



KDIGO 2025 IgAN Guideline Update A New Framework for Management and Therapeutic Approach

60th AZNSN Annual Congress

3rd September 2025

Perth, WA

DISCLOSURES

Served as medical advisor for Traverre, Otsuka, Kira Pharma, Eledon, CSL-Behring, Dimerix, Alpine, Arrowhead, Novartis (Chinook), .

Received honorarium from AstraZeneca, Amgen, Eli Lilly and Baxter, Novartis.

Served as a DMSC members in HEFEF trial (investigator initiated), ARGX-113-2203/AL-1103-014 Trial

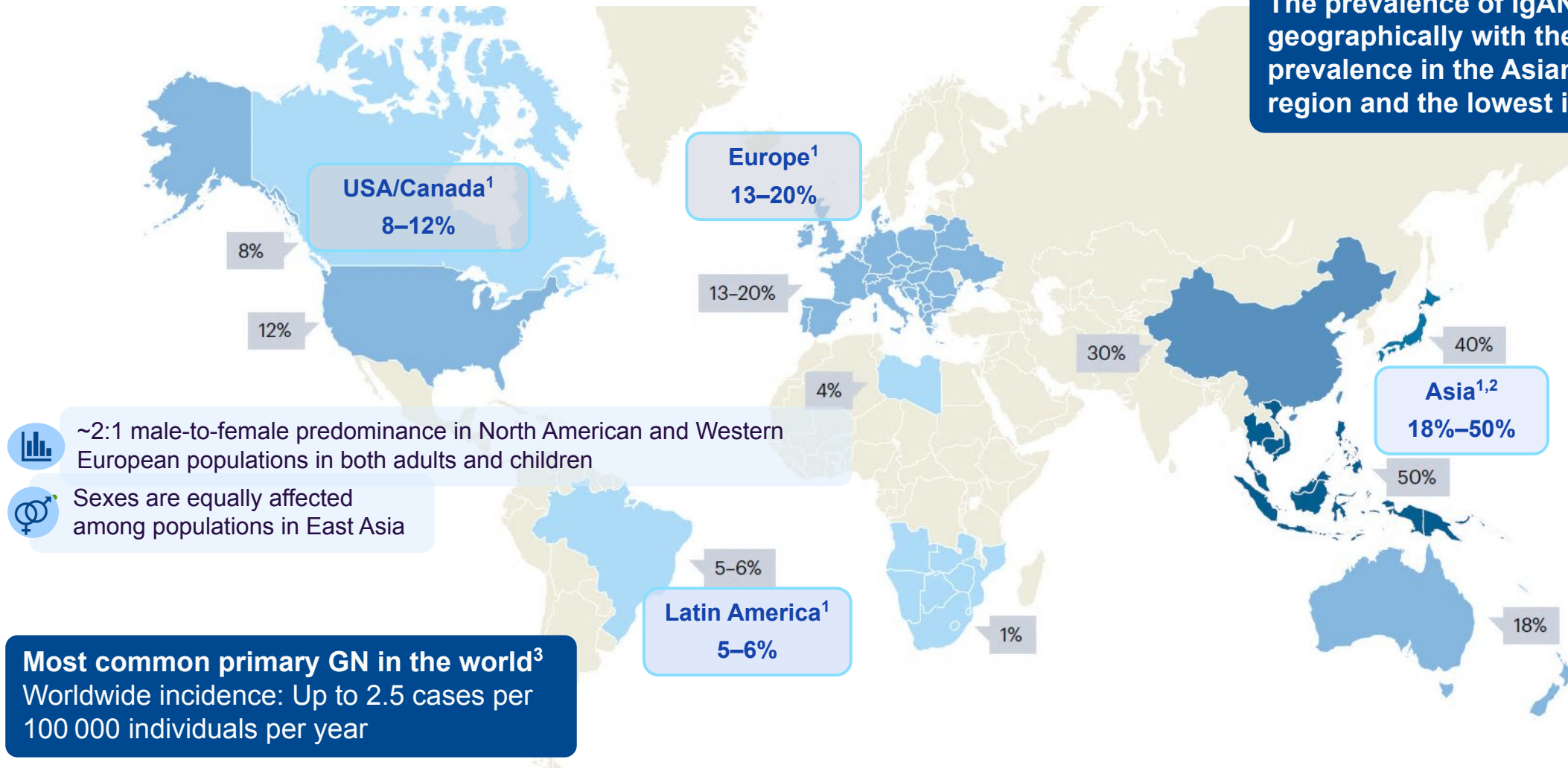
Honorary Executive Officer of Australia New Zealand Society of Nephrology (ANZSN) that received industry sponsorship for ANZSN activities

Overview

- What are the changes?
- Why the changes?
- Guidelines recommended treatment options and considerations.
- Predictor/s of treatment response

IgA nephropathy is the most common primary glomerulonephritis in the world

The prevalence of IgAN varies geographically with the highest prevalence in the Asian Pacific region and the lowest in Africa



Incidence of IgAN in Australia

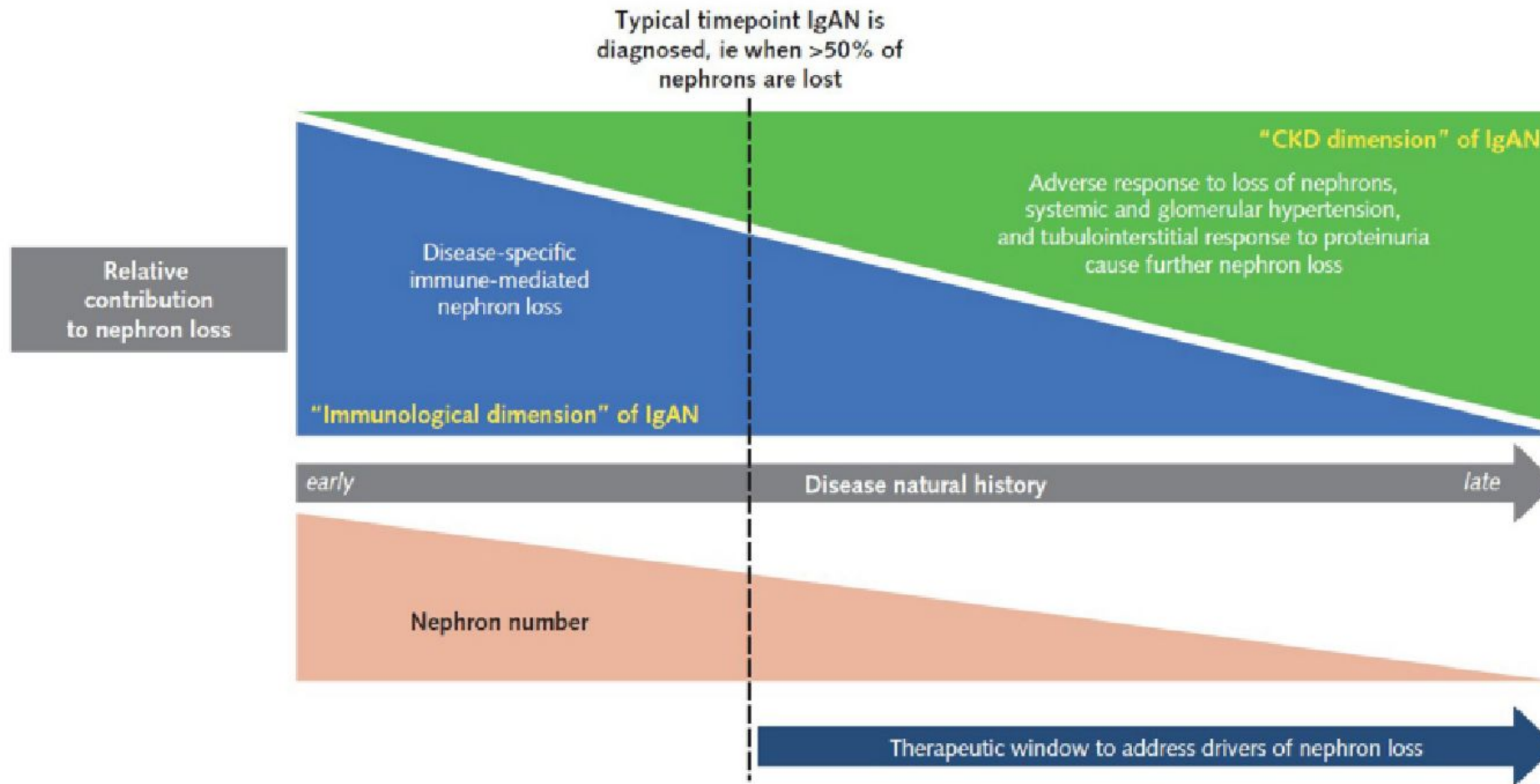
Author	EXTEND 45		Briganti et al (2)	Jegatheesan et al (3)
Population Age group Time period Total population	NSW* Age \geq 45 years 2005-2014 215,029		Victoria All age groups 1995-1997 4,560,155	Queensland Age \geq 18 years 2002-2011 3,404,000 in 2011
Glomerular disease	N = 170 (%)	Incidence per 100,000 person-years [95% CI]		
Min change disease	<5# (3)	0.08 [0.002-0.43]	0.6	0.29
FSGS	21 (12)	1.6 [1.0-2.5]	2.1	1.02
Membranous GN	15 (9)	1.2 [0.6-1.9]	1.3	0.65
IgA nephropathy*	29 (17)	2.2 [1.5-3.2]	4.3	1.41
MPGN	<5# (3)	0.2 [0.02-0.6]	0.3	0.15
Crescentic GN	<5# (3)	0.3 [0.08-0.8]		0.73
Other GN	68 (40)	5.2 [4.1-6.6]		
AAV	25 (15)	2.0 [1.2-2.8]	1.5	0.47
Anti-GBM disease	<5# (3)	0.3 [0.08-0.8]	0.1	0.08
Lupus nephritis	<5# (3)	0.08 [0.002-0.43]	1.7	0.69

**Aggarwal, et al. Unpublished
(2) NDT (2001) (3) Nephrology (2016)

KEY UPDATES OF KDIGO 2024 CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF IGA NEPHROPATHY (PUBLISH VERY SOON.....)

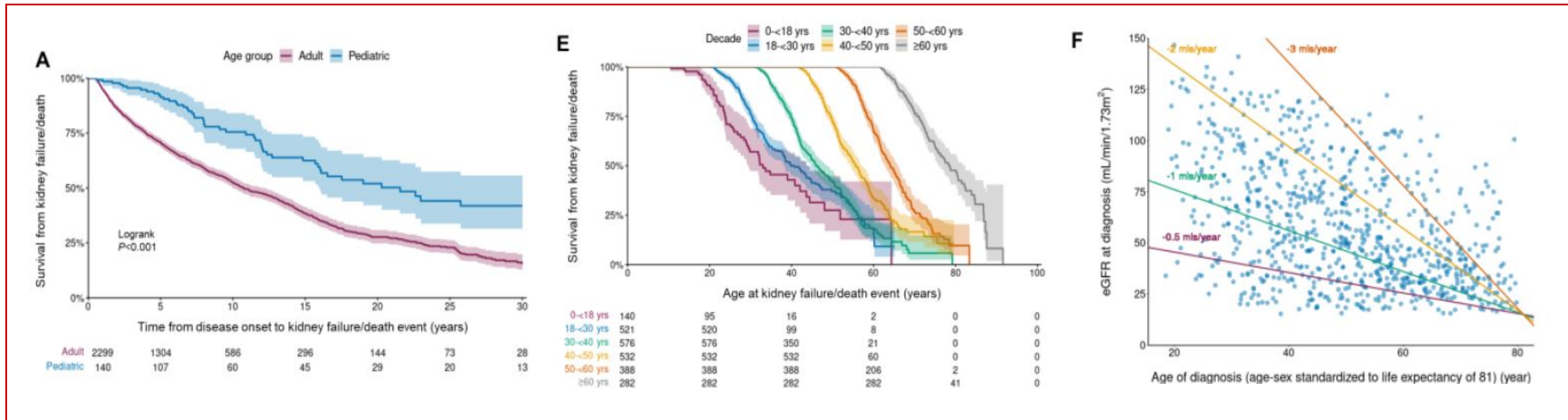
1. More liberal threshold for a kidney biopsy
2. Aims for lower proteinuria control, with goal of <0.5 g/d, ideally <0.3 g/d, and a stable eGFR
3. Treatment strategy should simultaneously pathomechanism of IgAN and the risk of progression of renal function
 - Reduce pathogenic forms of IgA (Gd-IgA1) for reduction or prevention of IgA immune complex formation
 - Anti-immune/ anti-inflammation treatment to prevent or reduce immune complex-mediated injury
 - Effective manage the risk of progression of chronic renal function due to IgAN-induced nephron loss

Change in concepts of therapeutic approach to IgAN



Almost all patients are at risk of progression to ESKD within their lifetime












UK national registry data showed that most patients progressed to kidney failure within 10–15 years



Even those patients historically categorized as “low-risk” (proteinuria < 0.88 g/g), had high rates of kidney failure within 10 years

Patients with proteinuria in IgAN are at high risk of progression to ESKD

Chinese large-scale cohort data: Time-varying proteinuria and progression of IgA nephropathy

Setting & Participants	Analysis	Results												
 <p>Observational cohort study</p>  <p>Single center Beijing, China</p>  <p>N = 1,530 patients</p> <ul style="list-style-type: none"> • IgA nephropathy (IgAN) • At least 12 months of follow-up 	 <p>Exposure: Time-varying proteinuria</p>  <p>Composite Kidney Outcome:</p> <ul style="list-style-type: none"> • 50% decline in eGFR • ESKD <p>Time-Dependent Confounders:</p>   <ul style="list-style-type: none"> • Age • Blood pressure • eGFR • Medications  	 <p>Median follow-up: 43.5 months</p>  <p>N = 254 (16.6%) patients developed composite kidney outcome</p> <table border="1"> <thead> <tr> <th>Proteinuria (g/d)</th> <th>HR (95% CI)</th> </tr> </thead> <tbody> <tr> <td>< 0.3</td> <td>Reference</td> </tr> <tr> <td>0.3 to < 0.5</td> <td>2.22 (0.88-5.58)</td> </tr> <tr> <td>0.5 to < 1.0</td> <td>4.04 (1.93-8.46)</td> </tr> <tr> <td>1.0 to < 2.0</td> <td>8.46 (3.80-18.83)</td> </tr> <tr> <td>≥ 2.0</td> <td>38.00 (17.62-81.95)</td> </tr> </tbody> </table>	Proteinuria (g/d)	HR (95% CI)	< 0.3	Reference	0.3 to < 0.5	2.22 (0.88-5.58)	0.5 to < 1.0	4.04 (1.93-8.46)	1.0 to < 2.0	8.46 (3.80-18.83)	≥ 2.0	38.00 (17.62-81.95)
Proteinuria (g/d)	HR (95% CI)													
< 0.3	Reference													
0.3 to < 0.5	2.22 (0.88-5.58)													
0.5 to < 1.0	4.04 (1.93-8.46)													
1.0 to < 2.0	8.46 (3.80-18.83)													
≥ 2.0	38.00 (17.62-81.95)													

