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 Travere, Otsuka, Kira Pharma, Eledon, CSL-Behring, Dimerix, Alpine, Arrowhead, Novartis (Chinook), .

Received honorarium from AstraZeneca, Amgen, Elli Lily and Baxter, Novartis.

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

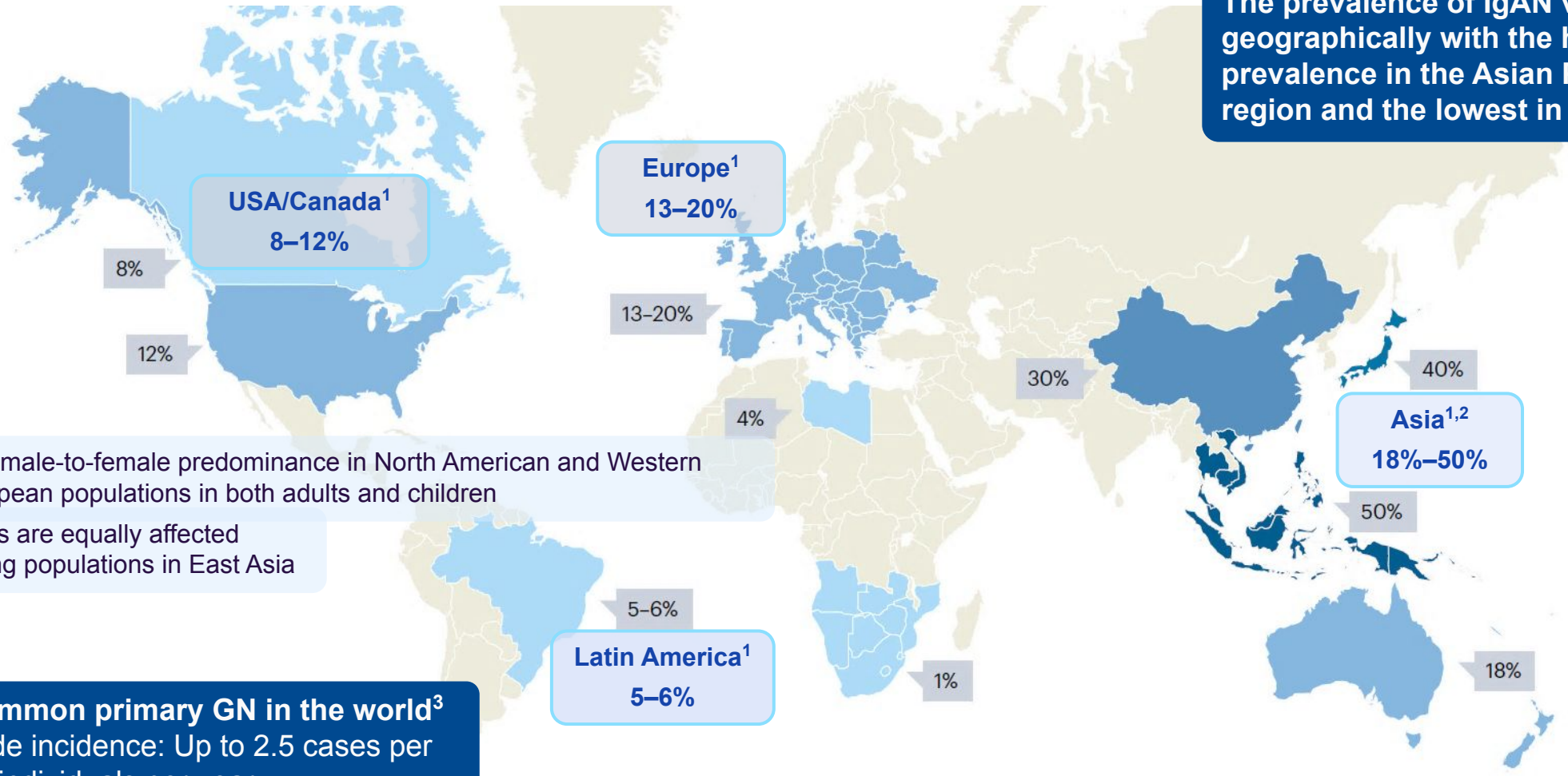
Honorary Executive Officer of Australia New Zealand Society of Nephrology (ANZSN) that received industry sponsorship for ANZSN activities

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



~2:1 male-to-female predominance in North American and Western European populations in both adults and children

Sexes are equally affected among populations in East Asia

Most common primary GN in the world[3]
Worldwide incidence: Up to 2.5 cases per 100 000 individuals per year

Incidence of IgAN in Australia

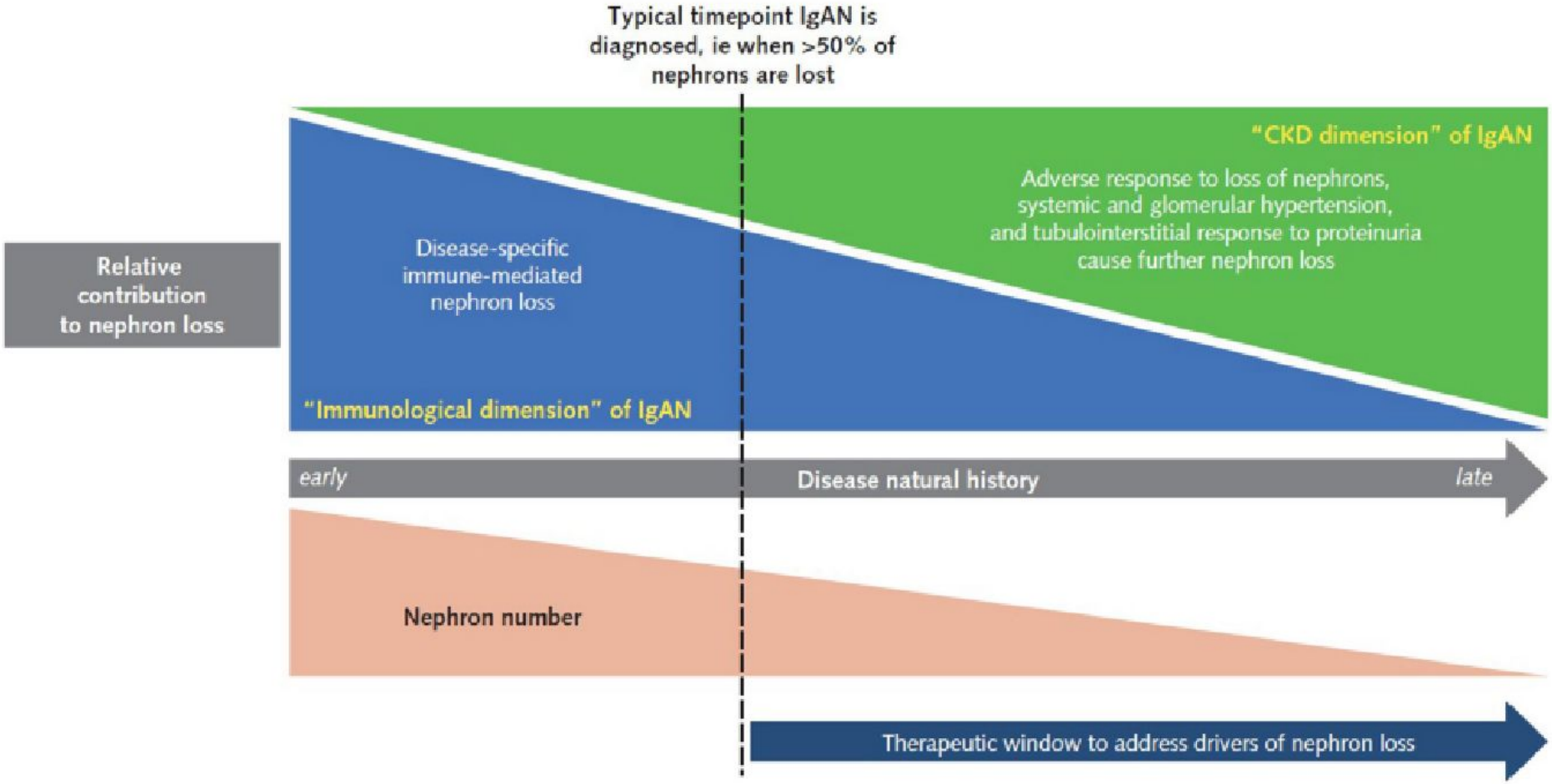
Author	**EXTEND 45**		**Briganti et al (2)**	**Jegatheesan et al (3)**
Population **Age group** **Time period** **Total population**	NSW* Age ≧ 45 years 2005-2014 215,029		Victoria All age groups 1995-1997 4,560,155	Queensland Age ≧ 18 years 2002-2011 3,404,000 in 2011
Glomerular disease	**N = 170 (%)**	**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

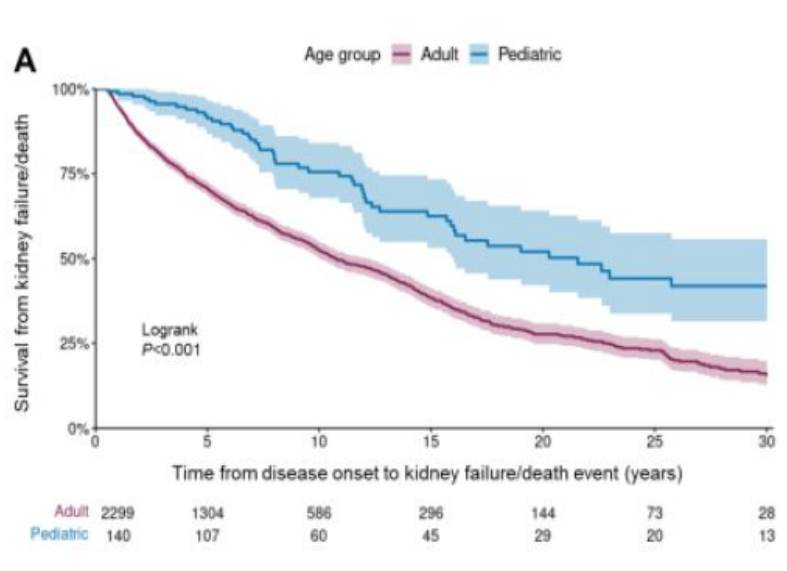
Change in concepts of therapeutic approach to IgAN

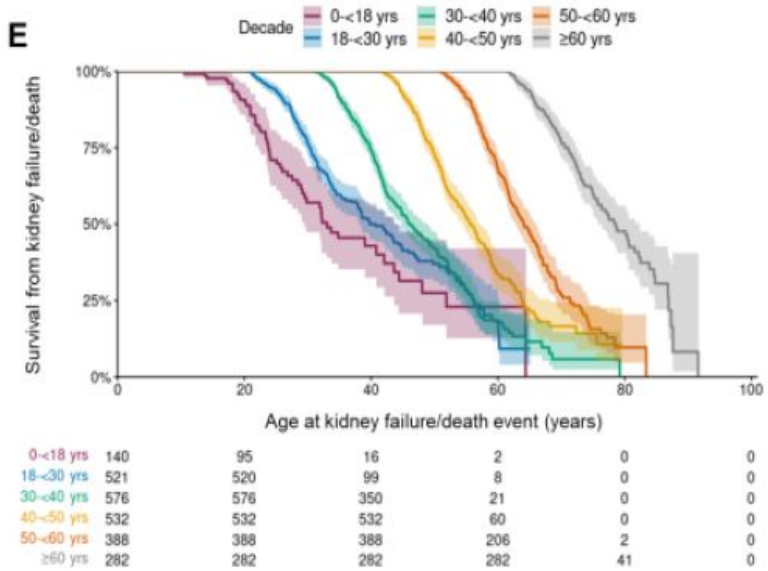


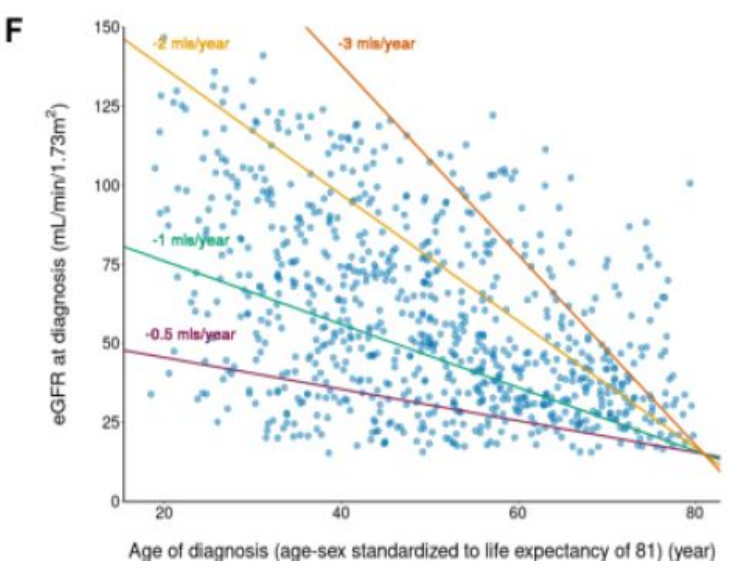
Barratt et al, Frontier in Medicine 2024

