# GLOMERULONEPHRITIS:

## What's new that changes clinical practice ?

John Feehally

# GLOMERULONEPHRITIS:

## What's new that changes clinical practice ?

**IgA Nephropathy**

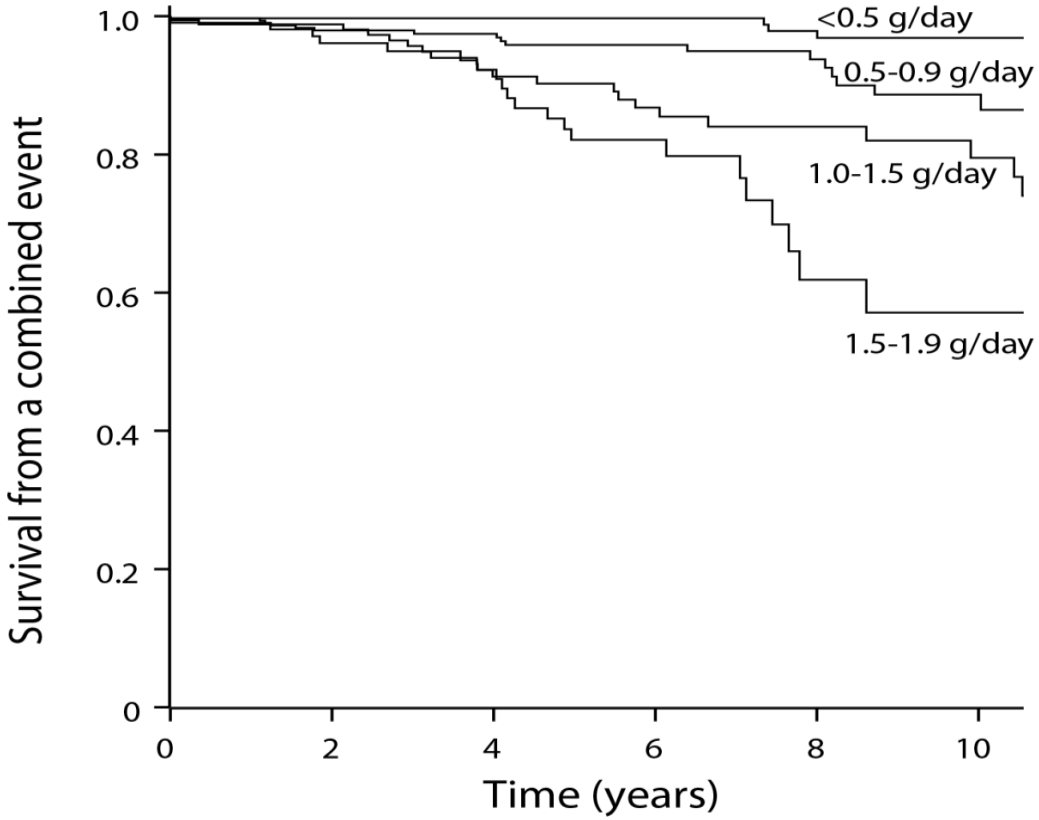
**Membranous Nephropathy**

# Management of IgA Nephropathy

## Predicting clinical outcome

# VALIGA Study
## Predictive value of follow-up time average proteinuria

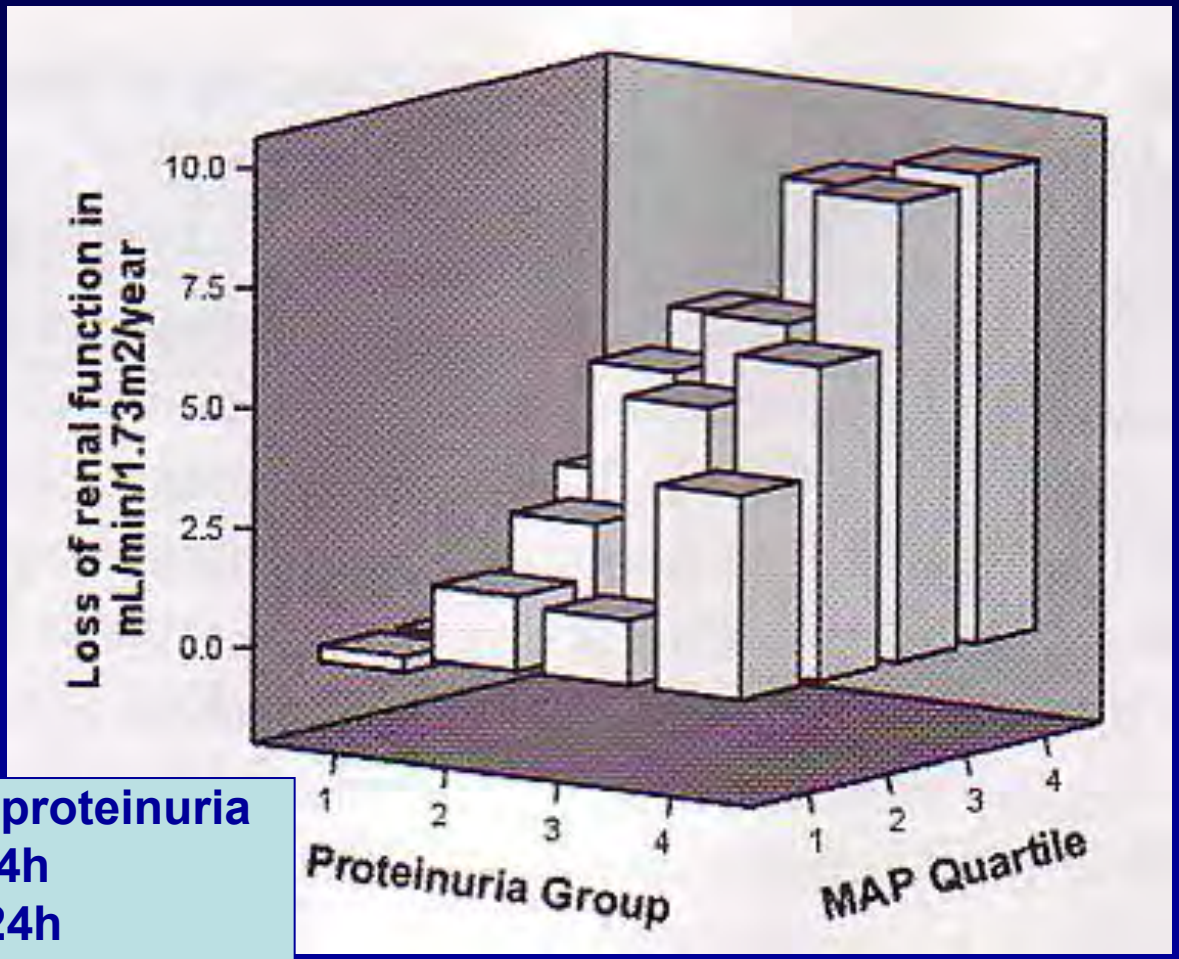
**50% decrease in eGFR and/or ESRD**




| | | | |
|---|---|---|---|
| <0.5 g/day | 338 | 198 | 97 |
| 0.5-0.9 g/day | 315 | 185 | 77 |
| 1.0-1.5 g/day | 167 | 97 | 46 |
| 1.5-1.9 g/day | 107 | 68 | 14 |

Coppo R. Kidney Int. 2014; 86: 828

# PREDICTING OUTCOME IN IgA NEPHROPATHY

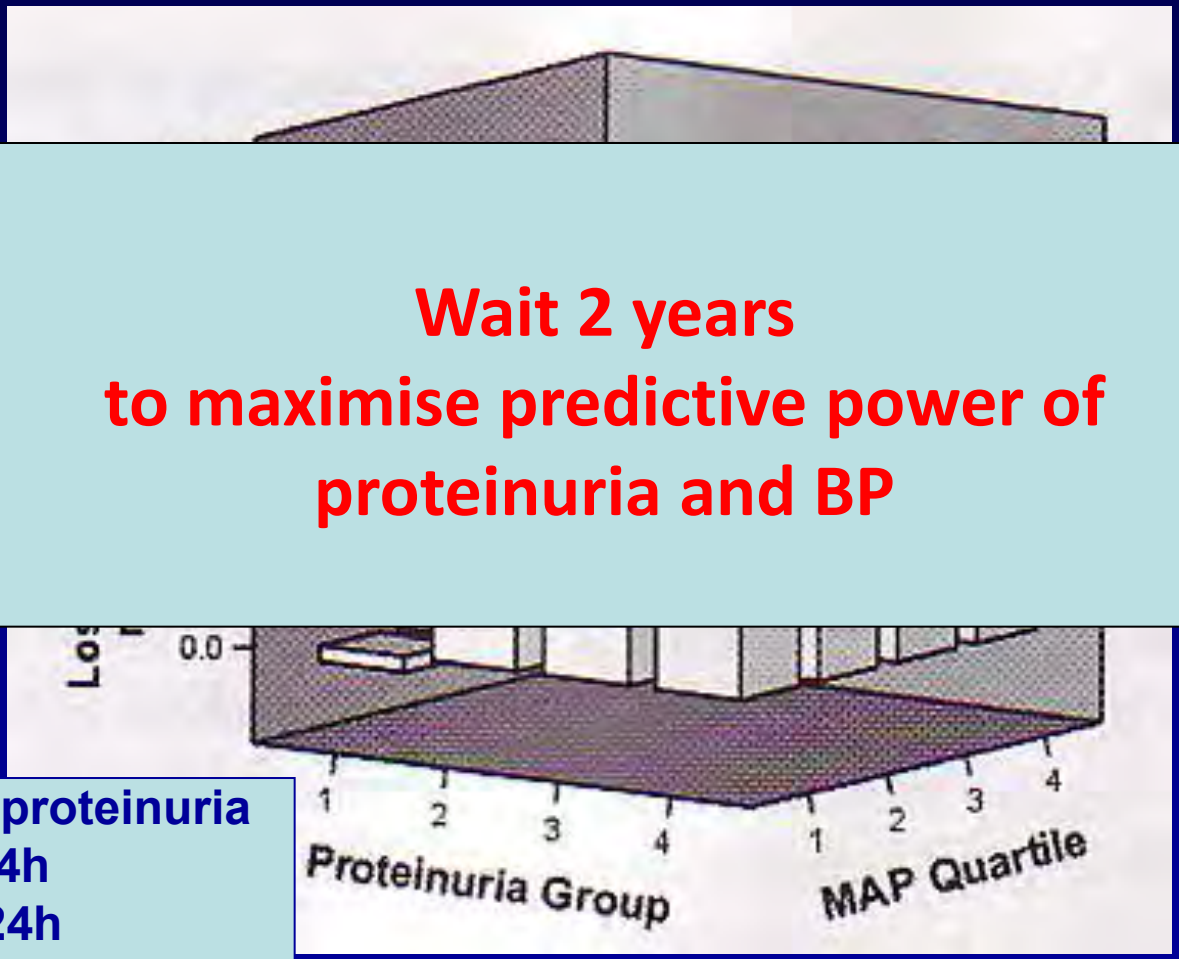



**Time-average proteinuria**

1 - < 1g/24h
2 – 1-2 g/24h
3 – 2-3g/24h
4 - >3g/24h

Reich H et al. JASN 2007; 18: 3177

# PREDICTING OUTCOME IN IgA NEPHROPATHY




**Wait 2 years**
**to maximise predictive power of proteinuria and BP**

**Time-average proteinuria**
**1 - < 1g/24h**
**2 – 1-2 g/24h**
**3 – 2-3g/24h**
**4 - >3g/24h**

Reich H et al. JASN 2007; 18: 3177

# The Oxford classification of IgA nephropathy: rationale, clinicopathological correlations, and classification

A Working Group of the International IgA Nephropathy Network and the Renal Pathology Society:

| | |
|---|---|
| **Mesangial hypercellularity - in > or <50% of glomeruli** | **M0 or M1** |
| **Endocapillary hypercellularity – present/absent** | **E0 or E1** |
| **Segmental sclerosis/adhesions – present/absent** | **S0 or S1** |
| **Tubular atrophy/interstitial fibrosis – 0-25%, 26-50%, >50%** | **T0 or T1 or T2** |

# The Oxford classification of IgA nephropathy: rationale, clinicopathological correlations, and classification

A Working Group of the International IgA Nephropathy Network and the Renal Pathology Society:

**M E S T**

**Each adds predictive value to ….**

**Initial clinical features**

**Follow up clinical features**

# Oxford Classification of IgA nephropathy
# Systematic review and meta-analysis

**16 retrospective cohort studies**
**3,893 patients - 570 kidney failure events**

| *Multivariate model* | HR for kidney failure | |
|---|---|---|
| M1 | 0.6 (95% CI, 0.5-0.8) | P < 0.001 |
| E1 | 1.4; 95% CI, 0.9-2.0) | P = 0.1 |
| S1 | 1.8 (95% CI, 1.4-2.4) | P < 0.001 |
| T1/2 | 3.2 (95% CI, 1.8-5.6) | P < 0.001 |
| | | |

Lv J et al. AJKD 2013; 62: 891

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# Systematic review and meta-analysis

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| **C** | **2.3 95% CI, 1.6-3.4)** | **P < 0.001** |

Lv J et al. AJKD 2013; 62: 891

# DEVELOPING AND IMPROVING THE OXFORD CLASSIFICATION OF IgA NEPHROPATHY

Never intended to be 'the finished product'

Integrate newer retrospective cohorts

Develop prospective studies

Improving the classification

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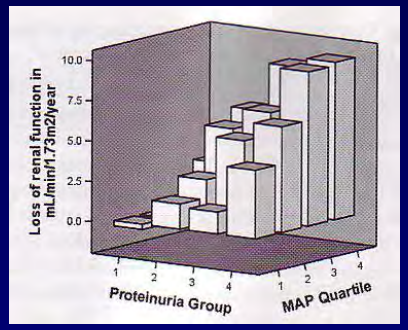
**Develop prospective studies**

**Improving the classification**

**Revised Oxford Classification of IgA**

Publication expected 2017

# PREDICTING OUTCOME IN IgA NEPHROPATHY



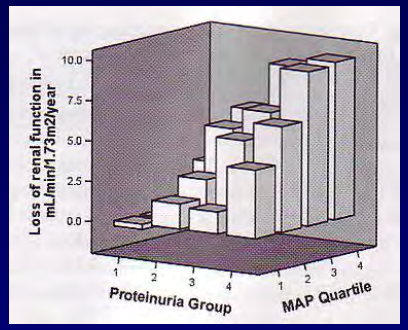

**OXFORD CLASSIFICATION**

**Predictive value of MEST**

**Degalactosylated IgA1 ?**

**Other biomarkers ?**

# PREDICTING OUTCOME IN IgA NEPHROPATHY

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**Predictive value of MEST**

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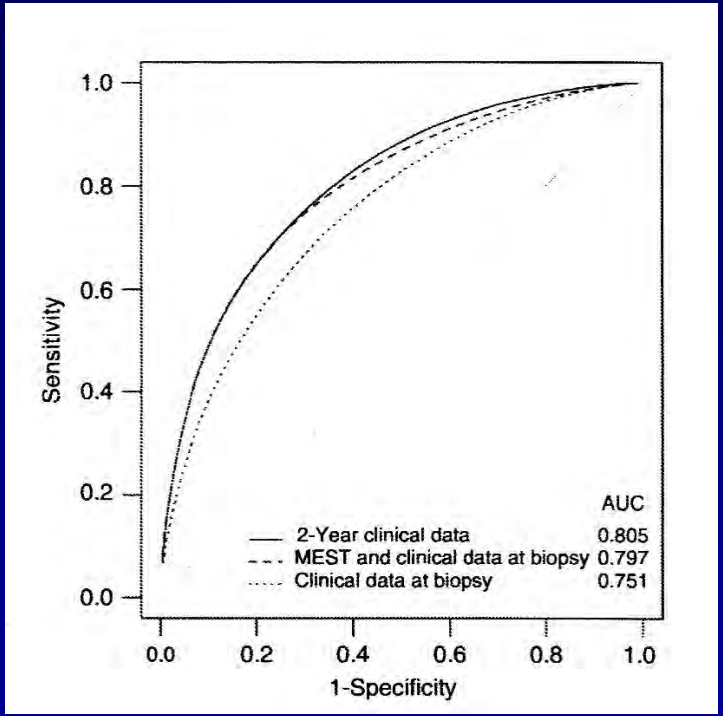
# PREDICTING PROGRESSION IN IgA NEPHROPATHY