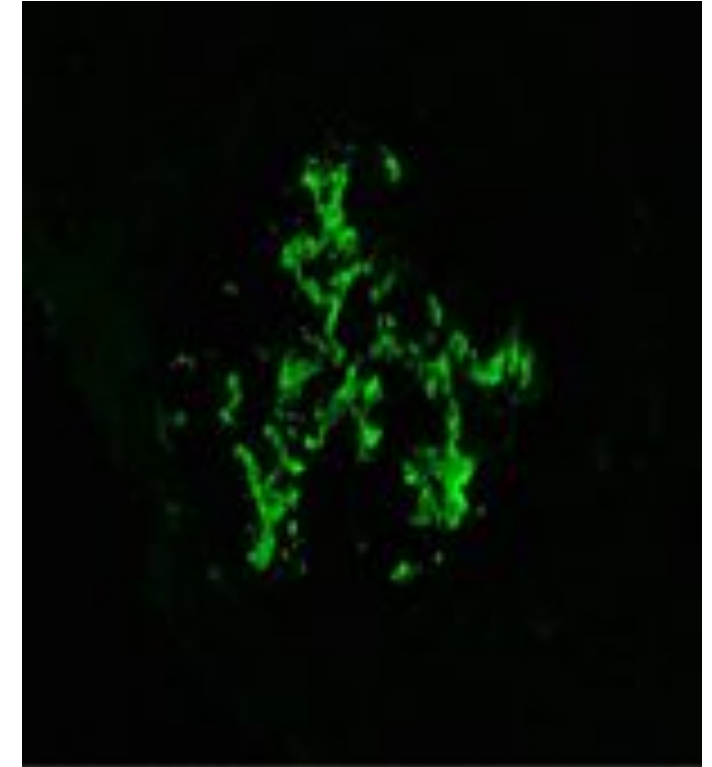
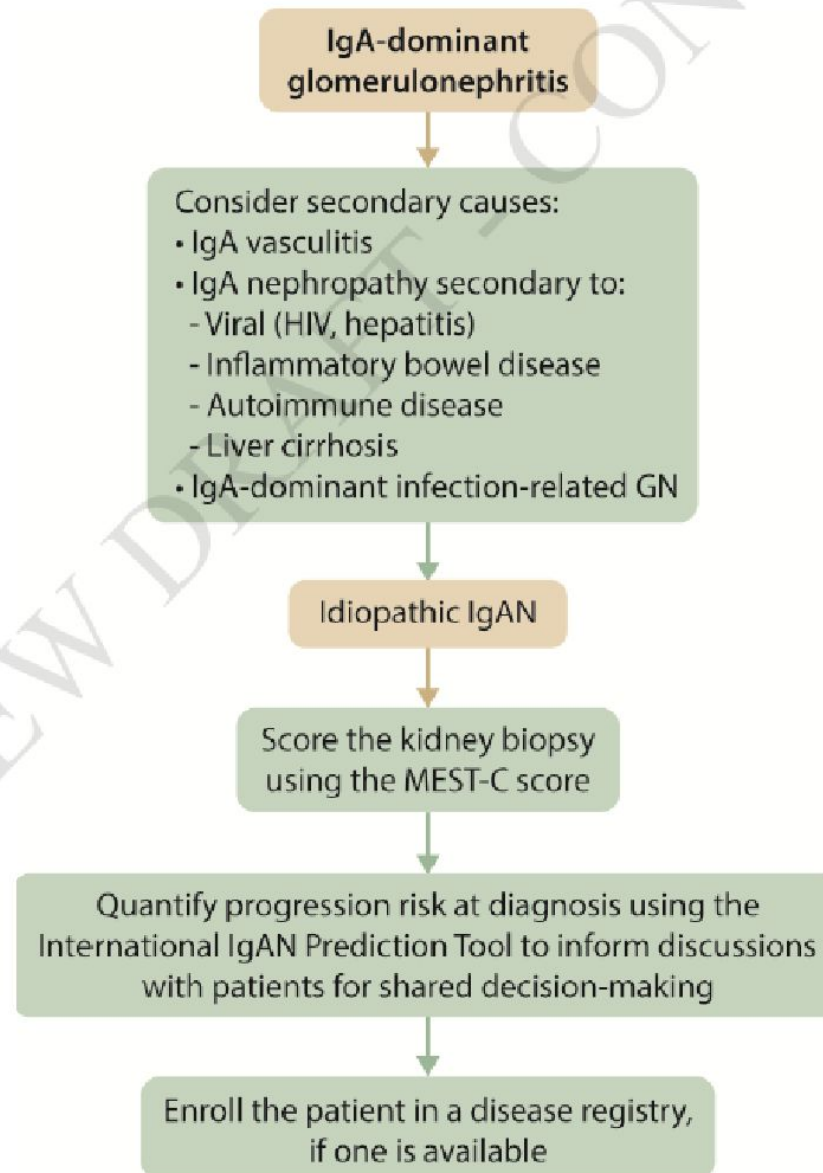
CONCLUSION: This study showed that patients with IgAN and proteinuria levels >0.5 g/d have an elevated risk of kidney failure, especially among patients with proteinuria levels ≥1.0 g/d before initiating treatment.

Chen Tang, Pei Chen, Feng-Lei Si, et al
@AJKDonline | DOI: 10.1053/j.ajkd.2023.12.016

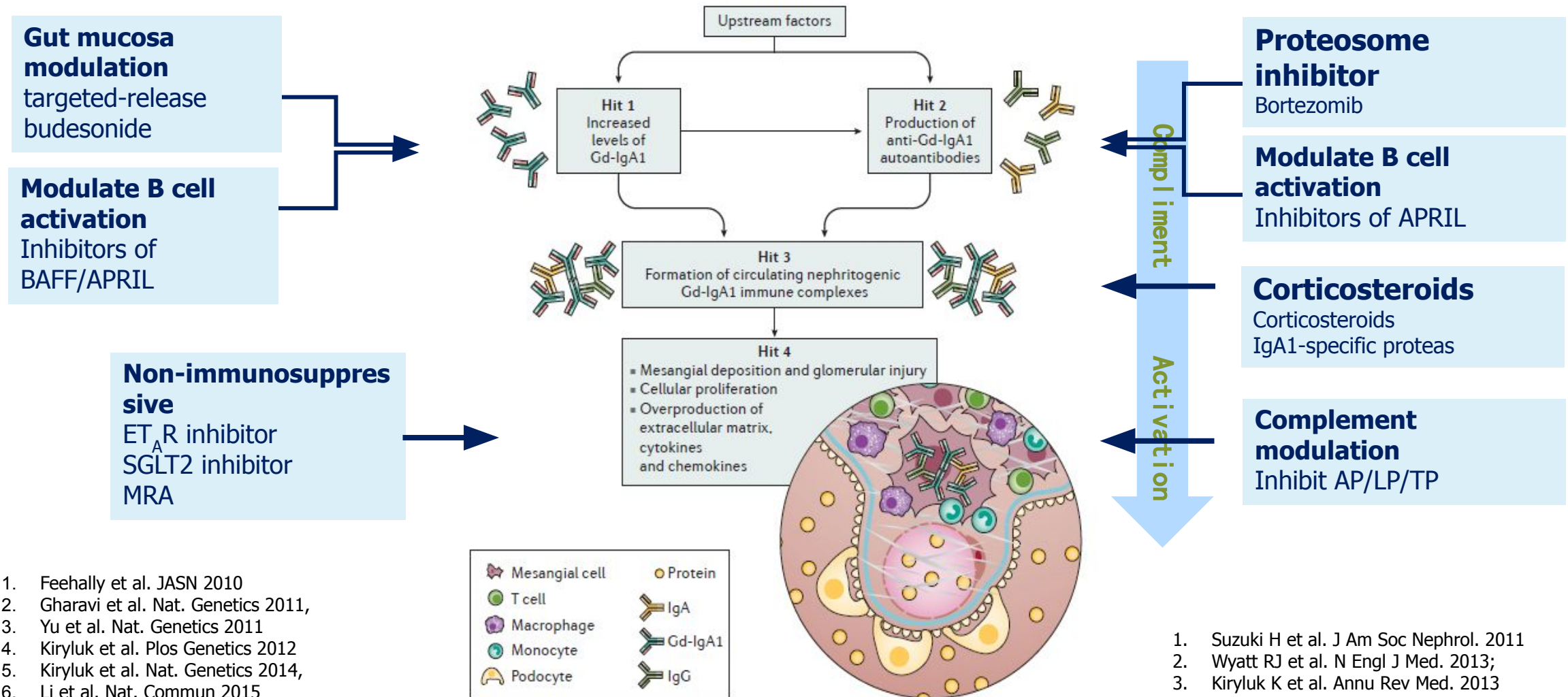


Diagnosis of IgAN can only be made by a kidney biopsy

- Exclude secondary IgAN
- Prognostication
- Large variability in kidney biopsy practices driven by cost, national screening program etc.



Potential therapeutic targets based on the current understanding for the pathogenesis of IgA nephropathy

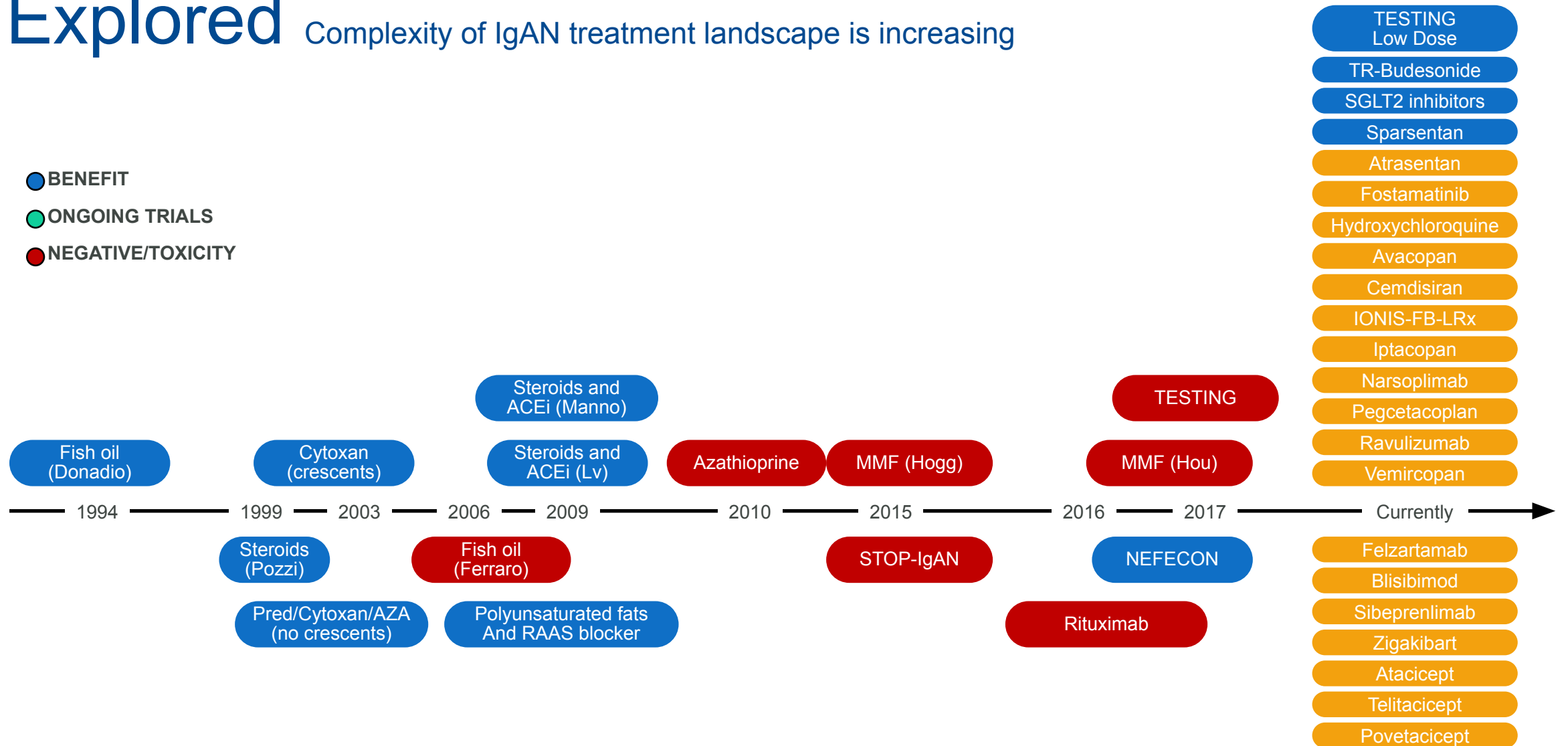


1. Feehally et al. JASN 2010
2. Gharavi et al. Nat. Genetics 2011,
3. Yu et al. Nat. Genetics 2011
4. Kiryluk et al. Plos Genetics 2012
5. Kiryluk et al. Nat. Genetics 2014,
6. Li et al. Nat. Commun 2015
7. Kiryluk et al. Nat. Genetics 2023,

1. Suzuki H et al. J Am Soc Nephrol. 2011
2. Wyatt RJ et al. N Engl J Med. 2013;
3. Kiryluk K et al. Annu Rev Med. 2013
4. Magistroni R et al. Kidney Int. 2015.

