



Treatment of IgA Nephropathy – New Guidelines and New therapies for 2026



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Potential Conflicts of Interest

Dr. Appel through the Glomerular Ctr at CUMC is involved with research through Columbia U. with Achilion-Alexion, Apellis, Calliditas, Genentech-Roche, Sanofi-Genzyme, Travers, Vera, Vertex, Novartis.

He lectures for Aurinia and Glaxo on Lupus Nephritis, and Calliditas on Mechanisms of IgA nephropathy and Travers on FSGS.

He has consultantships with : Alexion-Achilion, Apellis, Aurinia, Glaxo, Calliditas, Genentech-Roche, Up-to-Date, Sanofi-Genzyme, Travers, Vera, Vertex Novartis.

He has no major stock holdings.

IgA Nephropathy

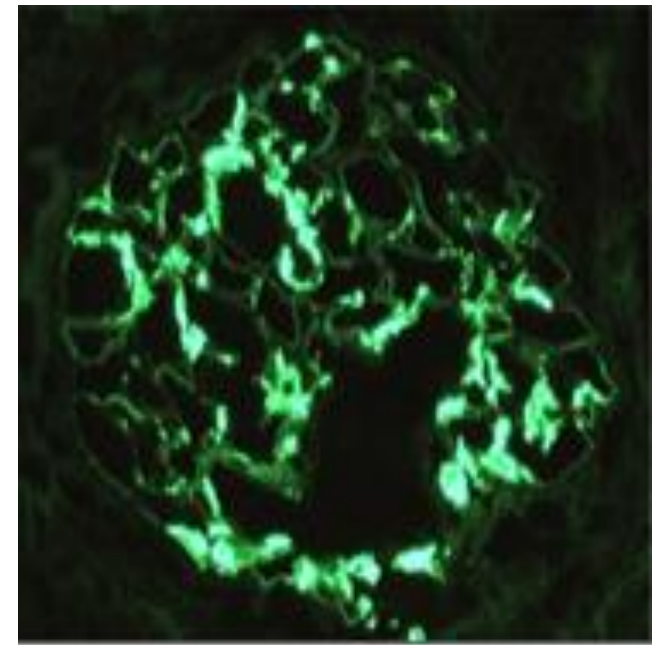
- **Defined by IgA glomerular deposition – IgA may be dominant or co-dominant (w IgG 40-50% IgM 70-80)**

