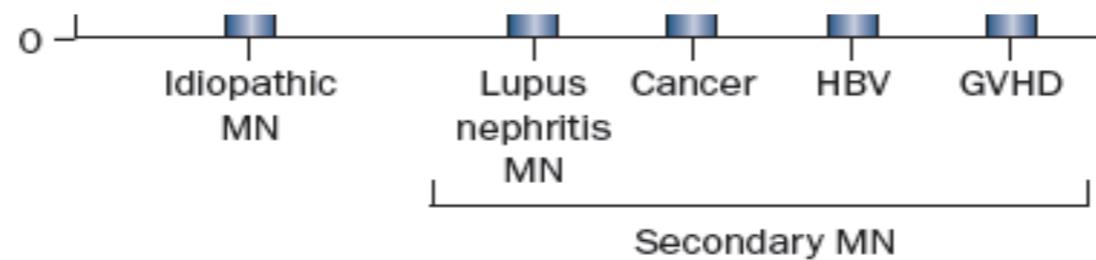
Laurence H. Beck, Jr., M.D., Ph.D., Ramon G.B. Bonegio, M.D., Gérard Lambeau, Ph.D., David M. Beck, B.A.,
David W. Powell, Ph.D., Timothy D. Cummins, M.S., Jon B. Klein, M.D., Ph.D., and David J. Salant, M.D.



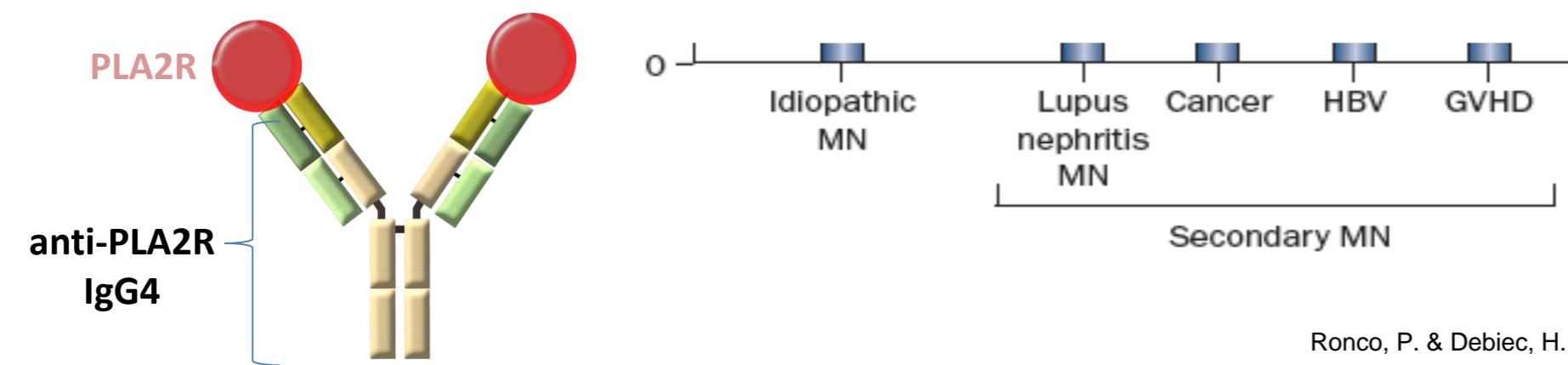
A $\tilde{\alpha}$ MN – antiPLA2R



Διάγνωση MN και anti-PLA2R

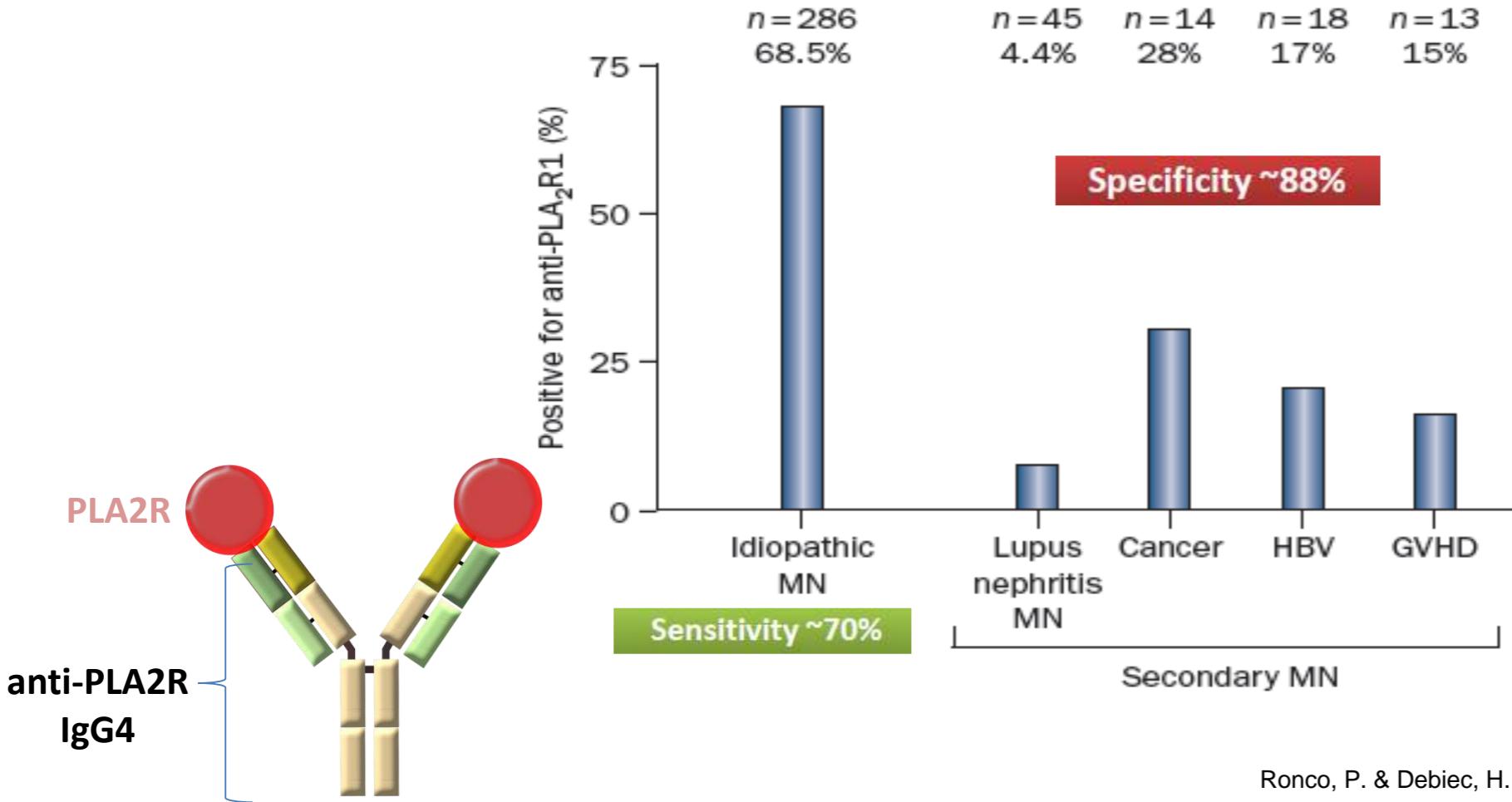


Διάγνωση MN και anti-PLA2R



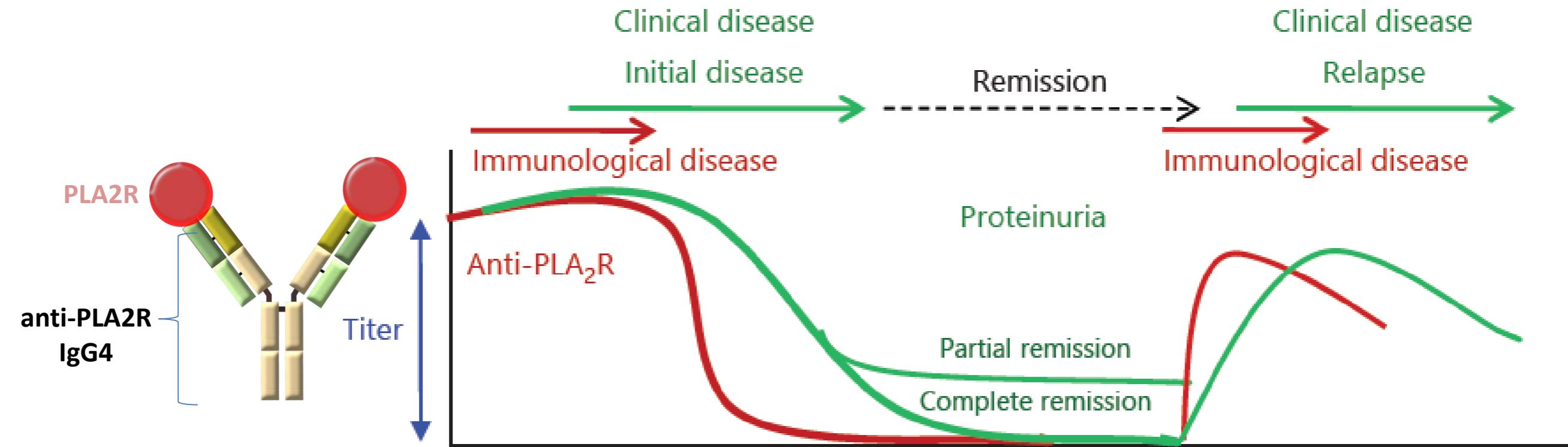
Ronco, P. & Debiec, H. Nat. Rev. Nephrol. 8, 203–213 (2012)

Διάγνωση MN και anti-PLA2R

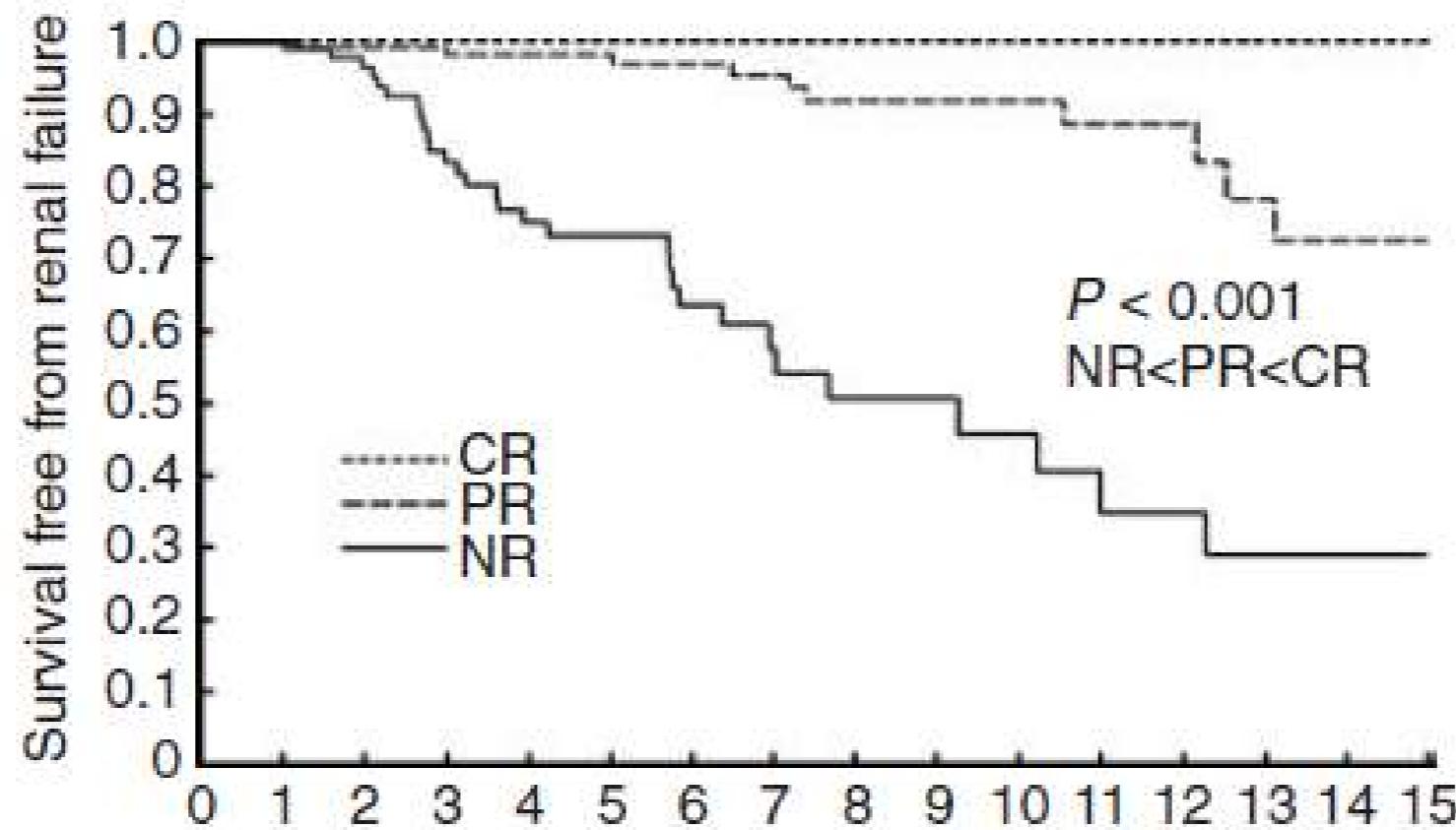


Ronco, P. & Debiec, H. Nat. Rev. Nephrol. 8, 203–213 (2012)