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





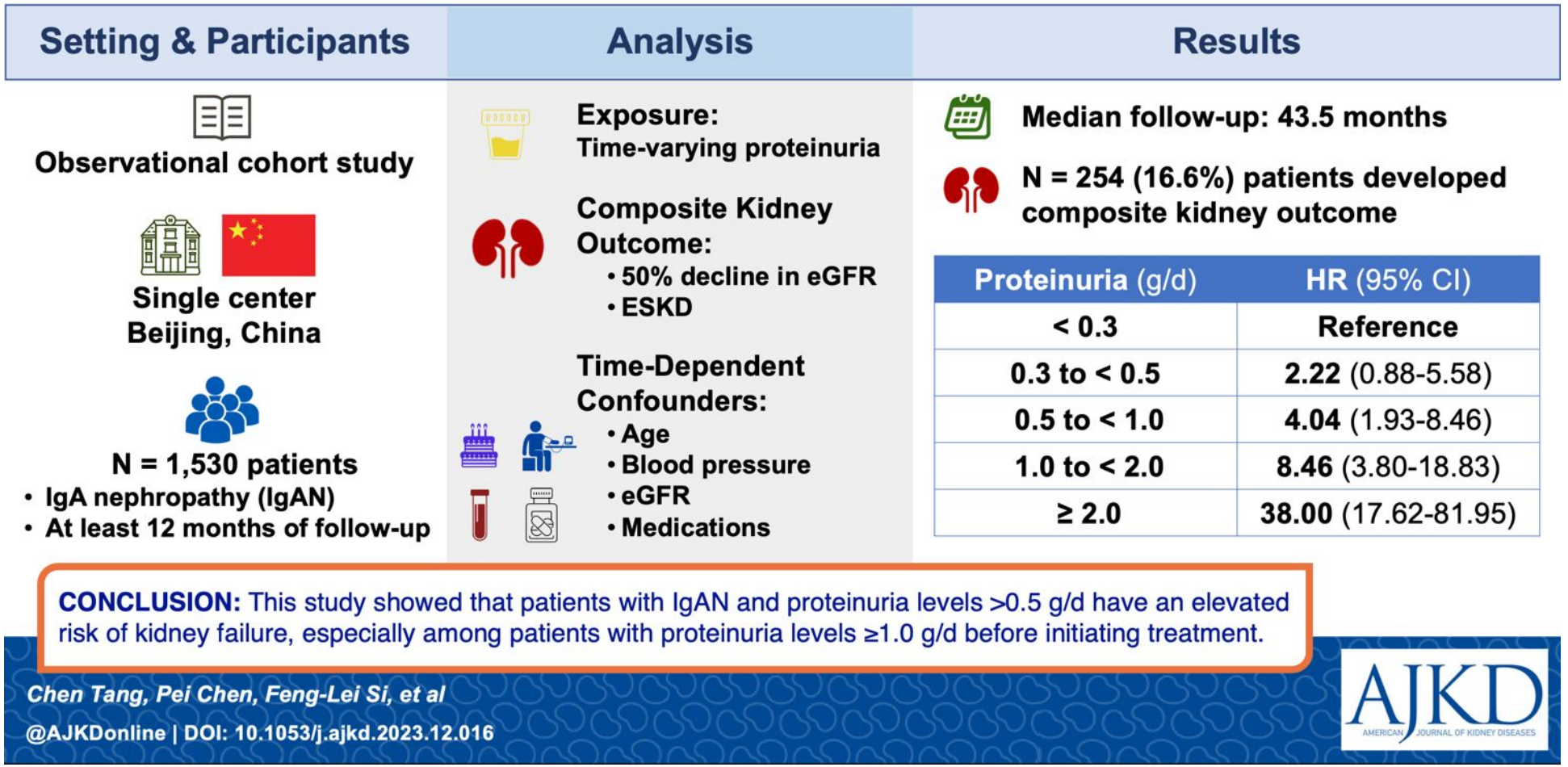


Even those patients historically categorized as "low-risk" (proteinuria <0.88 g/g), had high rates of kidney failure within 10 years

Pitcher D...Barratt J. Clin J Am Soc Nephrol. 2023 Apr 13. doi: 10.2215

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

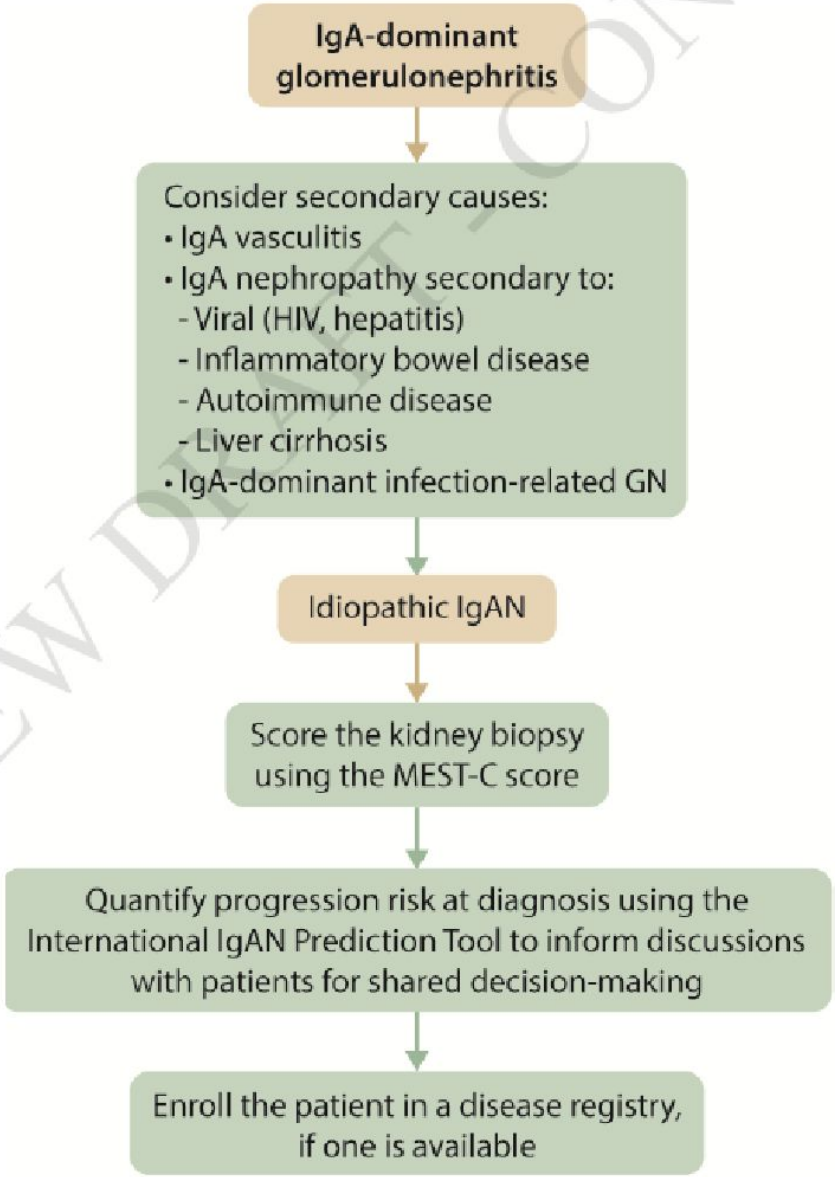


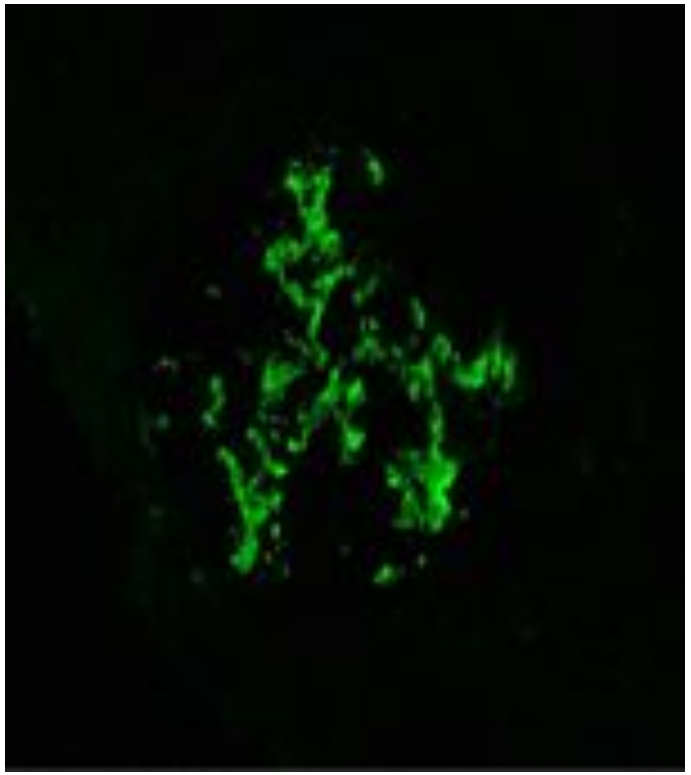
Chen Tang, … Hong Zhang. AJKD. 2023 Dec. doi: 10.1053

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.





VIEW DRAFT - CONF

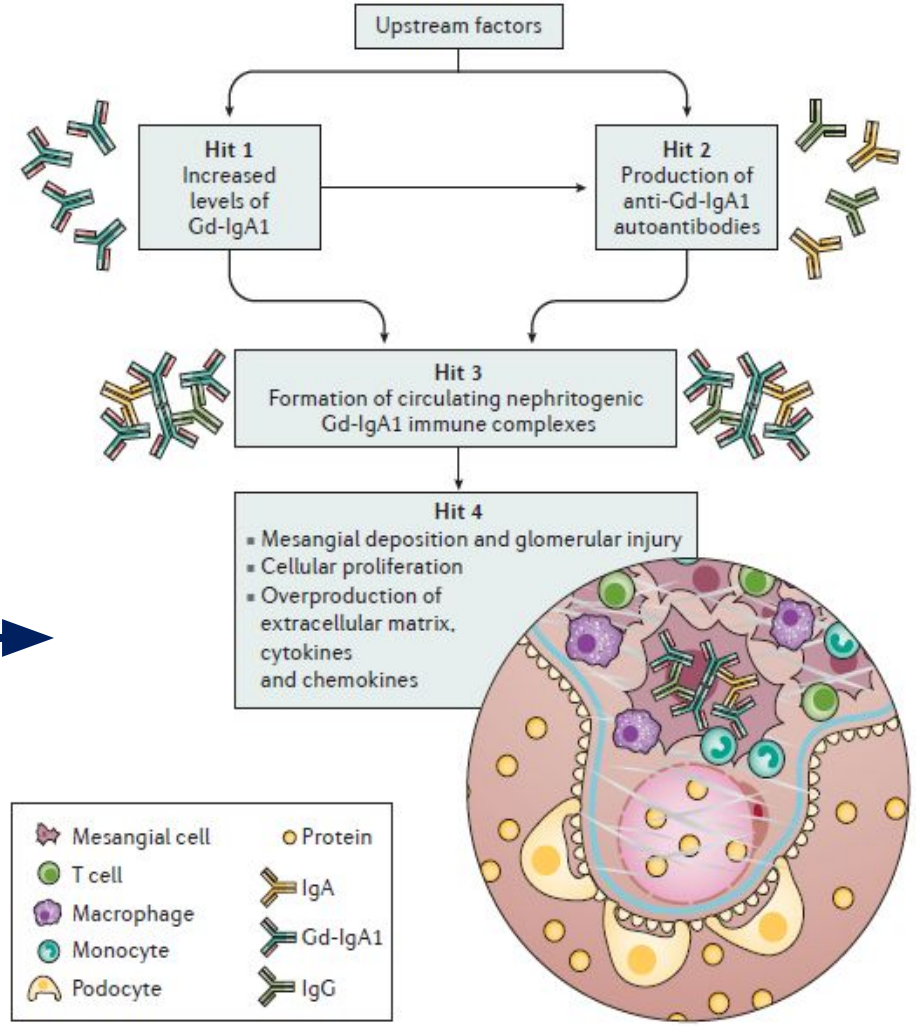
Potential therapeutic targets based on the current understanding for the pathogenesis of IgA nephropathy