Clinical data at time of biopsy:
Proteinuria
Blood pressure

**plus**

Pathological data
MEST score




**Outcome prediction as good as clinical data after 2 years follow up**

Barbour S et al. KI 2016; 89: 167

# Management of IgA Nephropathy

## Slowly progressive IgA nephropathy ……..

## The role of corticosteroids

**For which patients?**

**In what dose?**

**By what route?**

# KDIGO CLINICAL PRACTICE GUIDELINES FOR THE TREATMENT OF IgA NEPHROPATHY

## Corticosteroids for IgAN

We suggest that patients with persistent proteinuria ≥1 g/d,

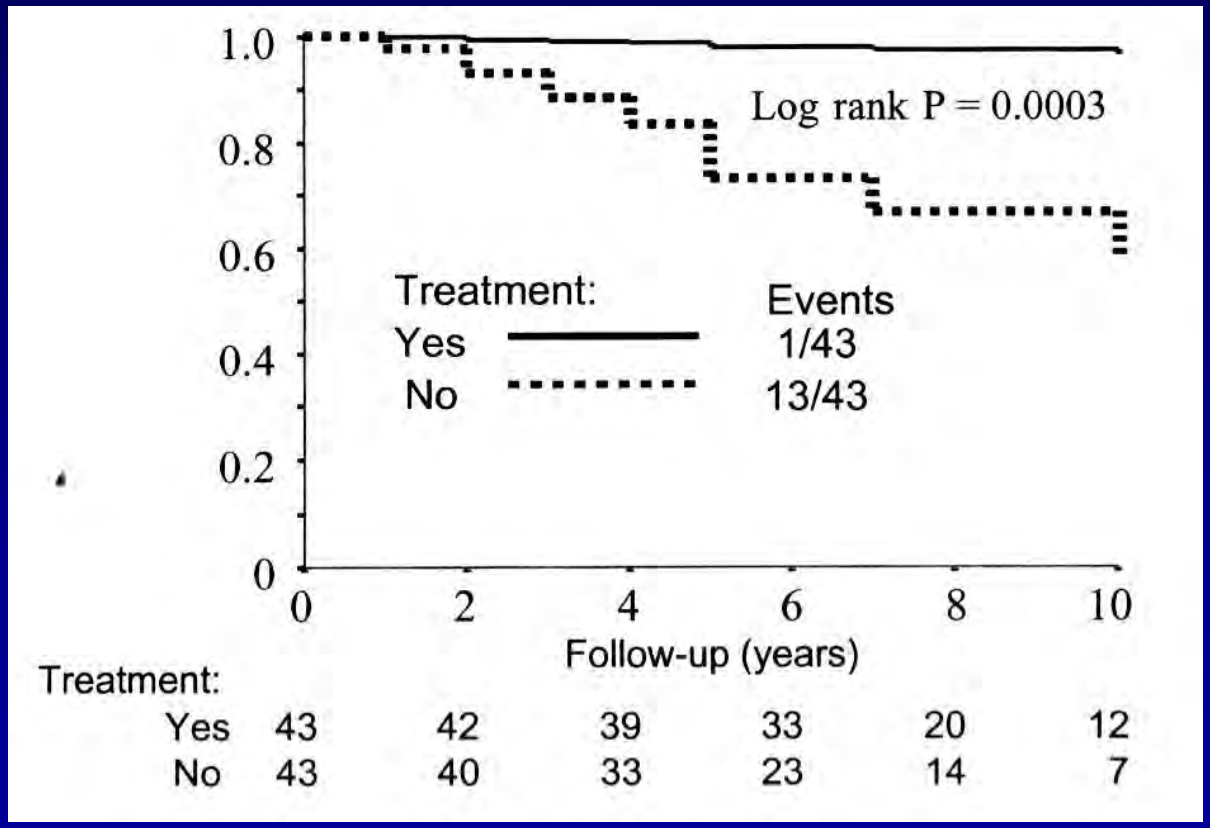
despite 3-6 months of optimized supportive care (including ACEi or ARBs and blood pressure control), and GFR >50 ml/min,

receive a 6-month course of corticosteroid therapy (2C)

# CORTICOSTEROID TREATMENT FOR IgA NEPHROPATHY

**Randomised controlled trial – serum creatinine < 130 µmol/L**

**Survival without end point - doubling of serum creatinine**




Pozzi C et al Lancet 1999; 353; 883 - JASN 2004; 15: 157

# *Management of IgA Nephropathy*

**CHALLENGE 5**

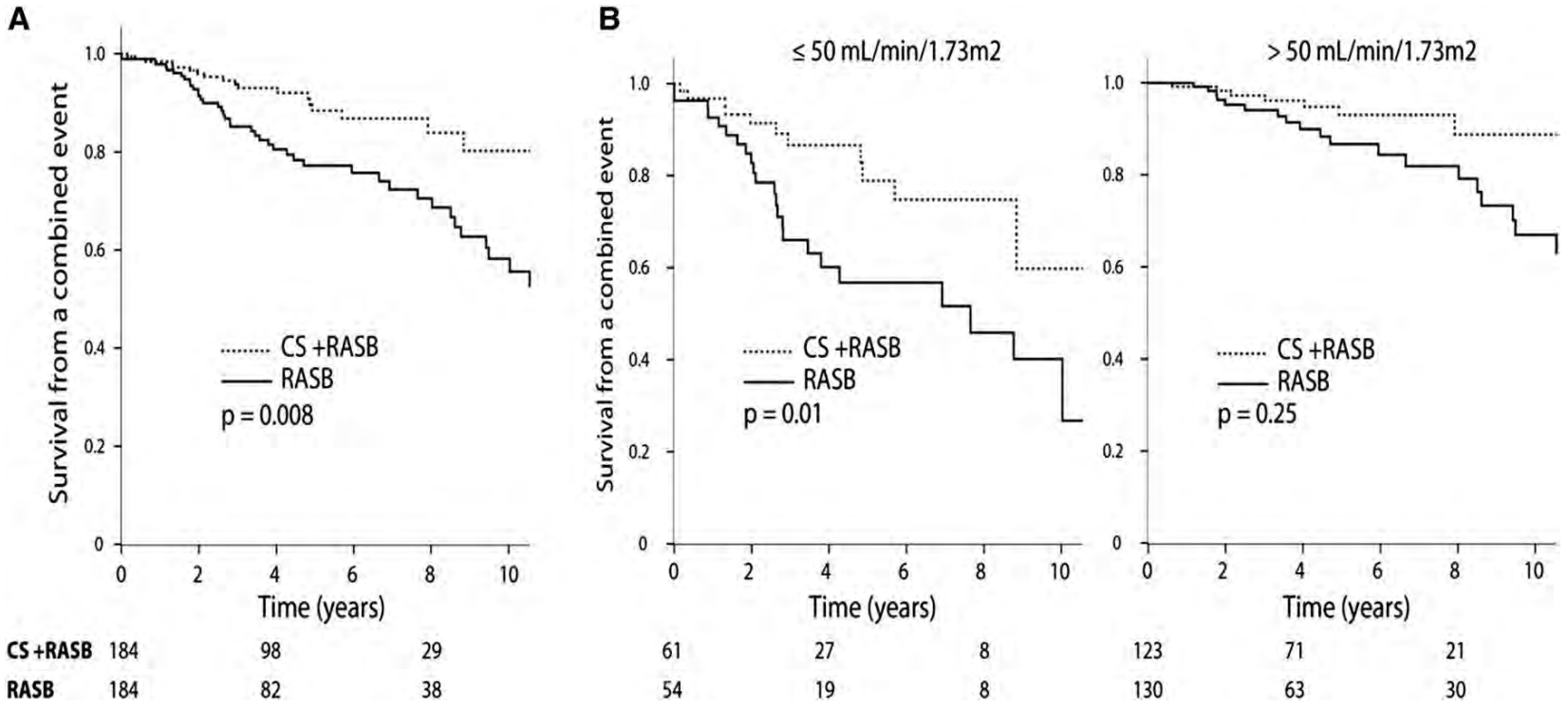
**Slowly progressive IgA nephropathy ……..**

**The role of corticosteroids ?**

**We still need studies with**

- **tight BP control**
- **full RAS blockade**
- **sufficient 'run-in'**

# Response to Corticosteroids and RAS blockers in IgA Nephropathy using Propensity Matching




Tesar V et al. JASN 2015;26:2248-2258

JASN

# CHANGES IN PROTEINURIA WITH STEROIDS AND AZATHIOPRINE

**CONCLUSIONS**

**In patients with IgAN, corticosteroids can reduce proteinuria and increase the possibility of maintaining time average proteinuria >1g/24hr**

**…..regardless of CKD stage and histologic damage**

**Sarcina C et al. CJASN June 2016 e-pub**

# CHANGES IN PROTEINURIA WITH STEROIDS AND AZATHIOPRINE

**325 patients IgAN & proteinuria >1g/24hr in 3 RCTs 1989-2005**
**'Individual patient data meta-analysis'**

| | n | sCr | Protocol | Reference |
|---|---|---|---|---|
| 1. | 86 | <1.5mg/dl | **corticosteroids *vs.* no treatment** | Pozzi C *et al.* Lancet 1999; 353: 883 |
| 2. | 207 | <2mg/dl | **corticosteroids *vs.* corticosteroids *plus* azathioprine** | Pozzi C *et al.* JASN 2010; 21: 1783 |
| 3. | 46 | >2mg/dl | **corticosteroids *vs.* corticosteroids plus azathioprine** | Pozzi C et al. J Nephrol 2013; 26: 86 |

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**In patients with IgAN, corticosteroids can reduce proteinuria and increase the possibility of maintaining time average proteinuria >1g/24hr**

**…..regardless of CKD stage and histologic damage**

| | No treatment | Corticosteroids | Corticosteroids plus azathioprine |
|---|---|---|---|
| n | 43 | 171 | 111 |
| RAS blockers at baseline | 12% | 54% | 60% |
| RAS blockers at follow up | 42% | 82% | 91% |

Sarcina C et al. CJASN June 2016 e-pub

# Study Design


Run-in Phase (6 Months)

Study-Phase (3 Years)

**IgAN, 18-70 years old, GFR > 30 ml/min, proteinuria > 0.75 g/d plus hypertension or GFR < 90 ml/min**

**Optimal supportive therapy**
(ACEi, ARB, target BP < 125/75 mm Hg, Statin, etc.)
Baseline after 6 months: BP, proteinuria, GFR

**Responder**
Proteinuria <0.75 g/d
optimal supp. therapy;
Check proteinuria

**Drop-Out**
Proteinuria > 3.5 g/d
GFR-loss > 30%

If proteinuria >0.75 g/d

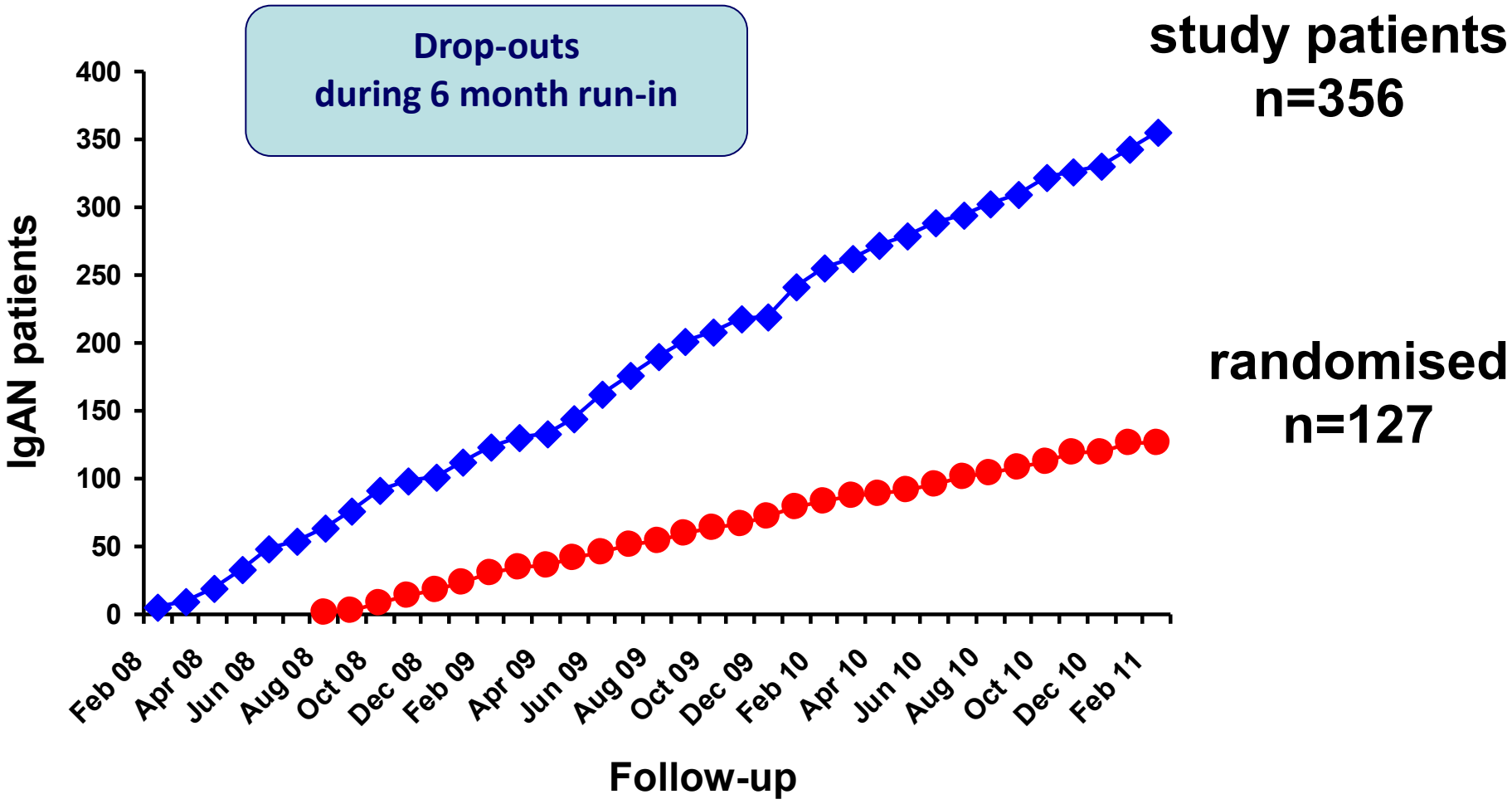
**Non-Responder**
Proteinuria >0.75 g/d

Randomisation

**Optimal supportive (n=74)**

**Optimal supportive + Immunosuppression (n=74)**

# Recruitment - STOP IgAN



# STOP IgAN: Results

**Two primary end points at 36 months**

1. **full clinical remission (uPCR <0.2g/g and stable kidney function, or fall in eGFR <5ml.min )**
2. **eGFR decrease >15ml/min/1.73m$^2$ from baseline at the end of the trial.**

**Full clinical remission - uPCR <0.2g/g**

**4/80 (5%) supportive care - 14/82 (17%) immunosuppression (p=0.01)**

**BUT**

**Mean proteinuria at 36 months not different (i.e. heterogeneous response)**

**eGFR at 36 months not different**

**Rauen T et al. NEJM 2015; 373:2225**

# STOP IgAN: Results

1. full clinical re… … eGFR <5ml.min )
2 …

Remission of proteinuria
without protection of eGFR

not a worthwhile goal
given adverse effects of immunosuppressions

Mea… …onse)

eGFR … different

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# STOP IgAN: Results


1. full clinical re… … eGFR <5ml.min )
2 …

**Remission of proteinuria**
**without protection of eGFR**

**not a worthwhile goal**
**given adverse effects of immunosuppressions**

Mea… …onse)

**With optimized supportive care .....**
**effects of immunosuppression are markedly blunted**
**in high risk IgAN**

Rauen T et al. NEJM 2015; 373:2225

# TESTING
# Therapeutic Evaluation of STeroids in IgA Nephropathy Global study

**Double-blind, multicentre, randomised, placebo-controlled trial**

**3 months of supportive therapy - including BP control & RAS blockade**

**If proteinuria > 1g/day & eGFR 20-120 ml/min/1.73m$^2$**

**0.8 mg/kg/day oral methylprednisolone (max 48 mg/day) weaning over 6-8 mth *or* placebo**

**Composite primary outcome: ESRD, death due to kidney disease, 40% drop in eGFR**

Lv J *et al.* ERA Abstract 2016

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**Study stopped early - excess of serious adverse events**

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# Therapeutic Evaluation of STeroids in IgA Nephropathy Global study

**262 randomised: mean age 38.6 ± 11.1 years, 36.6% female. Median f-up 1.5yrs**

**SERIOUS ADVERSE EVENTS:**

**20 (14.7%) steroids *vs.* 4 (3.2%) placebo**

**RR 4.63, 95% CI 1.63-13.18; p=0.0011)**

**….. mostly due to excess serious infections 12 *vs.* 0, 2 of which were fatal**

**Lv J *et al.* ERA Abstract 2016**

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**Time averaged proteinuria:**
**Reduced in the steroid treated arm (1.31 vs 2.19 g/day, p<0.001)**