Anti-PLA2R καὶ πορεία MN



Έγκεση λευκωματουρίας και νεφρική πρόγνωση



Ιδιοπαθής MN > νόσος από αντιPLA2R

Θεραπευτικός στόχος η απομάκρυνση των αντιPLA2R

Αντιμετώπιση ιδιοπαθούς/πρωτοπαθούς MN

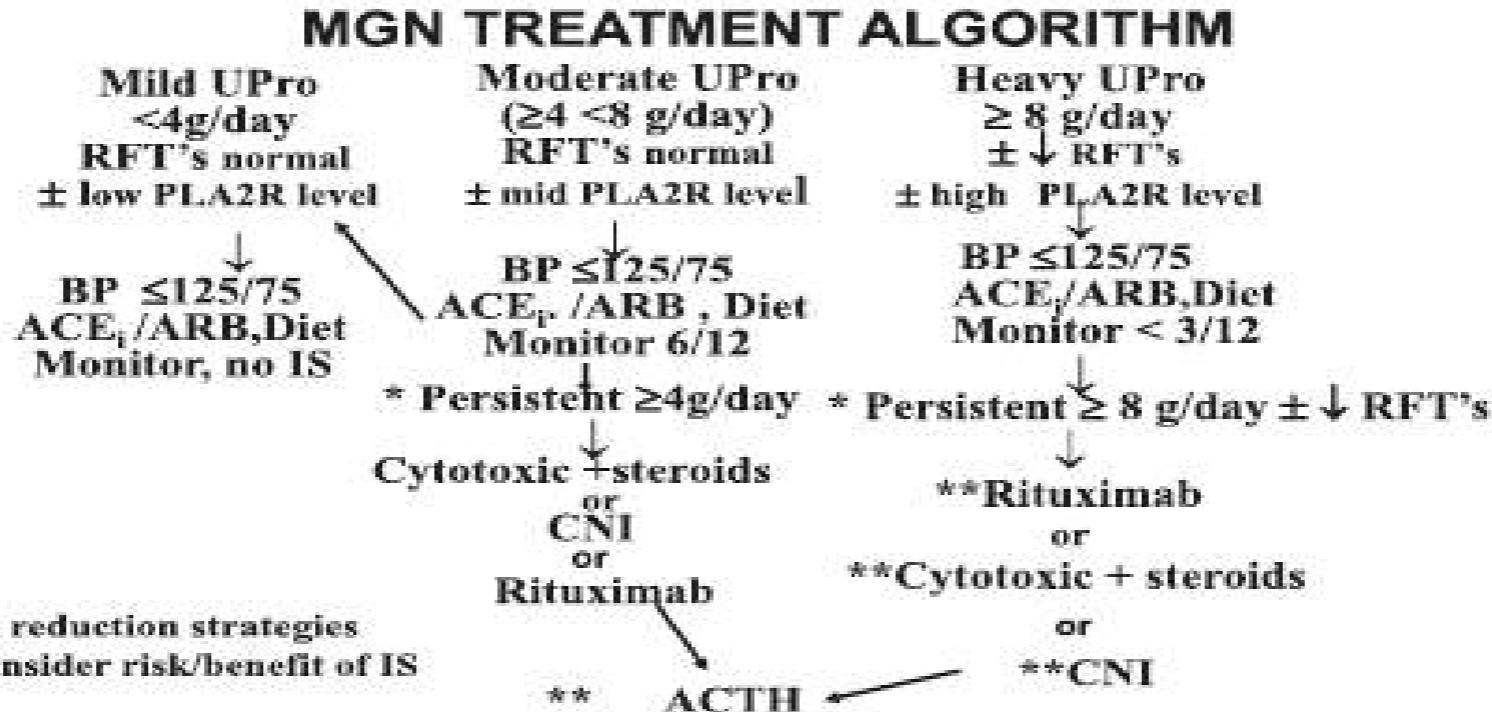
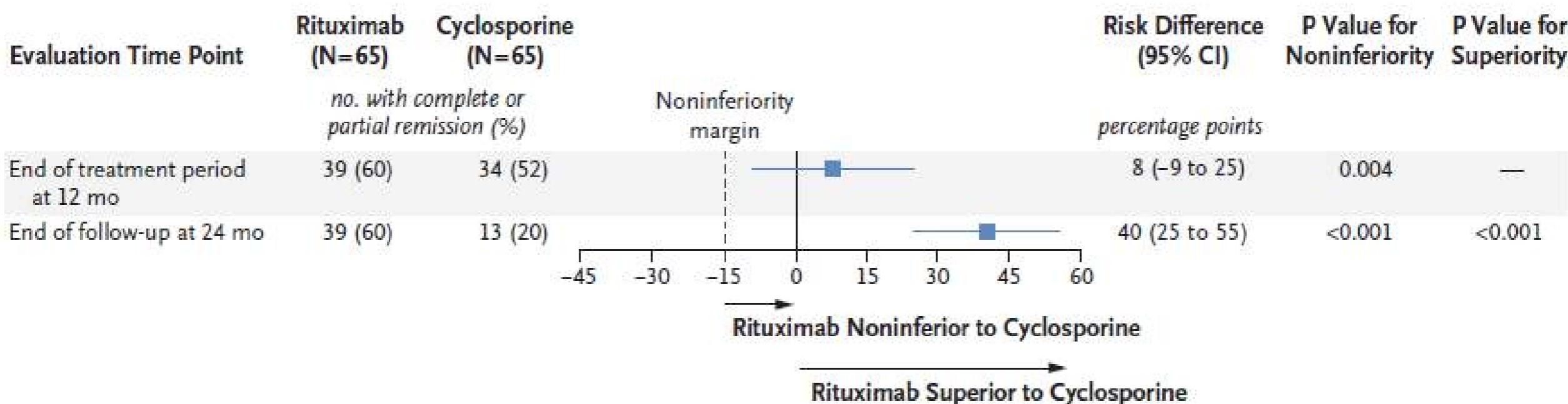


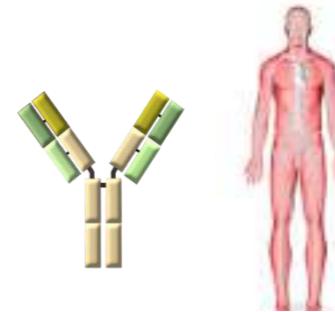
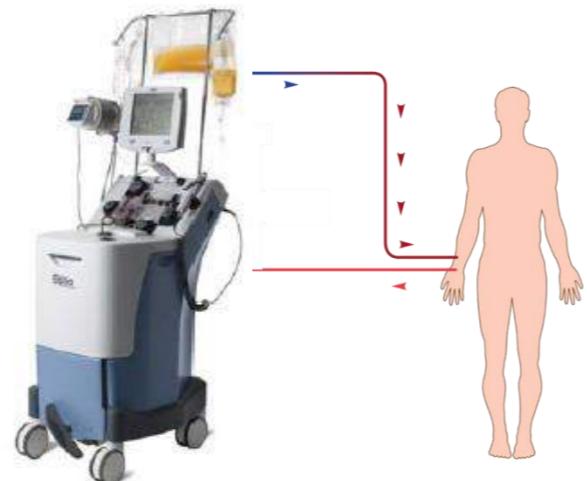
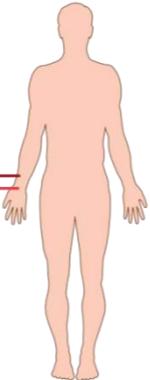
FIGURE 1: MN treatment algorithm. UPro, proteinuria; RFT, renal function tests; BP, blood pressure.

Rituximab or Cyclosporine in the Treatment of Membranous Nephropathy

F.C. Fervenza, G.B. Appel, S.J. Barbour, B.H. Rovin, R.A. Lafayette, N. Aslam, J.A. Jefferson, P.E. Gipson, D.V. Rizk, J.R. Sedor, J.F. Simon, E.T. McCarthy, P. Brenchley, S. Sethi, C. Avila-Casado, H. Beanlands, J.C. Lieske, D. Philibert, T. Li, L.F. Thomas, D.F. Green, L.A. Juncos, L. Beara-Lasic, S.S. Blumenthal, A.N. Sussman, S.B. Erickson, M. Hladunewich, P.A. Canetta, L.A. Hebert, N. Leung, J. Radhakrishnan, H.N. Reich, S.V. Parikh, D.S. Gipson, D.K. Lee, B.R. da Costa, P. Jüni, and D.C. Cattran, for the MENTOR Investigators



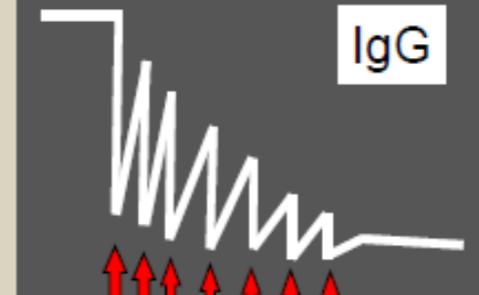
Αποκάκρυνση IgG με πλασμαφαίρεση



Removal of IgG

(Ward DM, *Updates to Harrison's Principles of Internal Medicine*, Volume V, 1984)

IgG Autoantibody titer



Plasmapheresis procedures

Most antibody mediated diseases:

- IgG is smaller (~146,000 Daltons)
- Only 30%-40% is intravascular

Plasmapheresis combined with rituximab for refractory idiopathic membranous nephropathy

Ming Wen · Claudio Küchle · Oliver Sarkar ·
Lutz Renders · Uwe Heemann · Christoph Schmaderer



Plasmapheresis combined with rituximab for refractory idiopathic membranous nephropathy

Ming Wen · Claudio Küchle · Oliver Sarkar ·
Lutz Renders · Uwe Heemann · Christoph Schmaderer

34-year-old male Caucasian

edema

proteinuria 6.2 g protein/g creatinine

serum albumin 2.6 g/dl

Kidney biopsy showed membranous glomerulopathy.

The causes of secondary membranous were excluded.

Plasmapheresis combined with rituximab for refractory idiopathic membranous nephropathy

Ming Wen · Claudio Küchle · Oliver Sarkar ·
Lutz Renders · Uwe Heemann · Christoph Schmaderer

Initially, the patient was treated with an **ACE inhibitor**, an **angiotensin II receptor blocker**, an **anticoagulant** and **prednisolone** (60 mg/day, progressively tapered to 5 mg/day).

Plasmapheresis combined with rituximab for refractory idiopathic membranous nephropathy

Ming Wen · Claudio Küchle · Oliver Sarkar ·
Lutz Renders · Uwe Heemann · Christoph Schmaderer

Initially, the patient was treated with an **ACE inhibitor**, an **angiotensin II receptor blocker**, an **anticoagulant** and **prednisolone** (60 mg/day, progressively tapered to 5 mg/day).

Six months later, his condition **deteriorated**. Serum **creatinine** level increased to **1.5 mg/dl** (135 μmol/l) while serum **albumin** declined to **1.5 g/dl** (15 g/l). The patient was still heavily proteinuric (**4.6 g protein/g creatinine**).

Plasmapheresis combined with rituximab for refractory idiopathic membranous nephropathy

Ming Wen · Claudio Küchle · Oliver Sarkar ·
Lutz Renders · Uwe Heemann · Christoph Schmaderer

The treatment was then complemented by **cyclosporine** (CsA) and switched later to **tacrolimus** (Tac) due to side effects.