Gut mucosa modulation
targeted-release budesonide

Plasma cell depleter
Felzartamab, mezagitamab

Modulate B cell activation
Inhibitors of BAFF/APRIL

Non-immunosuppressive
ET_AR inhibitor
SGLT2 inhibitor
MRA, DEARA



NATURE REVIEWS | DISEASE PRIMERS 2016;2:1-20

Complement Activation

Proteinases

Modulate B cell activation
Inhibitors of APRIL

Corticosteroids
Corticosteroids
IgA1-specific proteas

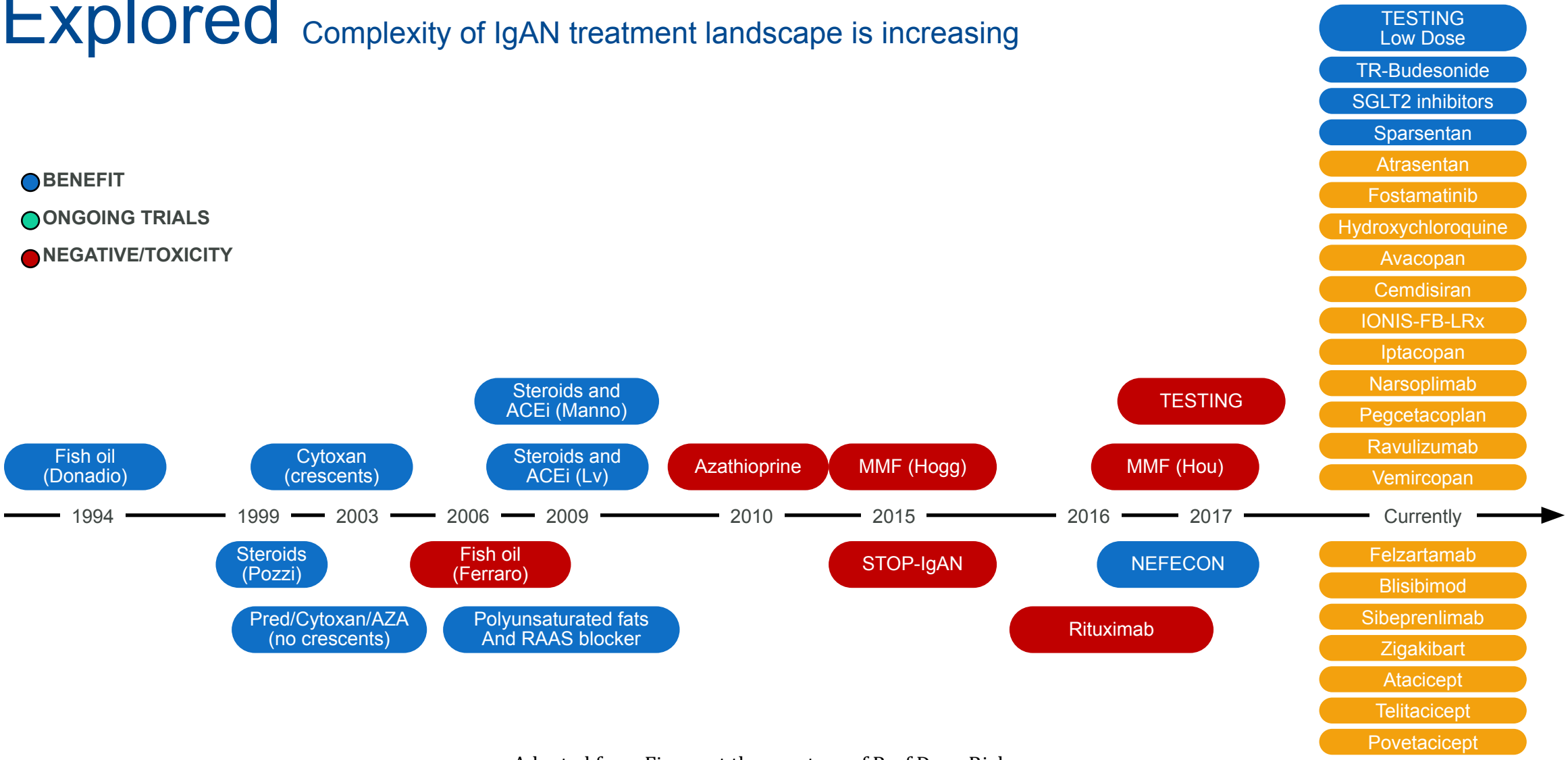
Complement modulation
Inhibit AP/LP/TP

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.

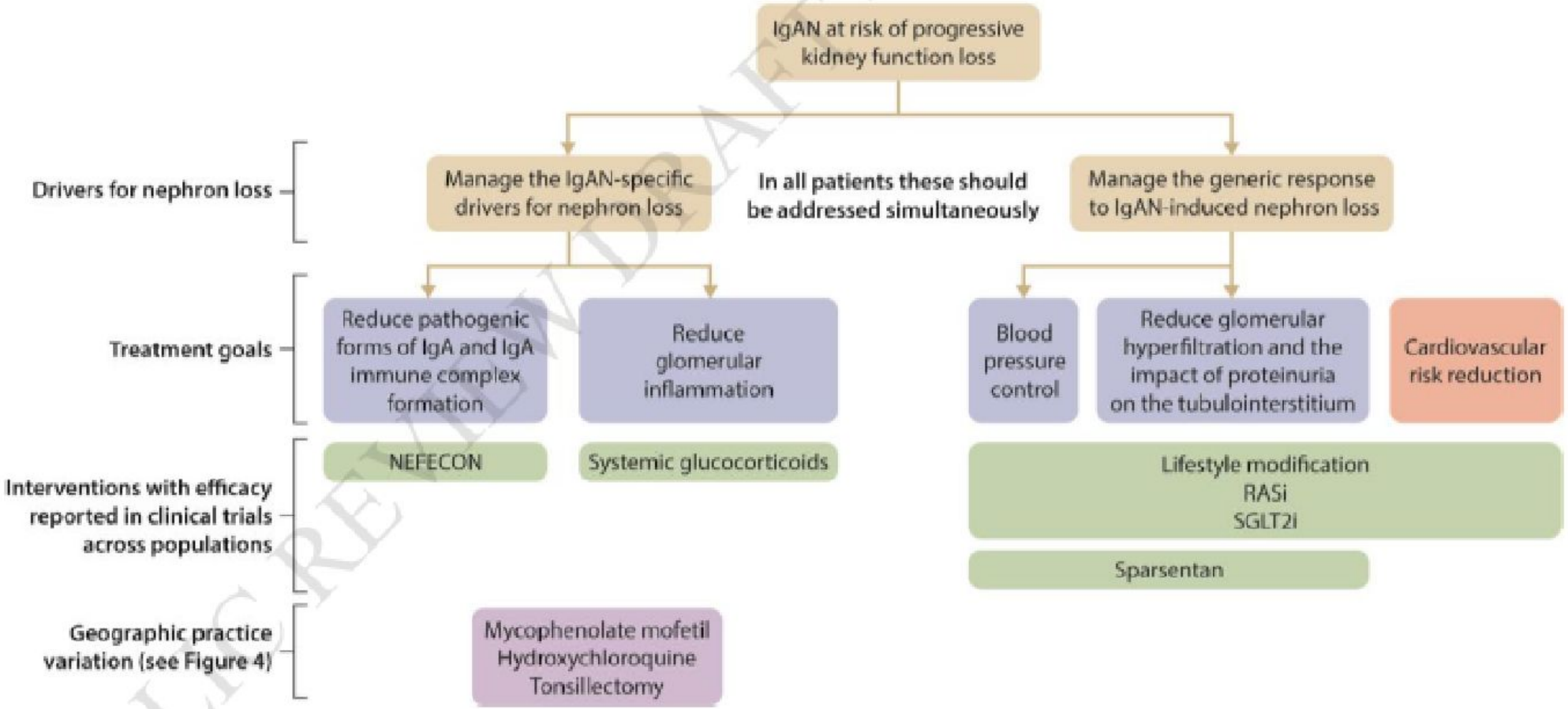
Many New Agents with Different MOAs Being Explored

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)



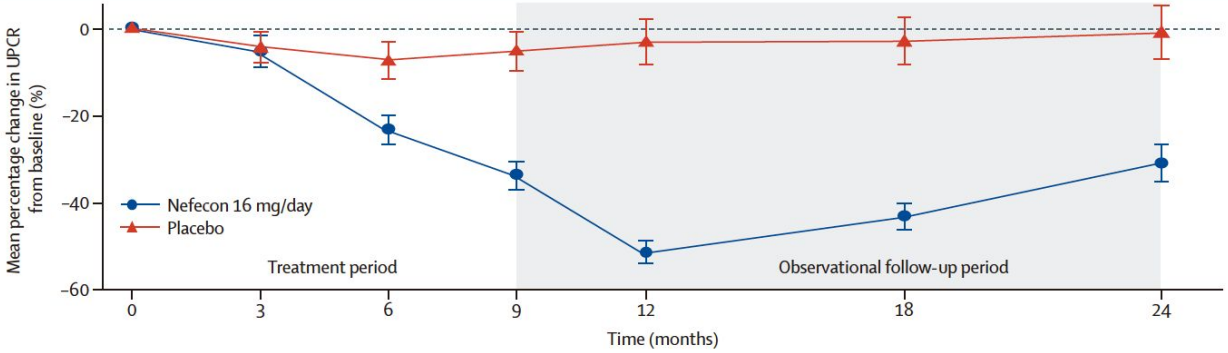
The definition of patients with IgA nephropathy at risk for progressive loss of kidney function

- **Proteinuria≥0.5g/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

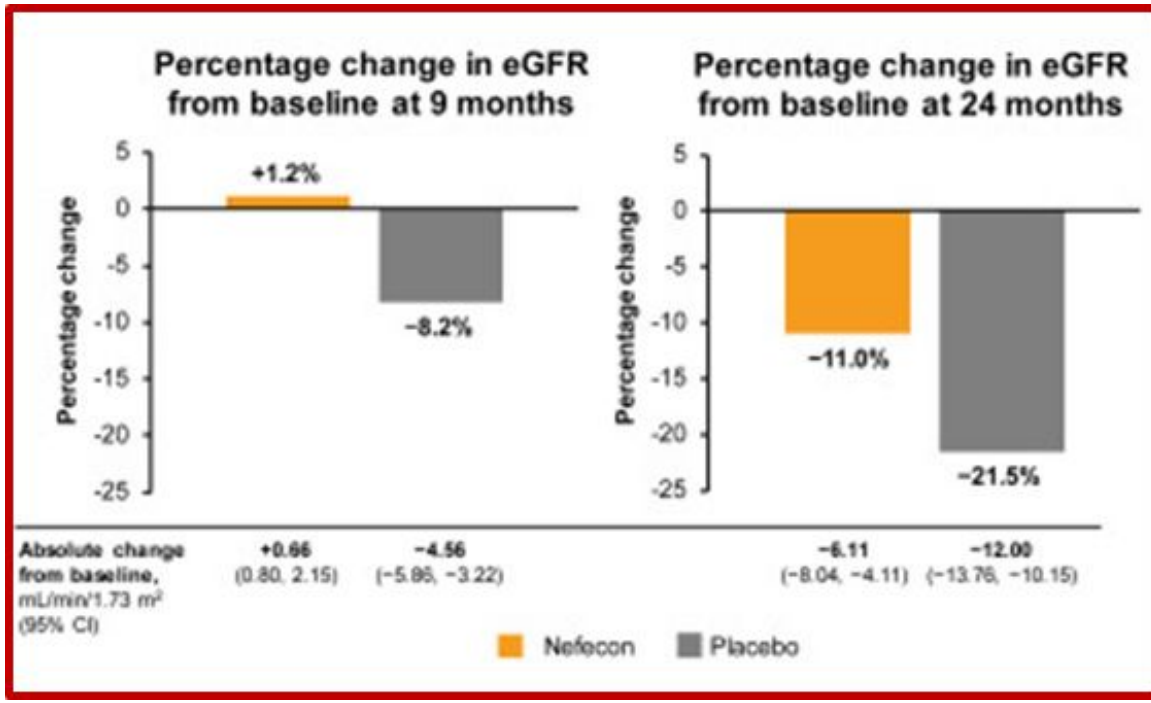
- Reduce the rate of loss of kidney function to **<1 ml/min/year**

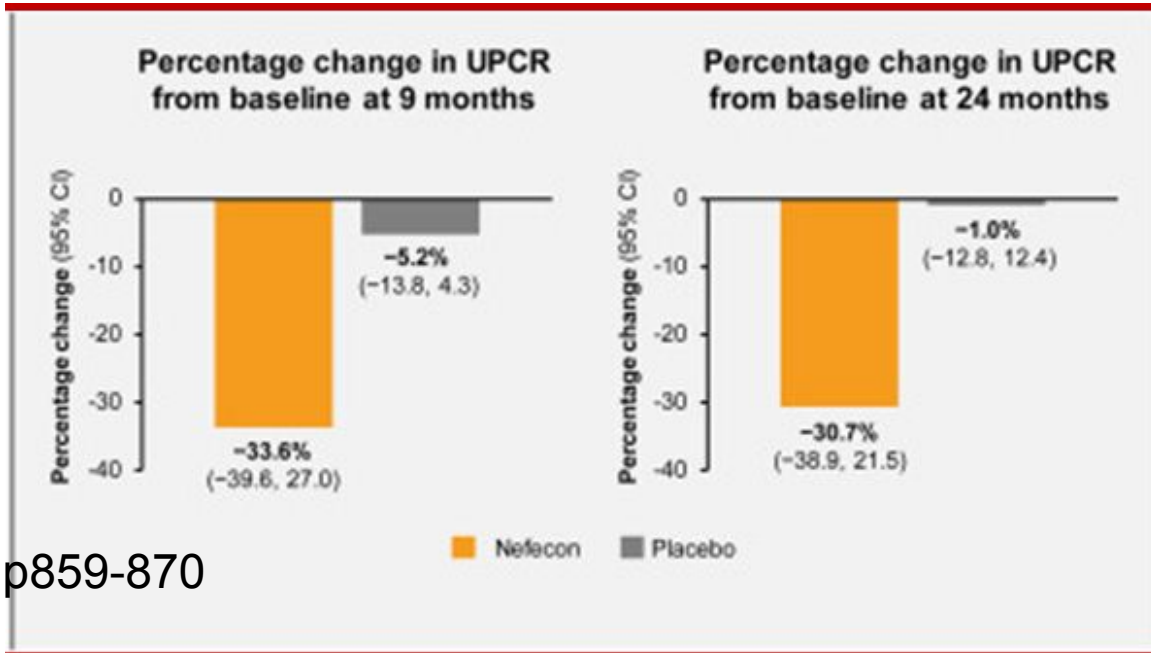
A 9-month treatment period with Nefecon provided a clinically relevant reduction in eGFR decline and a durable reduction in proteinuria that sustained at 24 months NefIgArd (Phase 3)



Nefecon, n	182	173	169	166	157	155	145
Placebo, n	182	176	169	164	160	151	142
Mean percentage change (95% CI) from baseline, %							
Nefecon 16 mg/day		−5·2 (−11·8 to 1·9)	−23·1 (−29·5 to −16·1)	−33·6 (−39·6 to −27·0)	−51·3 (−56·2 to −45·9)	−43·1 (−49·0 to −36·6)	−30·7 (−38·9 to −21·5)
Placebo		−4·3 (−10·9 to 2·9)	−7·3 (−15·0 to 1·2)	−5·2 (−13·8 to 4·3)	−3·2 (−12·8 to 7·5)	−2·9 (−13·0 to 8·3)	−1·0 (−12·8 to 12·4)
Percentage reduction (95% CI), %							
Nefecon 16 mg/day *vs* placebo		1·0 (−9·6 to 10·5)	17·1 (6·1 to 26·7)	30·0 (19·9 to 38·8)	49·7 (41·6 to 56·6)	41·4 (31·7 to 49·8)	30·1 (16·4 to 41·5)

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−ratio of geometric least squares means) × 100. UPCR=urine protein–creatinine ratio.