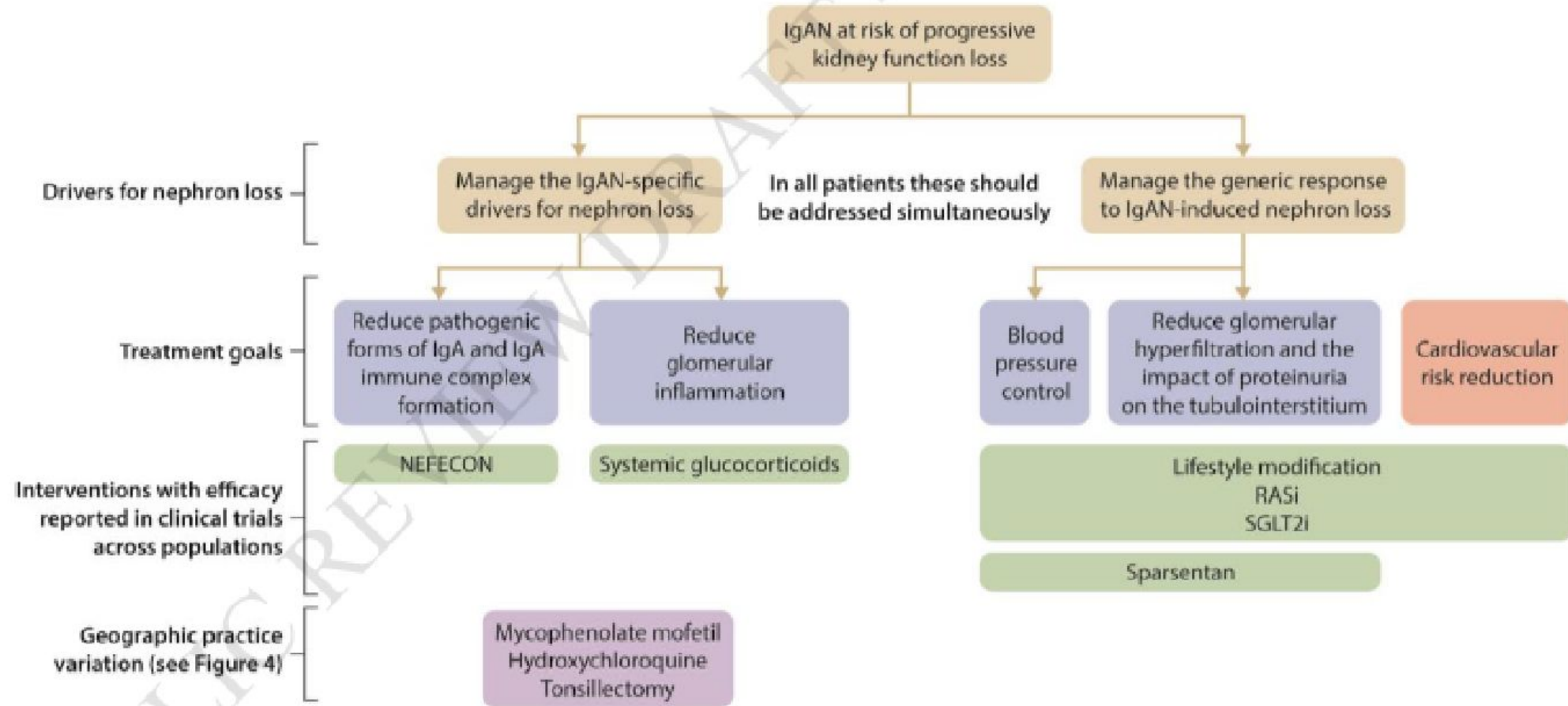
Many New Agents with Different MOAs Being Explored

Complexity of IgAN treatment landscape is increasing



Adapted from Figure at the courtesy of Prof Dana Rizk

Treatment targets in immunoglobulin A nephropathy (IgAN) and available to-date approved Rx (KDIGO 2024)



The definition of patients with IgA nephropathy at risk for progressive loss of kidney function

• Proteinuria $\geq 0.5\text{g/d}$ (or equivalent) is at risk of progressive loss of kidney function.
 Treatment goals for patients with IgA nephropathy at risk for progressive loss of kidney function

• Reduce the rate of loss of kidney function to $<1\text{ ml/min/vear}$ for the rest of the patient's life.

A 9-month treatment period with Nefecon provided a clinically relevant reduction in eGFR decline and a durable reduction in proteinuria that sustained at 24 months NefIgArd (Phase 3)

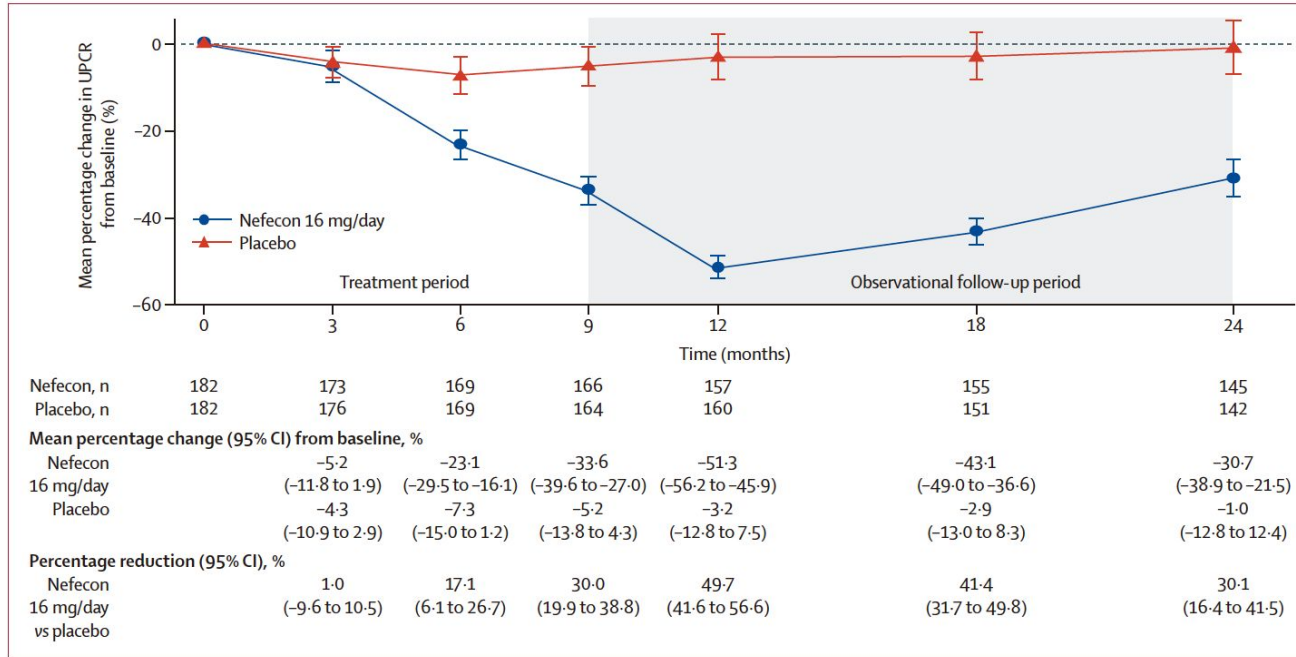
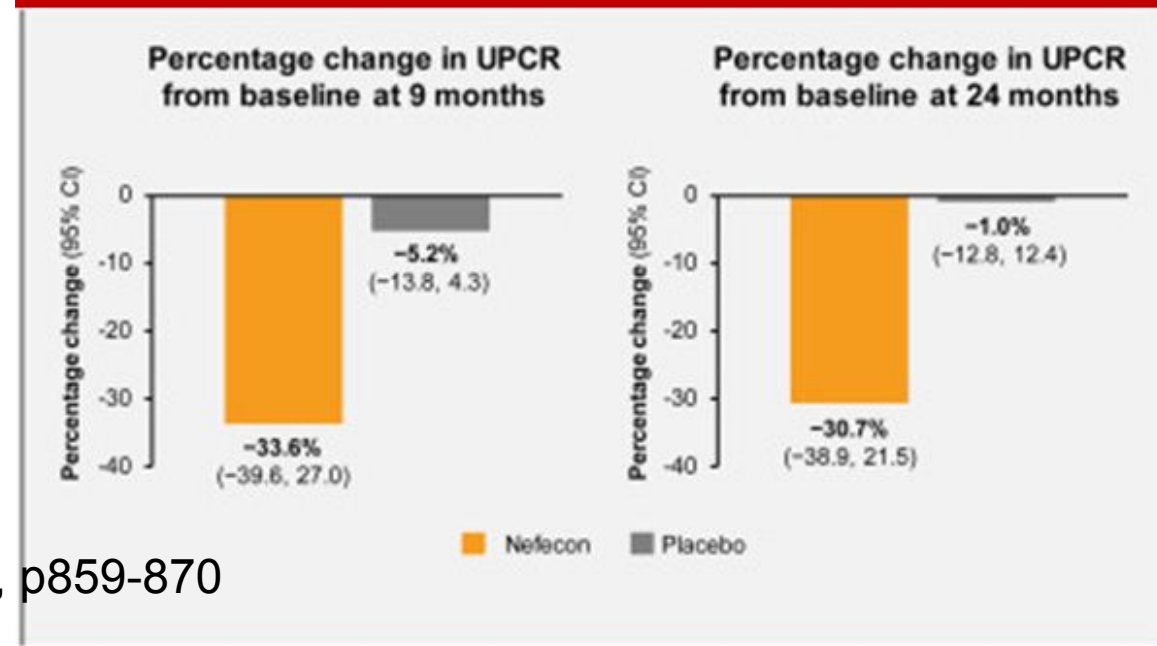
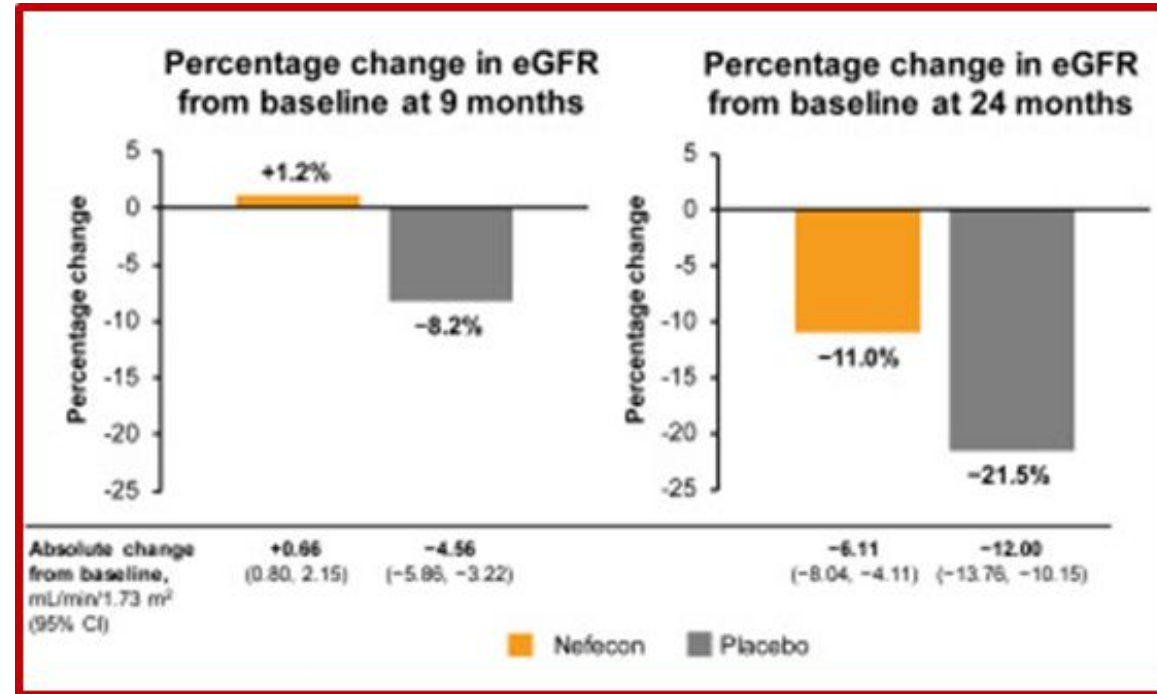


Figure 2: Mean percentage change in UPCR (g/g) from baseline to 24 months (full analysis set)
 Estimated geometric mean percentage change (and standard error) was calculated from a mixed-effects model for repeated measures of log-transformed post-baseline to baseline ratios at 3, 6, 9, 12, 18, and 24 months. Data included at baseline and 24 months are the log of the geometric mean of the two replicate values recorded at each timepoint, respectively. The corresponding percentage reduction and confidence interval was derived from $(1 - \text{ratio of geometric least squares means}) \times 100$. UPCR=urine protein-creatinine ratio.



NefIgArd (Phase 3)

Nefecon was also well tolerated, with a safety profile as expected for a locally acting oral budesonide product.

	9-month treatment period*		15-month observational follow-up period†	
	Nefecon 16 mg/day (n=182)	Placebo (n=182)	Nefecon 16 mg/day (n=175)‡	Placebo (n=174)‡
All treatment-emergent adverse events	159 (87%)	125 (69%)	127 (73%)	124 (71%)
Mild	93 (51%)	75 (41%)	62 (35%)	73 (42%)
Moderate	57 (31%)	46 (25%)	49 (28%)	43 (25%)
Severe	9 (5%)	4 (2%)	16 (9%)	8 (5%)
Any treatment-emergent serious adverse events	18 (10%)	9 (5%)	14 (8%)	14 (8%)
Any treatment-related treatment-emergent serious adverse events	4 (2%)	4 (2%)	0	1 (1%)
Any treatment-emergent adverse events leading to death	1 (1%)	0	1 (1%)	0
Any treatment-emergent adverse events leading to discontinuation of study treatment	17 (9%)	3 (2%)	NA	NA

Data are number of patients (%). NA=not applicable. *Includes adverse events that started or worsened during treatment, up to 14 days (inclusive) after the last treatment dose (ie, the last dose the patient received including the tapering period, regardless of treatment duration). Five patients (two in the Nefecon group and three in the placebo group) did not start study treatment. †Includes adverse events that started more than 14 days after the last treatment dose. ‡Number of patients who had a study visit during the observational follow-up period.