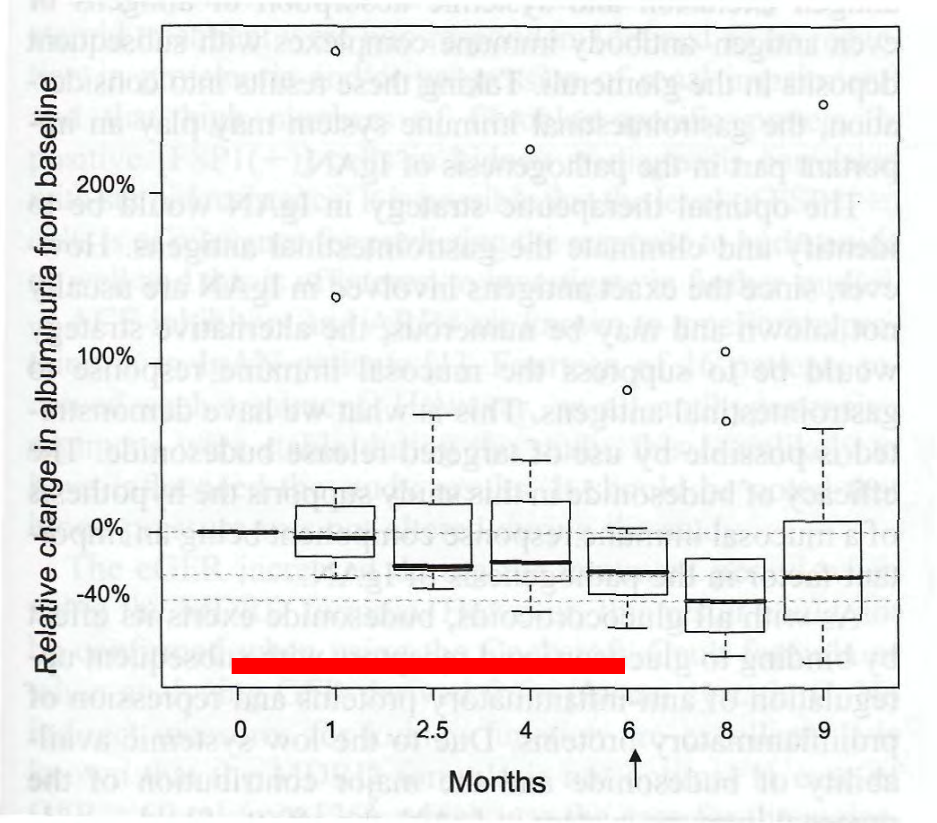
**Primary composite renal outcome:**
**7 (5.1%) with steroids and 18 (14.3%) with placebo**
**(HR 0.35; 95% CI 0.15 to 0.85; P=0.019)**

**Lv J *et al.* ERA Abstract 2016**

# PILOT STUDY OF ENTERIC BUDESONIDE IN PROTEINURIC IgA NEPHROPATHY

**Enteric corticosteroid preparation designed for ileo-caecal release of active compound with limited systemic effect**

**n = 16 - Ualb > 500mg/d - sCreatinine < 200µmol/l**




Smerud HK et al. NDT 2011; 26: 3237

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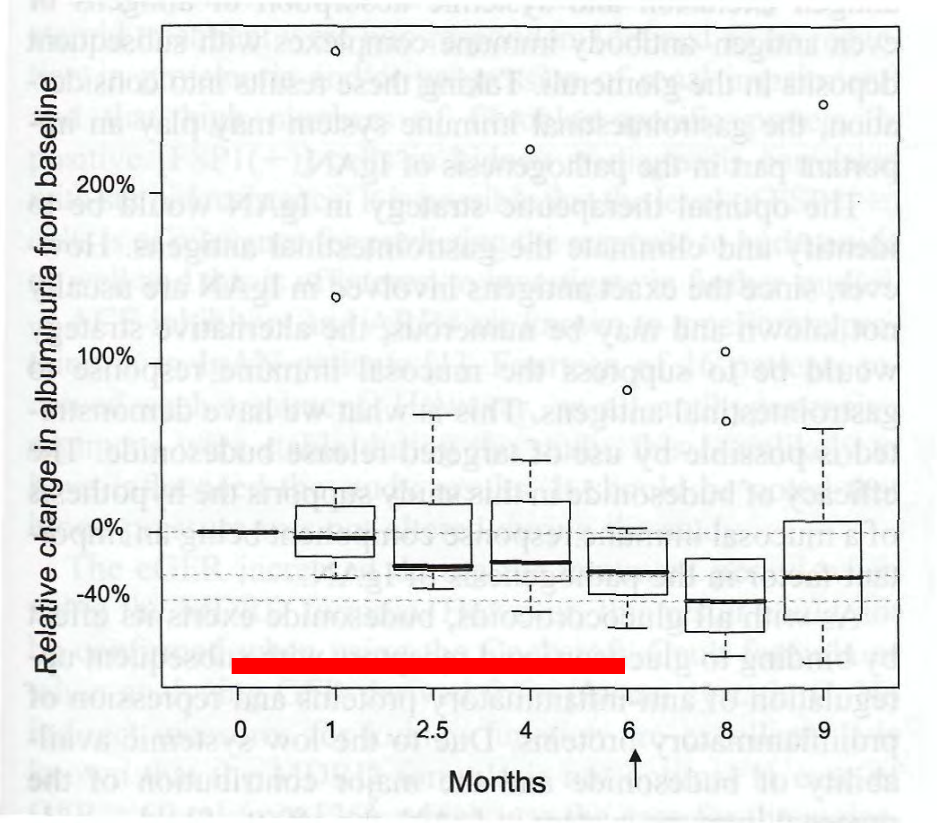