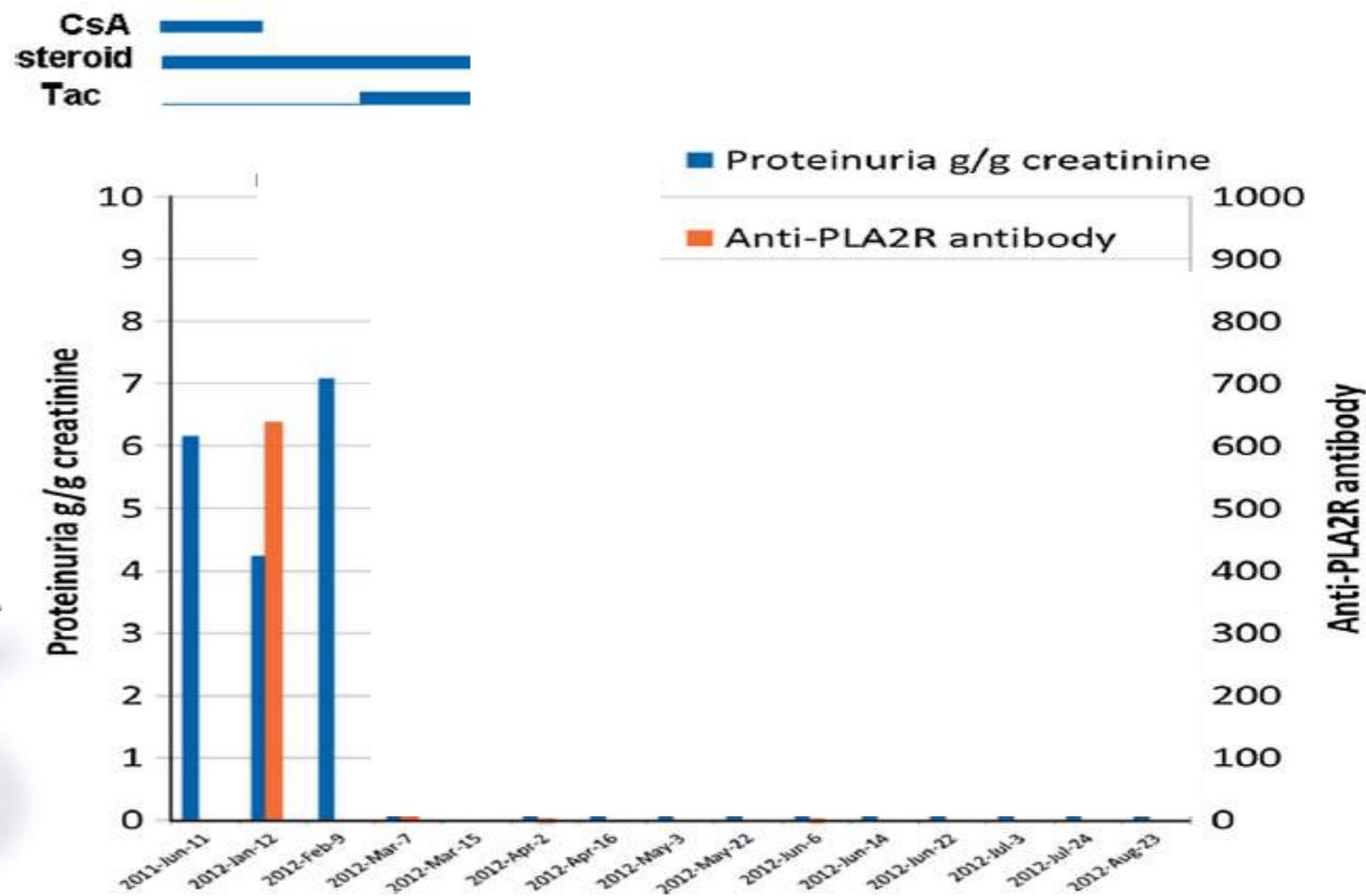
However, his condition further deteriorated rapidly with **increased protein excretion** (8.8 g protein/g creatinine). He **gained 20 kg in 3 weeks** and showed increased peripheral **edema** and **dyspnea**

Plasmapheresis combined with rituximab for refractory idiopathic membranous nephropathy

Ming Wen · Claudio Küchle · Oliver Sarkar ·
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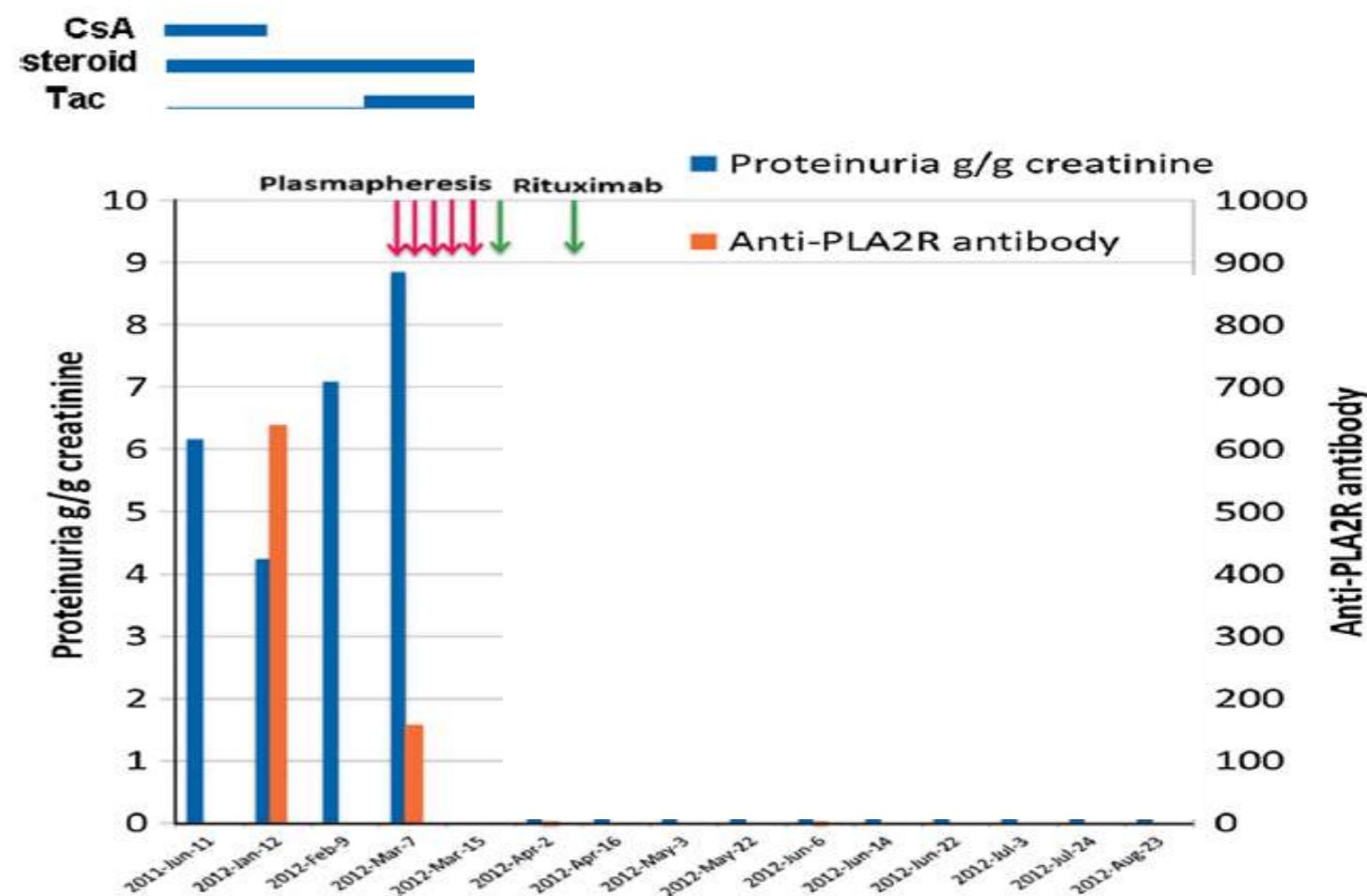
However, his condition further deteriorated rapidly with **increased protein excretion** (8.8 g protein/g creatinine). He **gained 20 kg in 3 weeks** and showed increased peripheral **edema** and **dyspnea**



Plasmapheresis combined with rituximab for refractory idiopathic membranous nephropathy

Ming Wen · Claudio Küchle · Oliver Sarkar ·
Lutz Renders · Uwe Heemann · Christoph Schmaderer

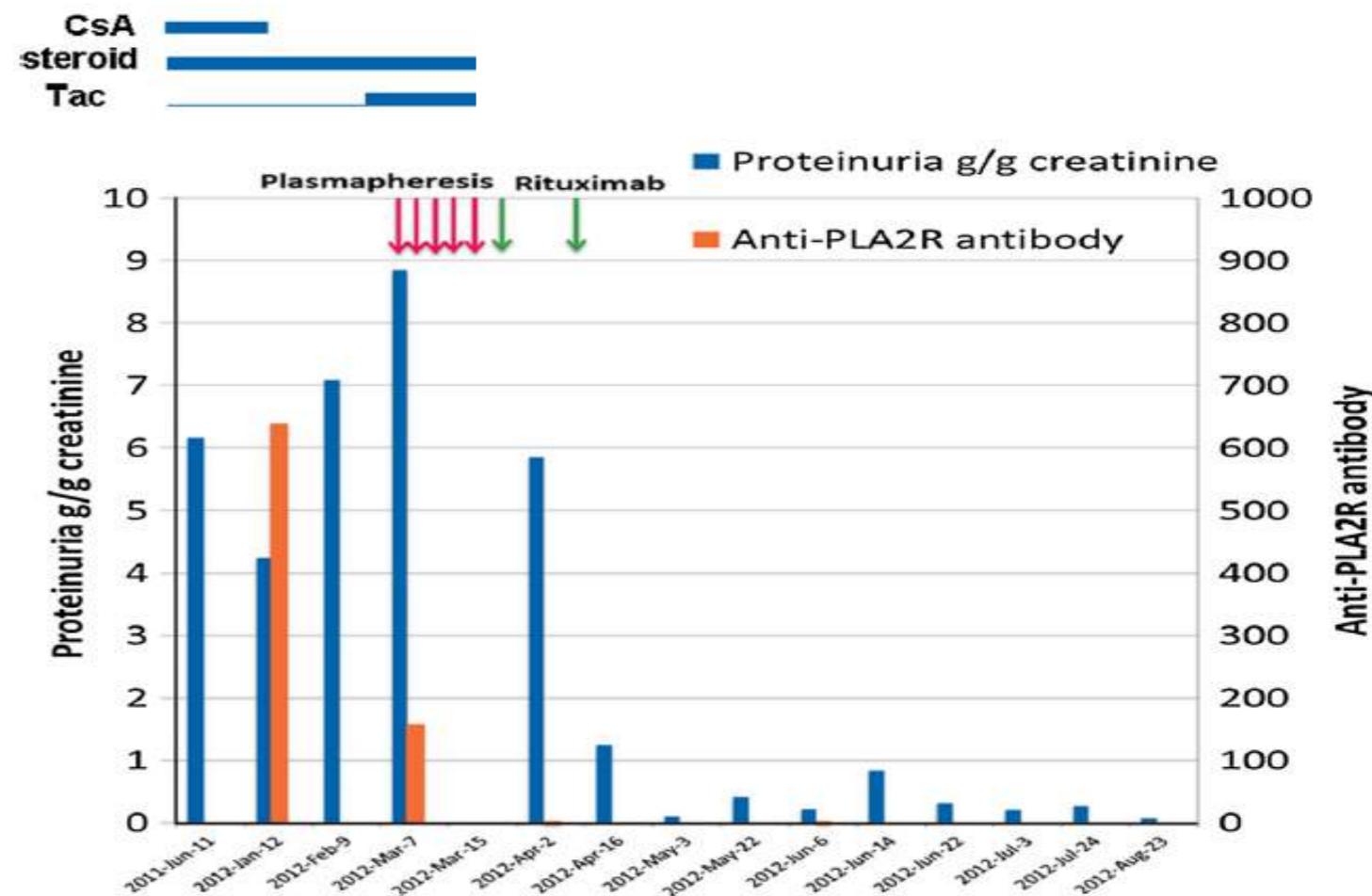
We decided to perform a combined treatment with **plasmapheresis** (d1-3, d5, d7) followed by two infusions of **rituximab** (d8 + d28). Each plasmapheresis was performed over 2–3 h, using **5,000 ml of fresh frozen plasma (FFP)**, approximately **1.2 times the circulating plasma volume**, as a replacement fluid. Subsequently, the patient received intravenous infusions of **rituximab (375 mg/m², d8 + d28)**.