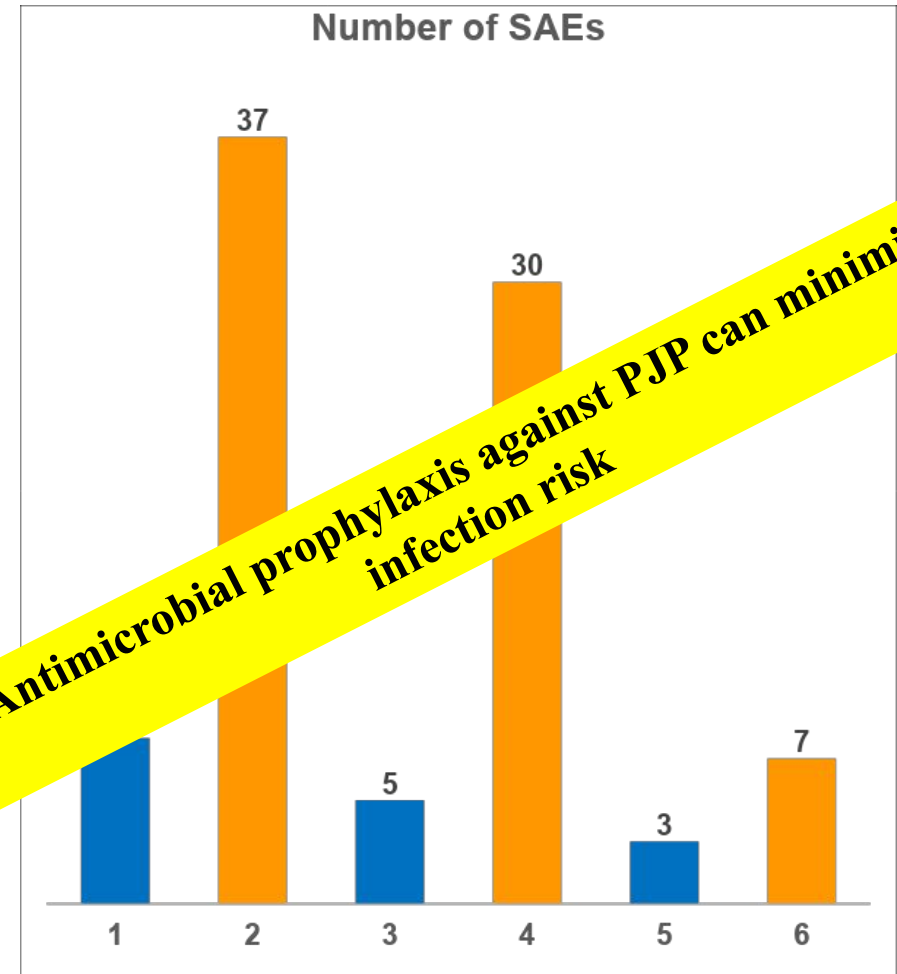
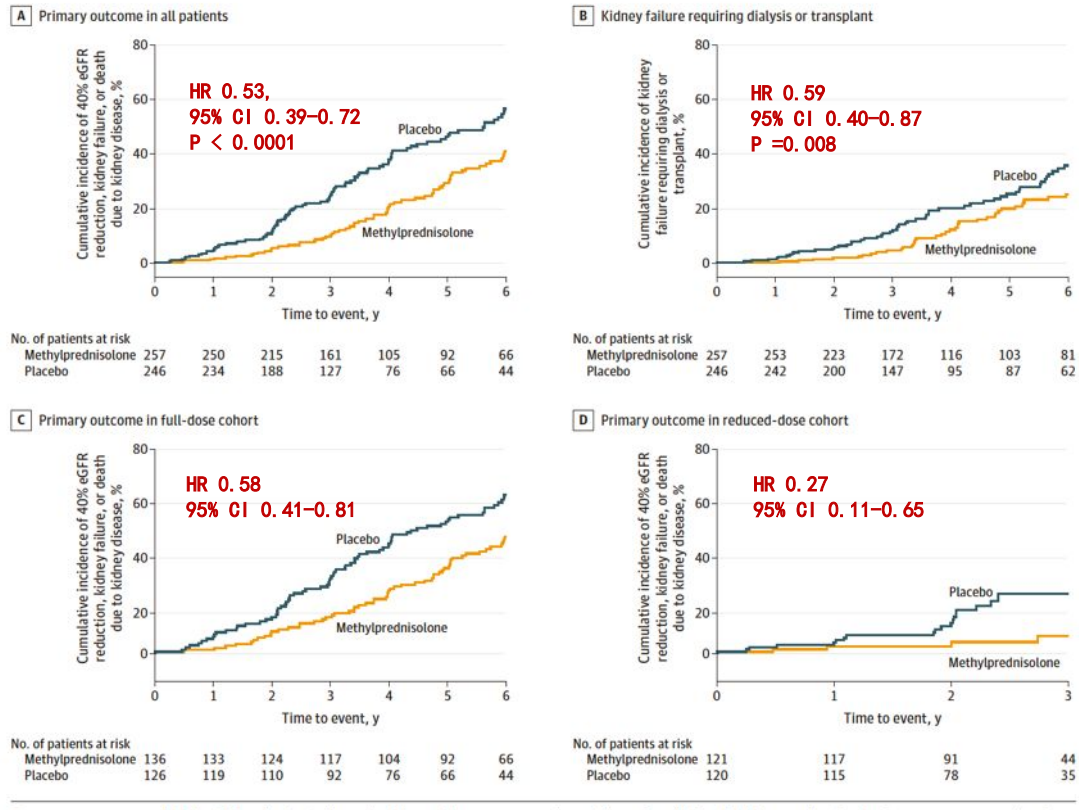
Table 3: Key safety variables (full analysis set)

- Generally well-tolerated, consistent with low systemic exposure
- Infection rate is uncommon (<5%) and no severe infection events were observed
- Discontinuations due to TEAEs occurred in 9% and 2% of patients in the Nefecon and placebo arms, respectively
- No adverse events on body weight or blood pressure
- No adverse events on HbA1c

Nefecon (targeted-release budesonide) was approved by FDA, EMA and CFDA for treatment in adult IgA Nephropathy patients

TESTING Study: Corticosteroids in IgA Nephropathy

Figure 2. Time From Randomization to First Outcome in a Study of the Effect of Oral Methylprednisolone on Kidney Function Decline in Patients With IgA Nephropathy



Antimicrobial prophylaxis against PJP can minimise infection risk

The full dose arm and reduced dose arm showed the similar protects against kidney failure in IgAN, and Reduced dose of corticosteroids with antibiotic prophylaxis acted much lower risk of SAEs

Lv J et al. JAMA. 2017;318(5):432–42;
 Lv J et al. JAMA. 2022; 327,1888 ;

The Efficacy and Safety of Reduced-Dose Oral Methylprednisolone in High-Risk IgA Nephropathy



Cohort & Methods



TESTING study

- Secondary analysis
- International multicentre RCT



Patients with biopsy-proven IgA nephropathy
N= 241



2017-2019



Inclusion criteria:

- Proteinuria ≥ 1 g/day despite 3 months of RAS blockade
- eGFR 30-120 mL/min/1.73m²



Methylprednisolone vs Placebo:

HR 0.24 (0.10-0.58) Lower risk of primary outcome
40% eGFR decline, kidney failure, death from kidney disease

12 months from baseline



Lowered proteinuria

-1.15 g/day (0.62-1.68; P <0.001)



Reduced eGFR decline from baseline

7.9 mL/min/1.73 m² (4.3-11.5; P <0.001)

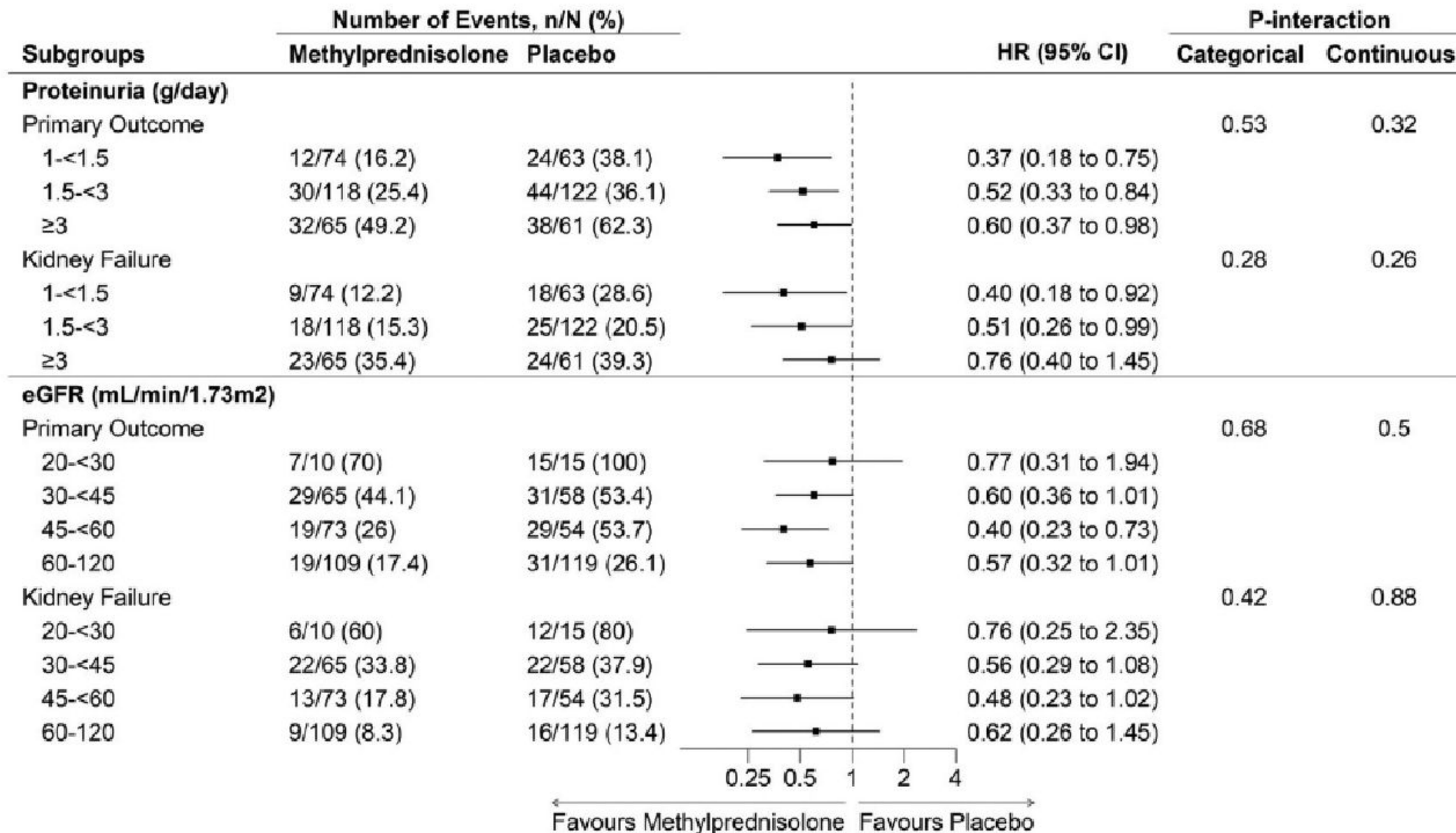


7 vs 3 serious adverse events

HR 1.97 (0.49-7.90)

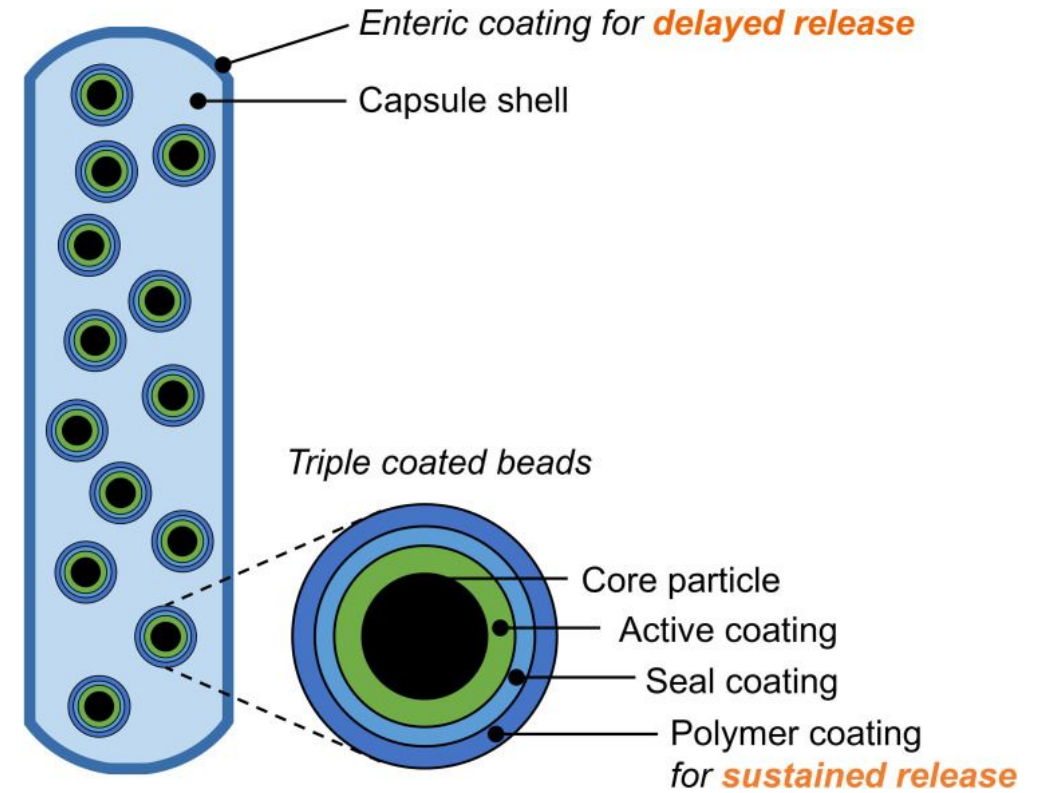
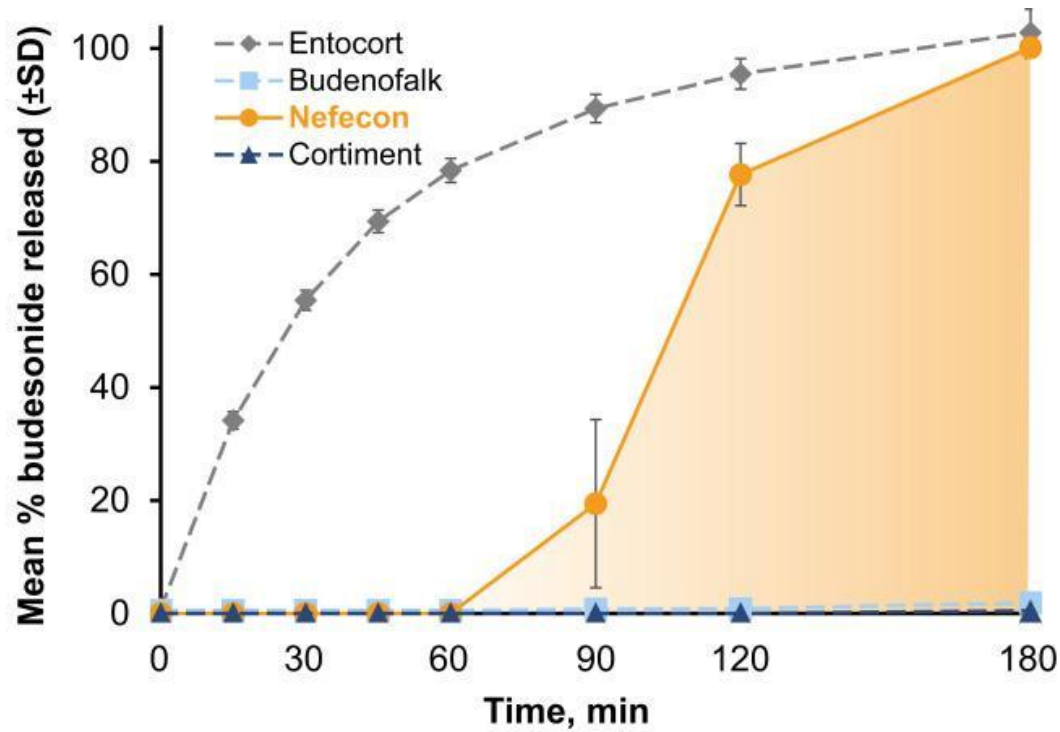
*maximum 32mg/day for 2 months then weaned over a total treatment duration of 6-9 months

Response to corticosteroids by baseline eGFR and proteinuria



Points to consider when choosing a treatment and/or treatment combinations for patients with IgAN

- **Age:** STOIgAN and TESTING studies participants are at least 7-9 years younger than that of Nefigard trial
- **Race:** The TESTING study was almost exclusively conducted in Asian patients. STOP-IgAN was exclusively conducted in Caucasians. In the NeflgArd Asian patients were relatively underrepresented compared with those in trials systemic glucocorticoids.
- **Accessibility:** Nefecon is not currently approved nor available in Australia and New Zealand



Not all budesonide formulations are equal

Barratt et al, Drug Des Devel Ther. 2024 Jul 3:18:3415-3428.