**RCT**
**presented at ASN 2015**
**12 month follow up:**

- **Proteinuria reduced**
- **eGFR preserved**

Smerud HK et al. NDT 2011; 26: 3237

# GLOMERULONEPHRITIS:

## What's new that changes clinical practice ?

IgA Nephropathy

**Membranous Nephropathy**

# MEMBRANOUS NEPHROPATHY – PATTERN OR DISEASE ?

**Primary**
**Idiopathic**

**Secondary**

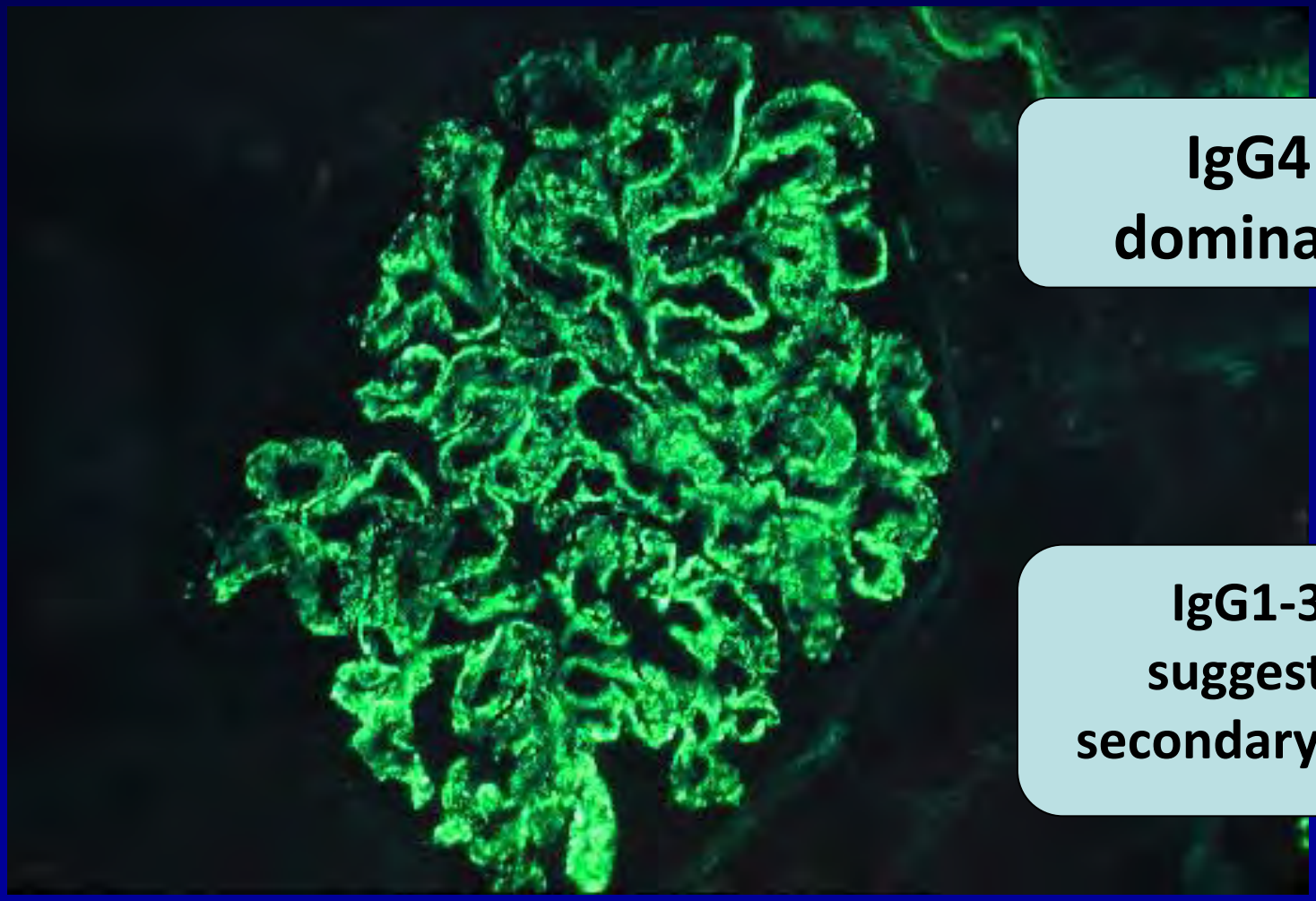
Immune disease

Infection

Drugs

Malignancy

# MEMBRANOUS NEPHROPATHY



**IgG4 dominant**

**IgG1-3 suggests secondary MN**

# MEMBRANOUS NEPHROPATHY – PATTERN OR DISEASE ?

**Primary Idiopathic**

Diagnosis by exclusion

**Secondary**

Infection

Drugs

Malignancy

# MEMBRANOUS NEPHROPATHY – PATTERN OR DISEASE ?

**Primary Idiopathic**

Diagnosis by exclusion

**Antigen unknown**

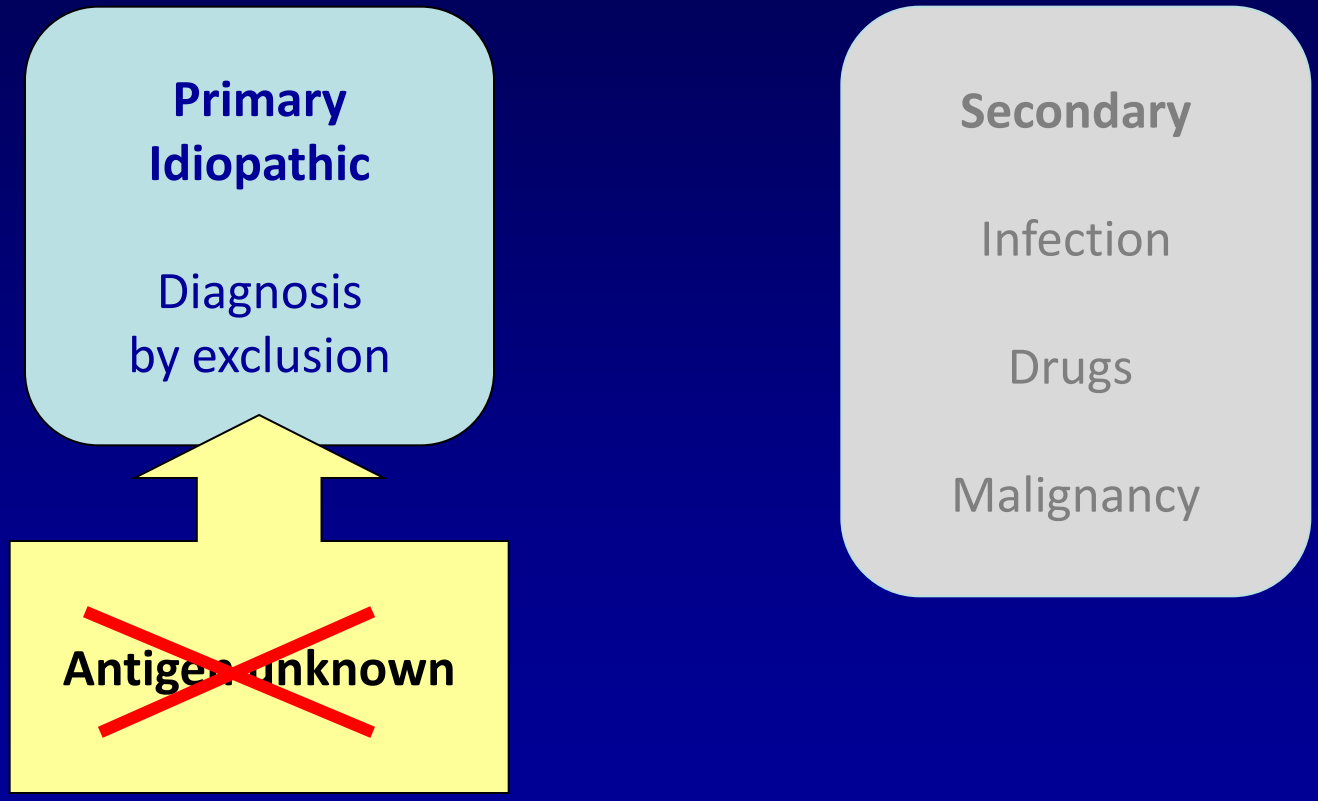
**Secondary**

Infection

Drugs

Malignancy

# MEMBRANOUS NEPHROPATHY – PATTERN OR DISEASE ?



# MEMBRANOUS NEPHROPATHY – PATTERN OR DISEASE ?

**Primary Idiopathic**

Diagnosis by exclusion

**70% - PLA2 Receptor**
***Circulating anti-PLA2R***

**30% - ?**

**Secondary**

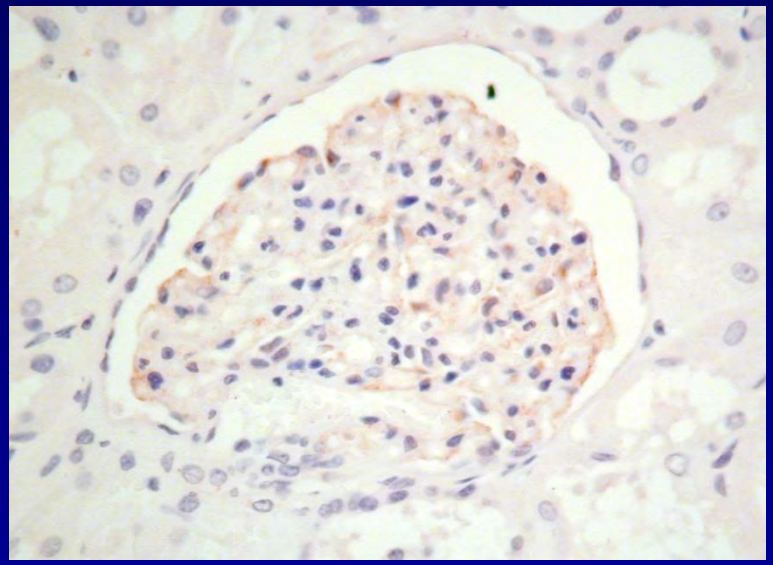
Infection

Drugs

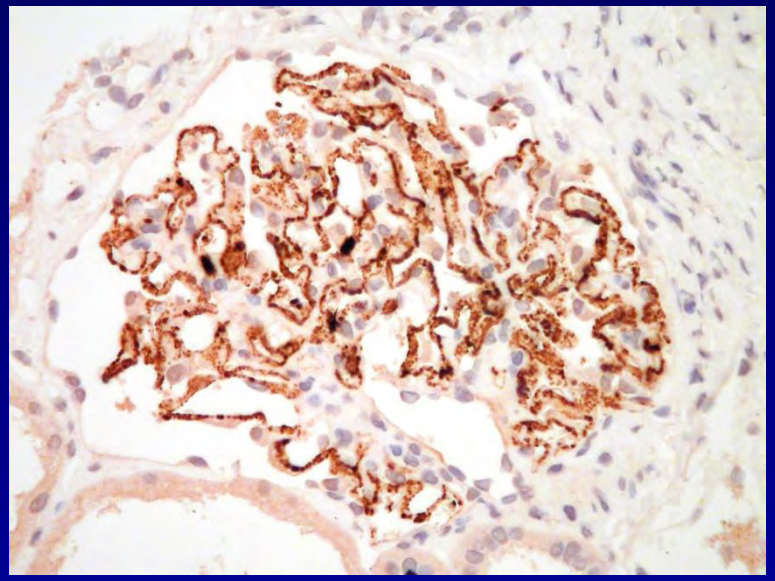
Malignancy

# PLA2R glomerular staining in membranous nephropathy

**NORMAL**

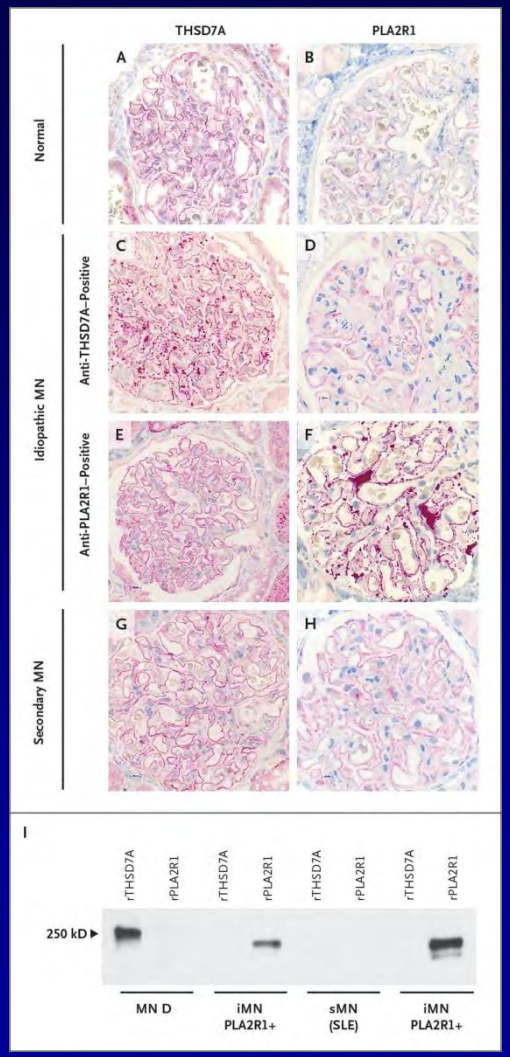


**MEMBRANOUS NEPHROPATHY**



Images courtesy of Prof. Ian Roberts

# THSD7A in Membranous Nephropathy




**Thrombospondin Type-1 Domain-Containing 7A**

**Circulating autoantibodies to THSD7A:**

**15/154 'Idiopathic' MN**

***….. all anti-PLA2R Ab negative***

*Tomas NM et al. N Engl J Med 2014;371:227*

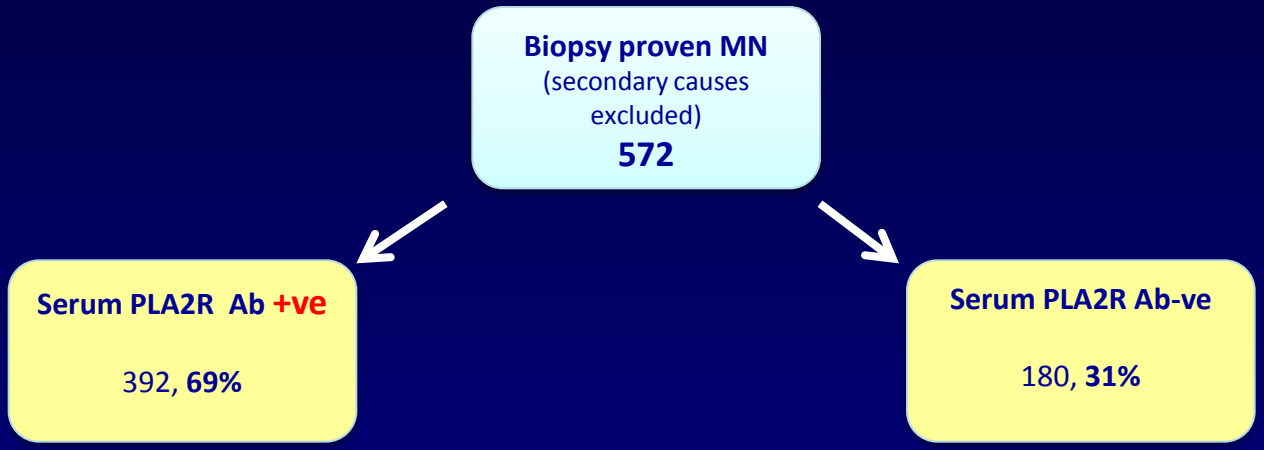
The NEW ENGLAND JOURNAL of MEDICINE

# PLA2R and THSD7A in Membranous Nephropathy

**Biopsy proven MN**
(secondary causes excluded)
**572**

Qin HZ et al. JASN 2016, e-pub

# PLA2R and THSD7A in Membranous Nephropathy

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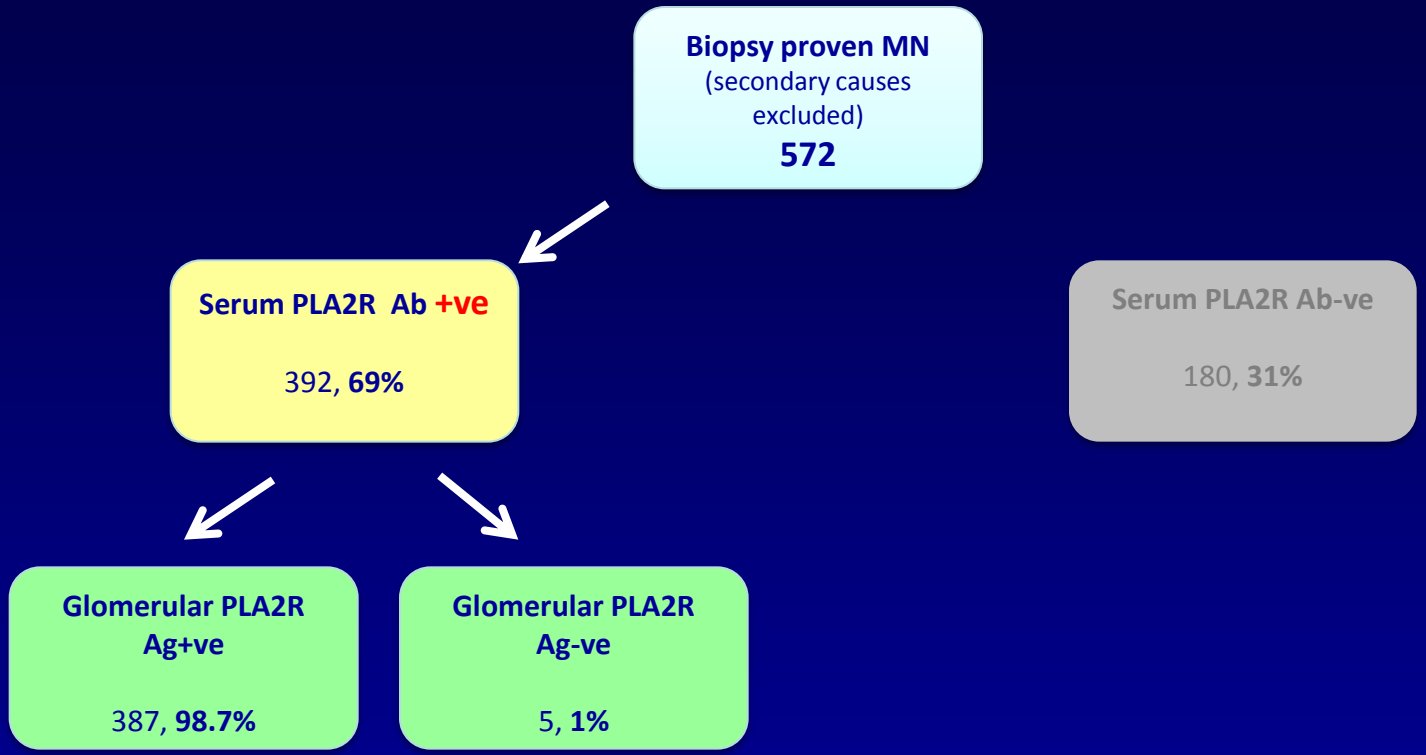


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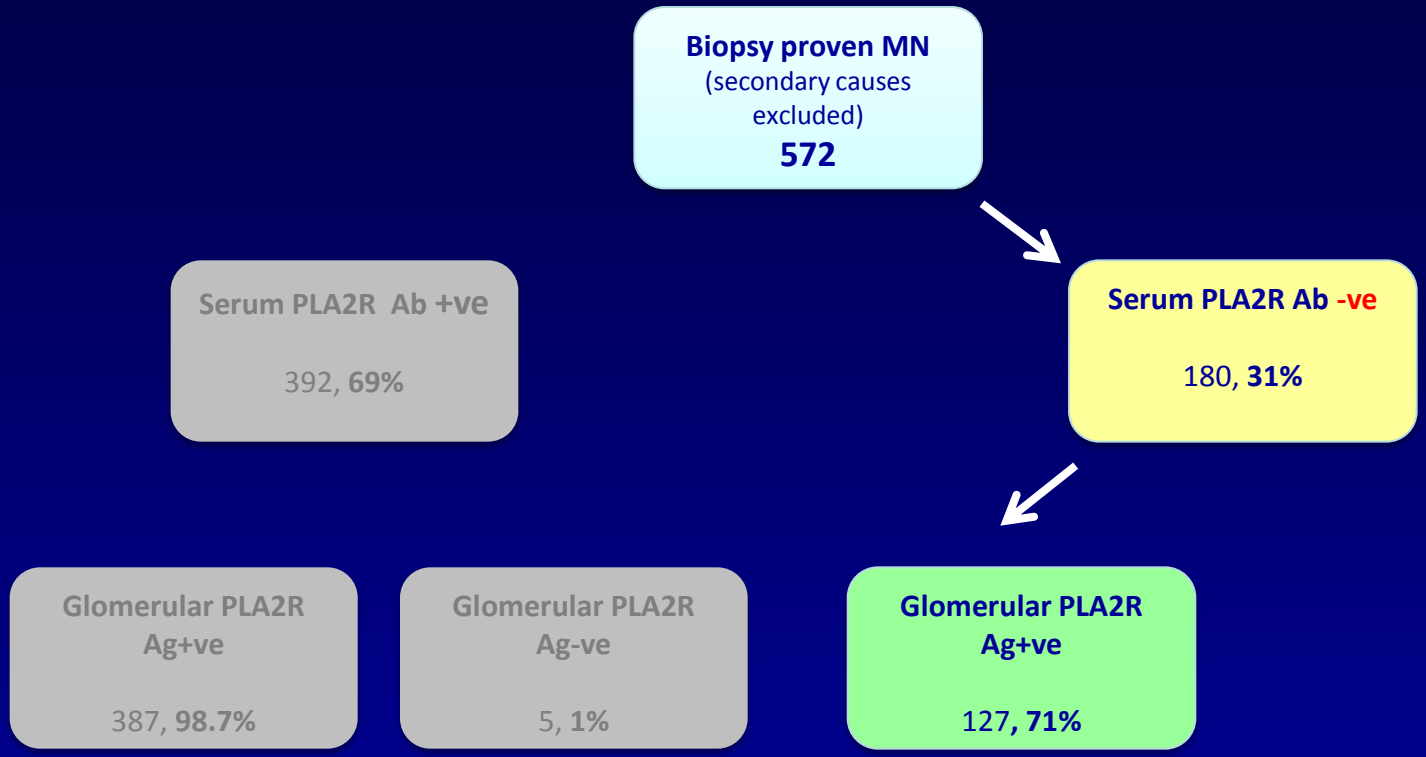


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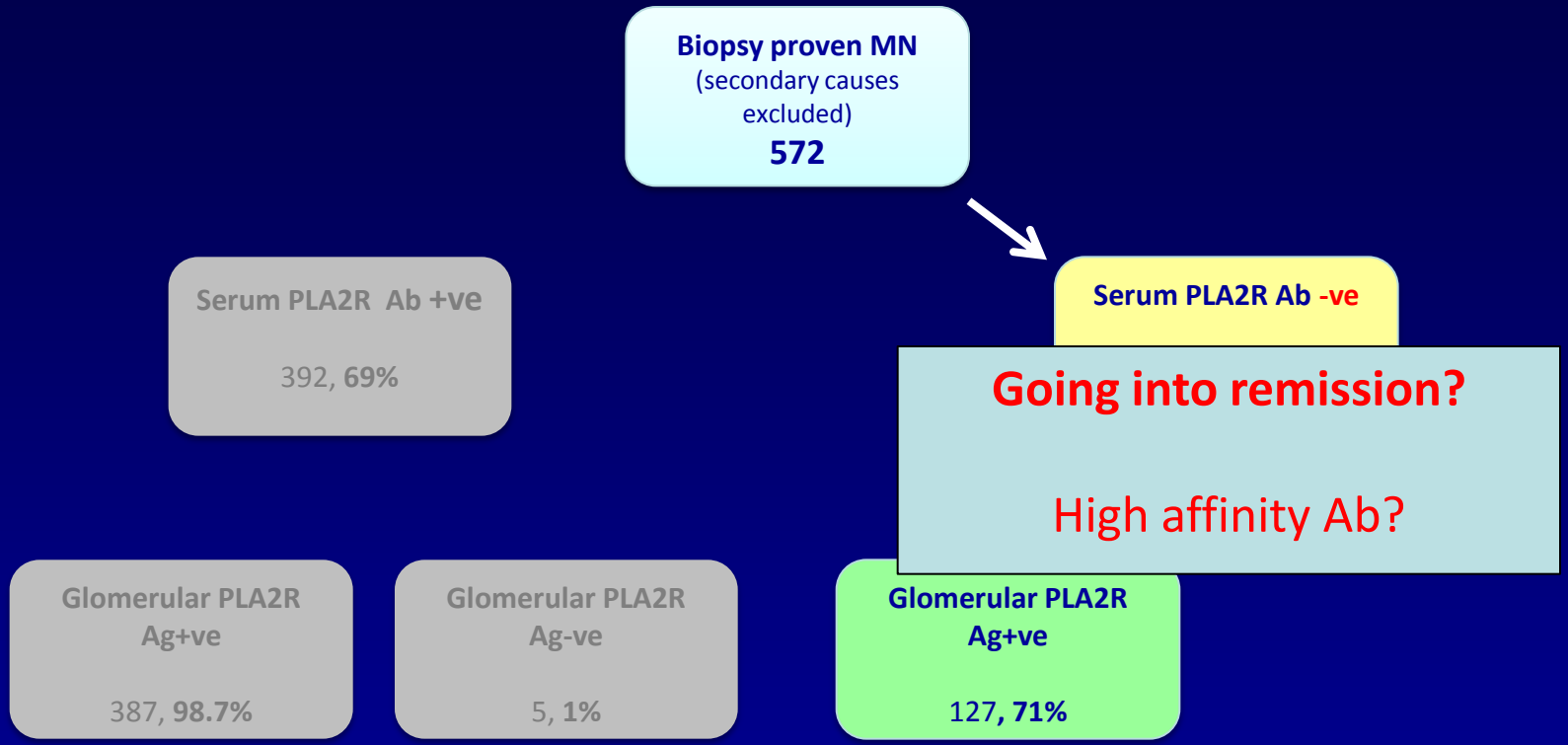
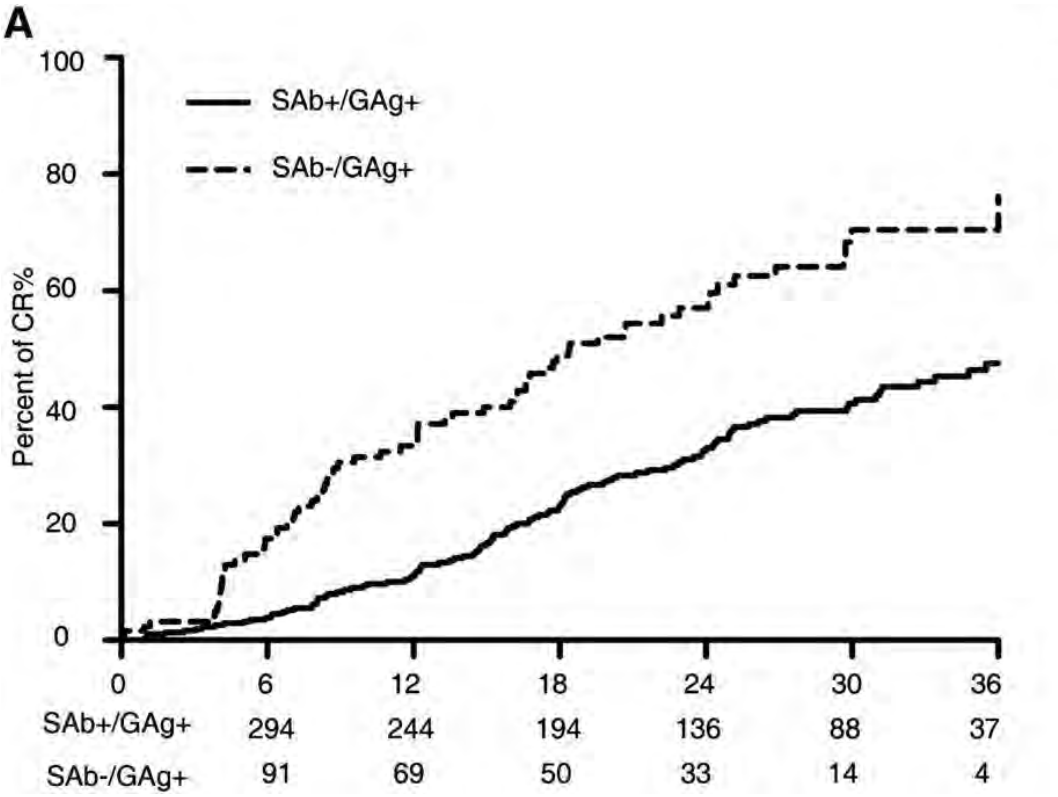