Lafayette et al. The Lancet Vol. 402, Issue 10405, 9–15 (2023), p859-870

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.

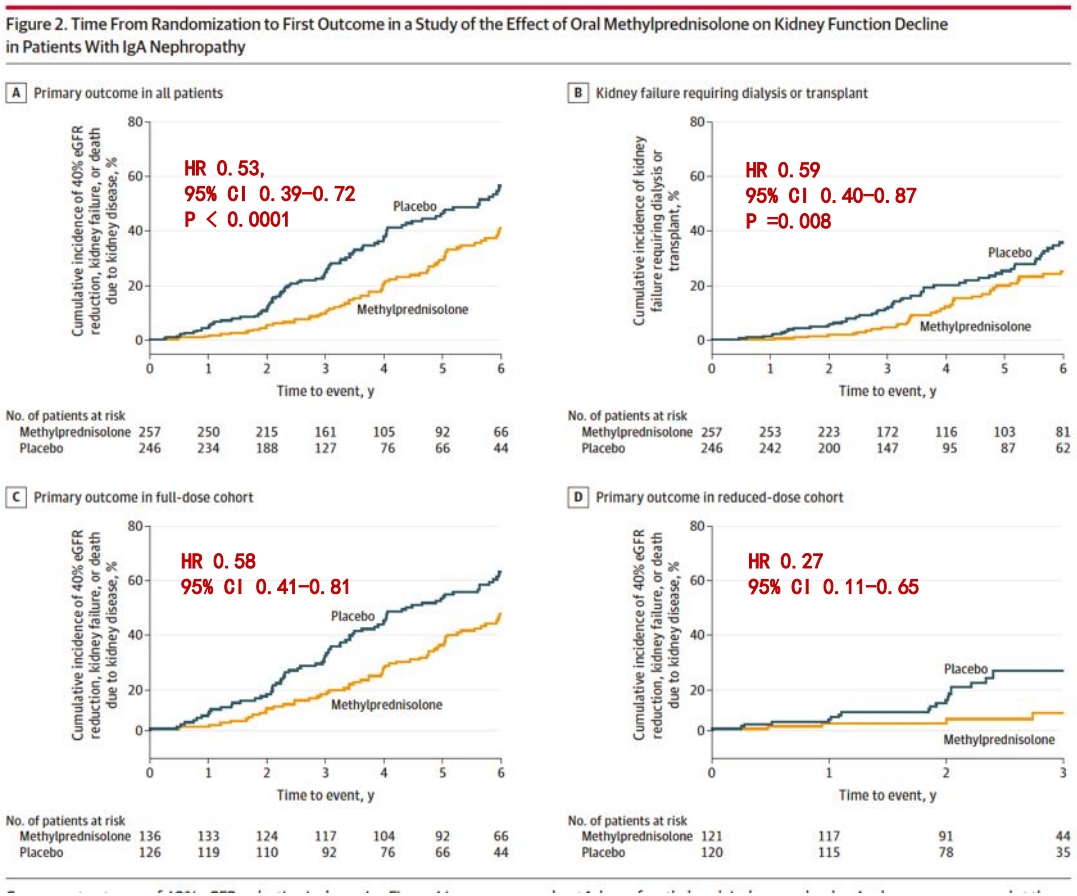
Table 3: Key safety variables (full analysis set)

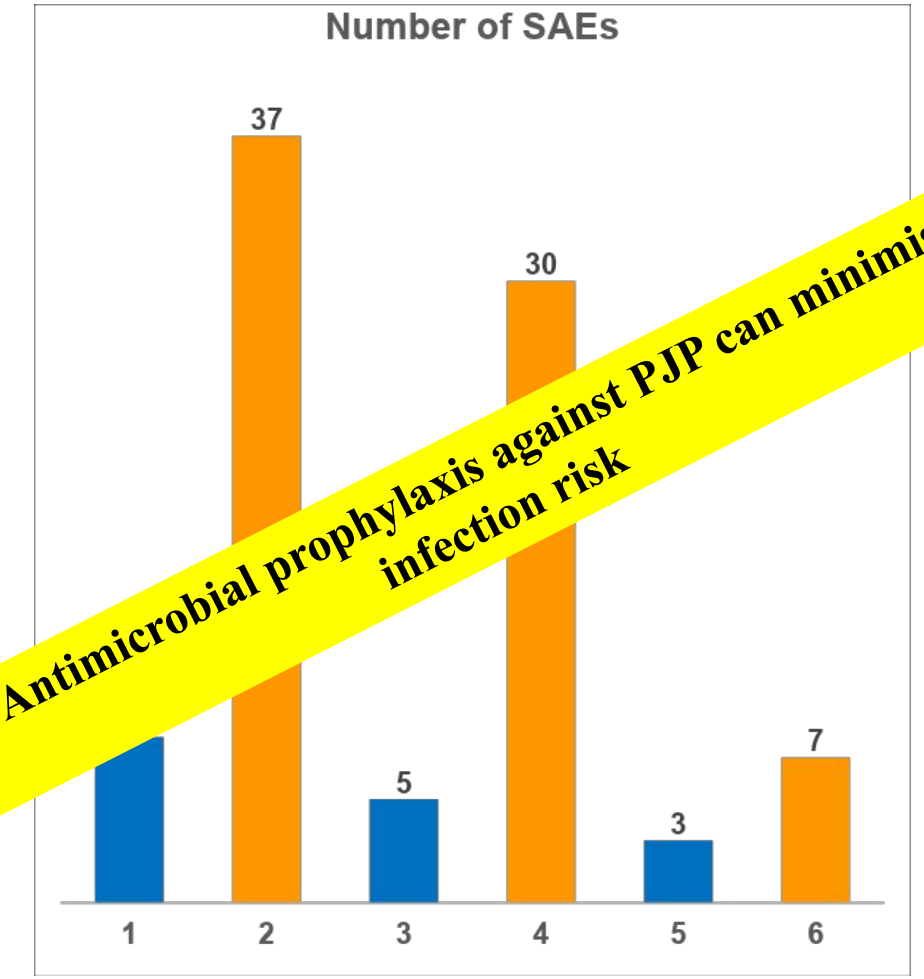
- Generally well-tolerated, consistent with low systemic exposure
- Infection rate is uncommon (<5%) and no severe infection events were observed
- Discontinuations due to TEAEs occurred in 9% and 2% of patients in the Nefecon and placebo arms, respectively
- No adverse events on body weight or blood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

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

Lafayette et al. The Lancet Vol. 402, Issue 10405, 9–15 (2023), p859-870

TESTING Study: Corticosteroids in IgA Nephropathy





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

ISN INTERNATIONAL SOCIETY OF NEPHROLOGY

Cohort & Methods

TESTING study
- Secondary analysis
- International multicentre RCT

Patients with biopsy-proven IgA nephropathy
N= 241

2017-2019

Inclusion criteria:
- Proteinuria ≥ 1g/day despite 3 months of RAS blockade
- eGFR 30-120 mL/min/1.73m^2

Reduced-dose methylprednisolone 0.4 mg/kg/day*

Randomized

median follow-up period of 2.5 years

Placebo

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

KI REPORTS
Kidney International Reports

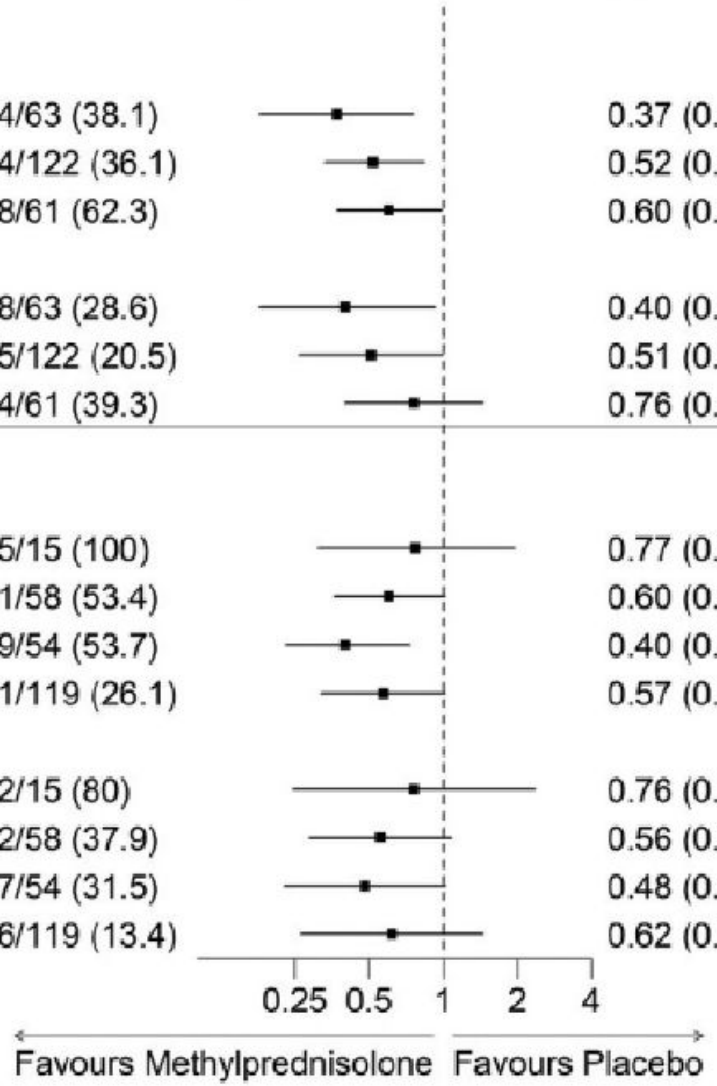
Kim D et al., 2024

Visual abstract by:
Eric Au, MBBS MPH PhD
@EricAu

Conclusion Reduced-dose methylprednisolone is effective in improving kidney outcomes in high-risk IgA nephropathy, however, is associated with a modestly higher number of serious adverse events compared to placebo.

Response to corticosteroids by baseline eGFR and proteinuria

Subgroups	Number of Events, n/N (%) Methylprednisolone	Placebo	HR (95% CI)	P-interaction Categorical	Continuous
Proteinuria (g/day)					
Primary Outcome				0.53	0.32
1-<1.5	12/74 (16.2)	24/63 (38.1)	0.37 (0.18 to 0.75)		
1.5-<3	30/118 (25.4)	44/122 (36.1)	0.52 (0.33 to 0.84)		
≥3	32/65 (49.2)	38/61 (62.3)	0.60 (0.37 to 0.98)		
Kidney Failure				0.28	0.26
1-<1.5	9/74 (12.2)	18/63 (28.6)	0.40 (0.18 to 0.92)		
1.5-<3	18/118 (15.3)	25/122 (20.5)	0.51 (0.26 to 0.99)		
≥3	23/65 (35.4)	24/61 (39.3)	0.76 (0.40 to 1.45)		
eGFR (mL/min/1.73m2)					
Primary Outcome				0.68	0.5
20-<30	7/10 (70)	15/15 (100)	0.77 (0.31 to 1.94)		
30-<45	29/65 (44.1)	31/58 (53.4)	0.60 (0.36 to 1.01)		
45-<60	19/73 (26)	29/54 (53.7)	0.40 (0.23 to 0.73)		
60-120	19/109 (17.4)	31/119 (26.1)	0.57 (0.32 to 1.01)		
Kidney Failure				0.42	0.88
20-<30	6/10 (60)	12/15 (80)	0.76 (0.25 to 2.35)		
30-<45	22/65 (33.8)	22/58 (37.9)	0.56 (0.29 to 1.08)		
45-<60	13/73 (17.8)	17/54 (31.5)	0.48 (0.23 to 1.02)		
60-120	9/109 (8.3)	16/119 (13.4)	0.62 (0.26 to 1.45)		



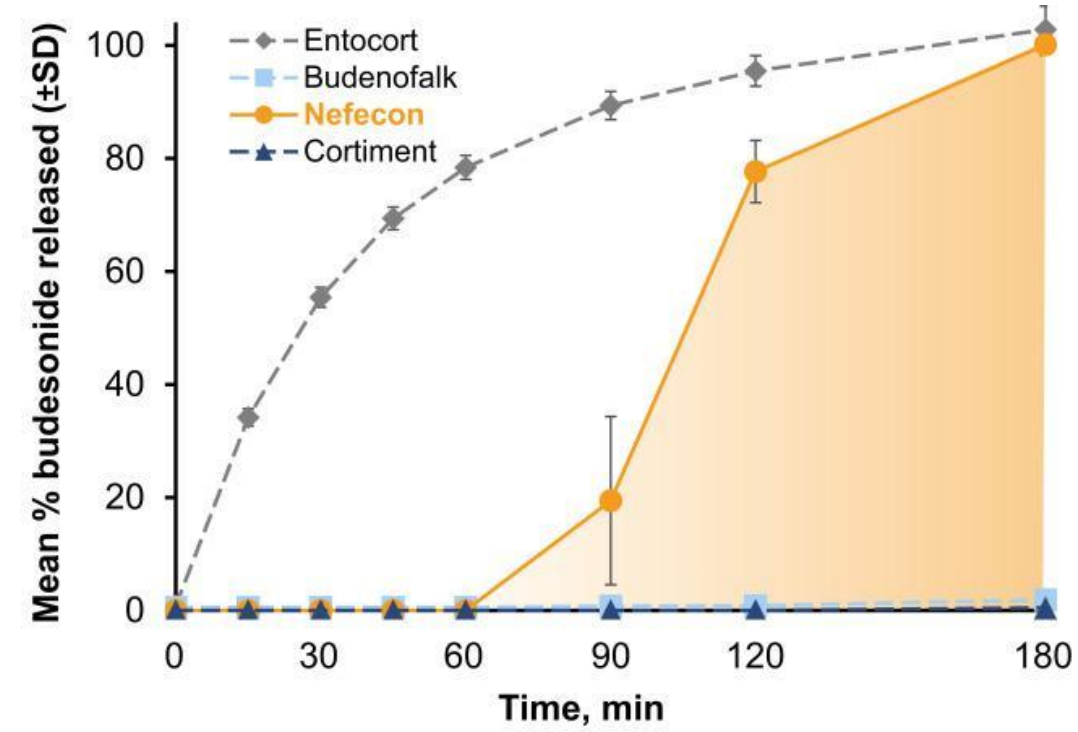
Kim et al. Kidney Int Rep (2025) doi.org/10.1016/j.ekir.2025.03.008)