2024 KDIGO Guidelines on Treatments : Beyond Supportive Care

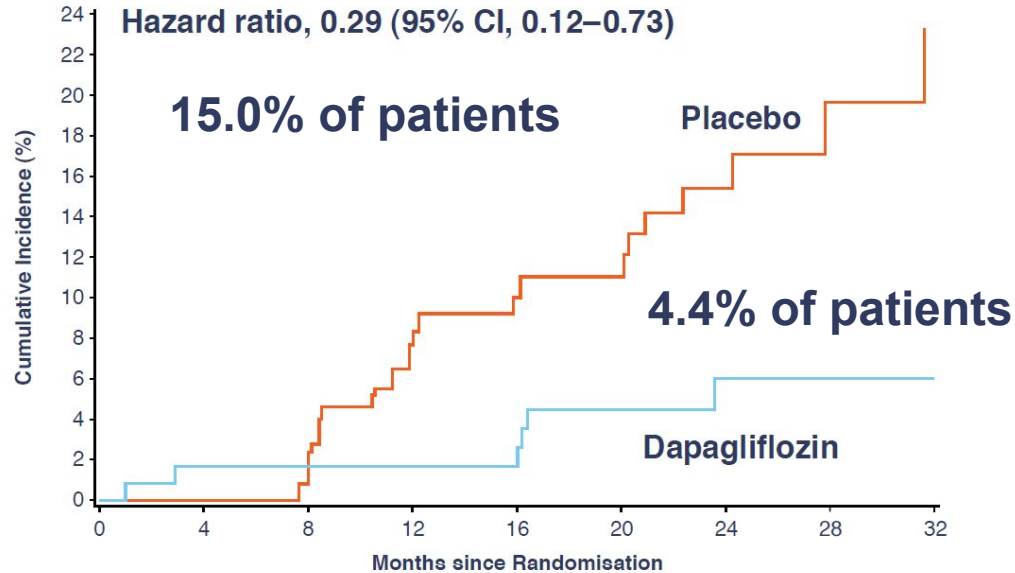
Agent	Suggested usage	Remarks
Antiplatelet agents	Not recommended	No evidence of efficacy
Anticoagulants	Not recommended	No evidence of efficacy
Azathioprine	Not recommended	No evidence of efficacy as monotherapy or when combined with glucocorticoids
Cyclophosphamide	Not recommended	Unless in the setting of rapidly progressive IgAN
Calcineurin inhibitors	Not recommended	No evidence of efficacy
Rituximab	Not recommended	No evidence of efficacy
Fish oil	Not recommended	Patients who wish to take fish oil should be advised of the dose and formulation used in the published clinical trials that reported efficacy.

Despite current available treatment options, there is an unmet need for an effective and safe disease-modifying treatment agent that can delay the onset of ESKD for patients with IgAN at high risk of progression^{1,2}

Treatment with systemic glucocorticoids should incorporate antimicrobial prophylaxis against *bacteria* and virus, along with gastroprotection and bone protection according to local guidelines

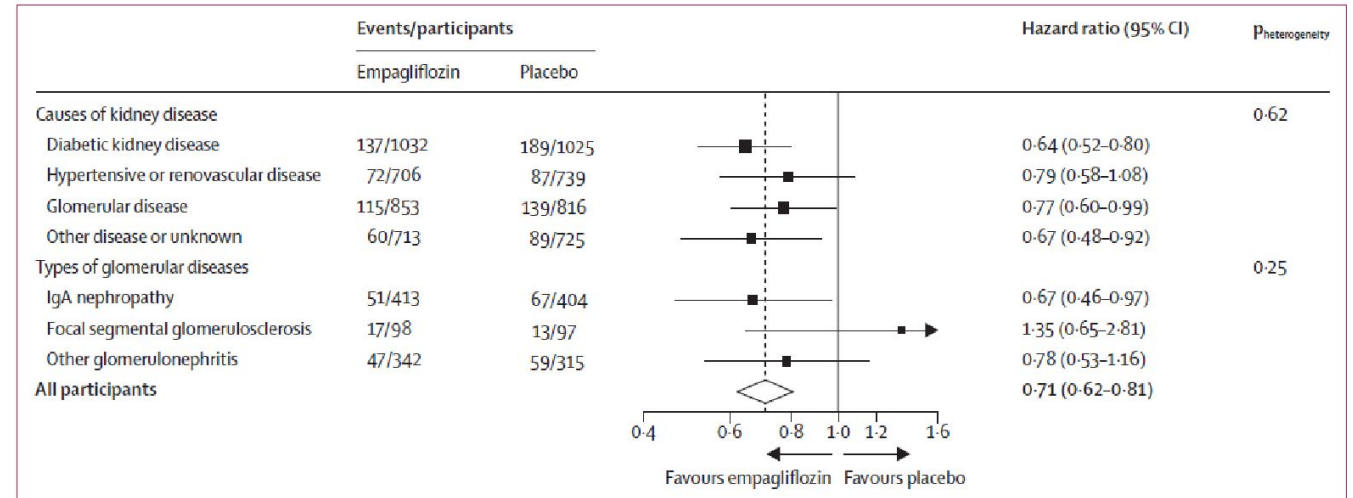
SGLT-2 inhibitors in IgA nephropathy

DAPA-CKD



No. at Risk	0	4	8	12	16	20	24	28	32
Dapagliflozin	137	107	106	105	104	98	61	43	17
Placebo	133	113	108	101	96	92	51	32	19

EMPA-KIDNEY



HR 0.67 95% CI 0.46-0.97

Kidney disease progression: as a sustained $\geq 40\%$ eGFR decline from randomisation, end-stage kidney disease, a sustained eGFR below 10 mL/min per 1.73 m², or death from kidney failure



Sparsentan received full FDA approval for Rx of IgAN

Efficacy and safety of sparsentan versus irbesartan in patients with IgA nephropathy (PROTECT): 2-year results from a randomised, active-controlled, phase 3 trial

Brad H Rovin*, Jonathan Barratt*, Hiddo J L Heerspink, Charles E Alpers, Stewart Bieler, Dong-Wan Chae, Ulysses A Diva, Jürgen Floege, Loreto Gesualdo, Julia K Inrig, Donald E Kohan, Radko Komers, Laura Ann Kooienga, Richard Lafayette, Bart Maes, Robert Malecki, Alex Mercer, Irene L Noronha, Se Won Oh, Chen Au Peh, Manuel Praga, Priscila Preciado, Jai Radhakrishnan, Michelle N Rheault, William E Rote, Sydney C W Tang, Vladimir Tesar, Howard Trachtman, Hernán Trimarchi, James A Tumlin, Muh Geot Wong, Vlado Perkovic, on behalf of the DUPRO steering committee and PROTECT Investigators†

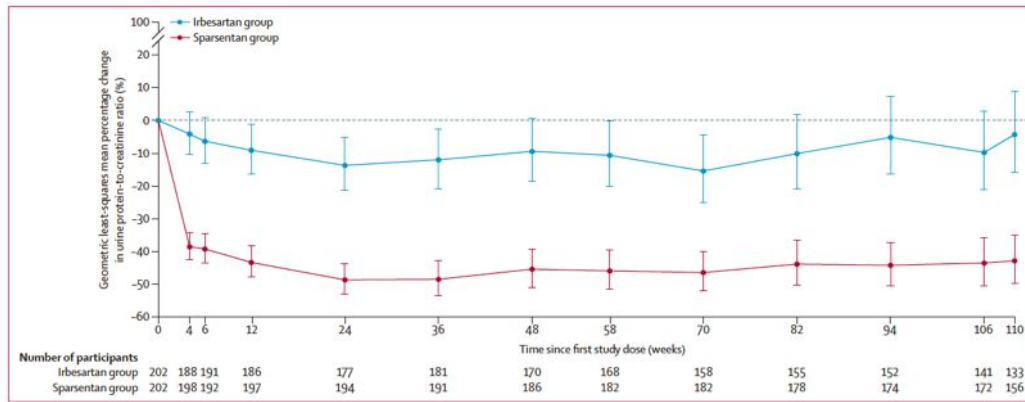


Figure 5: Geometric least-squares mean percentage change from baseline in the urine protein-to-creatinine ratio at each visit up to week 110. Error bars indicate 95% CIs.

Sparsentan treatment results in significantly greater decline in proteinuria than treatment with an ARB alone, and this decline in proteinuria is associated with a significant preservation of kidney function.

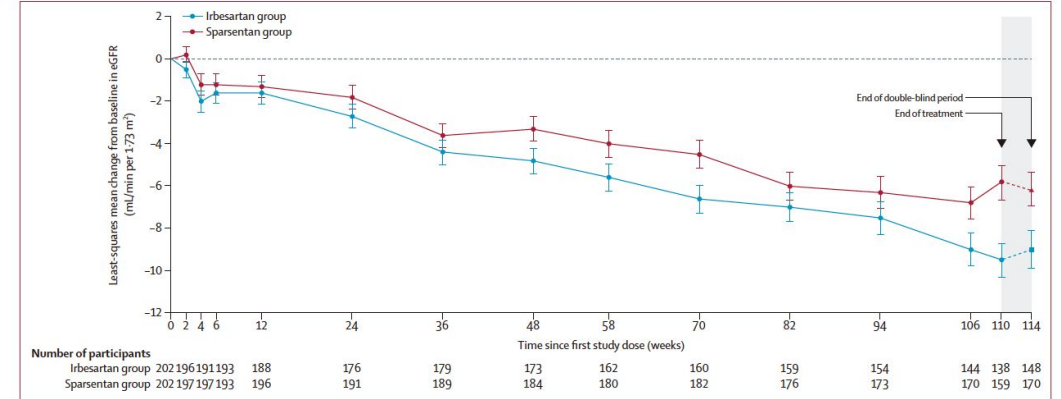


Figure 2: eGFR by visit up to week 114. Change from baseline in eGFR at week 6 or 114 was assessed with ANCOVA, and change from baseline in eGFR to other timepoints up to week 110 were analysed via a mixed model for repeated measures. Error bars indicate SEs. eGFR=estimated glomerular filtration rate.

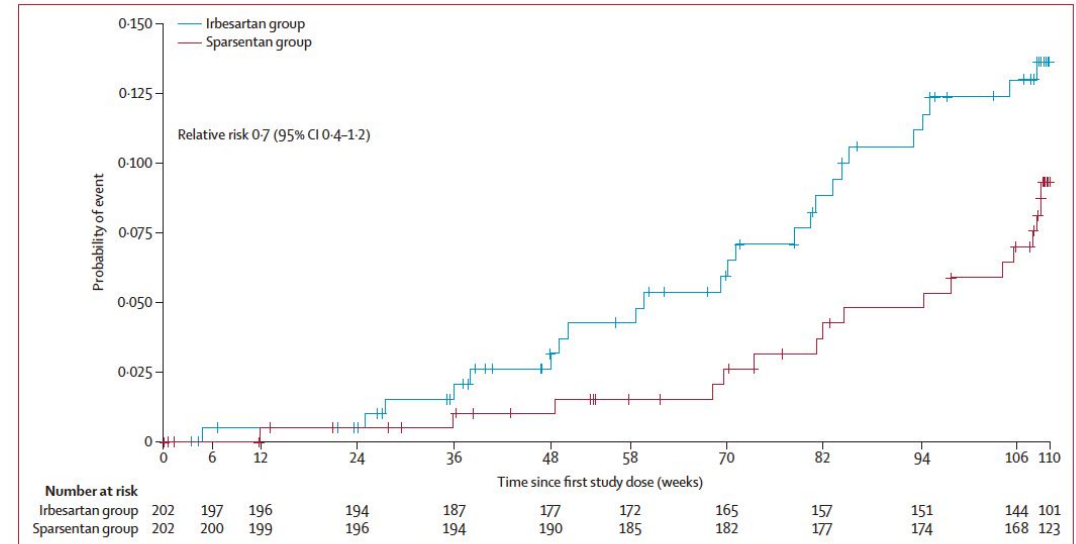
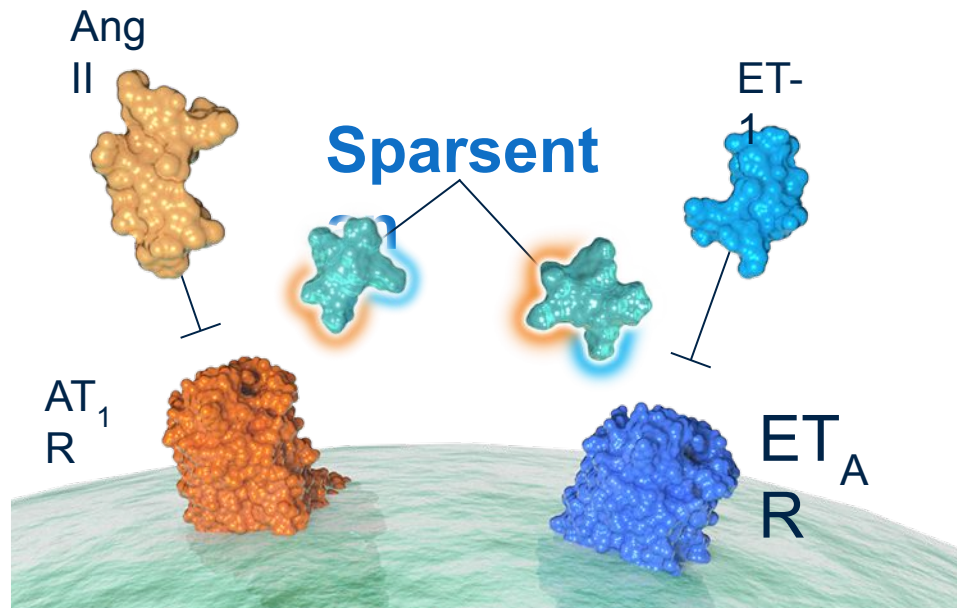


Figure 4: Time to reach the composite kidney failure endpoint of confirmed 40% eGFR reduction, end-stage kidney disease, or all-cause mortality. Vertical bars indicate censored patients. eGFR=estimated glomerular filtration rate.