Plasmapheresis combined with rituximab for refractory idiopathic membranous nephropathy

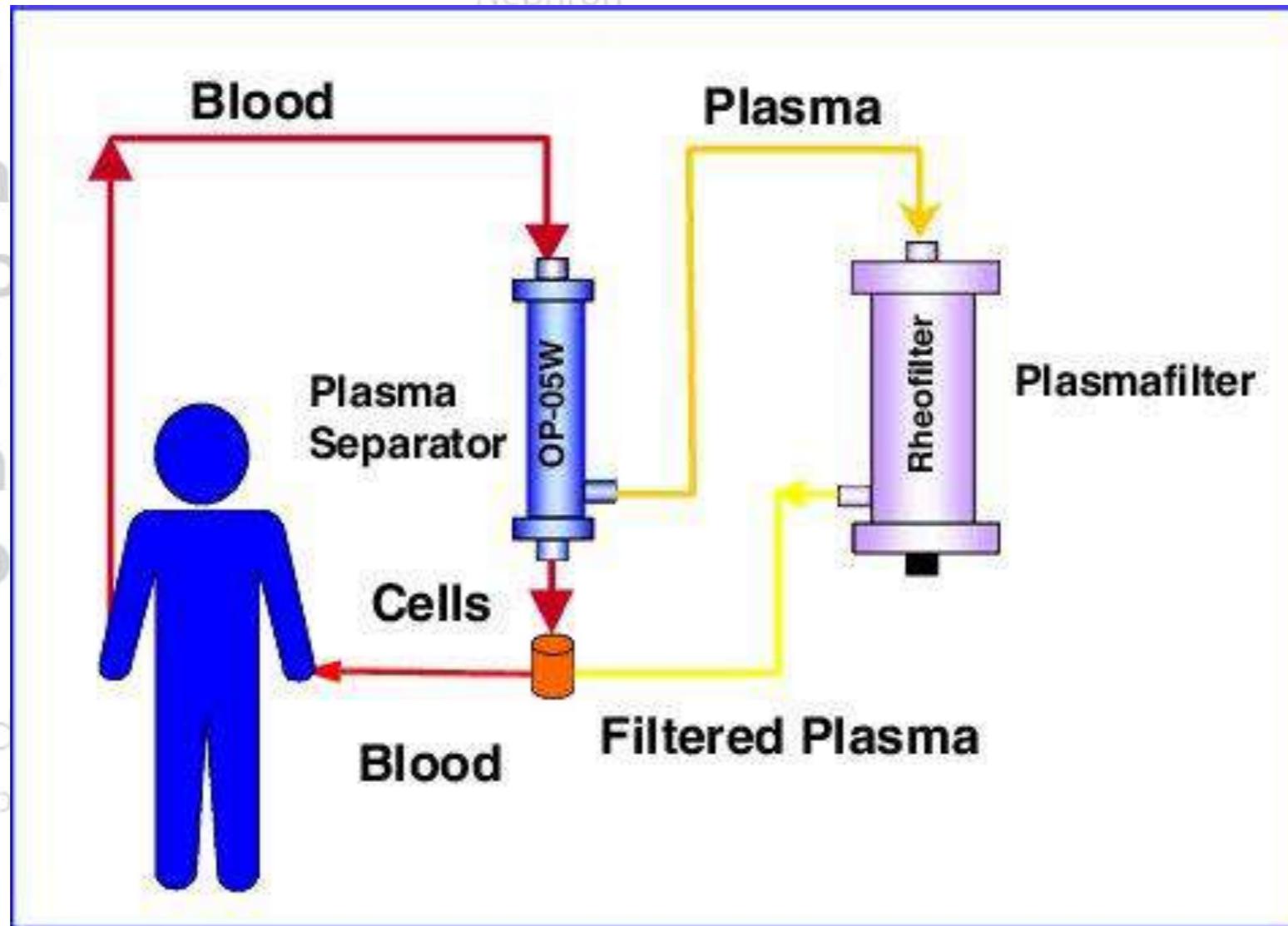
Ming Wen · Claudio Küchle · Oliver Sarkar ·
Lutz Renders · Uwe Heemann · Christoph Schmaderer

Complete remission of nephrotic syndrome was achieved 8 weeks later. The concentration of anti-PLA2R antibodies in the serum was continuously reduced during the treatment and eventually disappeared during remission. Protein excretion was below 0.3 g/day in eight consecutive visits under ACE inhibitor/ARB treatment.



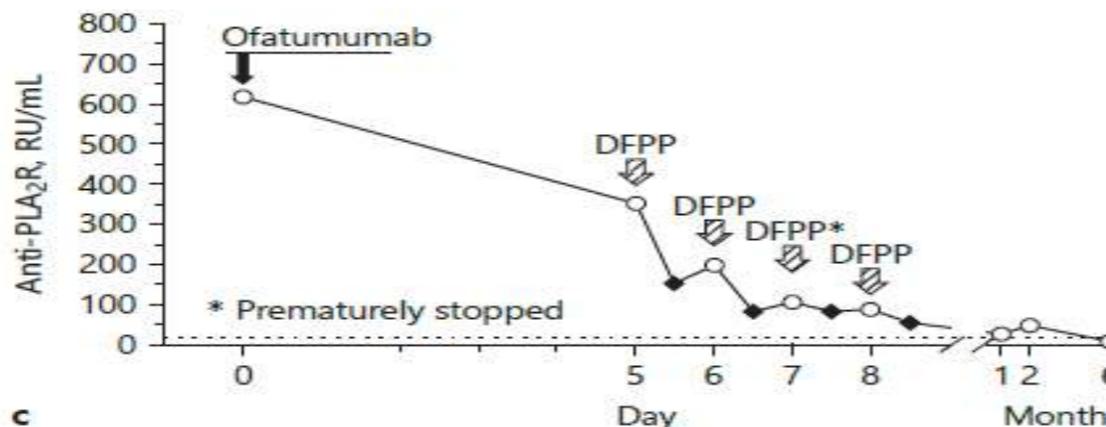
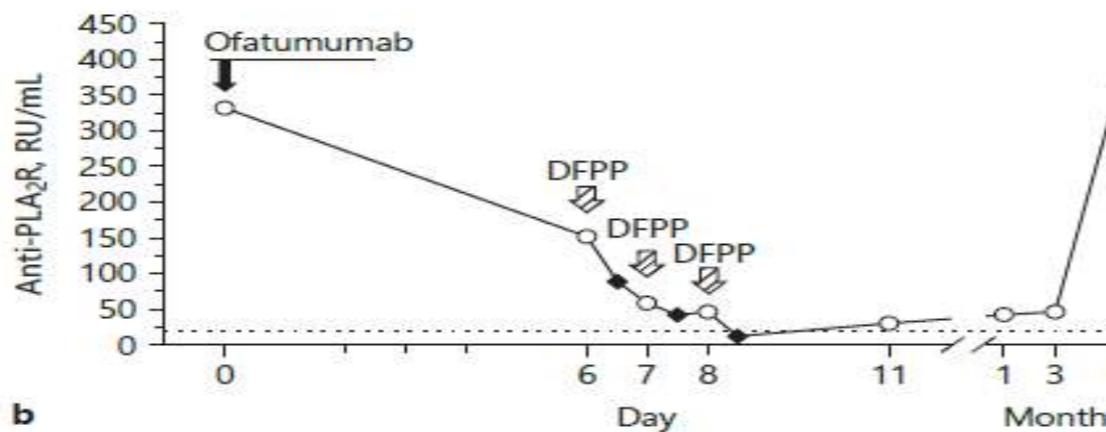
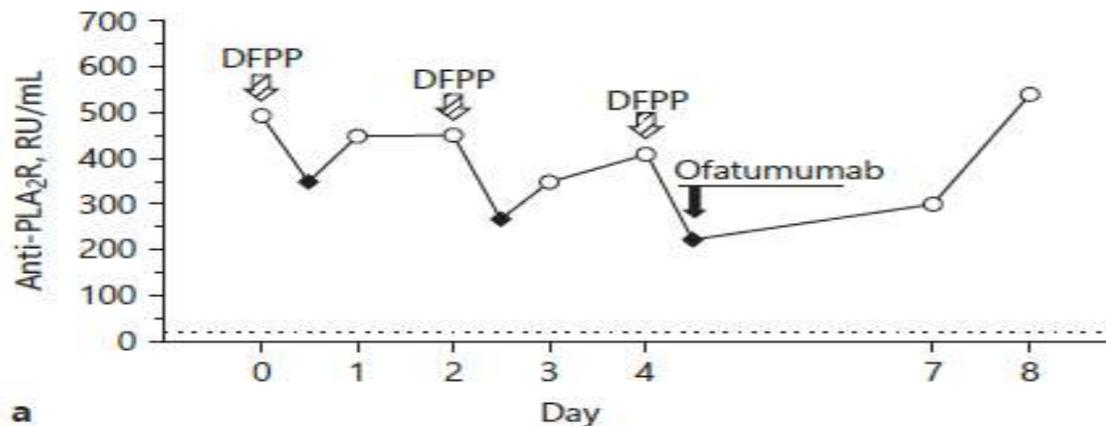
Accelerating the Depletion of Circulating Anti-Phospholipase A₂ Receptor Antibodies in Patients with Severe Membranous Nephropathy: Preliminary Findings with Double Filtration Plasmapheresis and Ofatumumab

Manuel Alfredo Podestà^{a, b} Alessia Gennarini^b Valentina Portalupi^b
Stefano Rota^b Maria Grazia Alessio^c Giuseppe Remuzzi^{a, d} Piero Ruggenenti^{a, d}



Accelerated Anti-F_{ab} Patient Preliminary Plasma

Manuel A
Stefano R

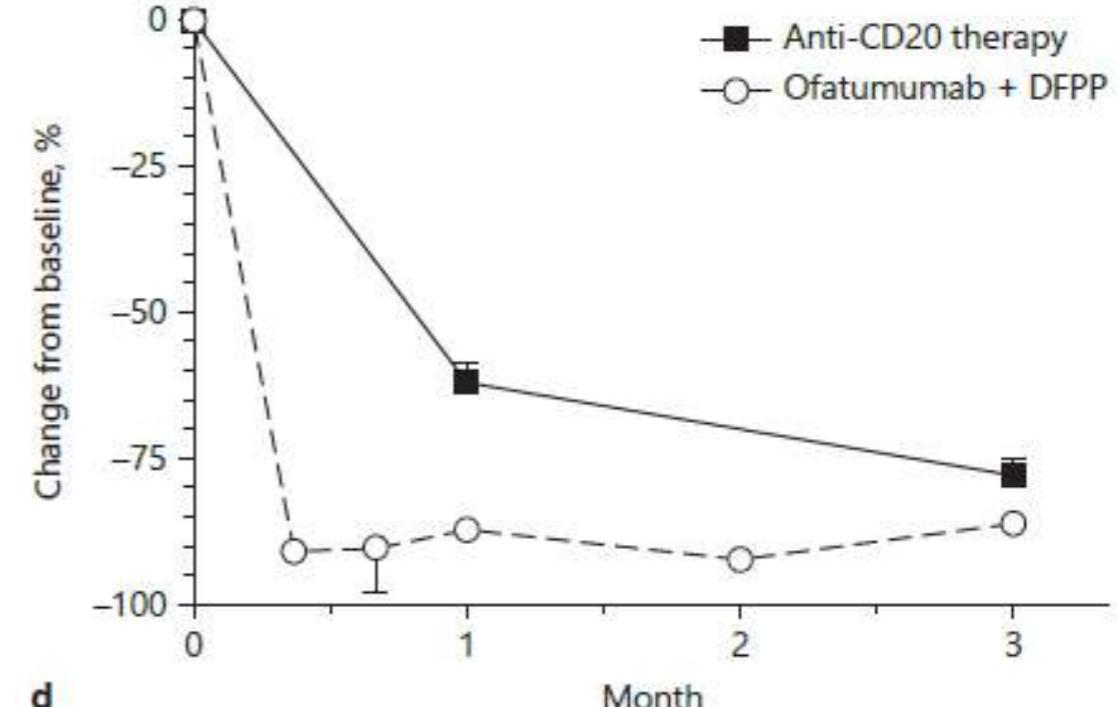


Circulating Anti-Autoantibodies in Lupus Nephropathy: Role Filtration Therapy

Silentina Portalupi^b
Mazzu^{a, d} Piero Ruggenenti^{a, d}

Accelerating the Depletion of Anti-Phospholipase A₂ Recombinant in Patients with Severe Membrane Angiopathy: Preliminary Findings with Plasmapheresis and Ofatumumab

Manuel Alfredo Podestà^{a,b} Alessia Genna
Stefano Rota^b Maria Grazia Alessio^c Giuseppe Remuzzi^{a,c} Piero Ruggenenti^{a,c}



A new rescue regimen with plasma exchange and rituximab in high-risk membranous glomerulonephritis

Janina Müller-Deile, Lena Schiffer, Marcus Hiss, Hermann Haller and Mario Schiffer

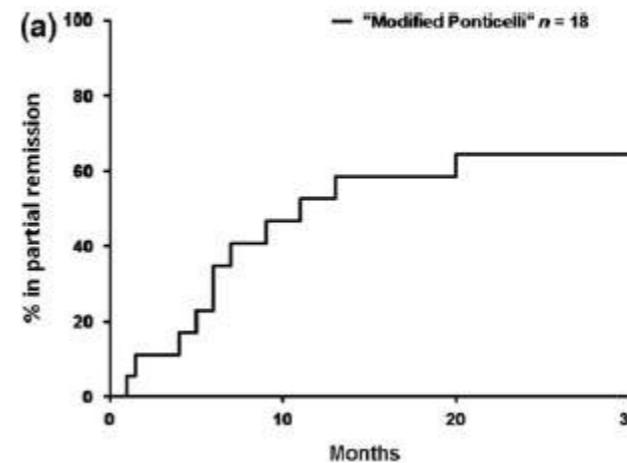
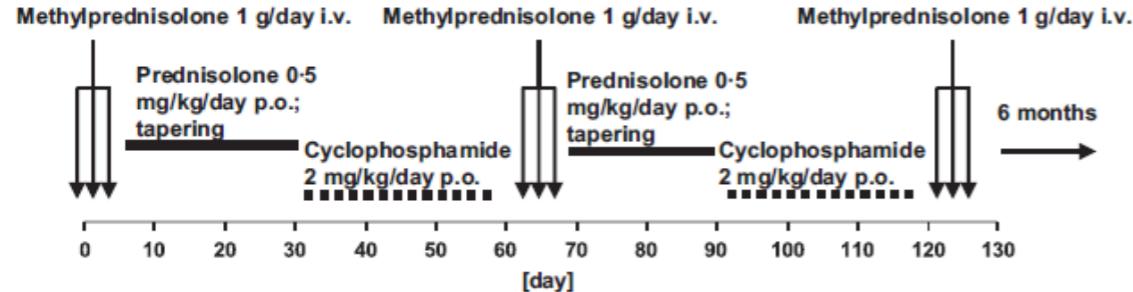
Division of Nephrology and Hypertension, Department of Medicine, Hannover Medical School, Hannover, Germany