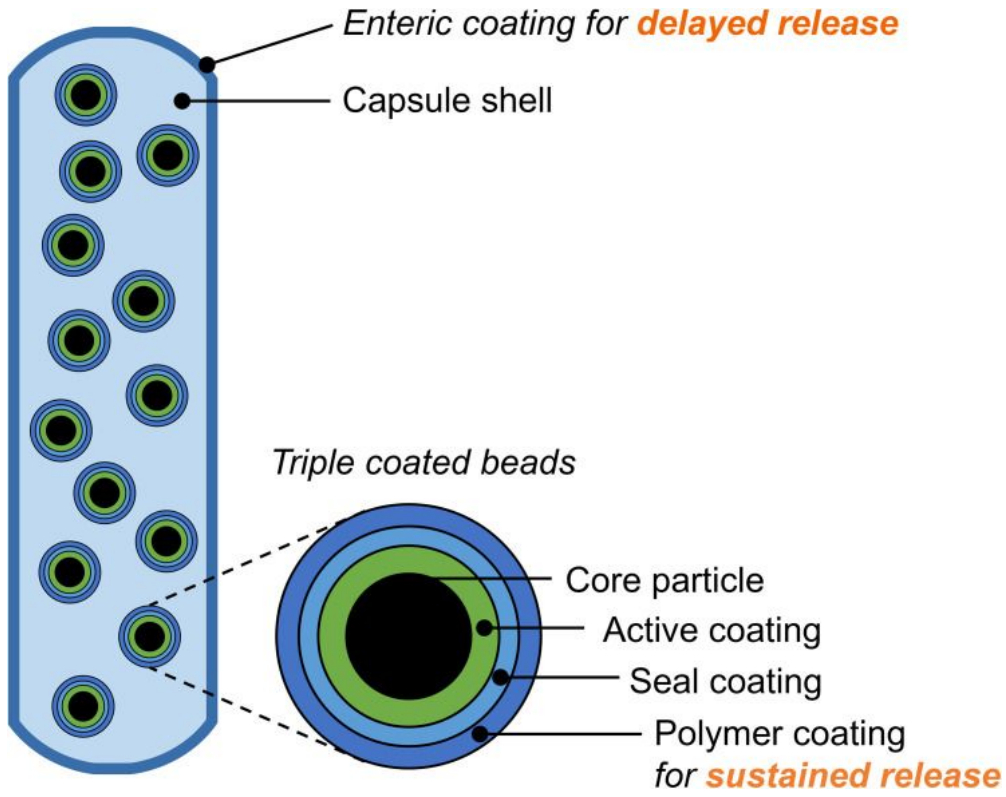
Points to consider when choosing a treatment and/or treatment combinations for patients with IgAN

- ***Race:*** The TESTING study was almost exclusively conducted in Asian patients. STOP-IgAN was exclusively conducted in Caucasians. In the NefIgArd Asian patients were relatively underrepresented compared with those in trials systemic glucocorticoids.

- ***Age:*** STOPIgAN and TESTING studies participants are at least 7-9 years younger than that of Nefigard trial

- ***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

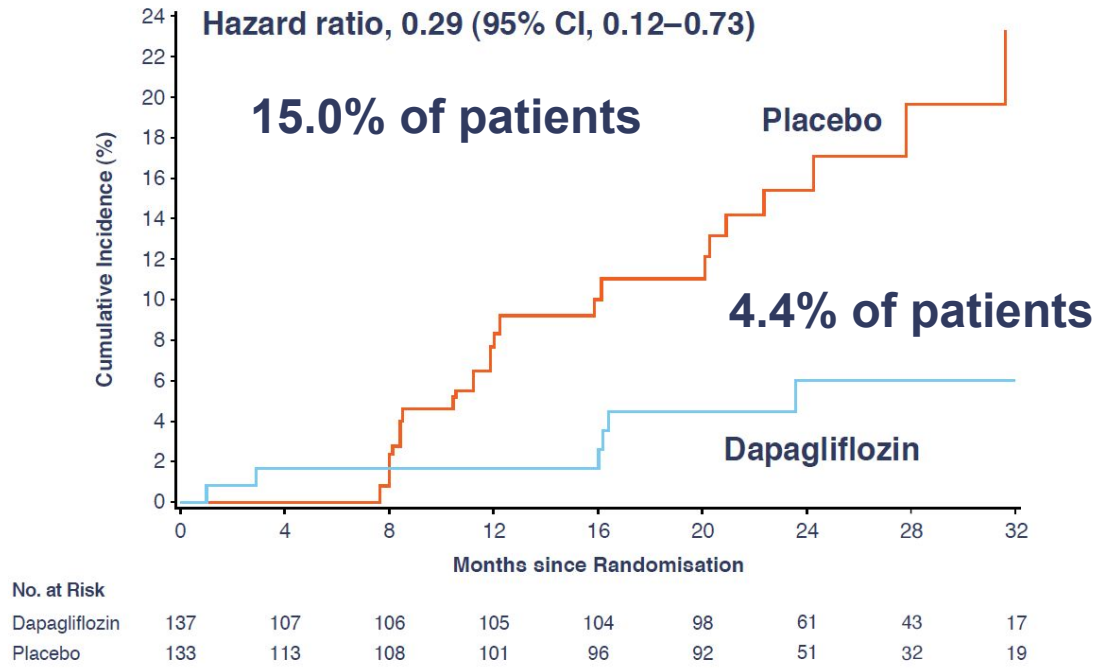
Agent	Suggested usage	Remarks
Antiplatelet agents	Not recommended	No evidence of efficacy
Anticoagulants	Not recommended	No evidence of efficacy
Azathioprine	Not recommended	No evidence of efficacy as monotherapy or when combined with glucocorticoids
Cyclophosphamide	Not recommended	Unless in the setting 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]

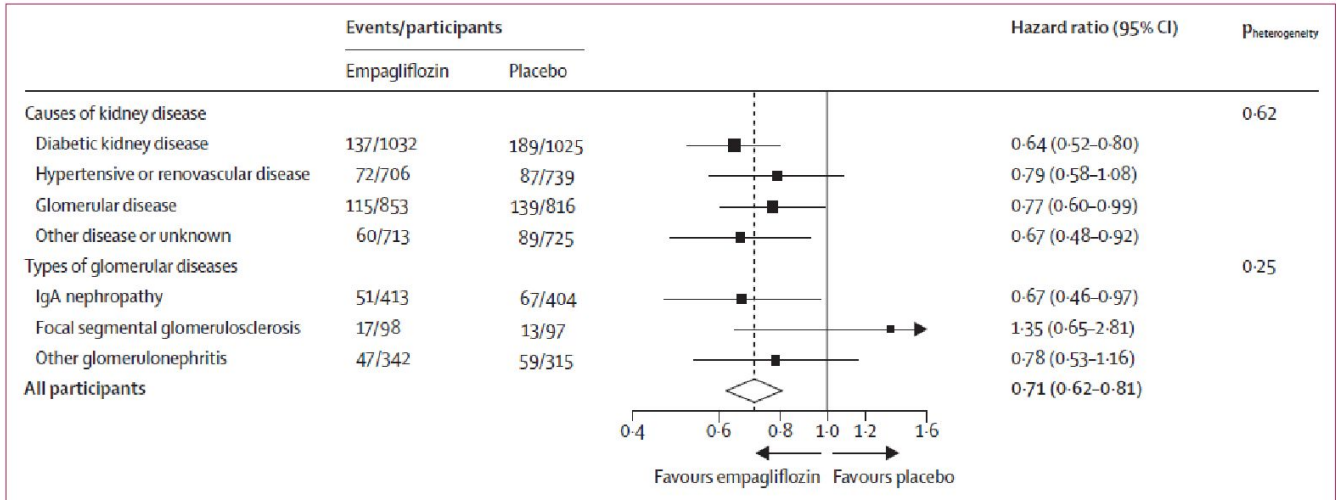
Treatment with systemic glucocorticoids should incorporate antimicrobial prophylaxis against *bacteria* and virus, along with gastroprotection and bone protection according to local guidelines

SGLT-2 inhibitors in IgA nephropathy

DAPA-CKD



EMPA-KIDNEY



HR 0.67 95% CI 0.46-0.97

Kidney disease progression: as a sustained ≥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

Wheeler DC et al, Kidney Int 2021 100(1):215-224.

The EMPA-KIDNEY Collaborative Group Lancet Diabetes Endocrinol 2024;12:15-60

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, Jula K Inrig, Donald E Kohan, Radko Komers, Laura Ann Kooienga, Richard Lafayette, Bart Maes, Robert Małecki, 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†*

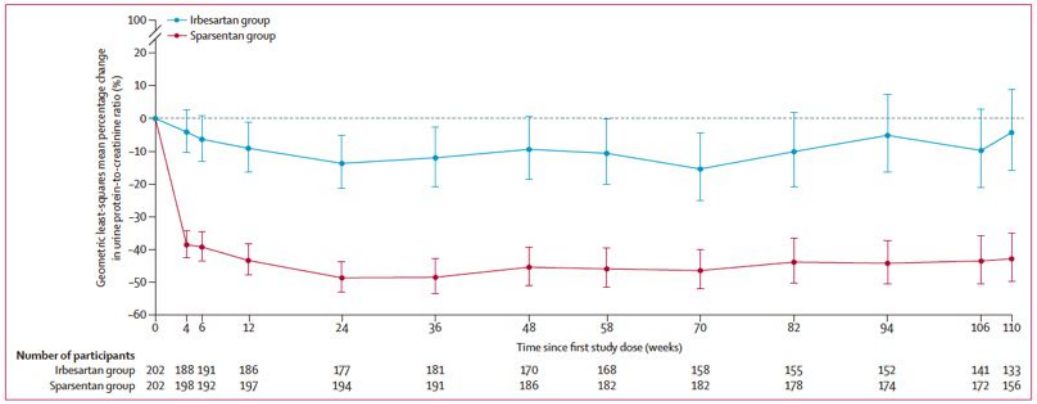


Figure 5: Geometric least-squares mean percentage change from baseline in the urine protein-to-creatinine ratio at each visit up to week 110
Error bars indicate 95% CIs.

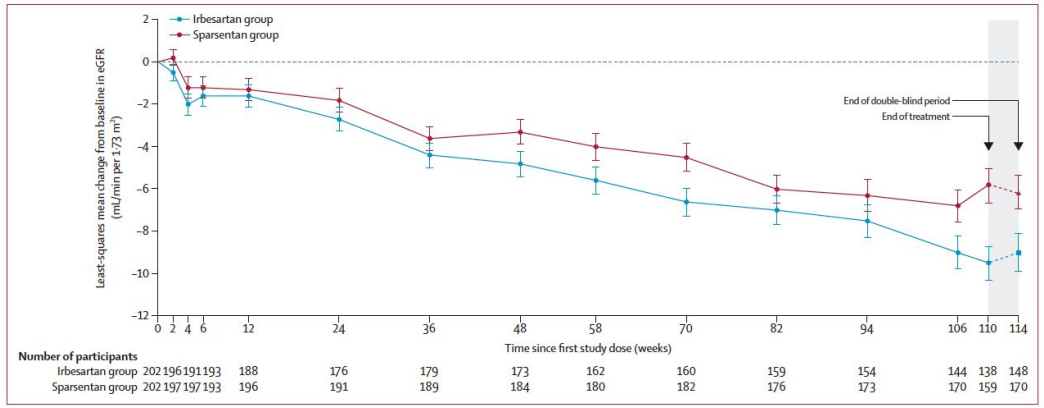


Figure 2: eGFR by visit up to week 114
Change from baseline in eGFR at week 6 or 114 was assessed with ANCOVA, and change from baseline in eGFR to other timepoints up to week 110 were analysed via a mixed model for repeated measures. Error bars indicate SEs. eGFR=estimated glomerular filtration rate.