Sparsentan- a dual ETR_A antagonist and A₁RB (DEARA)



International Journal of Nephrology and Renovascular Disease

Dovepress

open access to scientific and medical research

Open Access Full Text Article

REVIEW

Practical Considerations for the Use of Sparsentan in the Treatment of Patients with IgAN in Clinical Practice

Kirk N Campbell¹, Siân Griffin², Howard Trachtman³, Rob Geletka⁴,
Muh Geot Wong^{5,6}

¹Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, USA; ²Department of Nephrology, University Hospital of Wales, Cardiff, UK; ³Department of Pediatrics, University of Michigan, Ann Arbor, MI, USA; ⁴Travere Therapeutics, Inc., San Diego, CA, USA; ⁵Department of Renal Medicine, Concord Repatriation General Hospital, Concord, NSW, Australia; ⁶Concord Clinical School, University of Sydney, Concord, NSW, Australia

Correspondence: Kirk N Campbell, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, Box 1243, New York, NY, 10029, USA, Tel +1 212-241-6271, Fax +1 212-987-0389, Email kirk.campbell@mssm.edu



* Sparsentan is an investigational compound for treatment of primary or genetic FSGS and IgAN. It is not approved by any regulatory agency.

Ang II = angiotensin II; ARB = angiotensin receptor blocker; AT₁R = angiotensin II receptor type 1; CV = cardiovascular; ETR_A = endothelin receptor type A;

ET-1 = endothelin 1; IgA = immunoglobulin A.

1. Kowala MC, et al. *J Pharmacol Exp Ther* 2004; **309**:275–284; 2. Komers R & Plotkin H. *Am J Physiol Regul Integr Comp Physiol* 2016; **310**:R877–R884;

3. Trachtman H, et al. *J Am Soc Nephrol* 2018; **29**:2745–2754; 4. Heerspink HJL, et al. *Lancet* 2019; **393**:1937–1947; 5. Palmer SC et al. *Lancet* 2015; **385**:2047–2056;

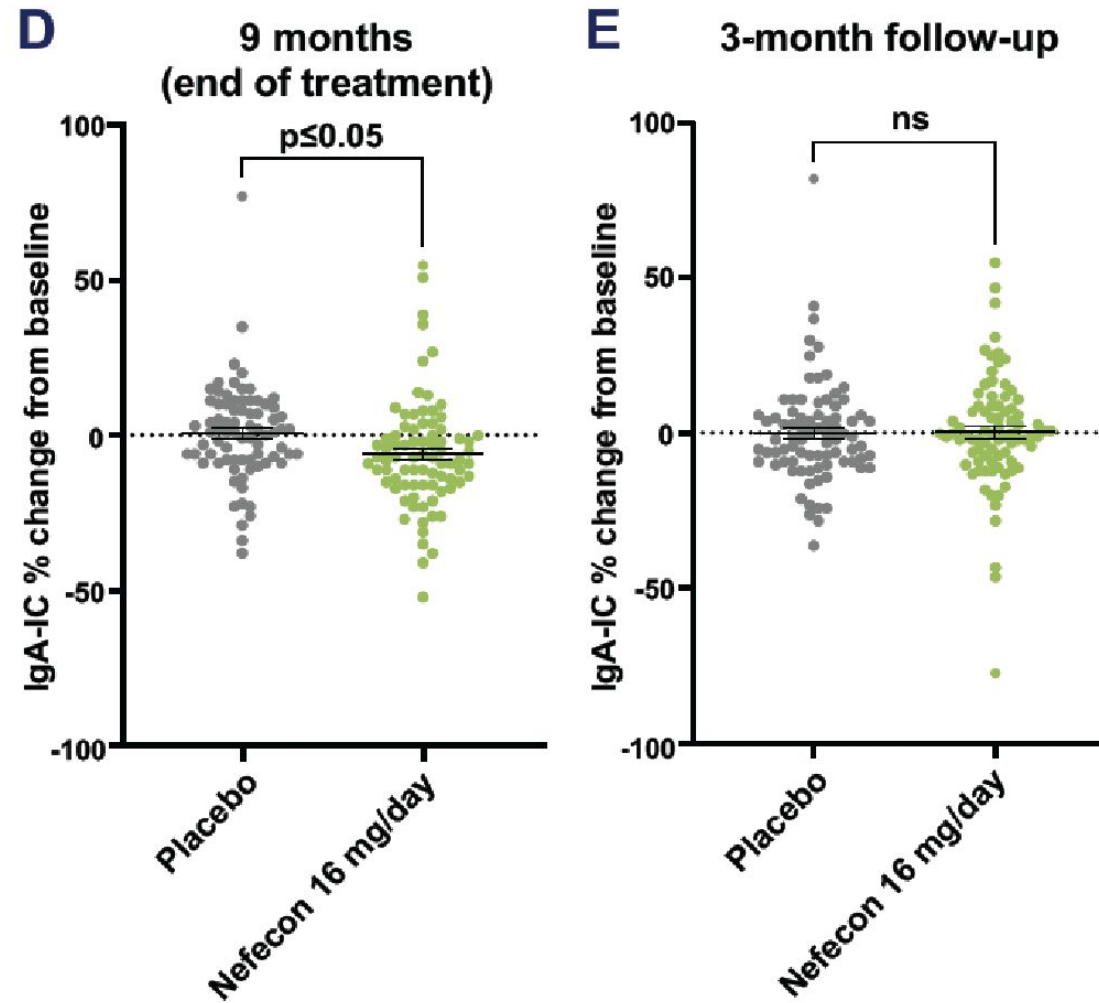
6. Dezsi CA. *Am J Cardiovasc Drugs* 2016; **16**:255–266. Figure © 2021 Travere Therapeutics, Inc. All rights reserved.



Points to consider when choosing a treatment and/or treatment combinations for patients with IgAN

- **Age:** Age: In the trials of SGLT2i, patients older. On average 6–8 years older than those recruited into the NeflgArd and PROTECT trials and 15–17 years older than those recruited into the STOPIgAN and TESTING studies.
- **eGFR:** In the trials of SGLT2i, the average eGFR at inclusion was 12–14 ml/min per 1.73 m² lower than that of patients included in the NeflgArd, PROTECT, STOP-IgAN, and TESTING studies.
- **RAASi optimization for 90 days:** Not required in the trials of SGLT2i.
- **Sparsentan** is the only drug to have shown efficacy beyond the in-trial uptitrated RASi.
- **SGLT2i** have been shown to both CV and renal protection, particularly in people with diabetes. They are also generally well tolerated.

9 months Rx of Nefecon reduced circulating GdIgA1 levels that reversed to baseline following cessation



Targeted-release budesonide modifies key pathogenic biomarkers in immunoglobulin A nephropathy: Insights from the NEFIGAN trial

Biomarkers with significant changes from baseline at 9 months with Nefecon 16 mg/d

Objective: To assess the effect of Nefecon on the various molecular mechanisms involved in the pathogenesis of IgAN



150 patients with IgAN

Randomized
and dosed

Nefecon 8 mg/d: n = 51

Nefecon 16 mg/d: n = 49

Placebo: n = 50

9 months of treatment → 3-month follow-up

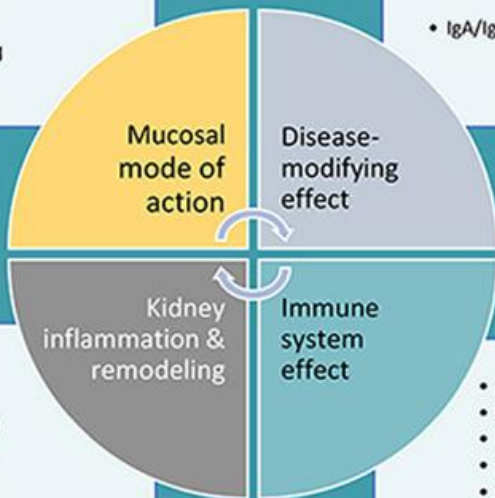


Blood and urine samples



Robust regression analysis
and protein-protein
interactions network

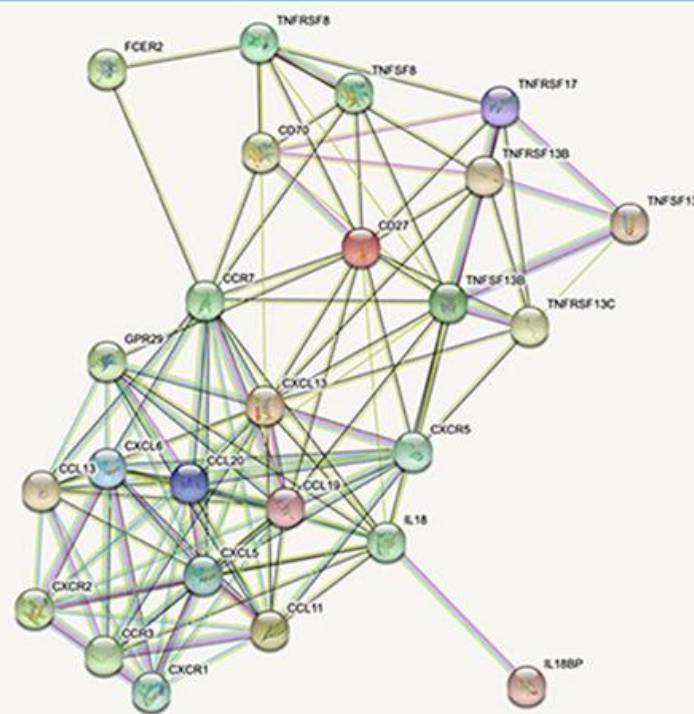
- FABP2
- Secretory IgA
- Antigliadin A
- Anticasein A
- Tetanus toxoid



- IgA1
- Total IgG
- Total IgA
- IgA/IgG immune complexes
- Gd-IgA1

- Plasma MASP3
- Urine MBL/Cr
- sCD163/Cr
- Urine C3M/Cr
- Plasma PRO-C6
- Plasma C3M

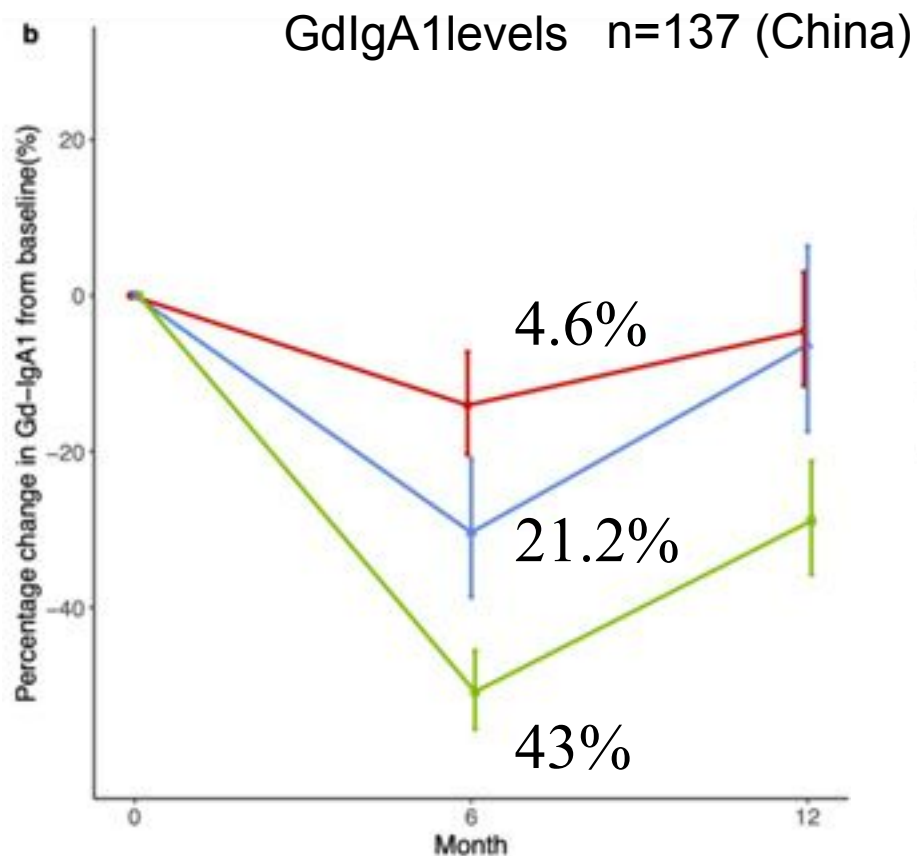
- APRIL
- BAFF
- BCMA
- sCD23
- sCD27
- sCD30
- CCL11
- CCL13
- CCL19
- CCL20
- CXCL5
- CXCL6
- CXCL13
- IL-18BPα