10 patients with a biopsy-proven diagnosis of iMGN
therapy-resistant to all conventional regimens
urinary protein to creatinine ratio of **more than 10 000 mg/g Crea.**

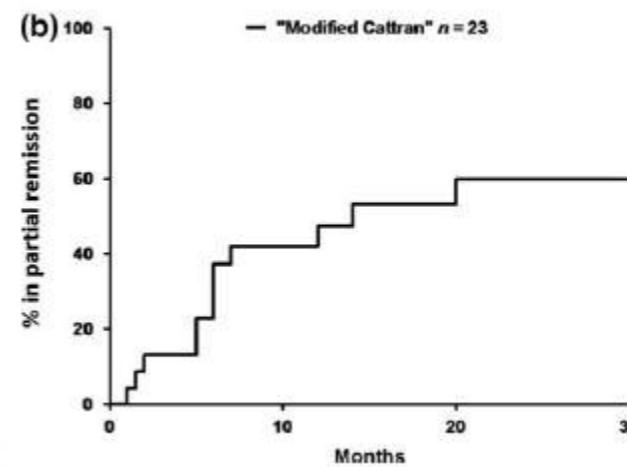
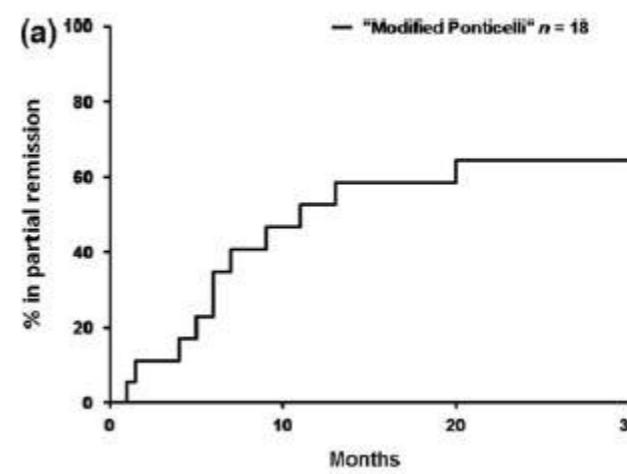
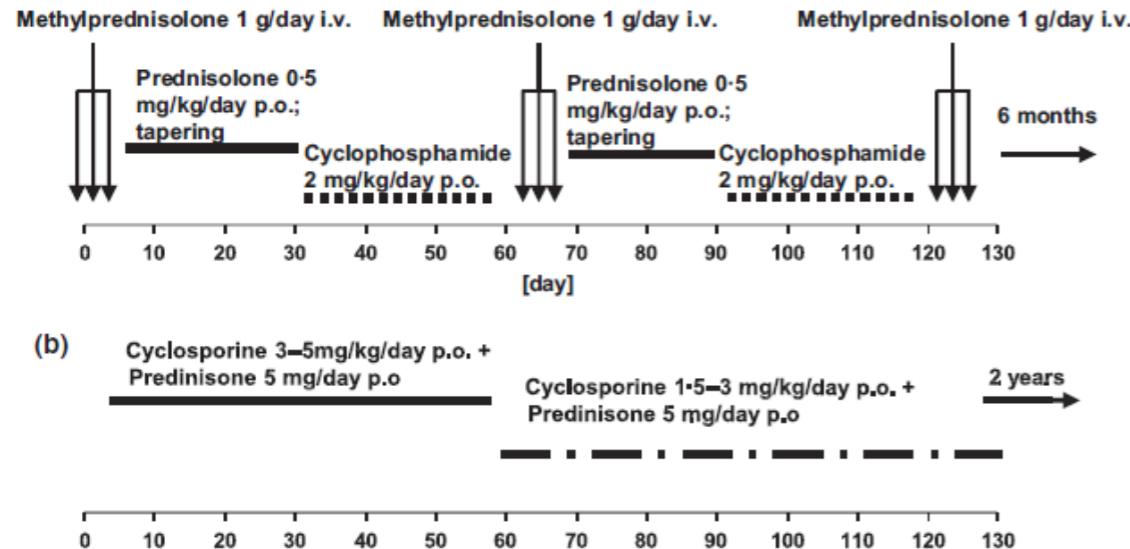
rescue protocol including
plasma exchanges (PE) against albumin, intravenous immunoglobulins (IVIGs) and rituximab

compared this protocol with standard immunosuppressive protocols including monthly alternating prednisolone plus cyclophosphamide (18 patients), cyclosporine plus prednisolone (23 patients) and rituximab alone (eight patients) in a retrospective design.

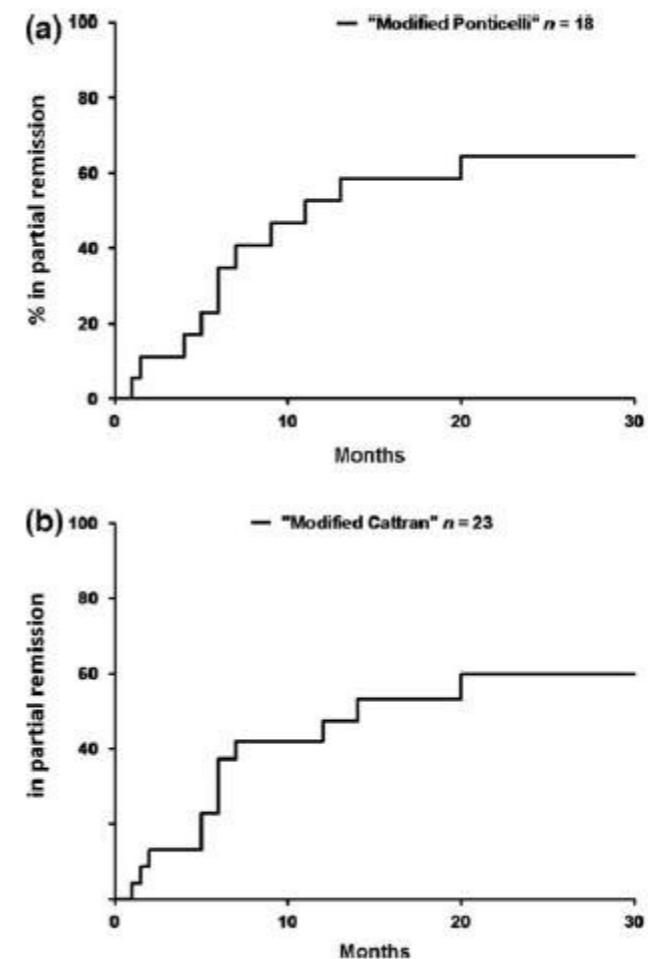
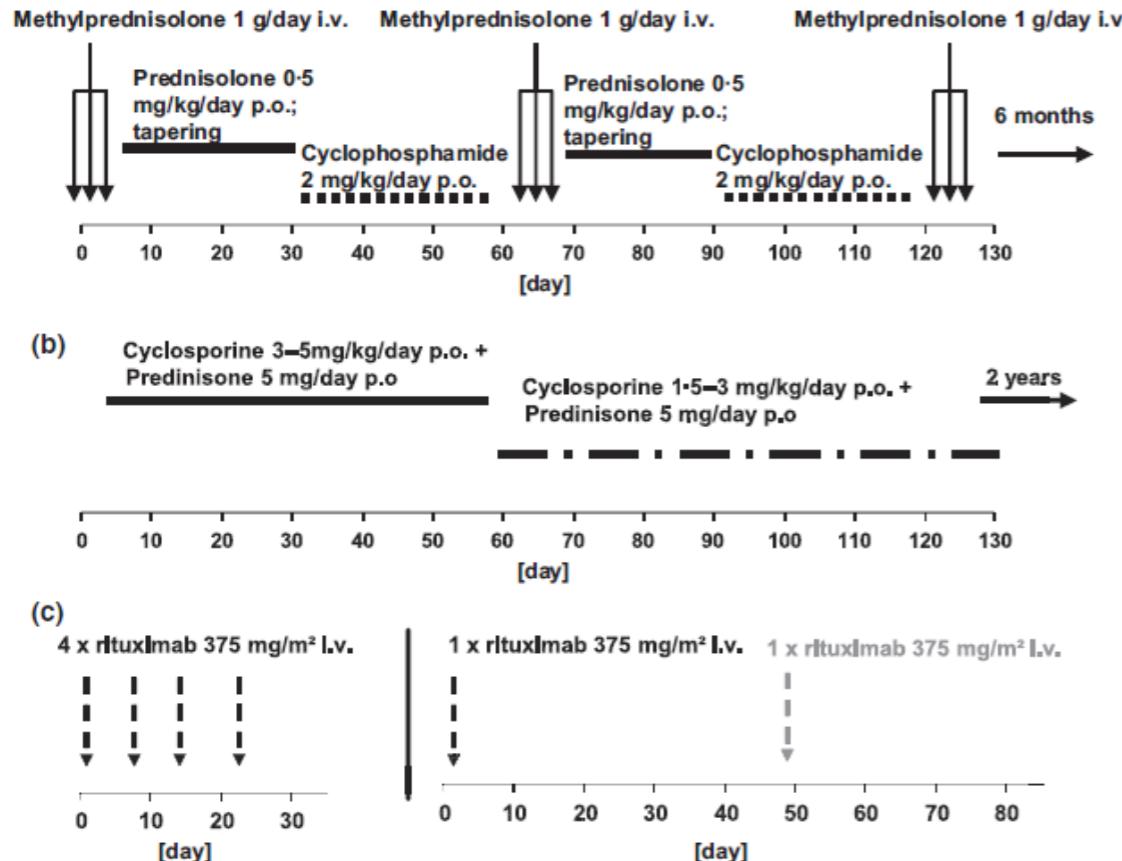
(a) **Different immunosuppressive regimes in iMGN**