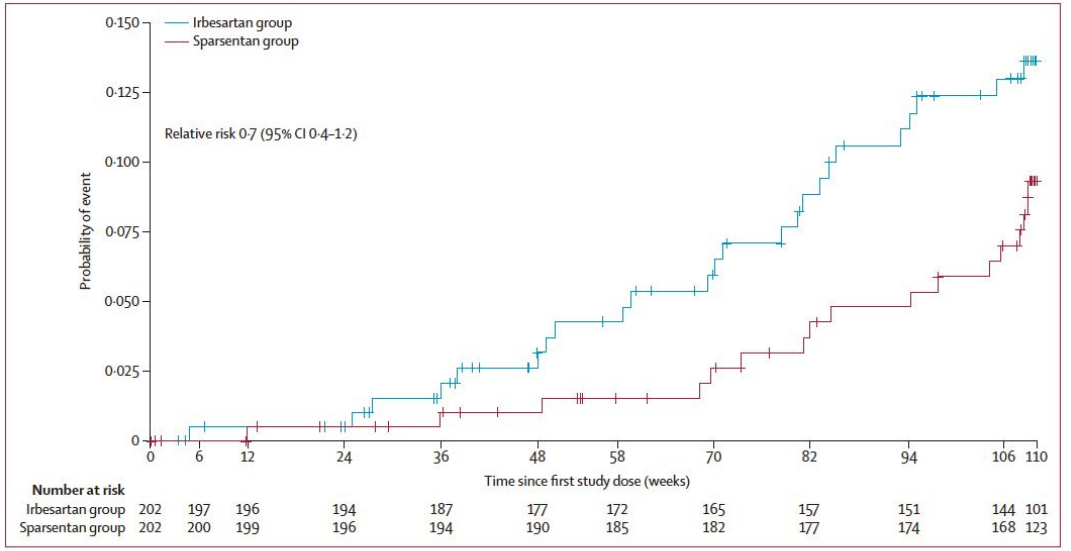
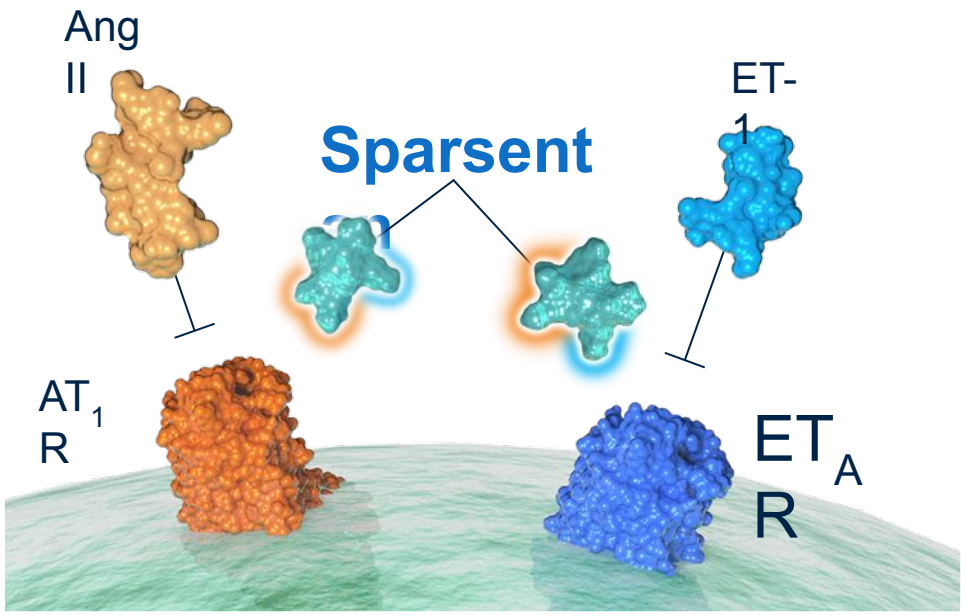


Figure 4: Time to reach the composite kidney failure endpoint of confirmed 40% eGFR reduction, end-stage kidney disease, or all-cause mortality
Vertical bars indicate censored patients. eGFR=estimated glomerular filtration rate.

Sparsentan 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.

Rovin B et al. The Lancet Vol 402, Issue 10417 p2077-2090 (2023)

Sparsentan- a dual ETR_A antagonist and A_1RB (DEARA)



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REVIEW

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

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Video abstract

Point your SmartPhone at the code above. If you have a QR code reader the video abstract will appear. Or use: https://youtu.be/Kp9x1WhIt1cU

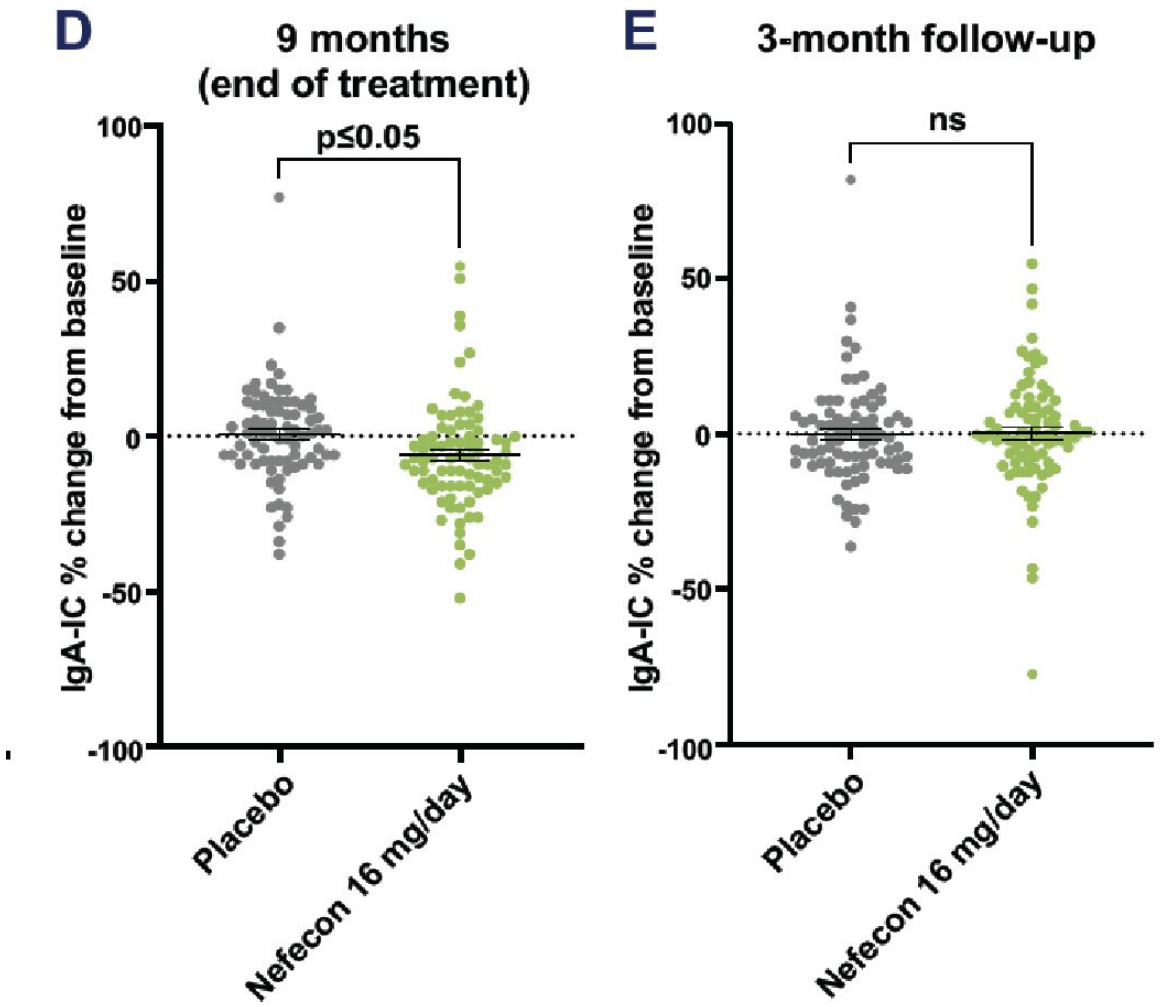
* Sparsentan is an investigational compound for treatment of primary or genetic FSGS and IgAN. It is not approved by any regulatory agency.
Ang II = angiotensin II; ARB = angiotensin receptor blocker; AT_1R = angiotensin II receptor type 1; CV = cardiovascular; ET_AR = endothelin receptor type A; ET-1 = 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:*** In the trials of SGLT2i, patients older. On average 6–8 years older than those recruited into the NefIgArd 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 m^2 lower than that of patients included in the NefIgArd, 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 GdIgA1levels that reversed to baseline following cessation



ERA Poster (2023)

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

kidney INTERNATIONAL

ISN INTERNATIONAL SOCIETY OF NEPHROLOGY

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

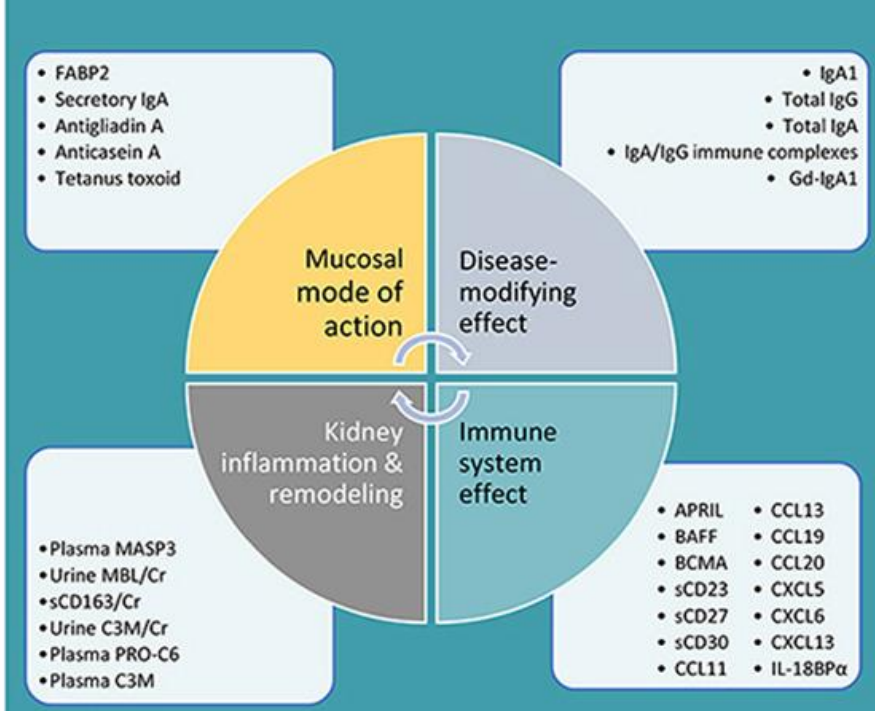
- **Nefecon** 8 mg/d: *n* = 51
- **Nefecon** 16 mg/d: *n* = 49
- **Placebo**: *n* = 50

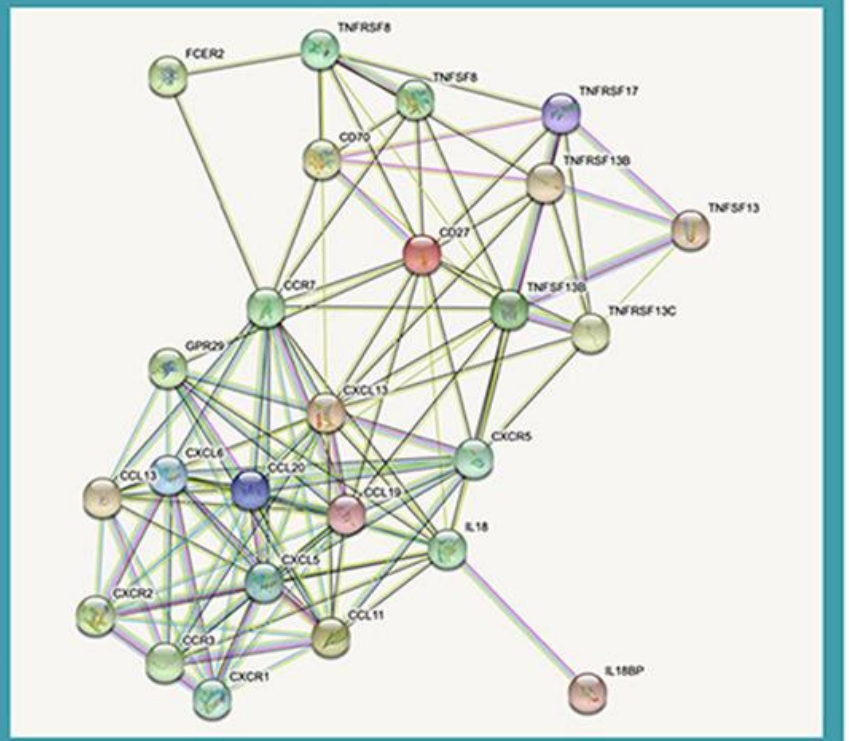
9 months of treatment → 3-month follow-up

Blood and urine samples

Robust regression analysis and protein-protein interactions network

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





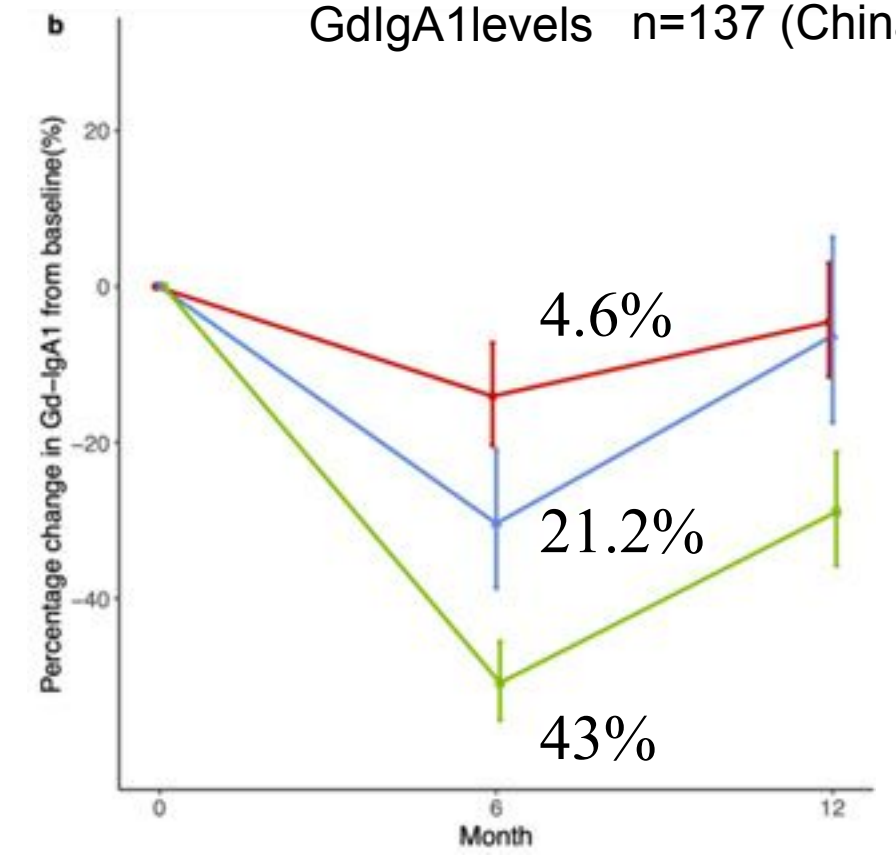
Wimbury D, Muto M, et al. 2023

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

GdIgA1levels n=137 (China)