Qin HZ et al. JASN 2016, e-pub

# Disease remission according to PLA2R serum Ab and glomerular Ag in Membranous Nephropathy

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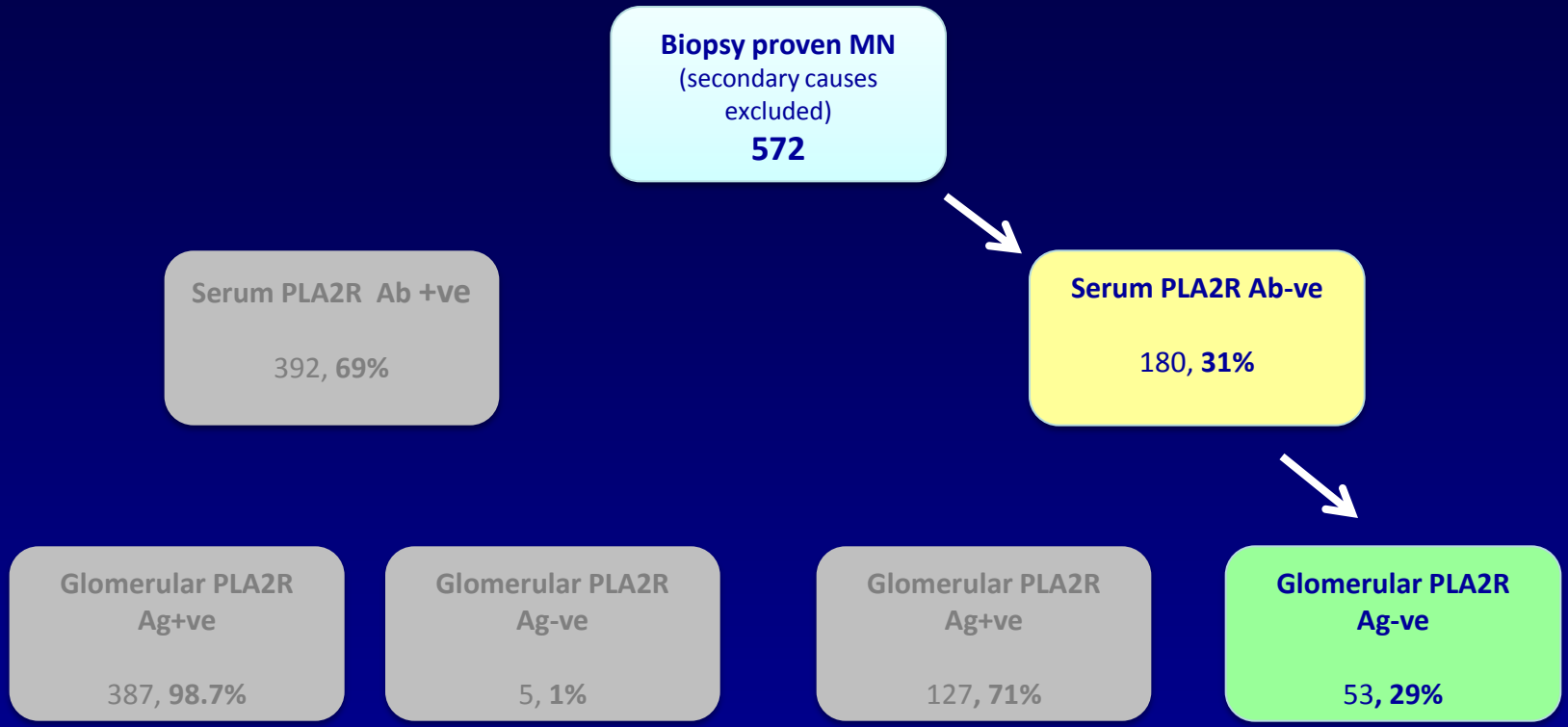


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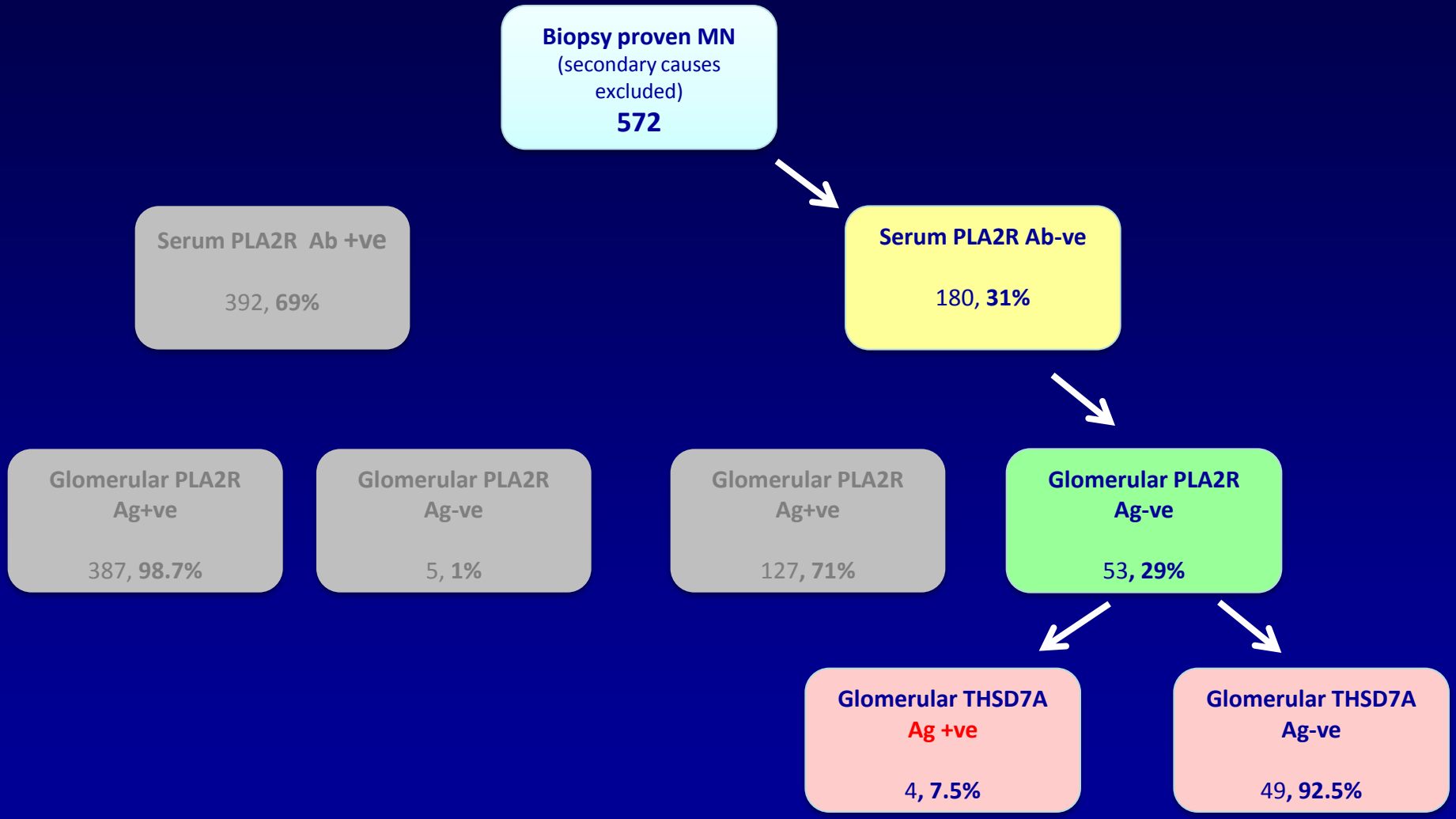


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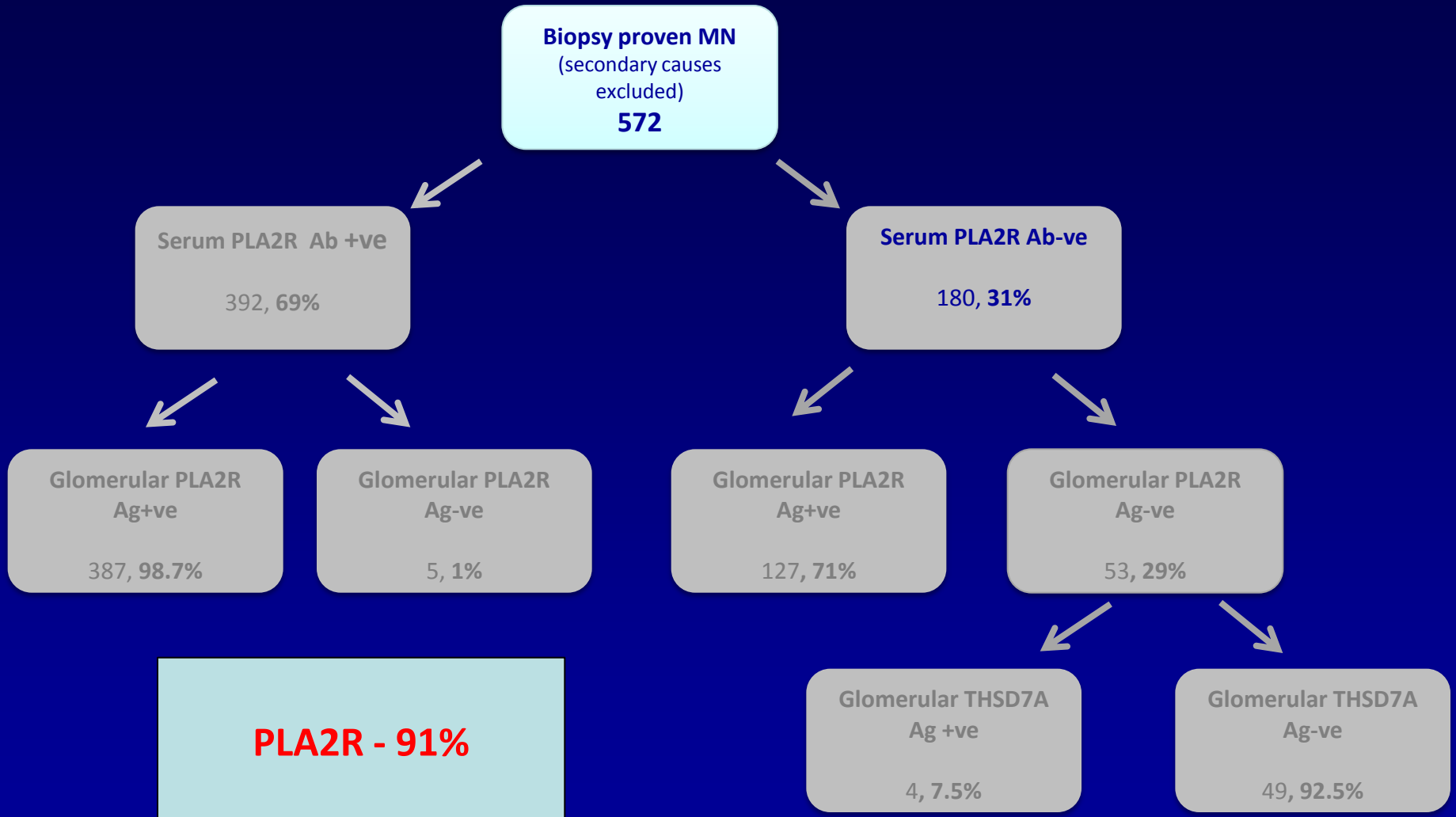


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# Anti-PLA2R as a marker in ‘idiopathic’ MN

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**Is anti-PLA2R specific for ‘idiopathic’ MN?**

# Is Anti-PLA2R specific for 'idiopathic' MN ?

**8 published studies – 616 IMN**

**3 different methods: Indirect IF (259) ELISA (207) Western blot (150)**

| Healthy controls | Other renal disease | 'Idiopathic' MN<br>Clinically active<br>No immunosuppression | Secondary MN<br>Tumours, lupus,<br>viral infection |
|---|---|---|---|
| 0/115 +ve | 0/276 +ve | **72%** | **5 – 30%** |

# Circulating levels and renal deposits of anti-PLA2R1 antibodies in membranous nephropathy

**64cases: 47 idiopathic, 17 secondary**

| Diagnosis of IMN | Sensitivity | Specificity |
|---|---|---|
| Circulating anti-PLA2R1 (>15RU/ml - IIF) | 74.5% | 94.2% |

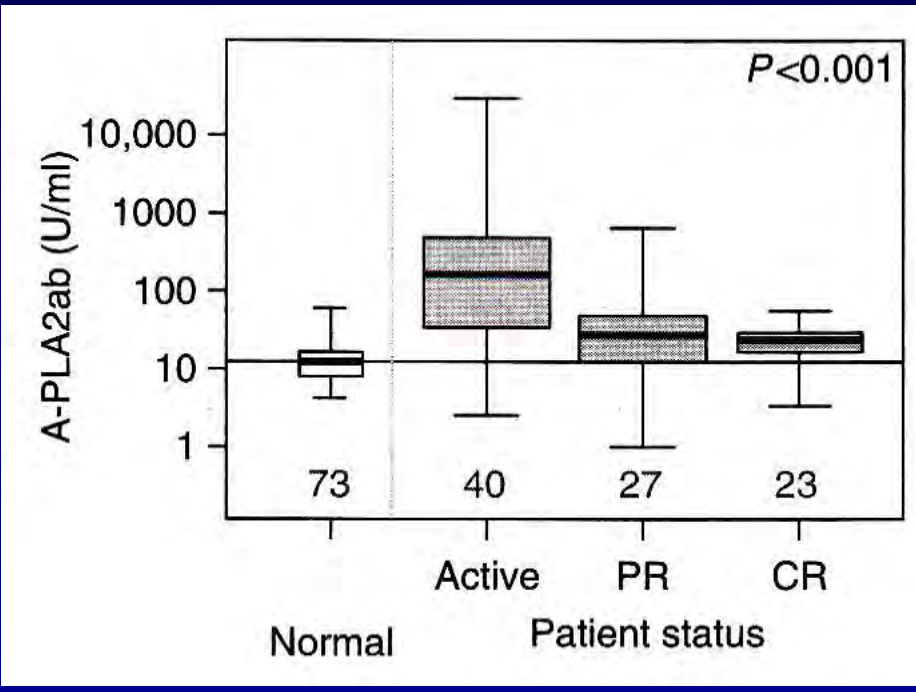
Segarra-Medrano A et al. Nefrologia 2014; 34: 353

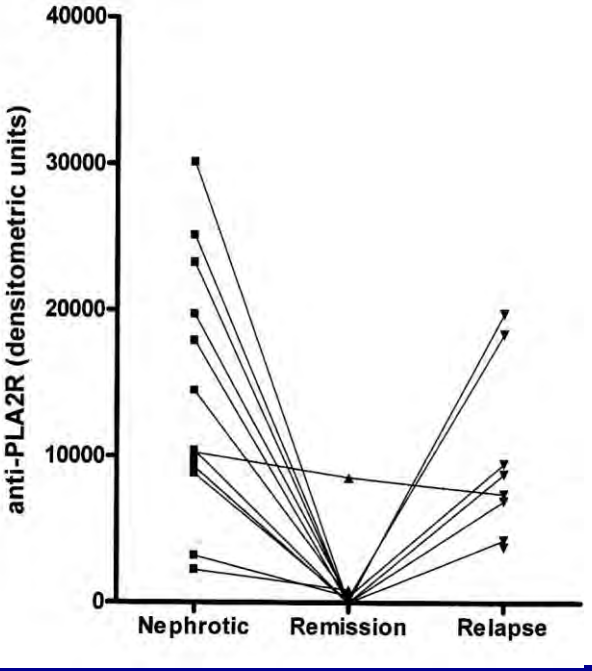
# Anti-PLA2R as a marker in ‘idiopathic’ MN

Is anti-PLA2R specific for ‘idiopathic’ MN?