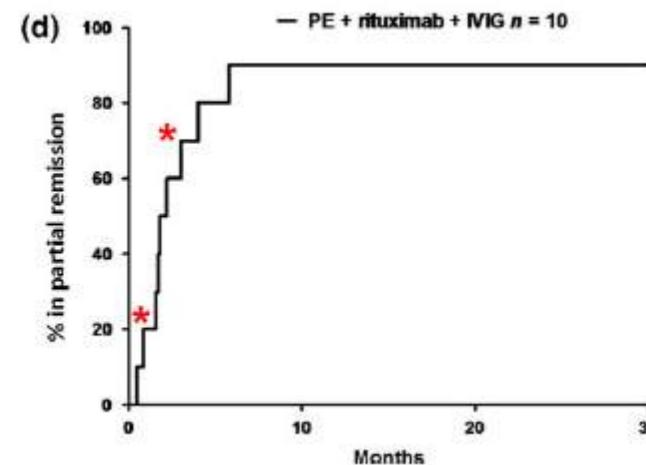
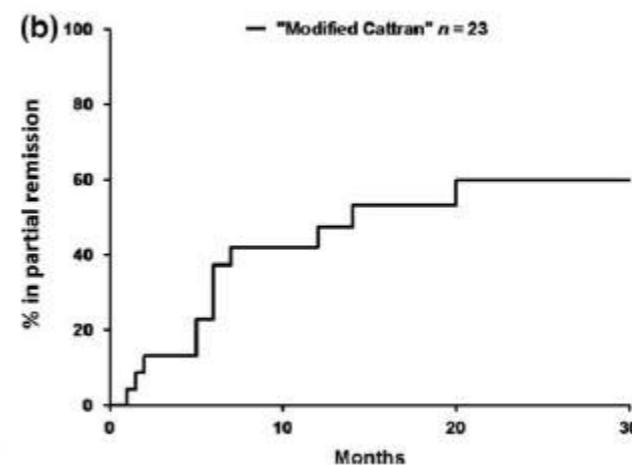
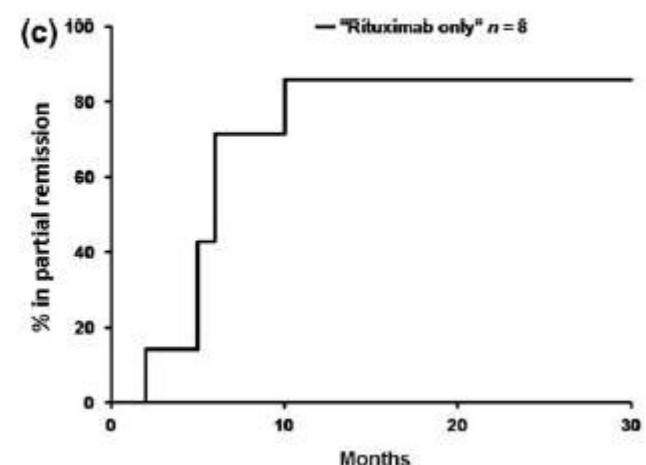
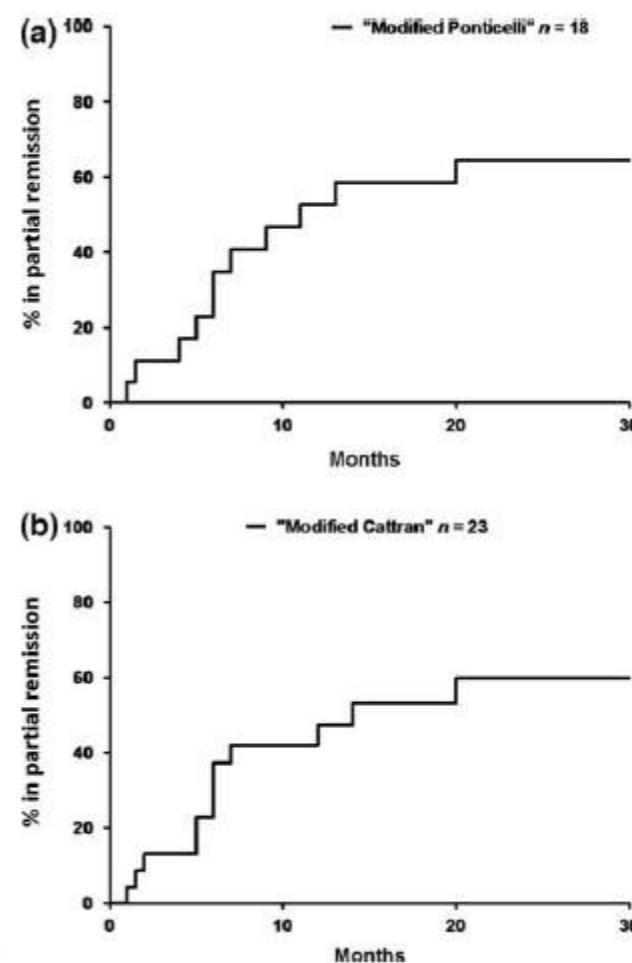
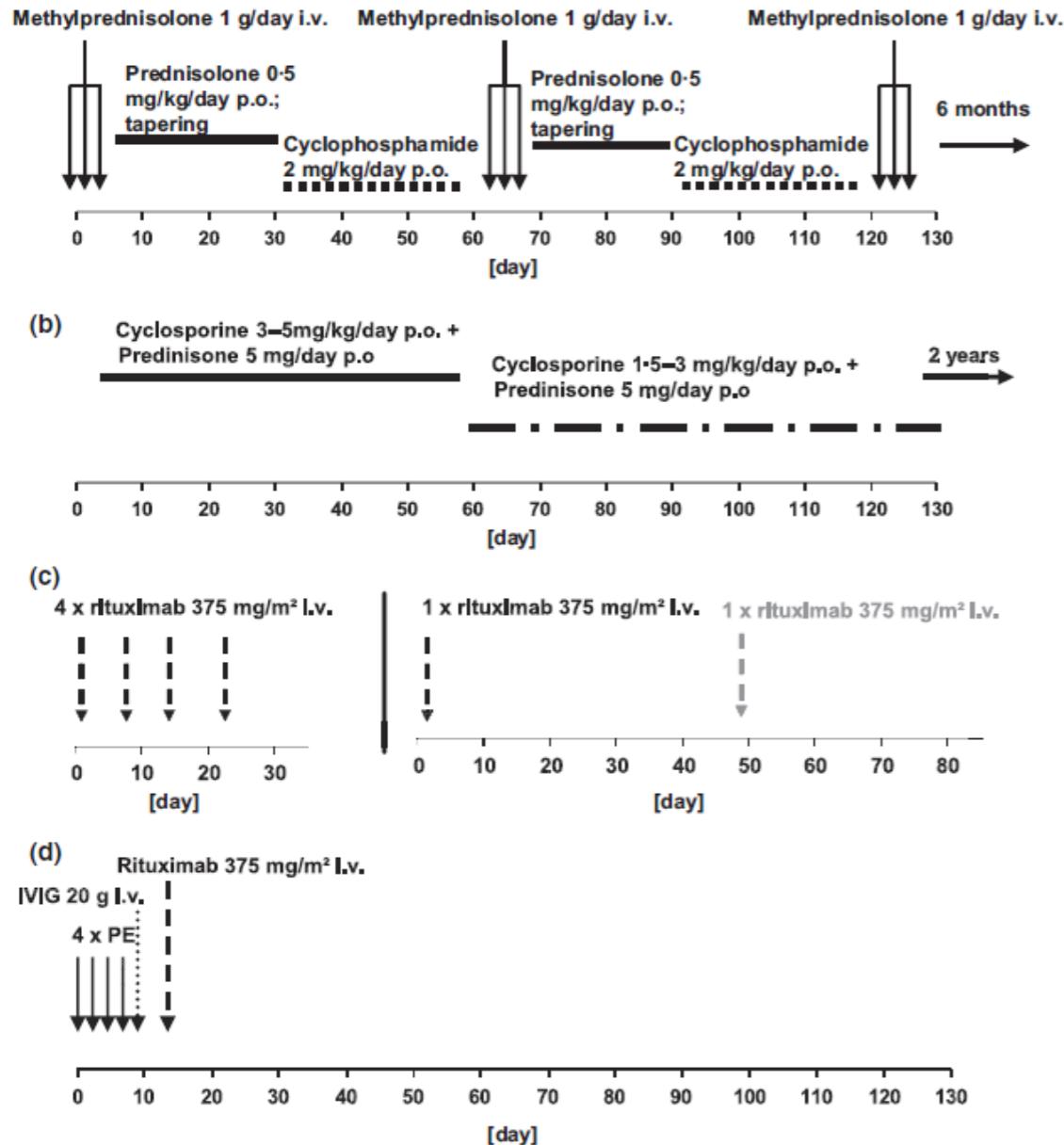
(a) **Different immunosuppressive regimes in iMGN**



(a) **Different immunosuppressive regimes in iMGN**

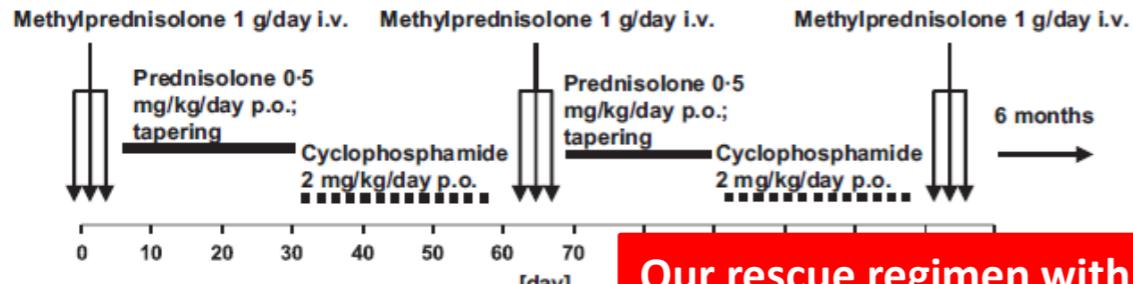


(a) **Different immunosuppressive regimes in iMGN**



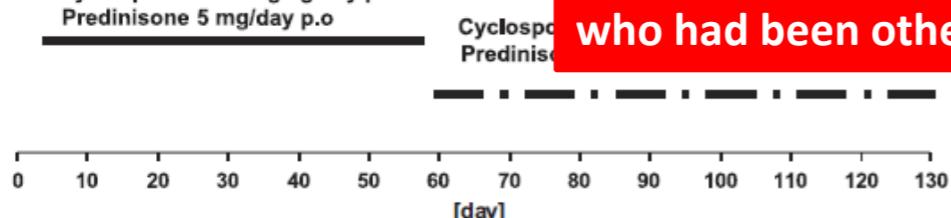
Red asterisks indicate partial remission in anti-PLA2R-antibody negative patients.

(a) **Different immunosuppressive regimens in iMGN**

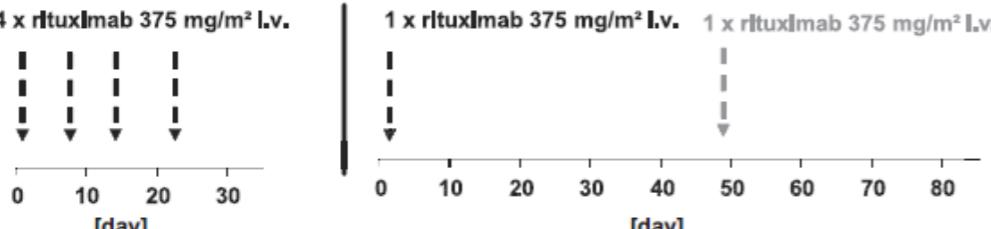


Our rescue regimen with PE, IVIGs and rituximab achieved partial remission in 90% of patients who had been otherwise refractory to therapy.

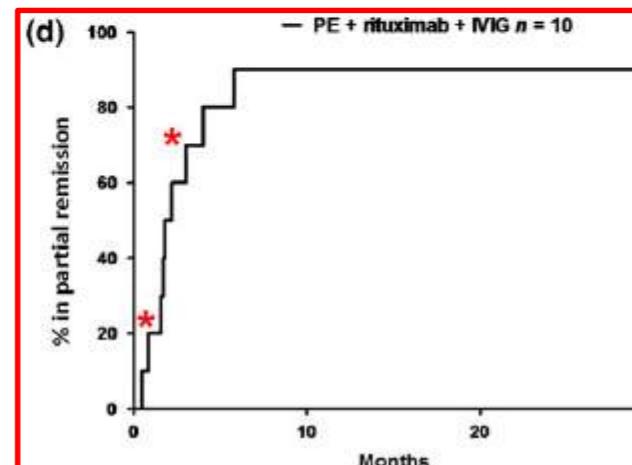
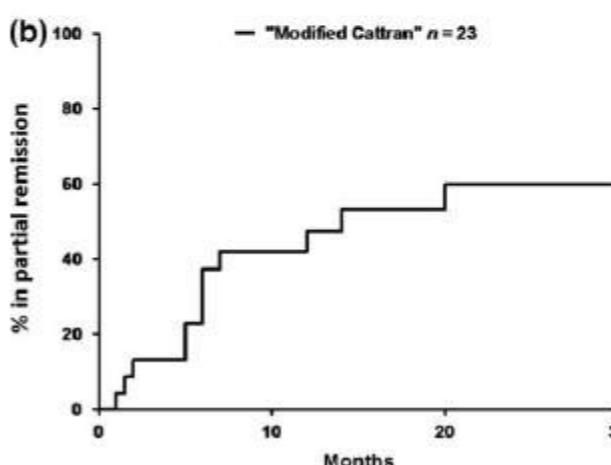
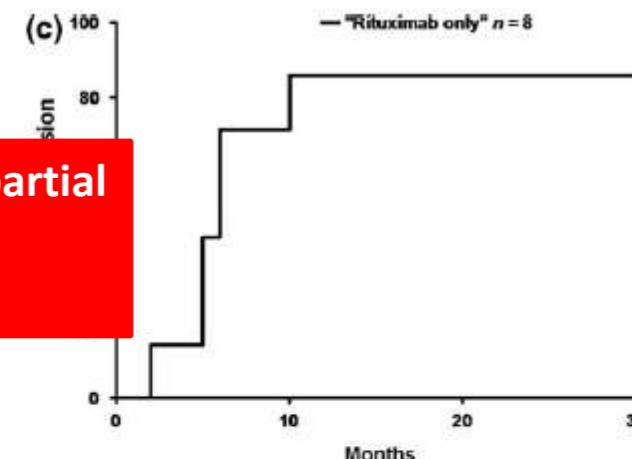
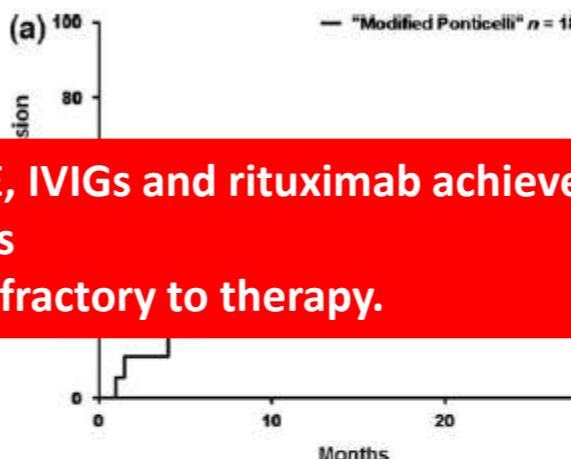
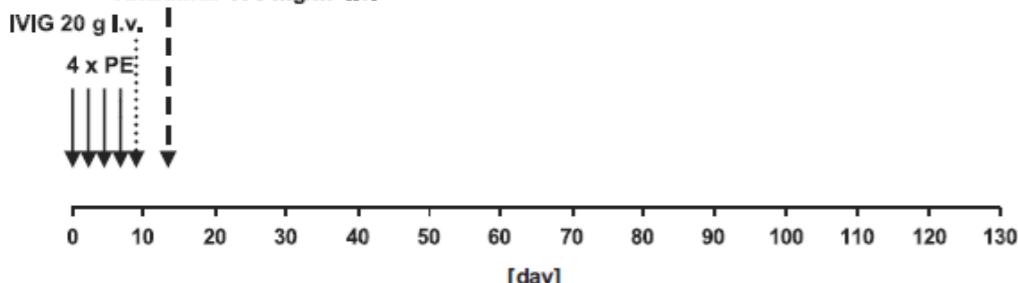
(b) Cyclosporine 3–5mg/kg/day p.o. + Prednisolone 5 mg/day p.o.