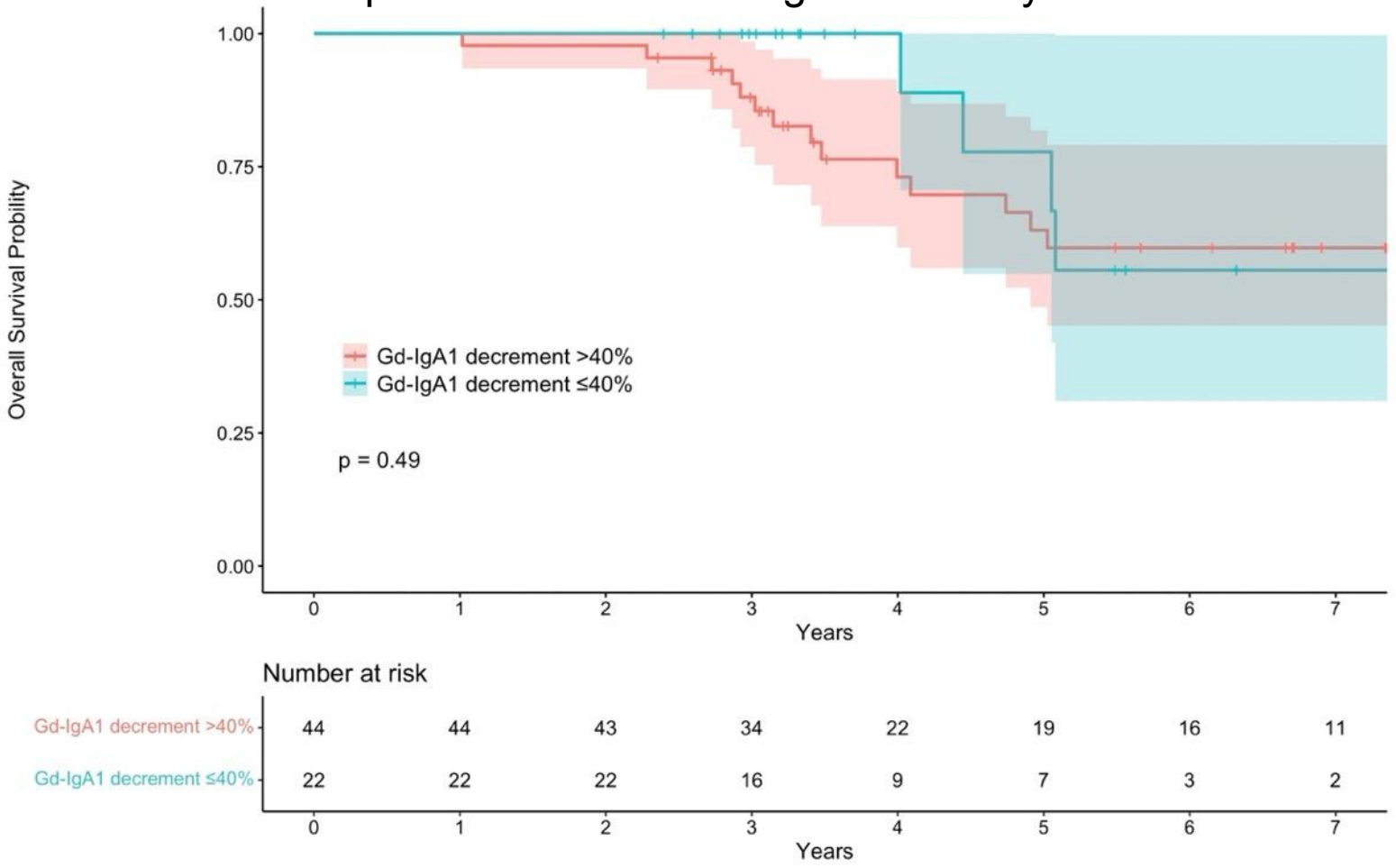


Placebo

Full dose

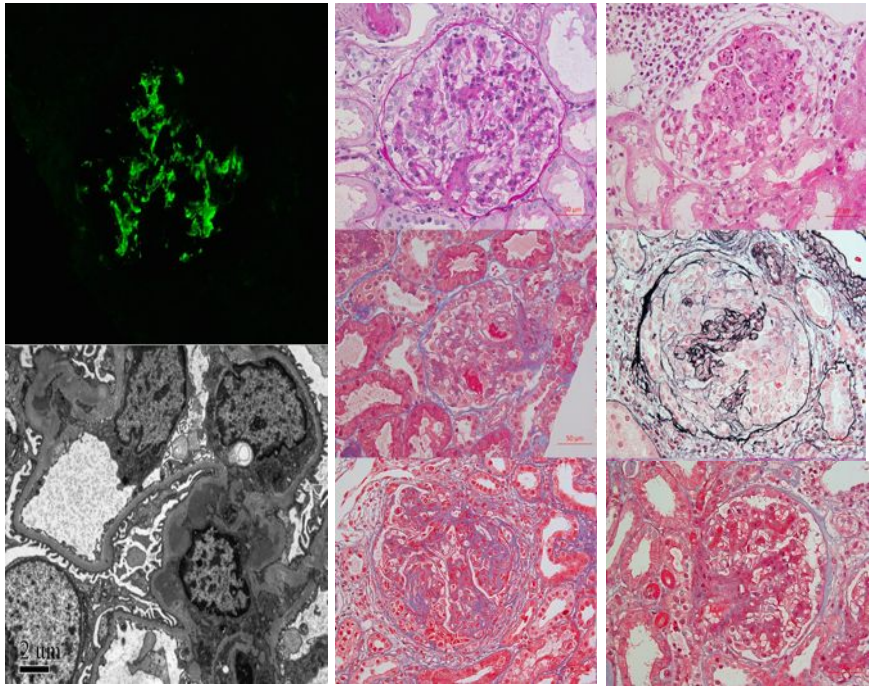
Reduced dose

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.

Al-Lawati AI et al. Nephrol Dial Transplant. 2017;32:i30–i36;
Tan M et al. Kidney Blood Press Res. 2015;40:200–206.

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

JASN
Journal of the American Society of Nephrology
Clinical Research

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 ≥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**

JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

Disagreement between local and central pathology review

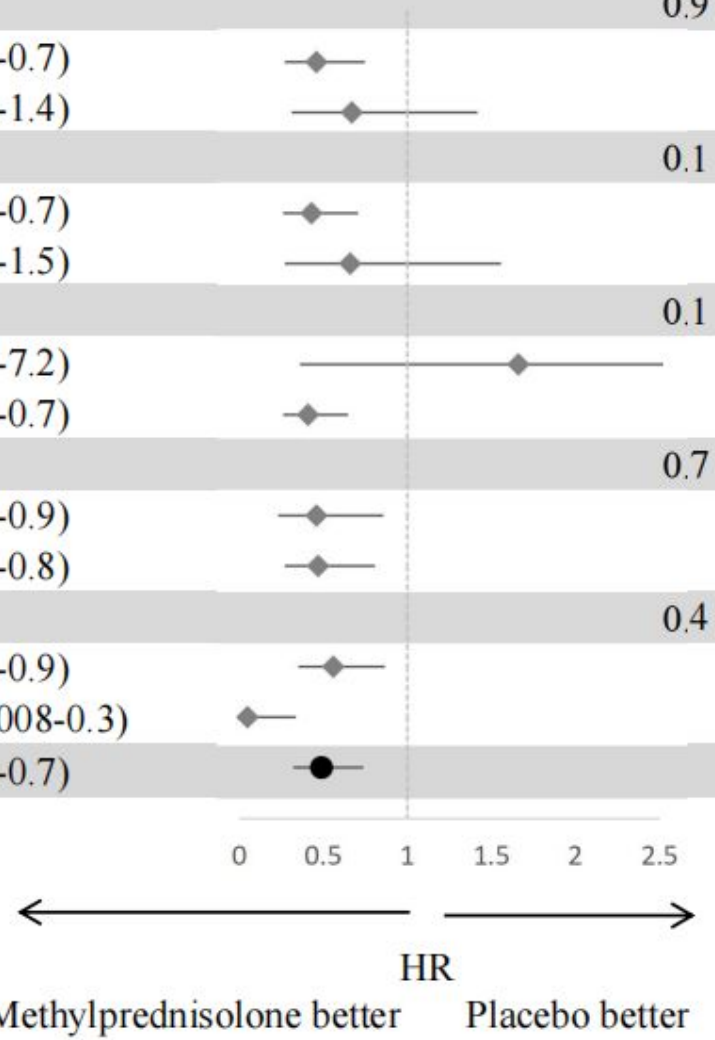
Pathology lesions	Central pathological review	Local pathology report	Kappa value
M1(%)	89/279(32)	160/272(59)	0.1
E1(%)	75/279(27)	82/279(29)	0.2
S1(%)	239/279(86)	200/272(74)	0.1
T0(%)	173/279(62)	114/272(42)	0.3
T1(%)	84/279(30)	110/272(40)	0.3
T2(%)	22/279(8)	48/272(18)	0.3
C0(%)	230/279(82)	102/274(37)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

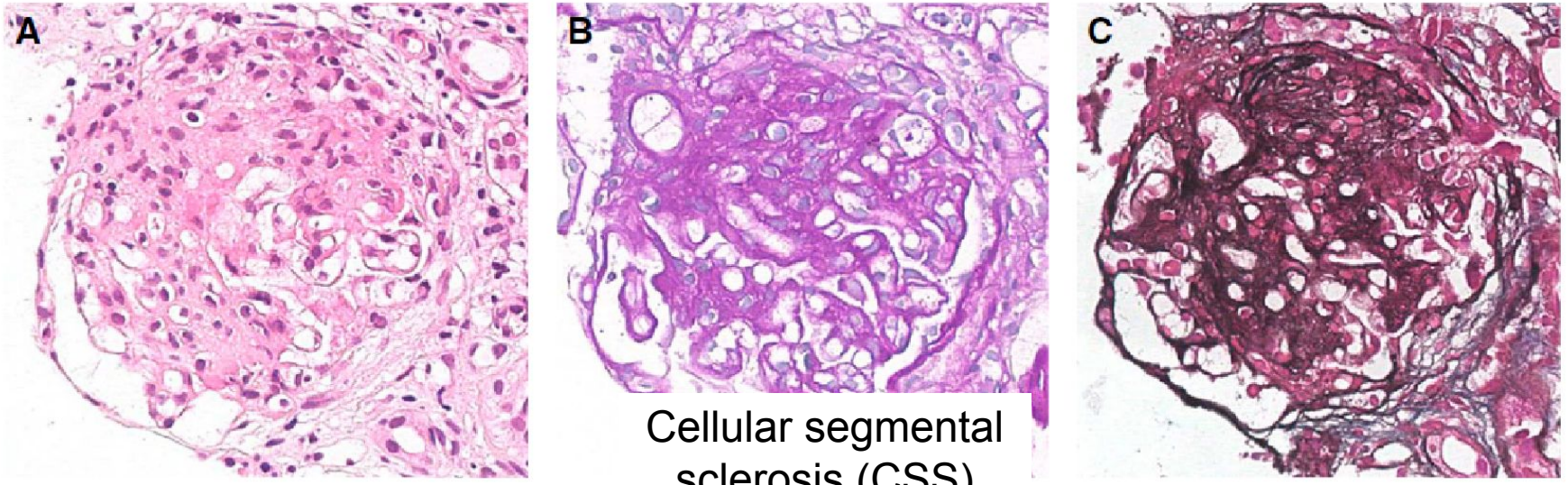
Characteristic	No./total No. (%) Methylprednisolone	Placebo	Hazard ratio 95%CI	*P* for interaction
Mesangial hypercellularity				0.9
M0	29/88(33)	52/102(51)	0.5(0.3-0.7)	
M1	19/51(37)	13/38(34)	0.7(0.3-1.4)	
Endocapillary hypercellularity				0.1
E0	36/106(34)	48/98(49)	0.4(0.3-0.7)	
E1	12/33(36)	17/42(40)	0.7(0.3-1.5)	
Segmental glomeruloscerlosis				0.1
S0	7/20(35)	6/20(30)	1.6(0.3-7.2)	
S1	41/119(34)	59/120(49)	0.4(0.3-0.7)	
Tubular atrophy/Interstitial fibrosis				0.7
T0	20/89(22)	23/84(27)	0.5(0.2-0.9)	
T1+T2	28/50(56)	42/56(75)	0.5(0.3-0.8)	
Crescents				0.4
C0	45/121(37)	51/109(47)	0.6(0.4-0.9)	
C1+C2	3/18(17)	14/31(45)	0.05(0.008-0.3)	
Overall	48/139(35)	65/140(46)	0.5(0.3-0.7)	