**Does anti-PLA2R correlate with disease activity ?**

# Anti-PLA2R antibodies & disease activity in Membranous Nephropathy




Hofstra J *et al*. CJASN 2011; 6: 1286

Kanigicherla D *et al*. Kidney Int 2013; 83: 940

# Anti-PLA2R as a marker in 'idiopathic' MN

**Is anti-PLA2R specific for 'idiopathic' MN?**

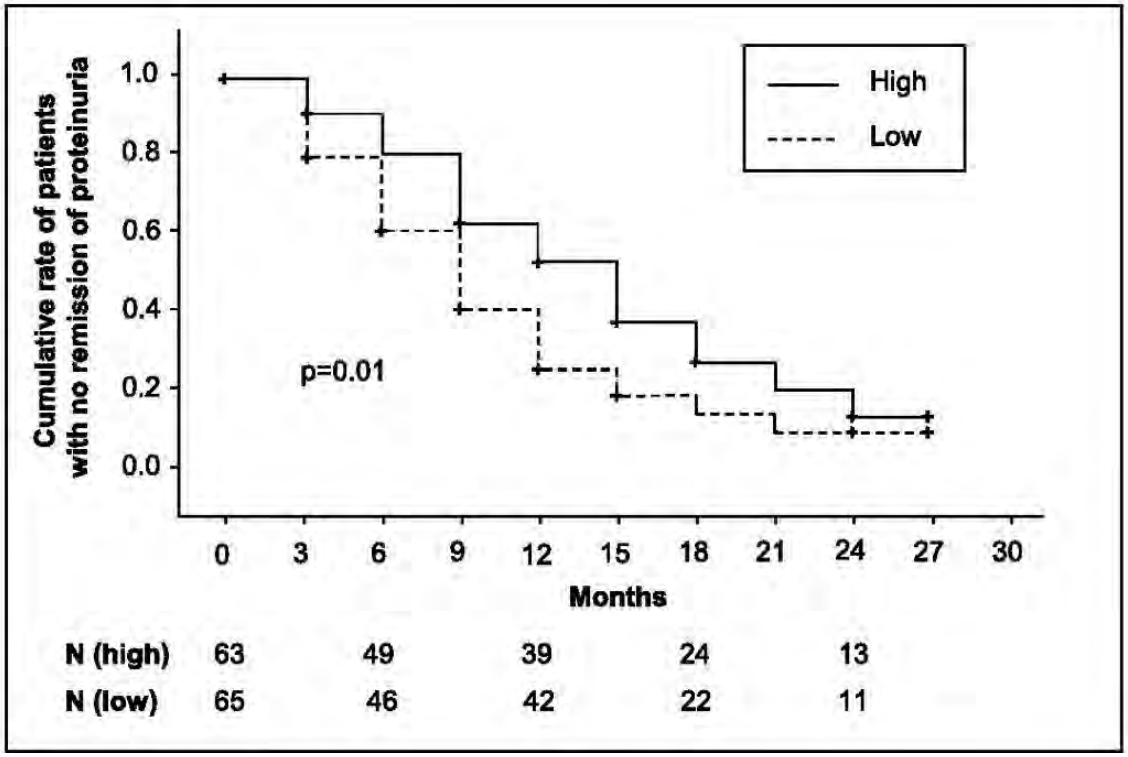
**Does anti-PLA2R correlate with disease activity ?**

**What is the temporal association of anti-PLA2R & proteinuria in**

- spontaneous remission?
- therapeutic remission ?
- relapse ?

# Time to remission of proteinuria high versus low PLA2R antibody levels in membranous nephropathy

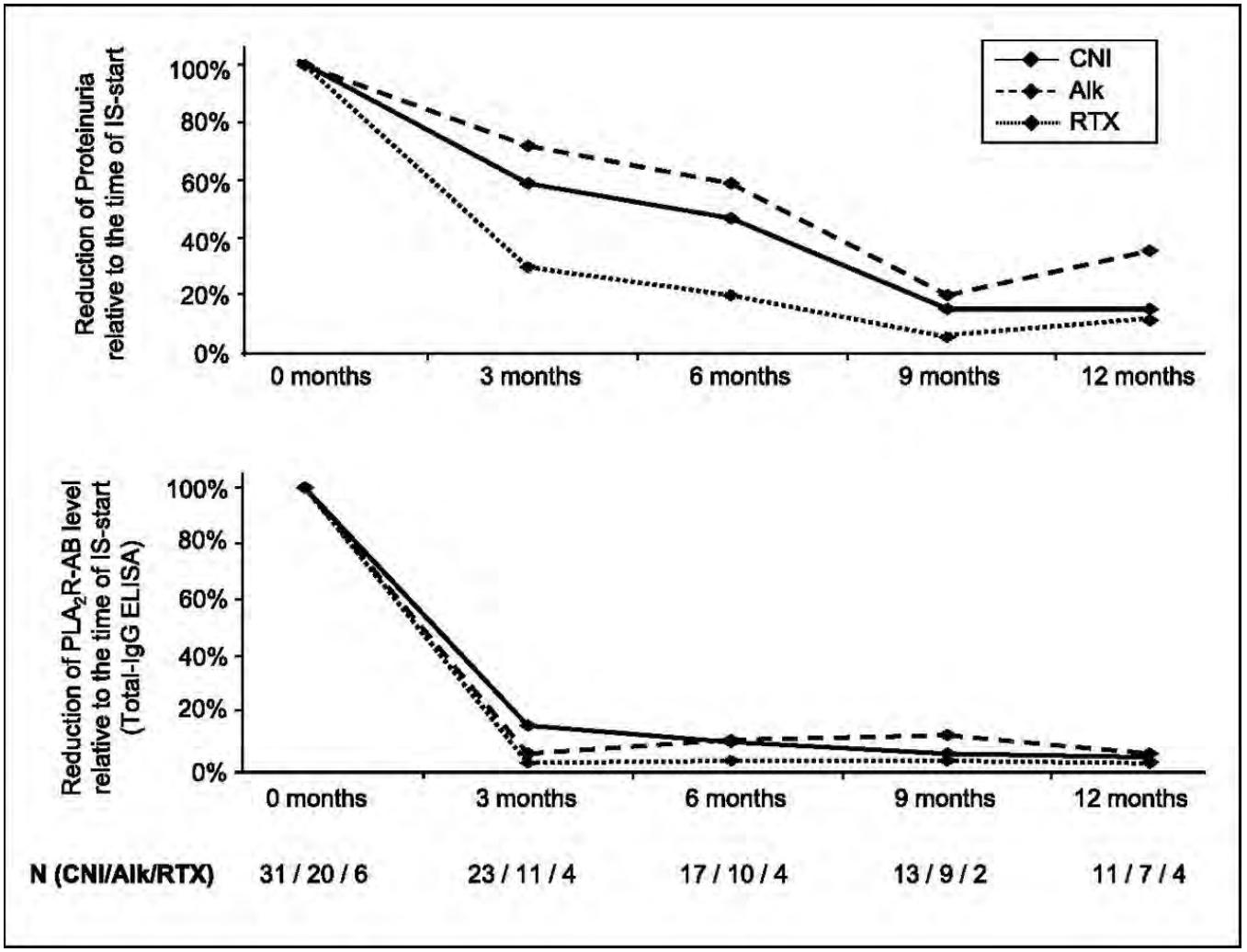
B




Hoxha E et al. JASN 2014;25:1357

JASN

# Changes in PLA2R antibody levels and proteinuria after immunosuppressive therapy in membranous nephropathy




Hoxha E et al. JASN 2014;25:1357

JASN

# Persistence of anti-PLA2R antibodies at the end of immunosuppressive treatment predicts subsequent course in Membranous Nephropathy

n = 48, retrospective observational 1997-2005
Corticosteroids *plus* cyclophosphamide or MMF

34 - anti-PLA2R positive at baseline

5 years

Anti-PLA2R negative at end of treatment - 24

58% **no** relapse

Anti-PLA2R positive at end of treatment - 9

100% relapse

Bech A *et al*. CJASN 2014; 9: 1386

# Anti-PLA2R as a marker in 'idiopathic' MN

Is anti-PLA2R specific for 'idiopathic' MN?

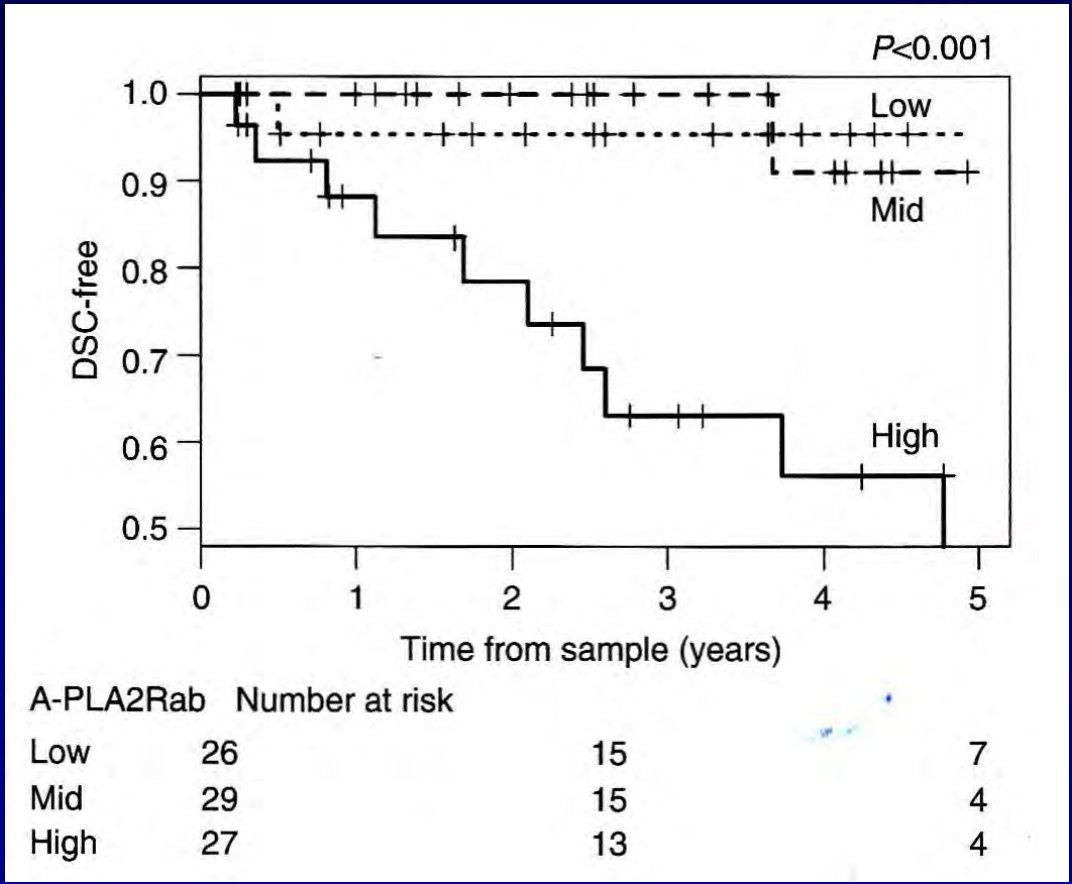
Does anti-PLA2R correlate with disease activity ?

What is the temporal association of anti-PLA2R & proteinuria in

•

**Does anti-PLA2R correlate with clinical outcome ?**

# Anti-PLA2R levels & time to doubling of serum creatinine in membranous nephropathy




Kanigicherla D et al. KI 2013; 83: 940

# Basics of treatment in idiopathic membranous nephropathy

**Exclude secondary causes**

**Anti-proteinuric therapy**

***BP control; RAS blockade; salt restriction***

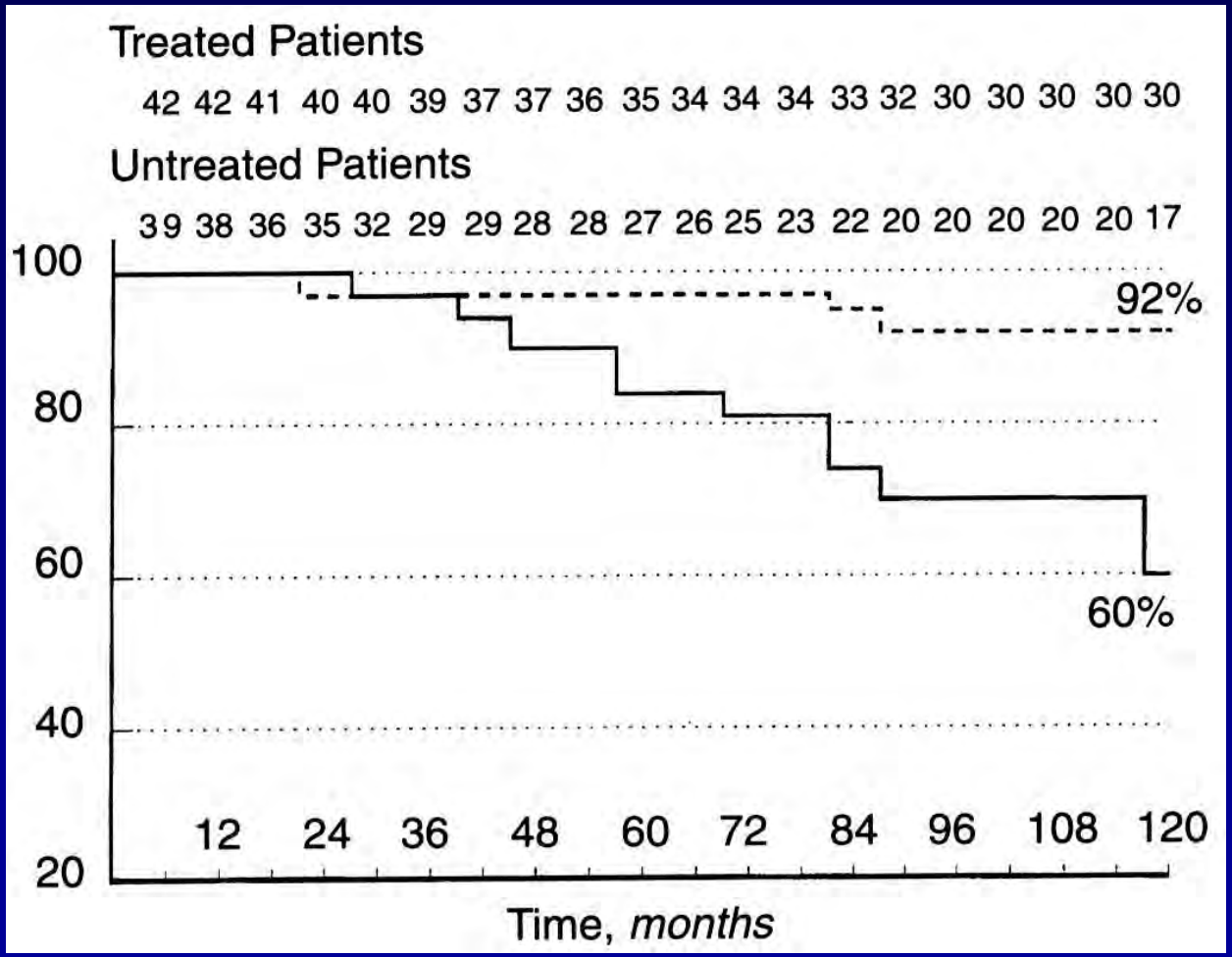
# Disease-specific immunotherapy for idiopathic membranous nephropathy

Corticosteroids plus alkylating agent

Calcineurin inhibitor

Rituximab

# 10 YEAR FOLLOW UP OF 'PONTICELLI REGIMEN' FOR IDIOPATHIC MEMBRANOUS NEPHROPATHY WITH NEPHROTIC SYNDROME




Ponticelli C *et al*. KI 1995; 48: 1600

# ‘PONTICELLI REGIMEN’
# FOR IDIOPATHIC MEMBRANOUS NEPHROPATHY
# WITH NEPHROTIC SYNDROME

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## Why is there controversy ?