(c) 4 x rituximab 375 mg/m² i.v.

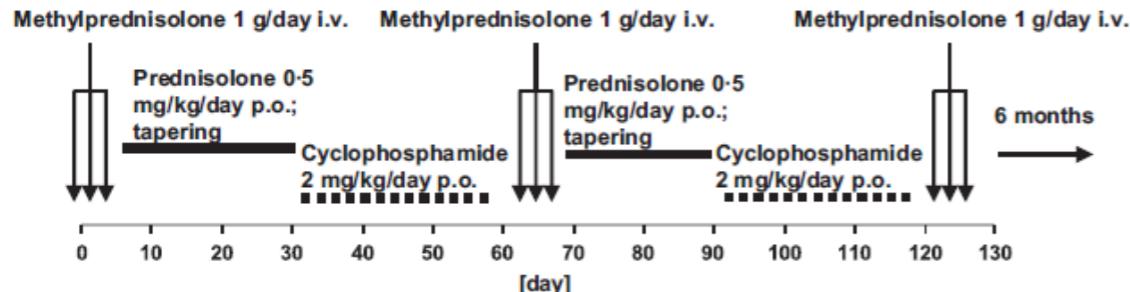


(d) Rituximab 375 mg/m² i.v.

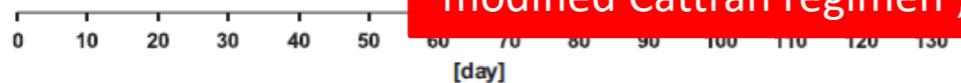


Red asterisks indicate partial remission in anti-PLA2R-antibody negative patients.

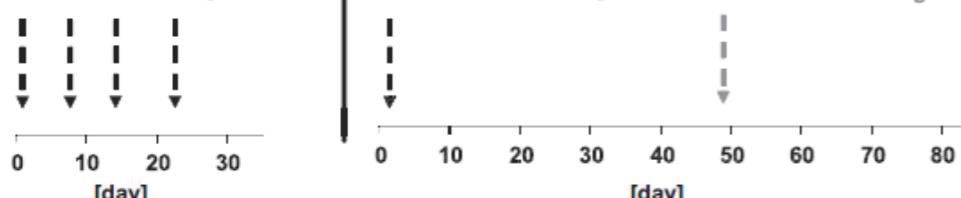
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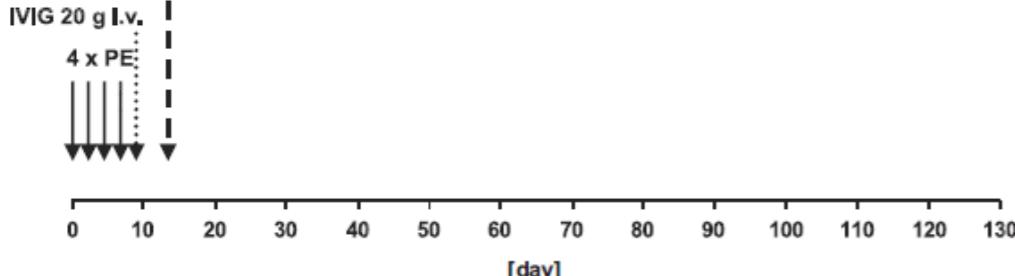
(b) Cyclosporine 3–5mg/kg/day p.o.
Prednisone 5 mg/day p.o.



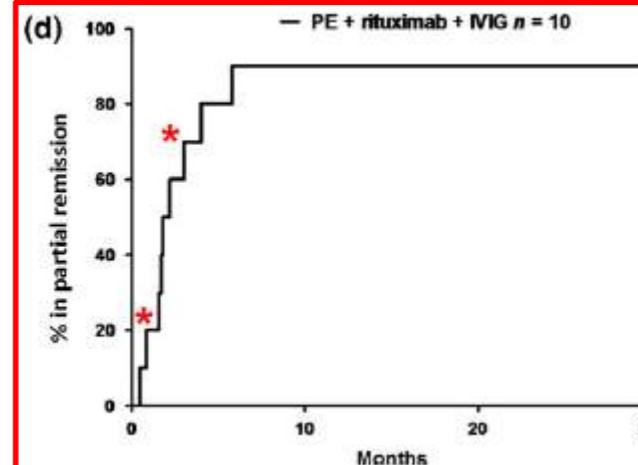
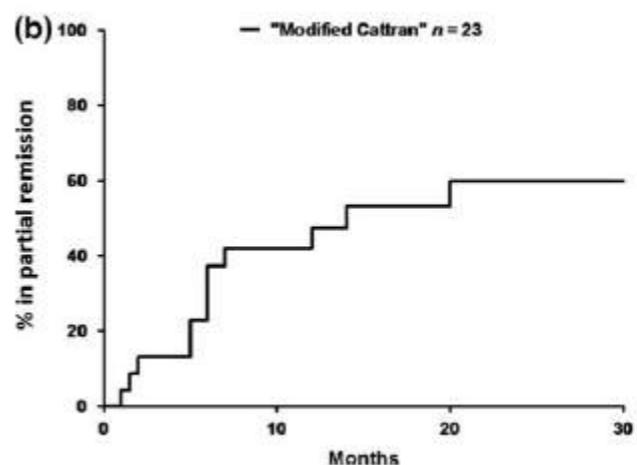
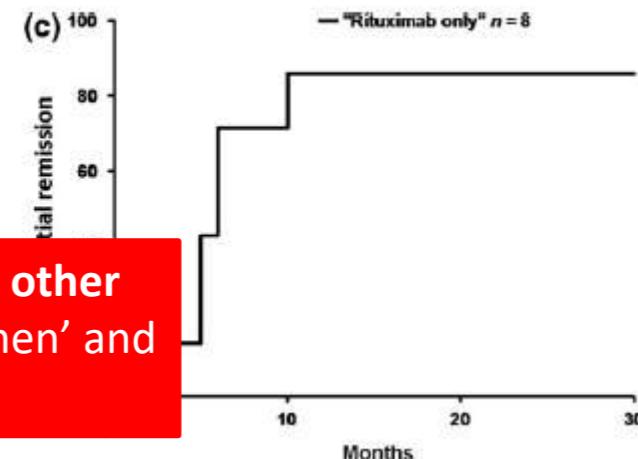
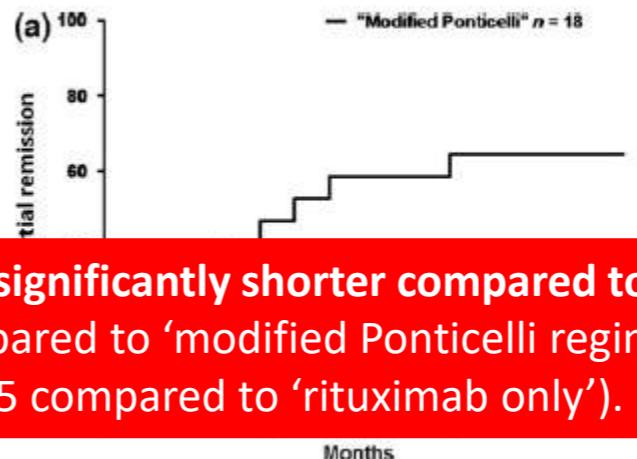
(c) 4 x rituximab 375 mg/m² i.v.



(d) Rituximab 375 mg/m² i.v.

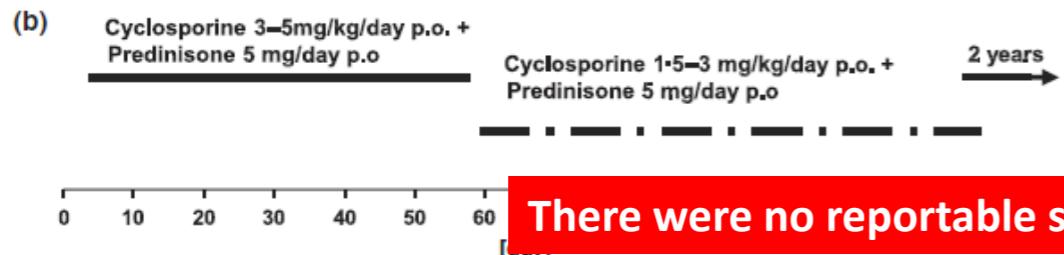
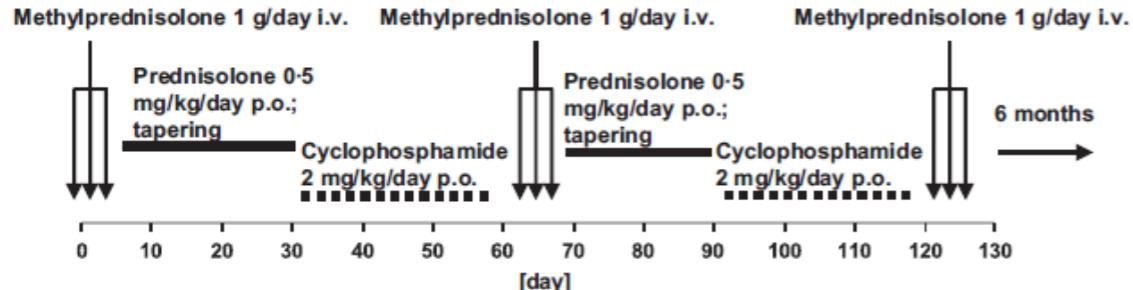


This time to partial remission was significantly shorter compared to other treatment regimens (P < 0.01 compared to 'modified Ponticelli regimen' and 'modified Cattran regimen'; P < 0.05 compared to 'rituximab only').