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

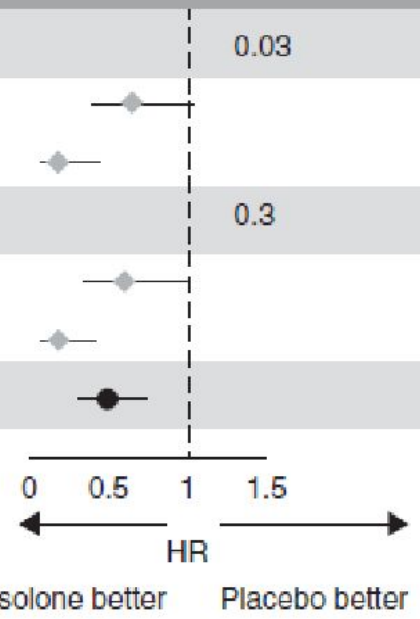
Subtype of S lesions

- Cellular segmental sclerosis



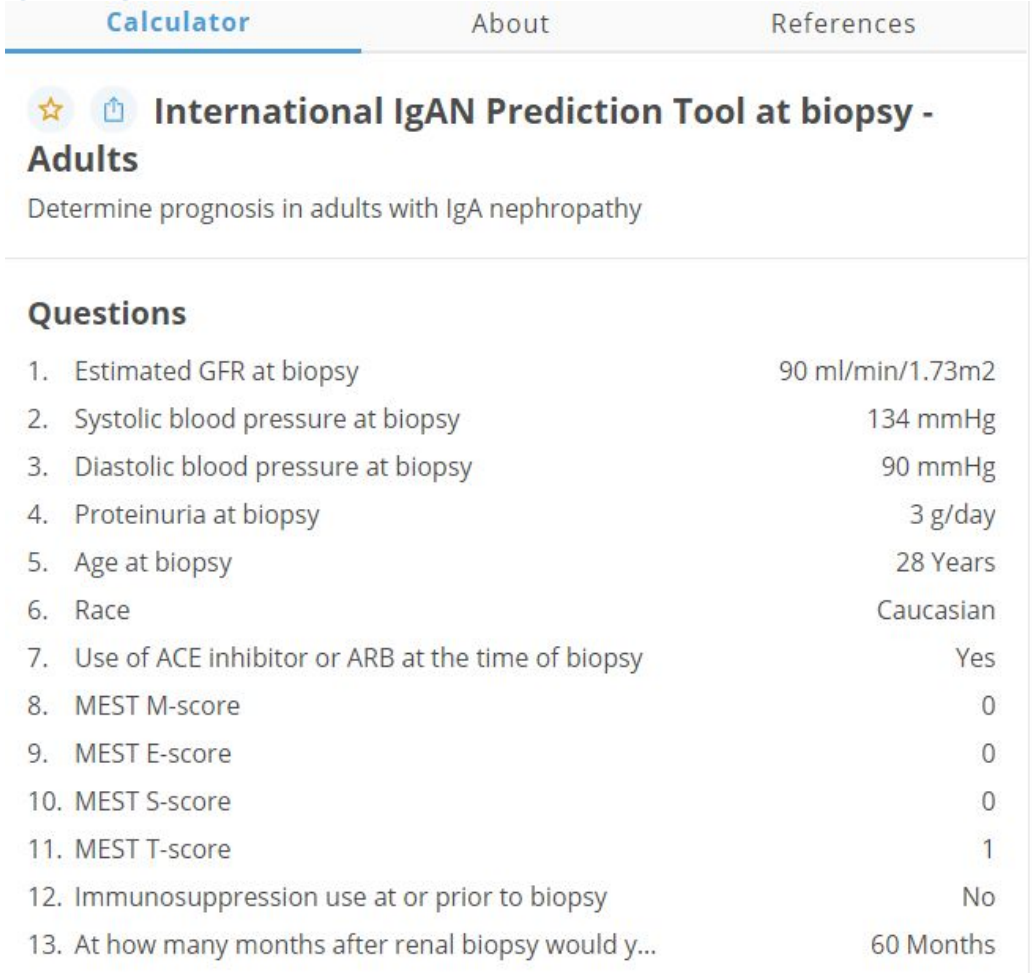
Cellular segmental sclerosis (CSS)

Characteristic	No./total No. (%) Methylprednisolone	Placebo	Hazard ratio (95%CI)	*P* for interaction
Cellular segmental sclerosis				0.03
No	37/104(36)	44/103(43)	0.6(0.4-1.0)	
Yes	11/35(31)	21/37(57)	0.2(0.07-0.4)	
podocytopathic segmental sclerosis				0.3
No	30/109(28)	39/102(38)	0.6(0.4-1.0)	
Yes	18/30(60)	26/38(68)	0.2(0.07-0.4)	
Overall	48/139(35)	65/140(46)	0.5(0.3-0.7)	



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%

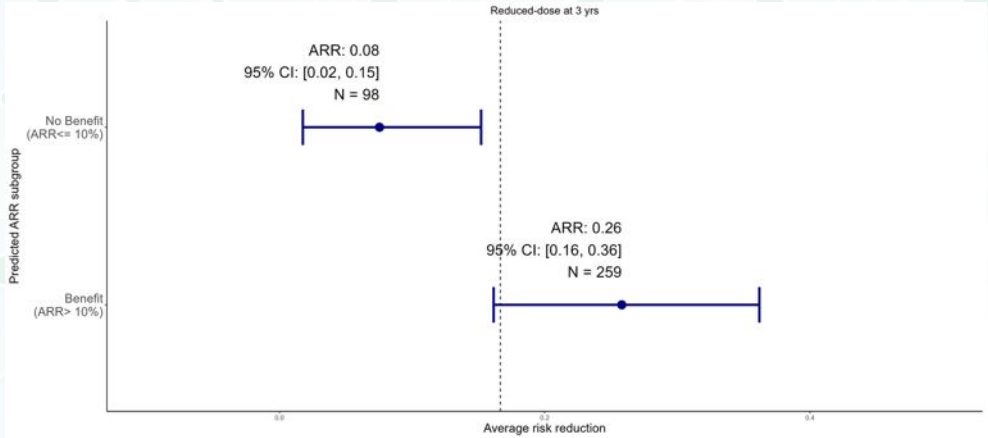
- **Caveats**
  - Requires recent kidney biopsy validated up to 2 years from kidney biopsy
  - Predict risk up to 5 years
  - Does not predict treatment response

Predicting who is more likely to benefit from corticosteroids

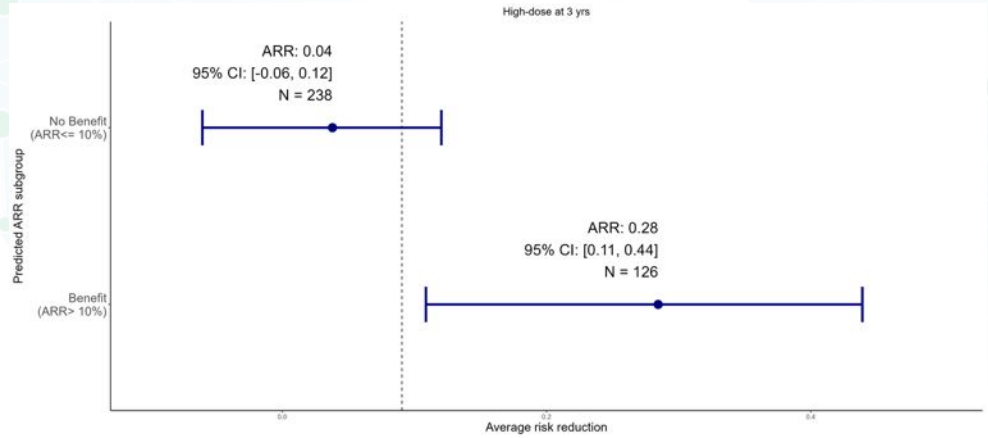
Main effects selected & interactions forced Variables	log-hazard (95% C.I)*
Treatment (Methylprednisolone vs. Placebo)	-0.14 [-0.59 ; -0.03]
eGFR (per 10 increase)	-0.22 [-0.40 ; -0.15]
Age (per 1 increase)	-0.03 [-0.05 ; -0.02]
Proteinuria (per 1 increase)	0.13 [0.07 ; 0.30]
Tubular atrophy	-0.10 [-0.52 ; 0.17]
T1 vs. T0	
T2 vs. T0	0.42 [0.04 ; 0.97]
RASB	0.09 [-0.16 ; 0.60]
50% - <80% vs. 0-50%	
>= 80% vs. 0-50%	0.22 [-0.00 ; 0.87]
C score	0.15 [-0.11 ; 0.55]
C1 vs. C0	
C2 vs. C0	-0.21 [-0.73 ; 0.38]
Race (Chinese vs. non-chinese)	-0.27 [-0.93 ; 0.02]
Time since biopsy (per 1 increase)	-0.00 [-0.00 ; 0.00]
SBP (per 1 increase)	0.01 [-0.00 ; 0.02]
Sex (Male vs. Female)	0.23 [-0.02 ; 0.63]
BMI (per 1 increase)	-0.02 [-0.06 ; 0.02]
Treatment * eGFR (per 10 increase)	-0.05 [-0.16 ; -0.02]
Treatment * Age (per 1 increase)	-0.00 [-0.01 ; 0.01]
Treatment * Proteinuria (per 1 increase)	0.07 [-0.03 ; 0.28]
Treatment * Tubular atrophy	-0.08 [-0.61 ; 0.33]
T1	
T2	-0.32 [-1.30 ; 0.14]
Treatment * RASB	0.05 [-0.32 ; 0.58]
>= 50% - <80%	
>=80	0.03 [-0.42 ; 0.46]
Treatment * C score	-0.14 [-0.67 ; 0.24]
C1	
C2	-0.42 [-1.74 ; 0.28]
Treatment * Race	0.09 [-0.13 ; 0.87]
Treatment * time since biopsy (per 1 increase)	0.00 [-0.01 ; 0.01]
Treatment * SBP (per 1 increase)	-0.00 [-0.01 ; -0.00]
Treatment * Sex	-0.09 [-0.57 ; 0.28]
Treatment * BMI (per 1 increase)	-0.00 [-0.01 ; 0.02]

* log-hazard estimates obtained from Ridge regression model with bootstrapped Conf. intervals

Reduced dose



Full dose

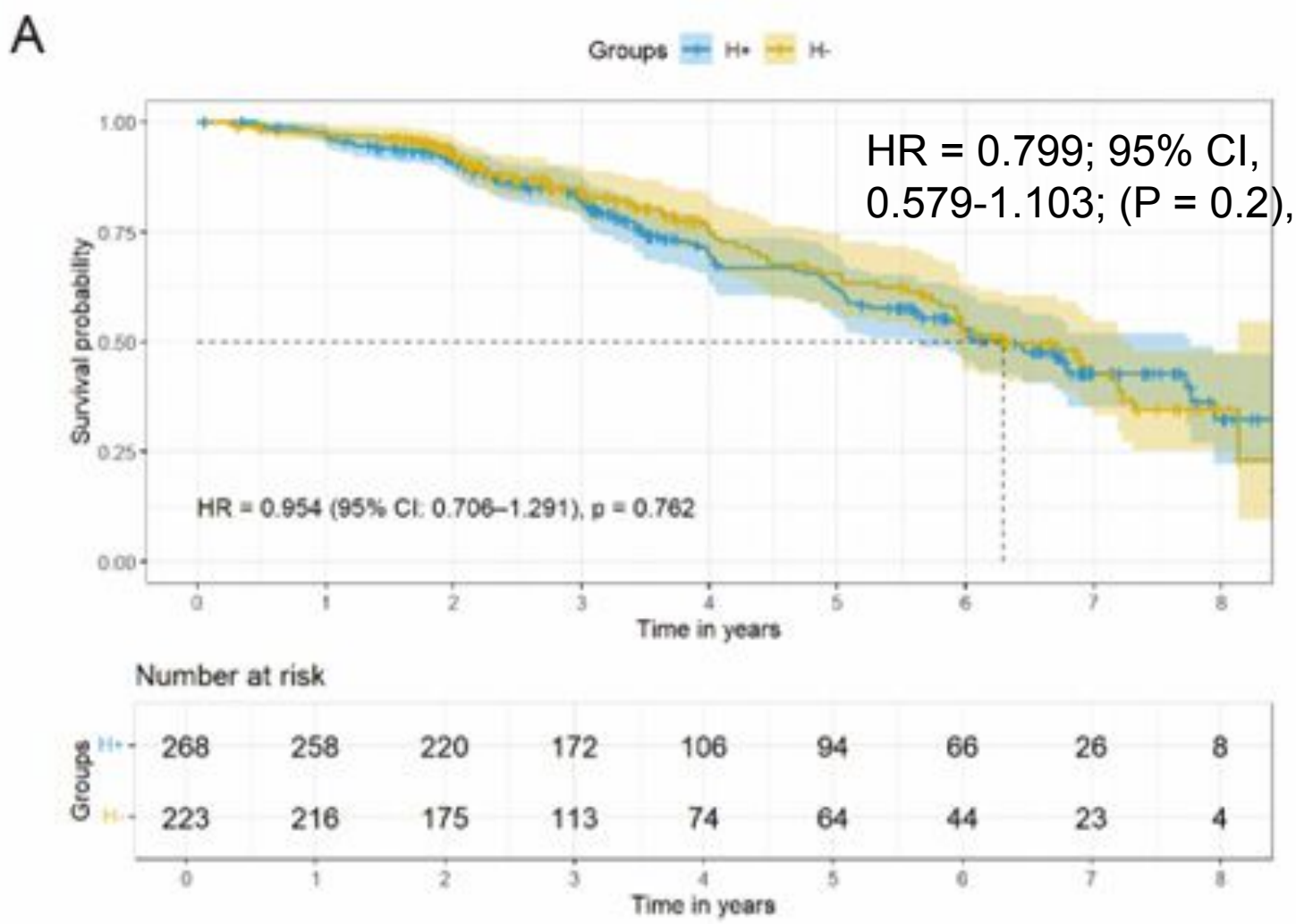


Manuscript under review

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



Manuscript under review

Sex Differences across Corticosteroid Response and Outcomes in IgA Nephropathy

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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/1.73m^2/year

KI REPORTS
Kidney International Reports

Kim D et al, 2025

Visual abstract by:
Husam Alzayer, MD
@HusamJZ

Conclusion: Methylprednisolone improves kidney outcomes in IgAN, regardless of sex, however males experience poorer kidney outcomes compared to females.

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 approach targeting both pathogenic IgA production, inflammation and the maladaptive responses

Better predictors to treatment response are needed

Thank you for your attention