## Toxicity

# ‘PONTICELLI REGIMEN’ FOR IDIOPATHIC MEMBRANOUS NEPHROPATHY WITH NEPHROTIC SYNDROME

**In 6 months the patient receives:**

**9 grams Methylprednisolone**
***and* oral Prednisolone 0.4mg/kg/alt day for 3 months**

***plus***

**Chlorambucil 0.2 mg/kg/day for 3 months**
***or***
**Cyclosphosphamide 2.5 mg/kg/day**

**Ponticelli C *et al*. KI 1995; 48: 1600**

# Cancer Risk after Cyclophosphamide in Idiopathic Membranous Nephropathy

**1995 – 2014 n = 272, mean age 50 yrs**

**Use of cyclophosphamide**

***Three*** **fold increase in cancer risk within 10-15 yr of starting treatment**

**Average 55 year old patient**

**Annual cancer risk increase 0.3% to 1%**

van den Brand J et al. CJASN 2014; 9: 1066

# CALCINEURIN INHIBITORS FOR IDIOPATHIC MEMBRANOUS NEPHROPATHY WITH NEPHROTIC SYNDROME

**Cyclosporine**

Cattran D *et al.* KI 2001; 59: 1484

**Tacrolimus**

Praga M *et al*. KI 2007; 71: 924

**Both are effective**

**… compared to placebo**

# Treatment Trials in Membranous Nephropathy

**Steroids+ alkylating agent**
***superior to***
**No immunosuppression**

**Calcineurin inhibitor**
***superior to***
**No immunosuppression**

# Treatment Trials in Membranous Nephropathy

Steroids+ alkylating agent
*superior to*
No immunosuppression

**BUT**
**no head to head comparison**

Calcineurin inhibitor
*superior to*
No immunosuppression

**… until recently**

# RCT of tacrolimus or cyclophosphamide combined with corticosteroids in idiopathic membranous nephropathy

**n = 100 Nephrotic syndrome, eGFR > 30 ml/min**

**Corticosteroids *plus* cyclophosphamide *or* tacrolimus**

**Remission rate higher with tacrolimus at 2 & 4 months**

**But *no difference* from 6 months to 18 months**

Xu J *et al*. Contrib Nephrol 2013; 181: 152

# RCT of tacrolimus plus corticosteroids vs. modified Ponticelli regimen in idiopathic membranous nephropathy

n = 70 Nephrotic syndrome, sCreat < 2.5 mg/dl

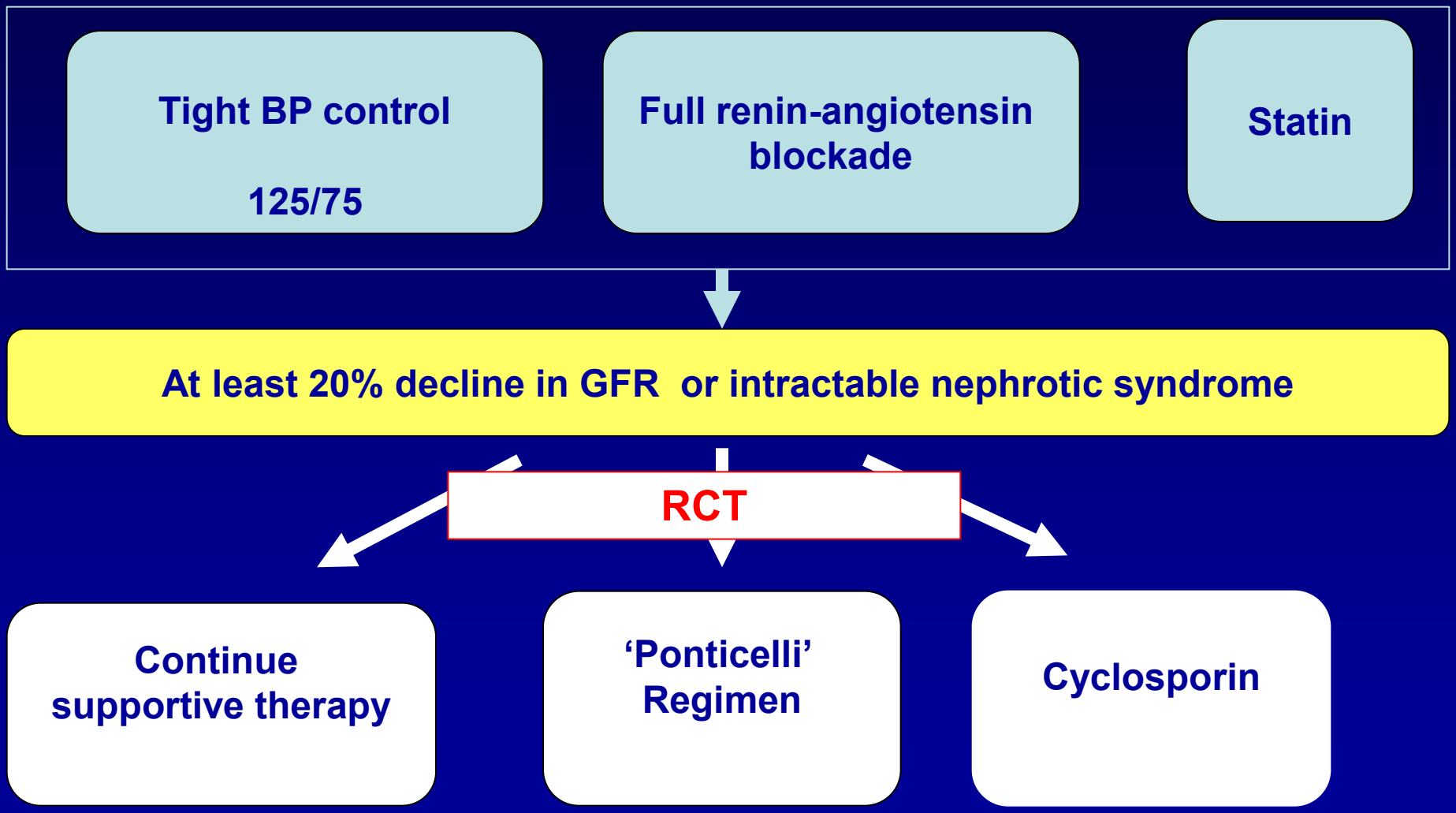
6 months supportive therapy *or* complications of nephrotic syndrome

Intention to treat analysis

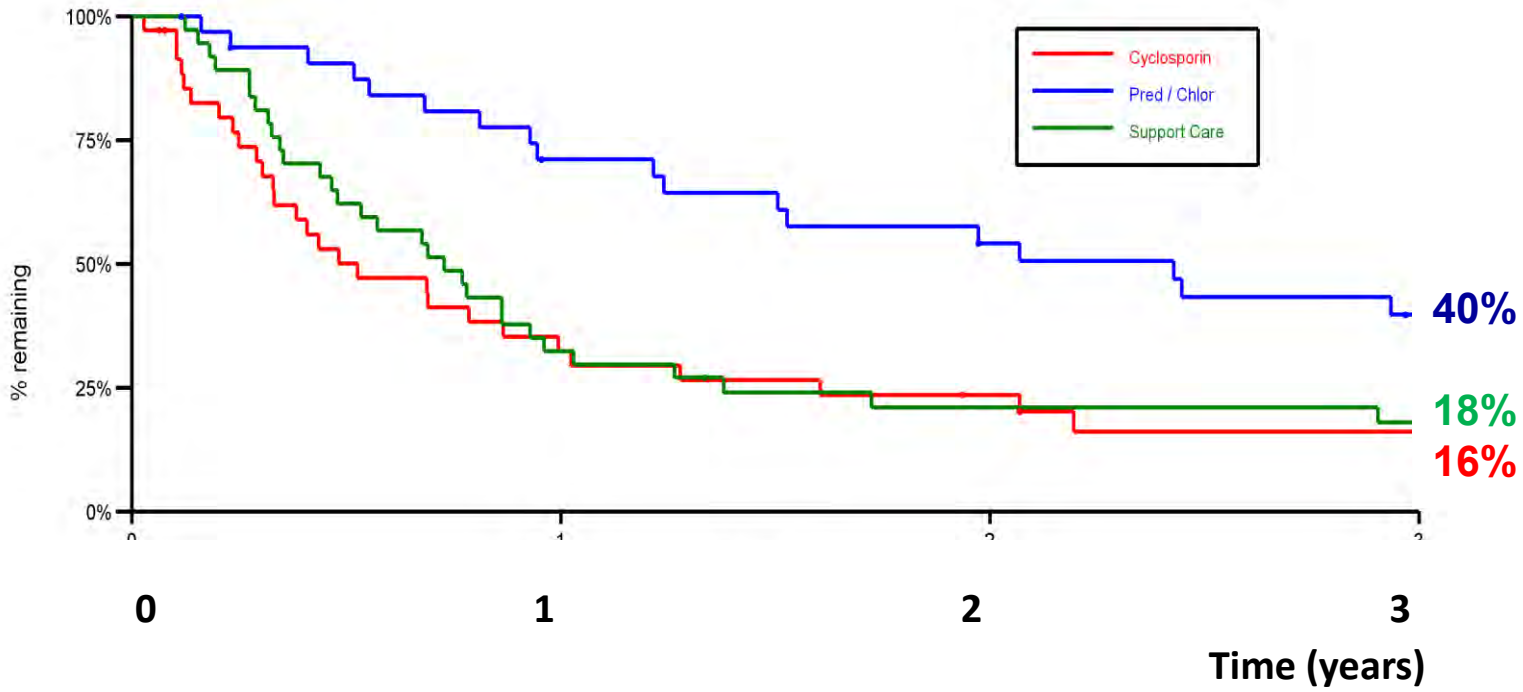
Remission rate (~70%) at 6 and 12 months ***not different***

Ramachandran R *et al*. Nephrology 2016; 21: 139

# THE UK RANDOMISED CONTROLLED TRIAL OF IMMUNOSUPPRESSION FOR PROGRESSIVE MEMBRANOUS NEPHROPATHY



# Time to 20% fall in GFR




***Hazard Ratio (95% CI):***

**Cyclosporin *vs* Supportive care: HR 1.17 (0.7, 1.95), 2p=0.5**

**Pred/Alkylating agent *vs* Supportive care: HR 0.44 (0.24, 0.78), 2p=0.0042**

# ‘PONTICELLI REGIMEN’
# FOR IDIOPATHIC MEMBRANOUS NEPHROPATHY
# WITH NEPHROTIC SYNDROME

---

**Why is there controversy ?**

**Toxicity**

**Is it necessary to treat *all* patients ?**

# Spontaneous remissions in primary membranous nephropathy

**328 patients with nephrotic syndrome – mean follow up 7.5 yrs**

**Spontaneous remission - 32%**

**Average time to remission: 15 months**

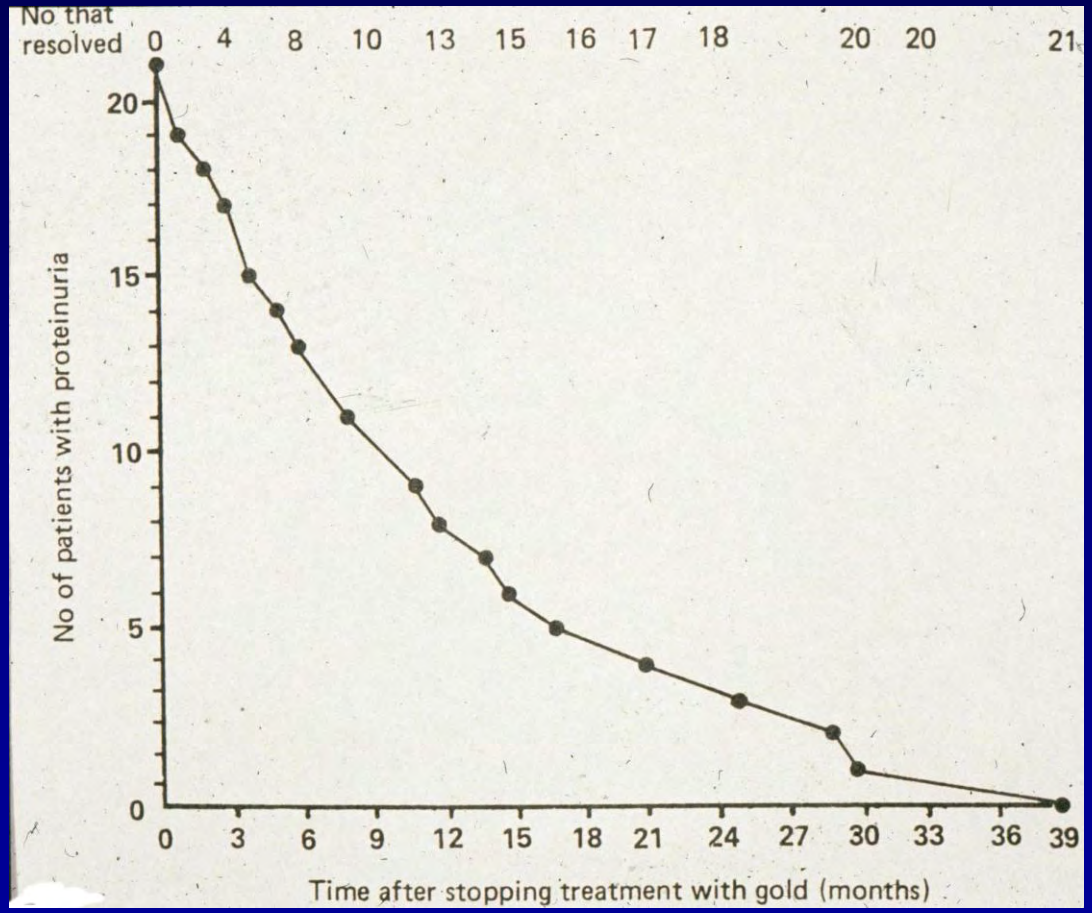
**22% with presenting proteinuria > 12 g/day spontaneously remit**

**Outcome if *no* spontaneous remission**

- ESRD 35% - 10 years
- 41% 15 years

**Polanco et al JASN 21:697, 2010**

# NATURAL HISTORY OF GOLD-INDUCED MEMBRANOUS NEPHROPATHY




Hall CL et al. Adv Exp Med Biol. 1989;252:247-56

# PREDICTING RISK IN MEMBRANOUS NEPHROPATHY

## TORONTO RISK SCORE

| | |
|---|---|
| **LOW RISK** | **normal renal function**<br>**proteinuria < 4g/day for 6/12** |
| **MEDIUM RISK** | **normal renal function**<br>**proteinuria > 4g/d < 8g/d for 6/12** |
| **HIGH RISK** | **abnormal renal function or/and**<br>**persistent proteinuria >8g/d for >6/12** |

# PREDICTING RISK IN MEMBRANOUS NEPHROPATHY

## TORONTO RISK SCORE

**LOW RISK** normal renal function

**MEDIUM RIS**

**HIGH RISK** g/d for >6/12

**Role of serial measurements of anti-PLA2R antibodies**

***Data still limited***

# Long-Term Outcomes in Idiopathic Membranous Nephropathy using a Restrictive Treatment Strategy

**n = 254 1995-2009 RAS blockade**

**Immunosuppression** (cyclophosphamide & steroids) ***only for*** **deteriorating renal function or untreatable nephrotic syndrome (49%)**

| % | 1 yr | 3 yrs | 5 yrs | 10 yrs |
|---|---|---|---|---|
| Partial remission | 39 | 70 | 83 | |
| Complete remission | 5 | 24 | 38 | |
| RRT | - | - | - | 3 |
| Death | - | - | - | 10 |