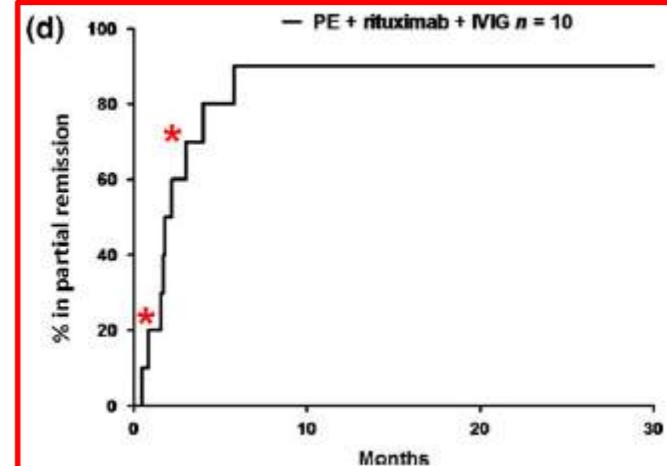
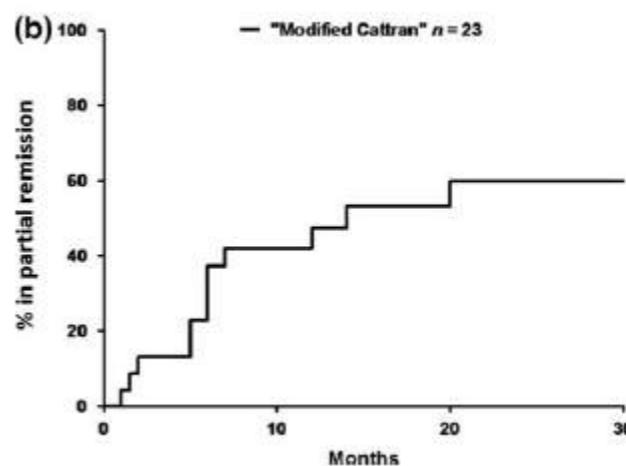
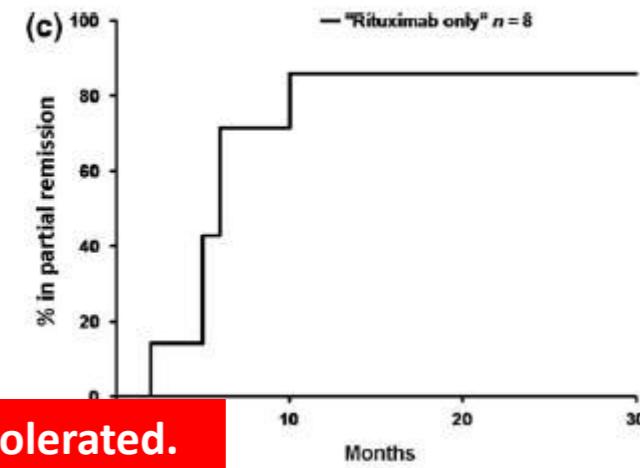
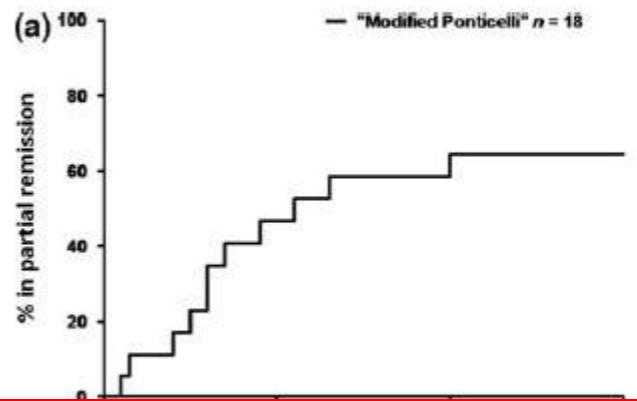
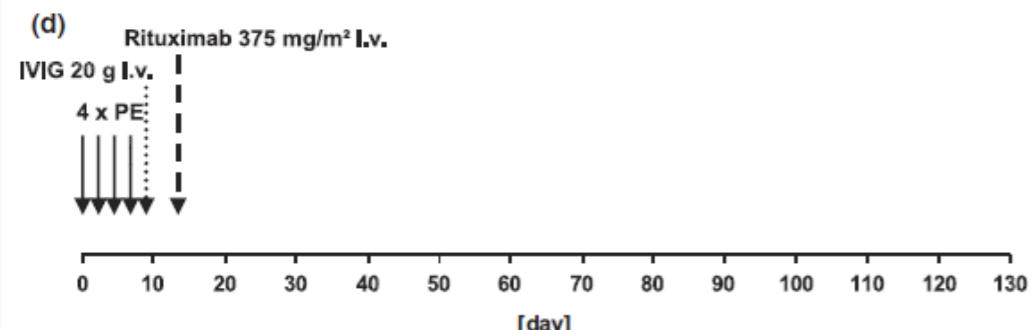
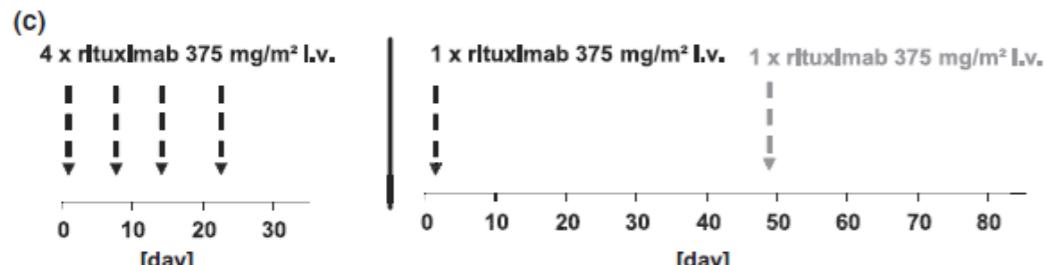


Red asterisks indicate partial remission in anti-PLA2R-antibody negative patients.

(a) **Different immunosuppressive regimes in iMGN**



There were no reportable side effects and the therapy was well tolerated.



Red asterisks indicate partial remission in anti-PLA2R-antibody negative patients.

Suggested therapy algorithm for iMGN

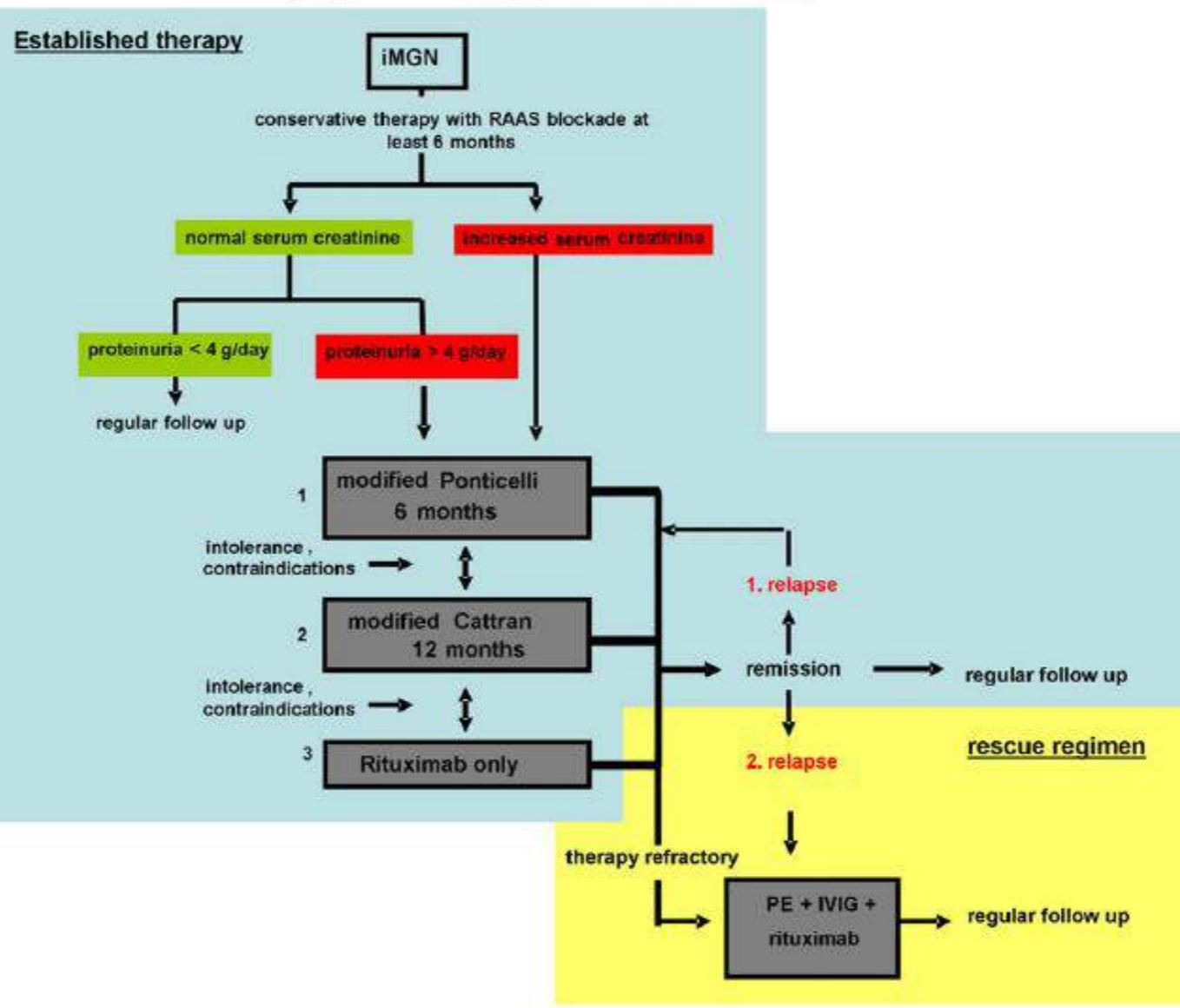
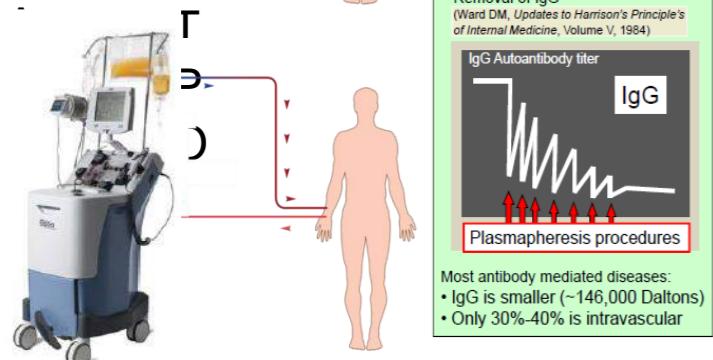
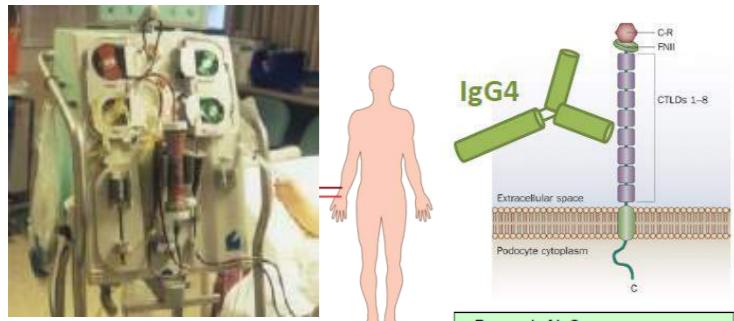
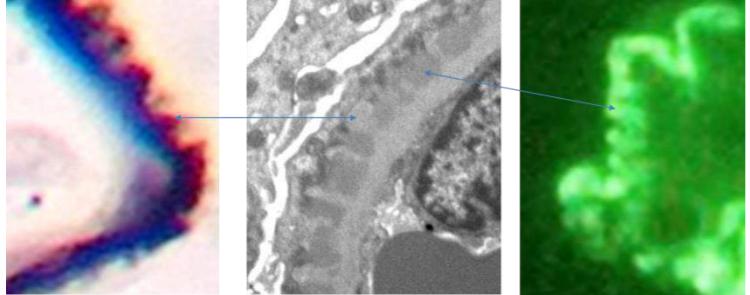
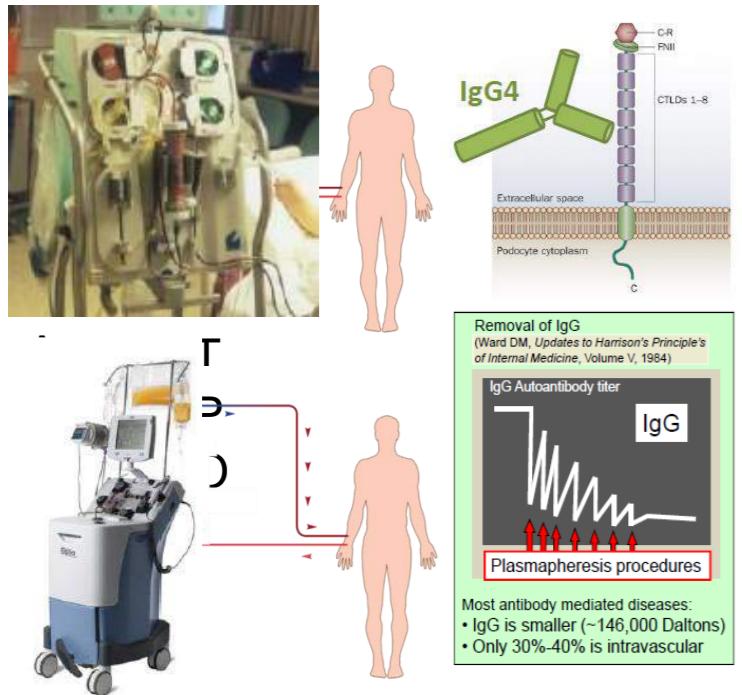
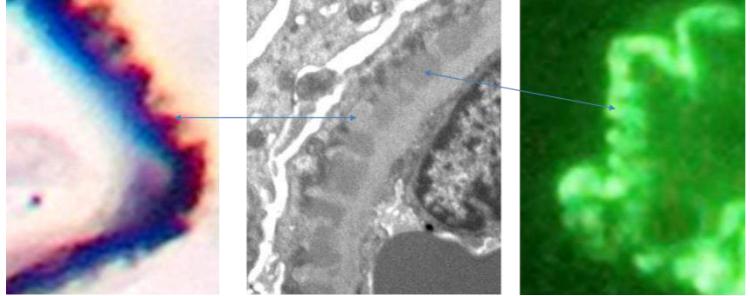


Figure 4 Suggested algorithm for iMGN including a new rescue regimen for therapy refractory patients. iMGN: idiopathic membranous glomerulonephritis; RAAS: Renin–angiotensin–aldosterone system.

Πλασμαφαίρεση σε ΜΝ



- Θεραπεία διάσωσης
- σε εμμένουσα βαριά λευκωματουρία
- ανθεκτική σε άλλες θεραπείες
- πάντα σε συνδυασμό με αντιCD20 αγωγή



Ευχαριστώ

*για την
προσοχή σας*