CONCLUSION

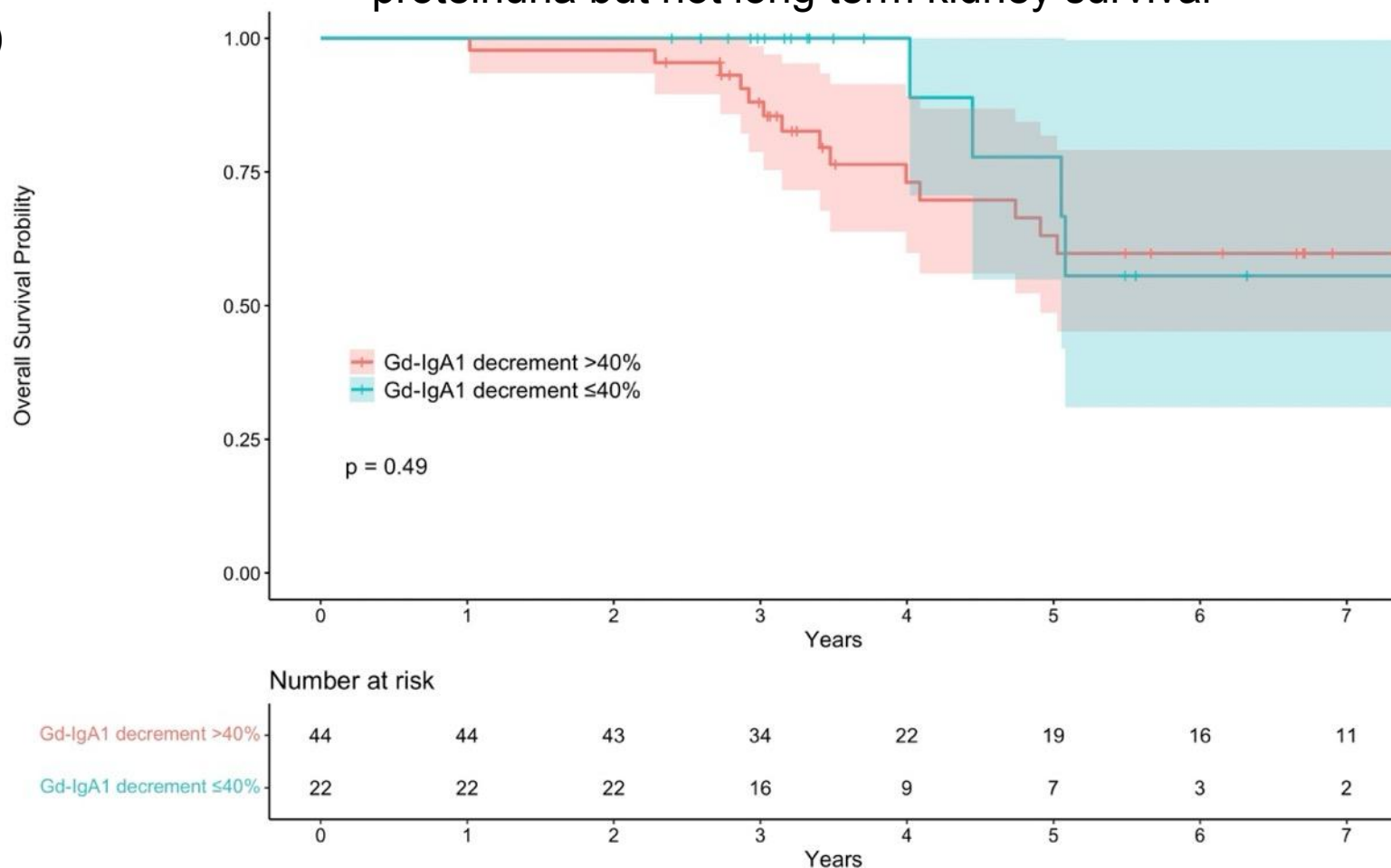
Nefecon exerts a direct disease-modifying effect in IgAN by targeting the GALT, regulating mucosal immune dysfunction and potentially modulating the systemic immune response

TESTING trial: Corticosteroids and circulating GdIgA1 levels



Placebo —
 Full dose —
 Reduced dose —

Greater reduction in GdIgA1 at 6 months correlates to proteinuria but not long term kidney survival

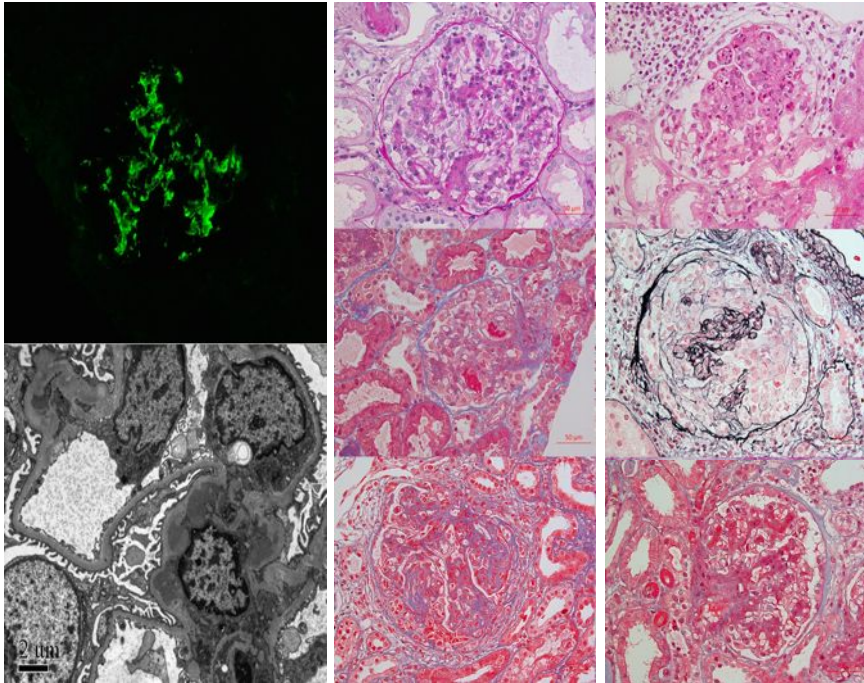


Zan et al (Accepted for publication, CJASN)



IgA nephropathy

Clinical-pathological presentation is highly variable



- ❑ Histopathology and clinical presentation: highly variable
- ❑ Oxford's classification: MEST-C scores widely used
- ❑ There is insufficient evidence to support the use of the Oxford Classification MEST-C score in determining which drug should be commenced in IgAN.

The mechanisms responsible for the presentation and development of IgAN are incompletely understood, and this has limited development of highly targeted therapies for this disease.

Predictive value of the Oxford Classification for the effect of glucocorticoid therapy in IgA nephropathy



Secondary analysis
of TESTING trial



N=279
Chinese participants
with kidney biopsy
slides available for
central pathology
review



Glucocorticoid
therapy

Median Bx → Rx = 4 months



Oxford classification



Composite outcome of $\geq 40\%$
reduction in eGFR, kidney failure,
or death due to kidney disease

No crescents (C0)

HR 0.6 [95% CI, 0.4–0.9]

With crescents (C1/C2)

HR 0.05 [95% CI, 0.008–0.3]

P for
interaction
=0.4



New subclassification
of segmental sclerosis (S1)



Risk of kidney failure

With hypercellularity
(cellular segmental sclerosis)

HR 0.2 [95% CI, 0.07–0.4]

Without hypercellularity

HR 0.6 [95% CI, 0.4–1.0]

P for
interaction
=0.03

Conclusions: Crescents and cellular segmental sclerosis in IgA nephropathy suggested a favorable response to glucocorticoid therapy.

Sufang Shi, Ian S.D. Roberts, Zixuan Wang, et al. **Predictive Value of the Oxford Classification for the Effect of Glucocorticoid Therapy in IgA Nephropathy.** JASN DOI: 10.1681/ASN.0000000796. Visual Abstract by Paolo Nikolai So, MD

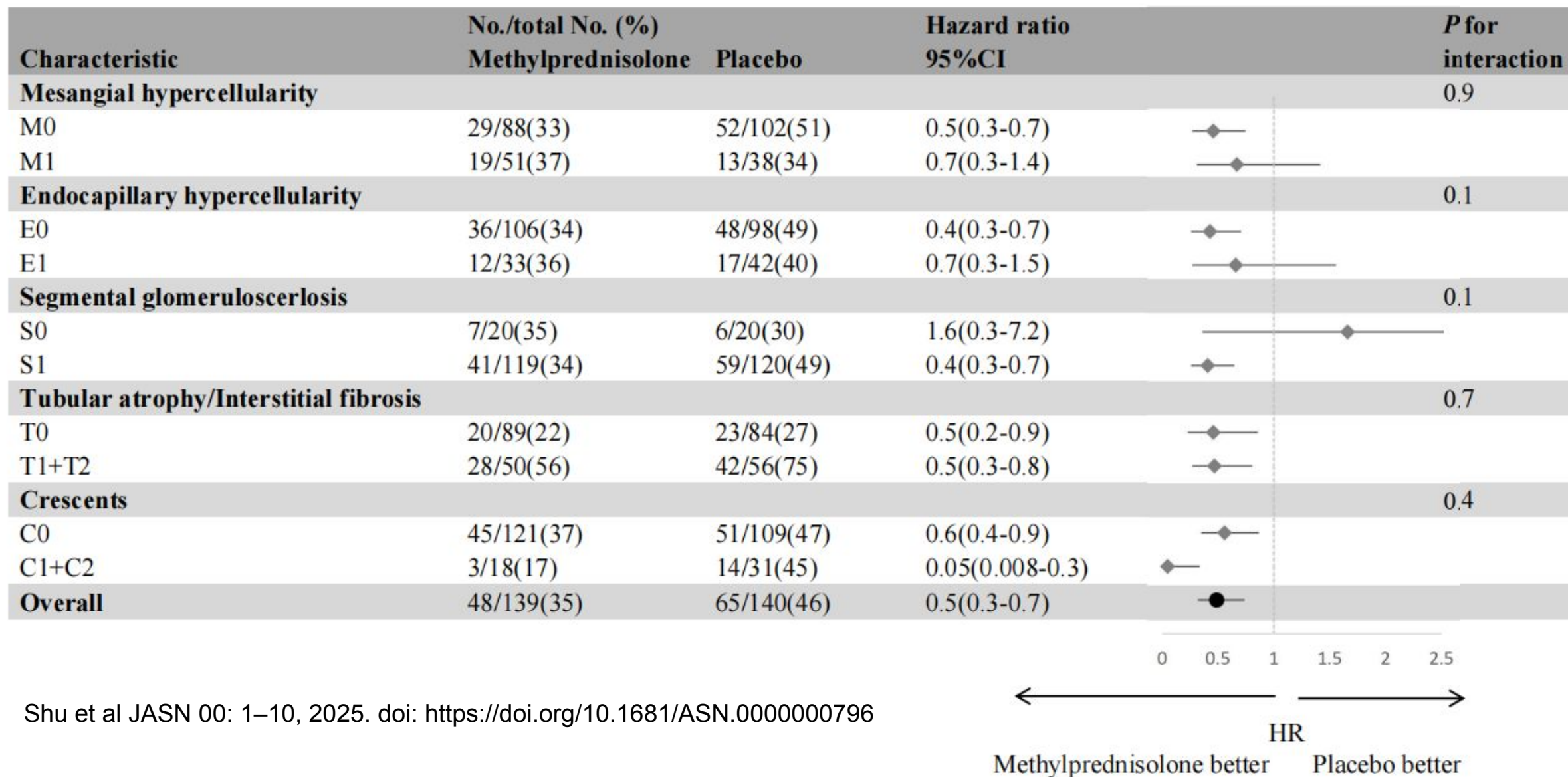
Disagreement between local and central pathology review

Pathology lesions	Central pathological review	Local pathology report	Kappa value
M1(%)	89/279(32)	160/272(59)	0.1
E1(%)	75/279(27)	82/279(29)	0.2
S1(%)	239/279(86)	200/272(74)	0.1
T0(%)	173/279(62)	114/272(42)	0.3
T1(%)	84/279(30)	110/272(40)	0.3
T2(%)	22/279(8)	48/272(18)	0.3
C0(%)	230/279(82)	102/274(37)	0.1
C1(%)	48/279(17)	127/274(46)	0.1
C2(%)	1/279(0.4)	45/274(16)	0.1

M, mesangial hypercellularity; E, endocapillary hypercellularity; S, segmental sclerosis; T, tubular atrophy/interstitial fibrosis; C, cellular/fibrocellular crescents.

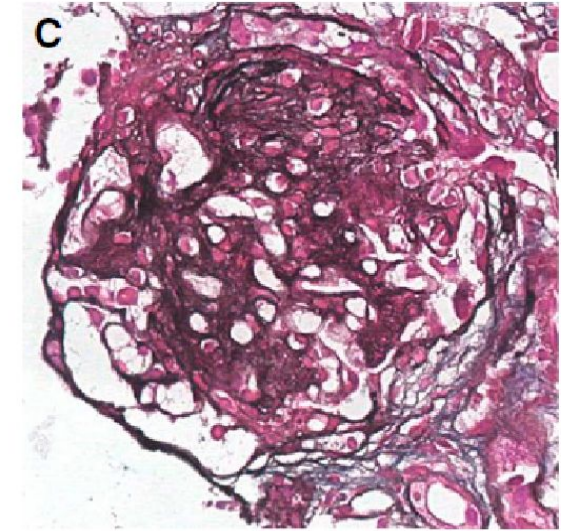
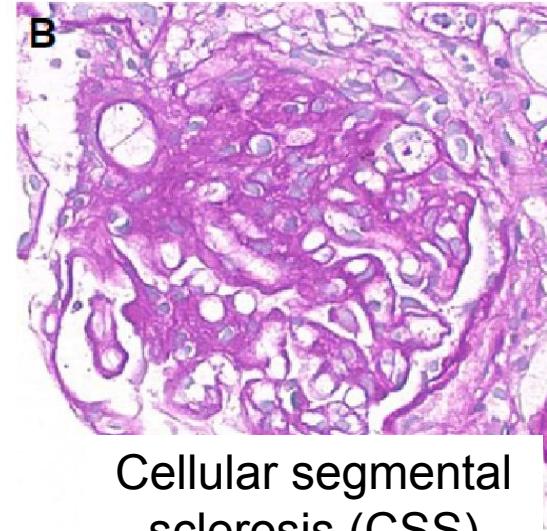
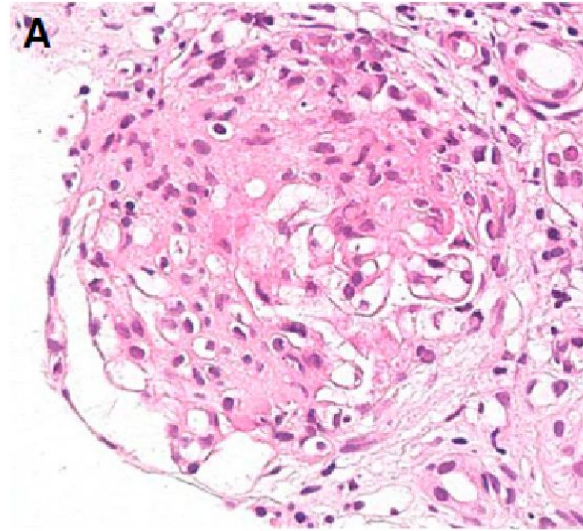
Shu et al JASN 00: 1–10, 2025. doi: <https://doi.org/10.1681/ASN.0000000796>

The effect of methylprednisolone treatment on the kidney outcomes stratified by centrally reviewed MEST-C scores