**Serious adverse events - 23%**

infections (17%), leukopenia (18%), CV events (13%), and malignancies (8%)

van den Brand JA *et al*. JASN 2014: 25; 150

# RITUXIMAB FOR IDIOPATHIC MEMBRANOUS NEPHROPATHY

**2003-2016**

**29 clinical reports - 430 patients treated**

**No RCT**

# RITUXIMAB FOR IDIOPATHIC MEMBRANOUS NEPHROPATHY WITH NEPHROTIC SYNDROME

**n = 100**

**Persistent uP >3.5g/d after 6 months ACE inhibitor**

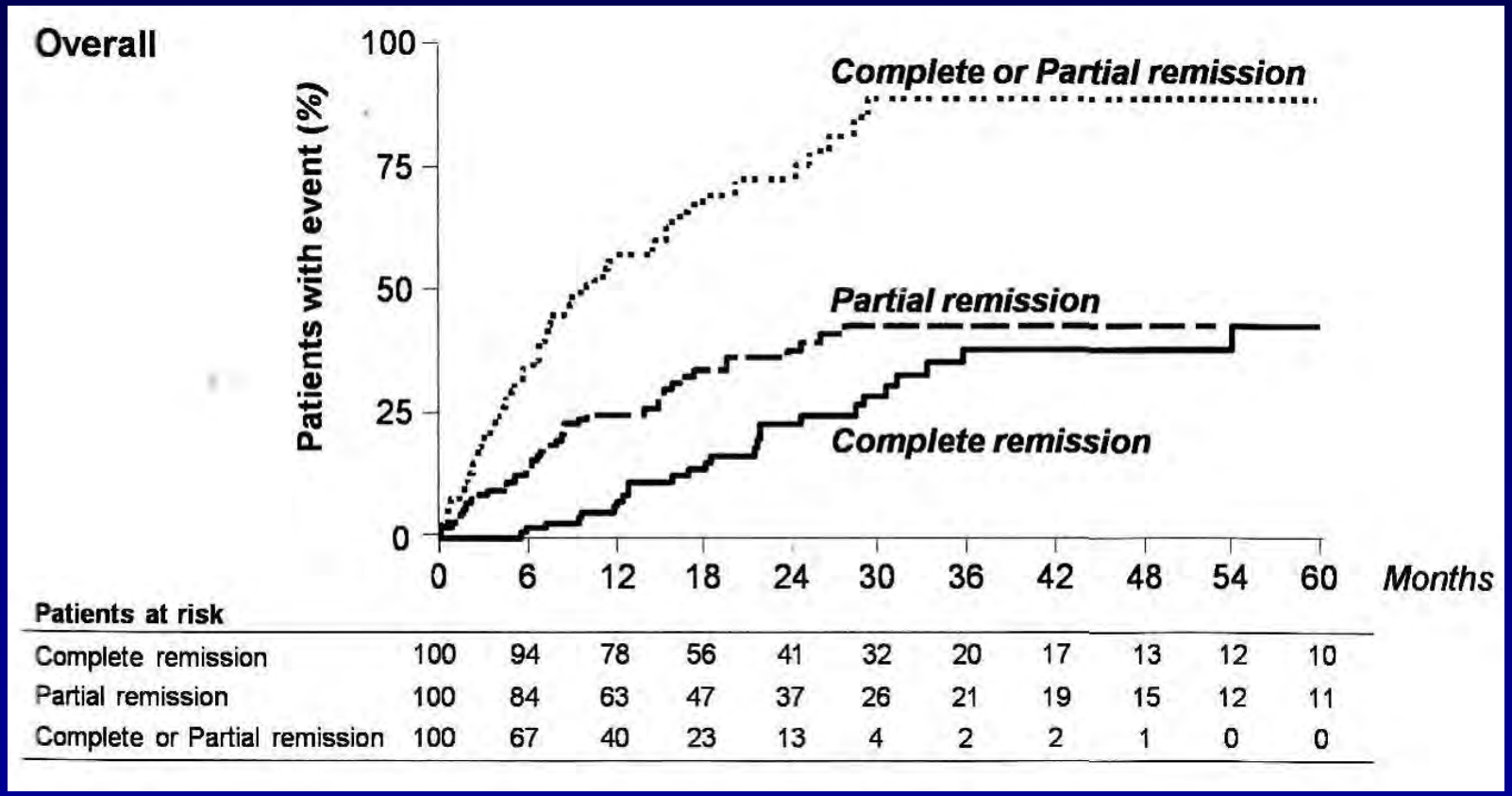
**10 year experience, at least 6 months follow up**

**32% previous immunosuppression**

**RITUXIMAB - most had 2 doses,**
**second dose when peripheral blood B cells recovering**

Ruggenenti P et al. JASN 2012; 23: 1416

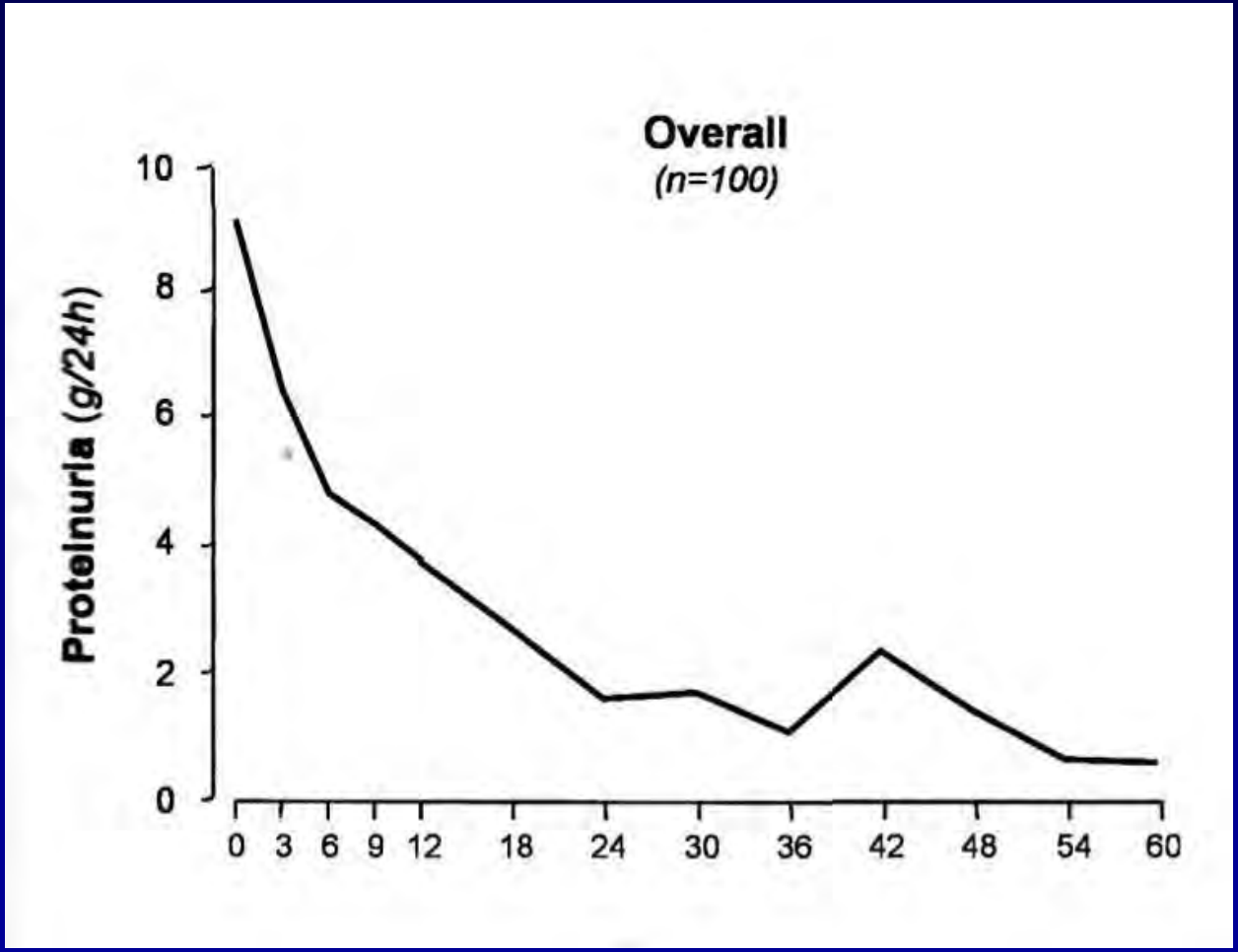
# RITUXIMAB FOR IDIOPATHIC MEMBRANOUS NEPHROPATHY WITH NEPHROTIC SYNDROME




| Patients at risk | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Complete remission | 100 | 94 | 78 | 56 | 41 | 32 | 20 | 17 | 13 | 12 | 10 |
| Partial remission | 100 | 84 | 63 | 47 | 37 | 26 | 21 | 19 | 15 | 12 | 11 |
| Complete or Partial remission | 100 | 67 | 40 | 23 | 13 | 4 | 2 | 2 | 1 | 0 | 0 |

Ruggenenti P et al. JASN 2012; 23: 1416

# RITUXIMAB FOR IDIOPATHIC MEMBRANOUS NEPHROPATHY WITH NEPHROTIC SYNDROME

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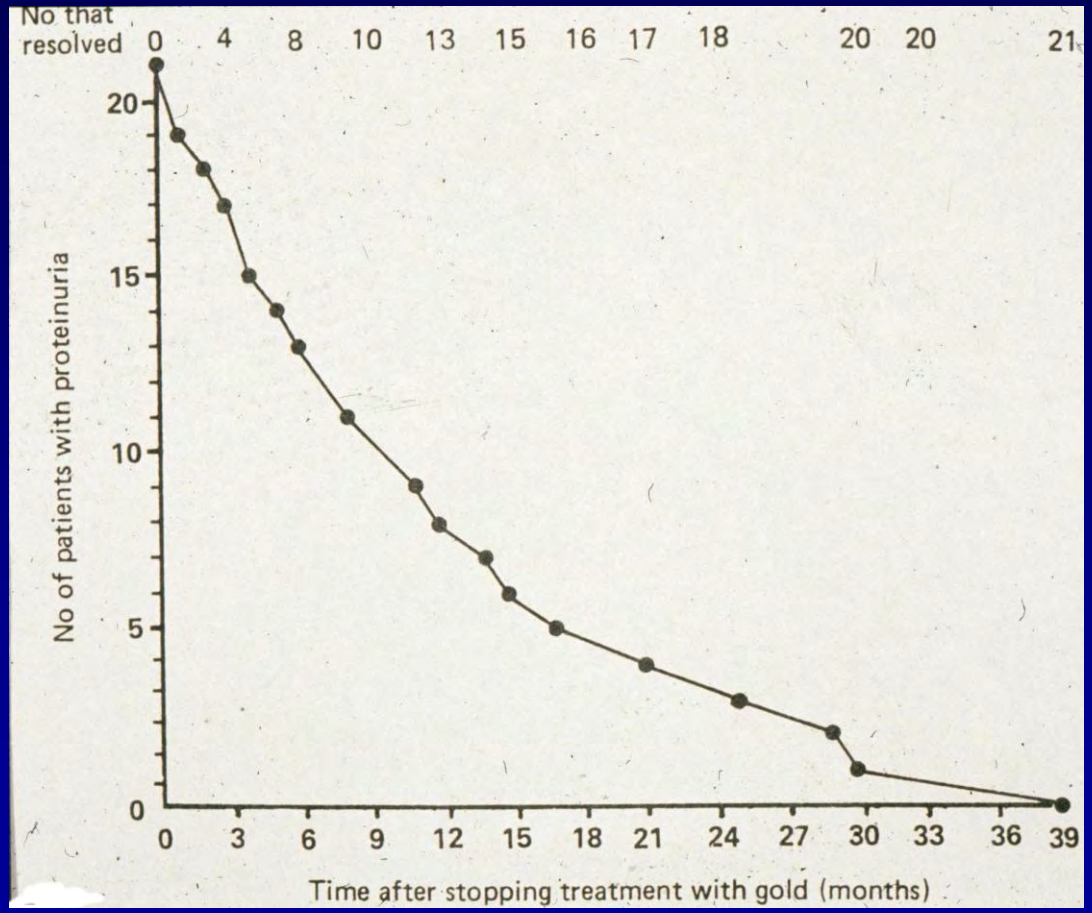



Hall CL et al. Adv Exp Med Biol. 1989;252:247-56

# COST OF RITUXIMAB

**1 dose of rituximab: $4,000** (? $1200 generic from India)

**Ponticelli regimen for 6 months: $ 600**

Does avoiding one hospital admission for a septic episode save the cost of rituximab ?

Ruggenenti P et al. JASN 2012; 23: 1416

# Treatment Trials in Membranous Nephropathy

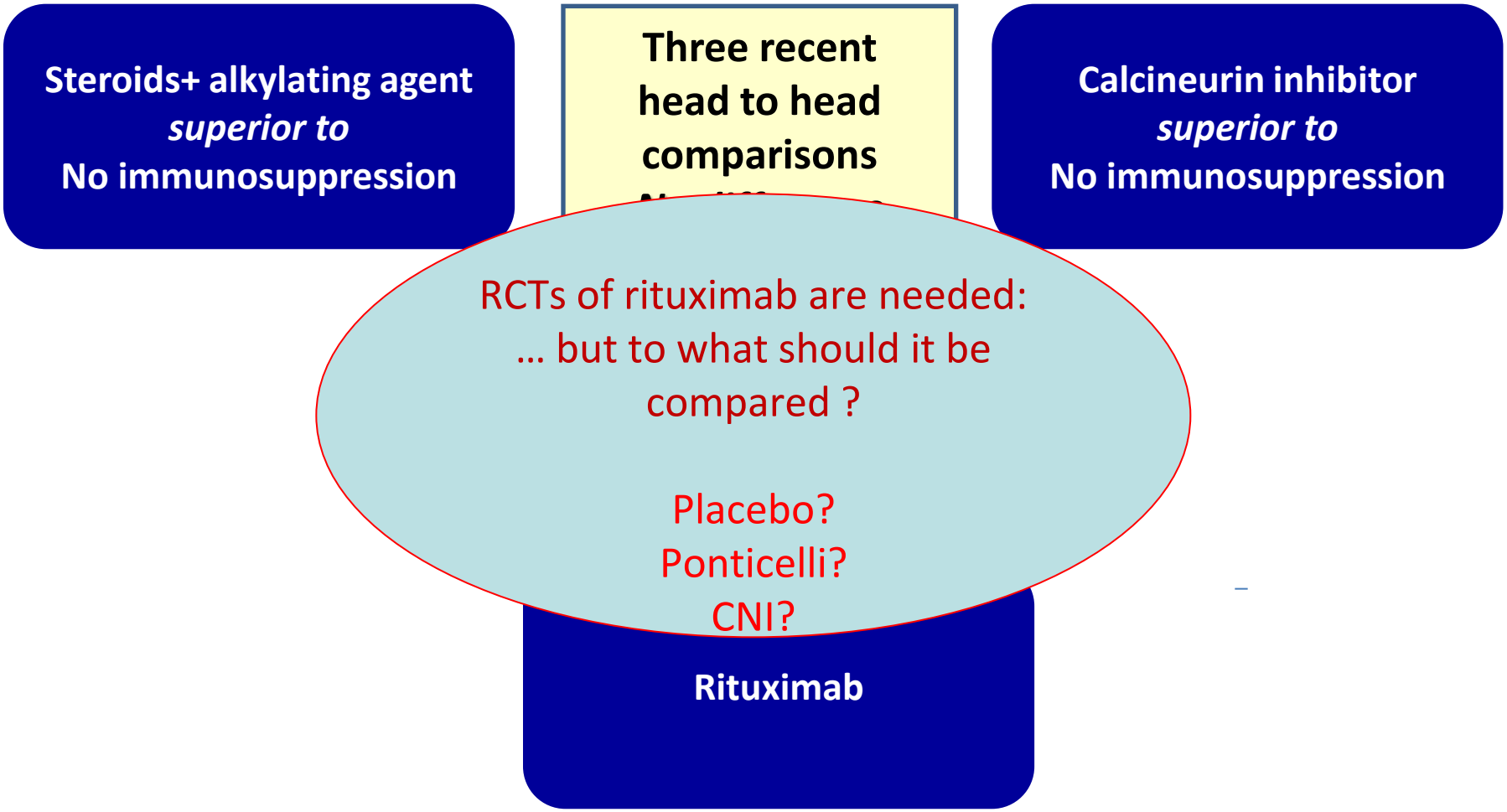
Steroids+ alkylating agent
*superior to*
No immunosuppression

Three recent head to head comparisons
***No difference***

Calcineurin inhibitor
*superior to*
No immunosuppression

Rituximab

# Treatment Trials in Membranous Nephropathy



# RCTs of RITUXIMAB for MEMBRANOUS NEPHROPATHY

**Paris**

**Rituximab**

***vs***

**Placebo**

**Mayo Clinic**

**3 months run in ….**

**Cyclosporine**
6 months

***vs***

**Rituximab**

# RCTs of RITUXIMAB for MEMBRANOUS NEPHROPATHY

## Paris

**Rituximab**

***vs***

**Placebo**

**Rituximab**
**is superior to placebo**

## Mayo Clinic

**3 months run in ….**

**Cyclosporine**
6 months

***vs***

**Rituximab**

# Management of Glomerular Disease

**Do the simple things properly**

**Resist the urge to 'do something'**

**Minimise adverse effects of treatment**

**Weigh risk vs. benefit**

**Use guidelines with judgment**

**Wait for evidence**

**Help create the evidence**