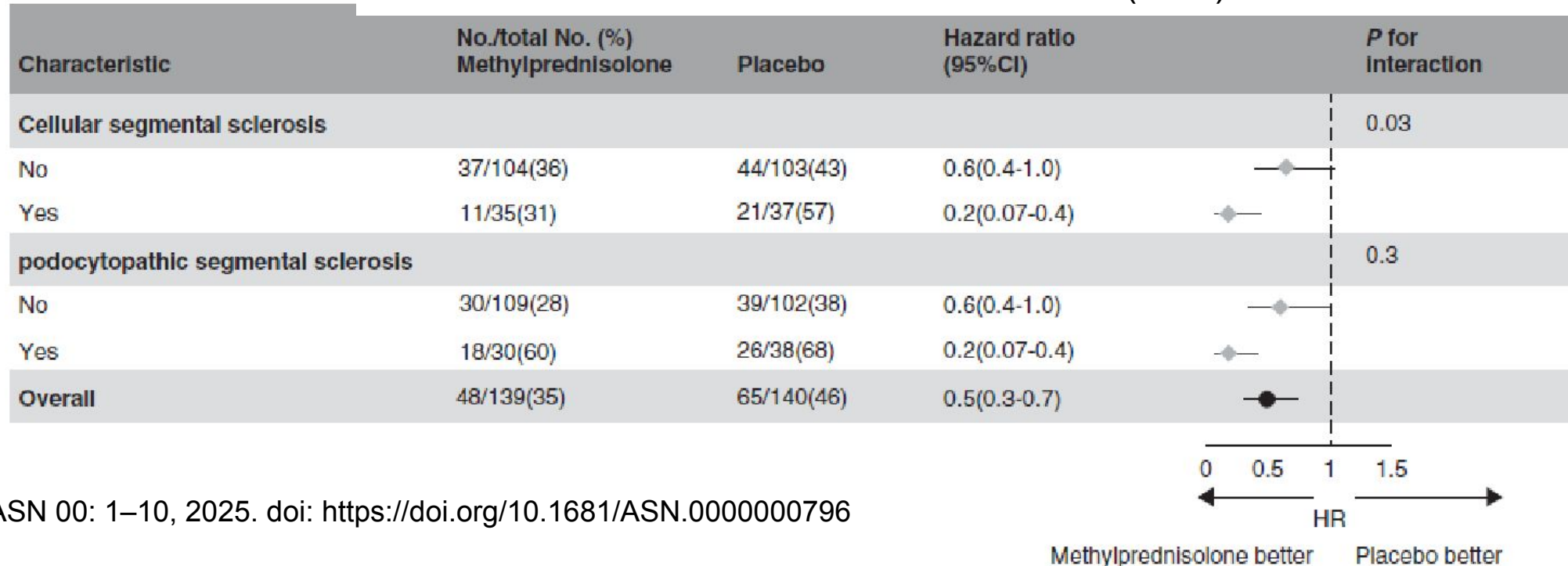


Subtype of S lesions

- Cellular segmental sclerosis



Cellular segmental sclerosis (CSS)



Shu et al JASN 00: 1–10, 2025. doi: <https://doi.org/10.1681/ASN.0000000796>

International IgAN (IIGAN) Prediction tool for adults

Calculator About References

★ 📌 International IgAN Prediction Tool at biopsy - Adults

Determine prognosis in adults with IgA nephropathy

Questions

1. Estimated GFR at biopsy	90 ml/min/1.73m2
2. Systolic blood pressure at biopsy	134 mmHg
3. Diastolic blood pressure at biopsy	90 mmHg
4. Proteinuria at biopsy	3 g/day
5. Age at biopsy	28 Years
6. Race	Caucasian
7. Use of ACE inhibitor or ARB at the time of biopsy	Yes
8. MEST M-score	0
9. MEST E-score	0
10. MEST S-score	0
11. MEST T-score	1
12. Immunosuppression use at or prior to biopsy	No
13. At how many months after renal biopsy would y...	60 Months

Results

★ Save 📄 Copy Results

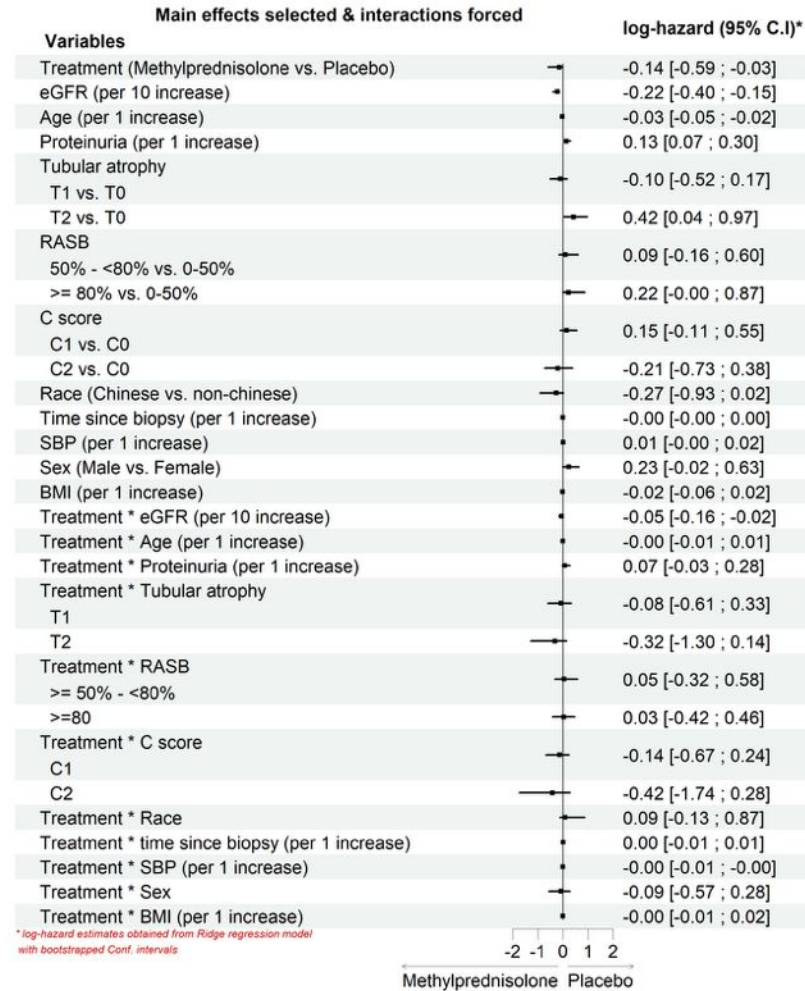
Risk of Progression

The risk of a 50% decline in estimated GFR or progression to end-stage renal disease 5.0 years after renal biopsy is 17.59%

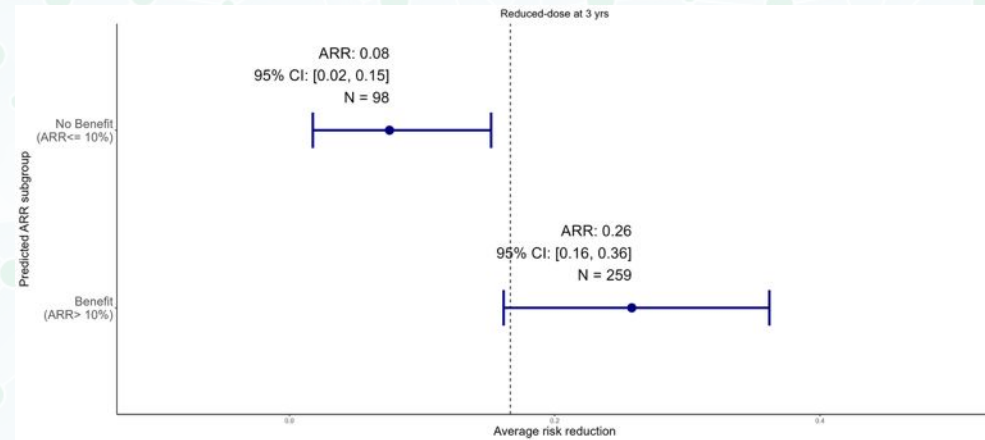
• Caveats

- Requires recent kidney biopsy validated up to 2 years from kidney biopsy
- Predict risk up to 5 years
- Does not predict treatment response

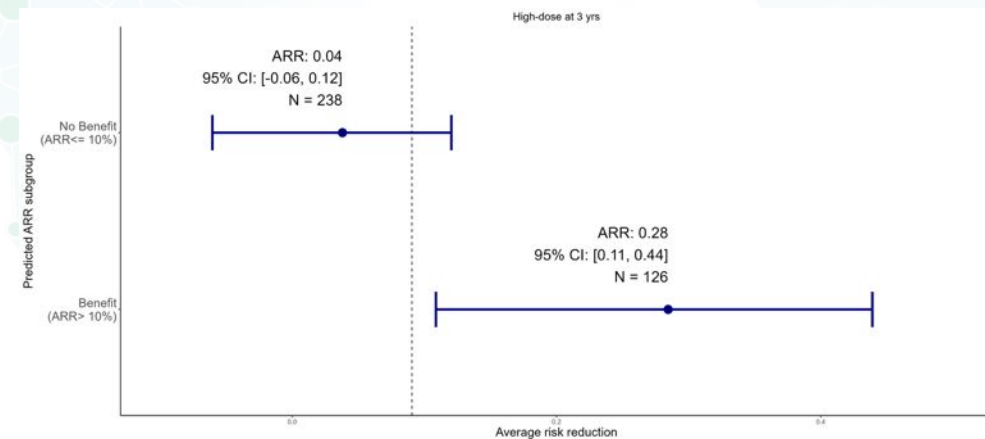
Predicting who is more likely to benefit from corticosteroids



Reduced dose



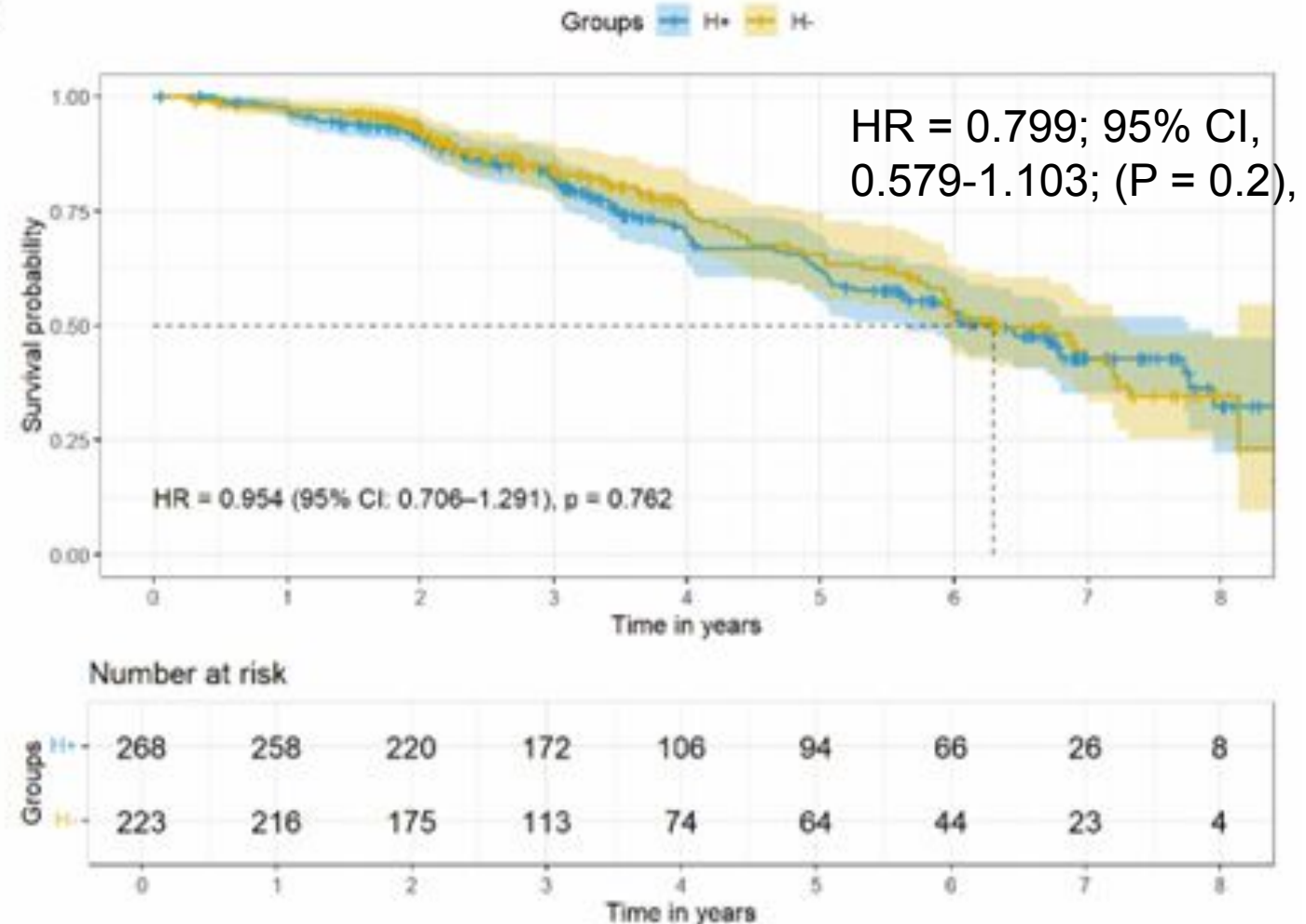
Full dose



HAEMATURIA AND KIDNEY OUTCOMES

- Post hoc analysis of TESTING trial (n=491/503 (>97%) participants)
- Hematuria remission: time-averaged hematuria ≤ 5 RBC/HPF.
- Proteinuria remission: time-averaged proteinuria < 1.0 g/day
- Composite kidney outcomes: 40% eGFR decline, Kidney failure and death dt kidney disease
- Median f/up of 3.5 years
- Methylprednisolone significantly increased remission rates of hematuria (50.8% vs. 39.9%, $P = 0.020$), haematuria remission is not associated with kidney outcomes

A



Sex Differences across Corticosteroid Response and Outcomes in IgA Nephropathy



Post-hoc analysis of the TESTING trial

Median follow-up of 4.2 years



Randomized Controlled Trial
International, multicenter, and double-blind study



Biopsy-proven IgA
with proteinuria >1g/day despite 12 weeks of supportive care



Oral Methylprednisolone
Full-dose (0.6-0.8mg/kg/day)
Reduced-dose (0.4mg/kg/day)



Sex and treatment interaction
on the primary outcome's risk

Primary Composite Outcome compared to a placebo

Sustained 40% ↓ in eGFR, KF, or death due to kidney disease



HR 0.64
CI 0.38-1.09



HR 0.51
CI 0.35-0.74

P-interaction=0.47



Methylprednisolone also decreased proteinuria from baseline at 12 months and slowed the overall decline of eGFR, with no differences between sexes



Males were at a greater risk of the primary outcome than females

HR 1.44
CI 1.05-1.97

Total eGFR rate of decline over 2 years was also greater in males

3.13
mL/min/1.73m²/year

Summary



Change in paradigm in managing patients with IgAN that aim at early detection, early prevention of nephron loss



RCT level evidence to provide a framework and guidance in therapeutic approach for IgAN



Combination therapies are needed to target both pathogenic IgA production, inflammation and the maladaptive responses



Better predictors to treatment response are needed



Thank you for your attention