- **Presentation- Young – gross hematuria**

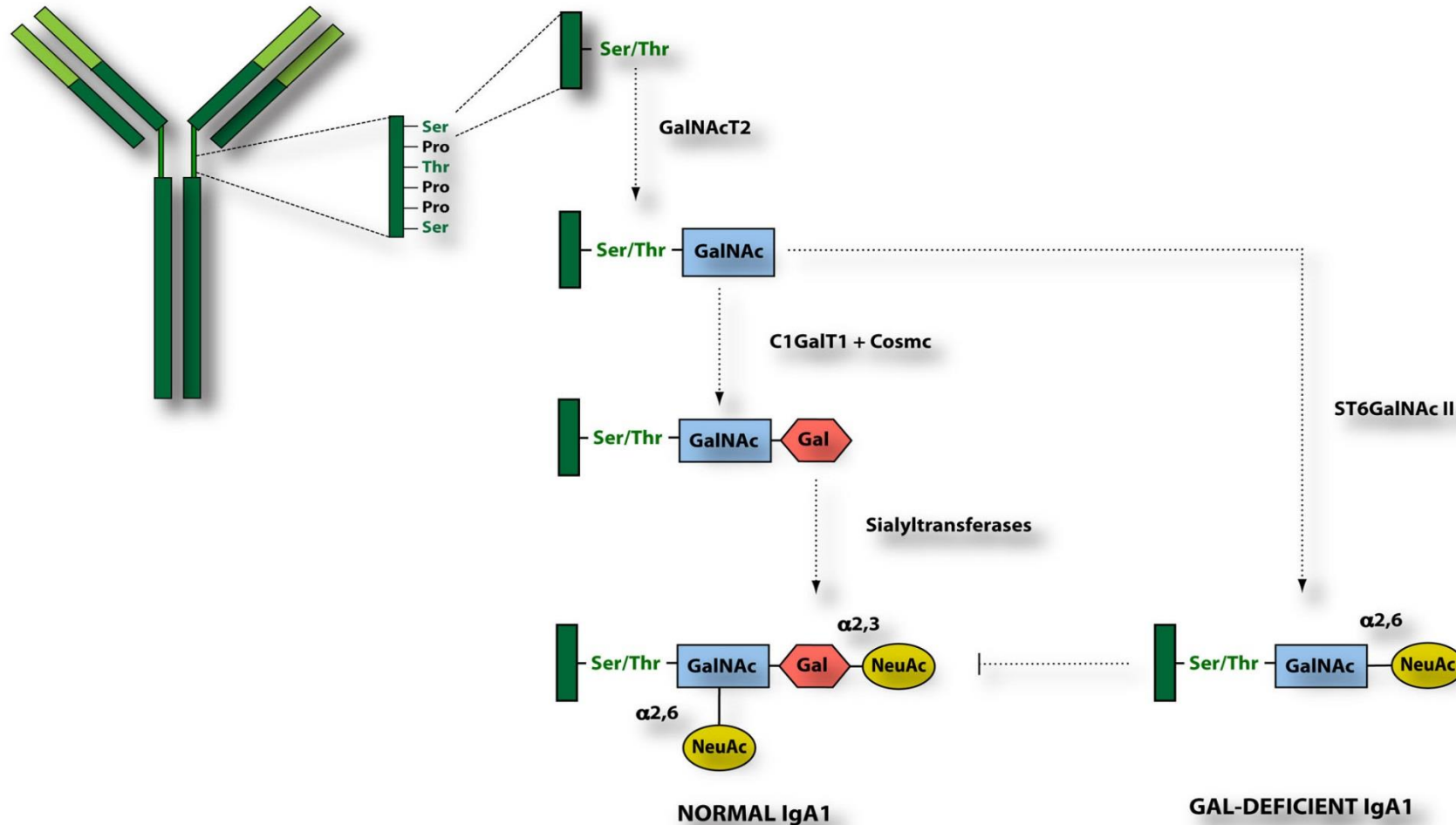
Adults – Proteinuria + hematuria

Pathogenesis – GdIgA1 – 4 Hit Hypothesis

- **ESKD in 15-20% by 10 yrs , 30-40 % by 20 yrs. Risk Far Greater in some!**
- **Progression Risk Factors - Proteinuria and rate of loss of GFR**
- **Treatment – Changing Views but clearly no SINGLE Therapy for All .**
- **Must diagnose earlier and treat all elements in the pathogenesis of IgAN in 2026.**



Low O-glycosylation of IgA1 and gal deficient IgA1 formation



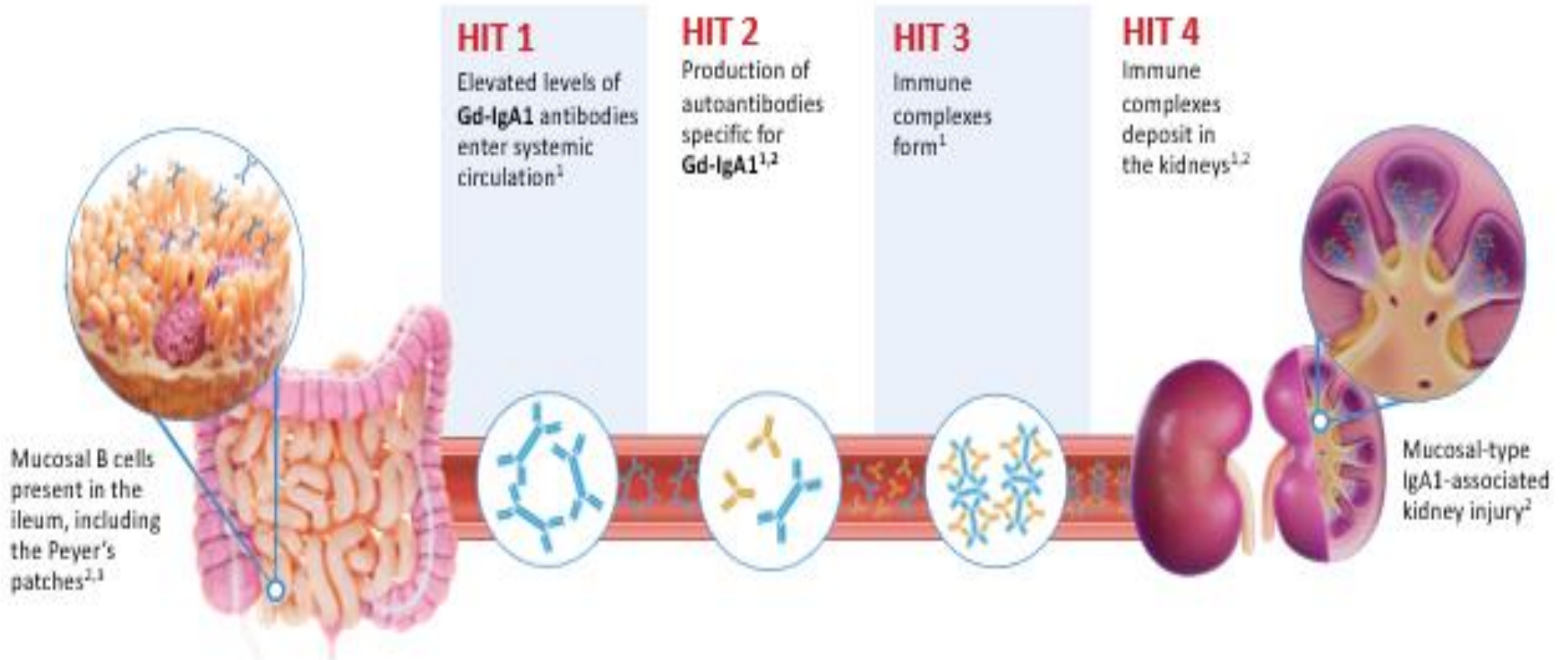
GalNAc = N-acetylgalactosamine

Gal = Galactose

NeuAc = Sialic Acid

Kiryluk et al. *Pediatr Nephrol* (2010)

“Four Hit Hypothesis” of Pathogenesis of IgA Nephropathy



Chang et al, Front Med 7:92, 2020

Barratt et al. Kidney Int Rep 5:1620-1624 2020

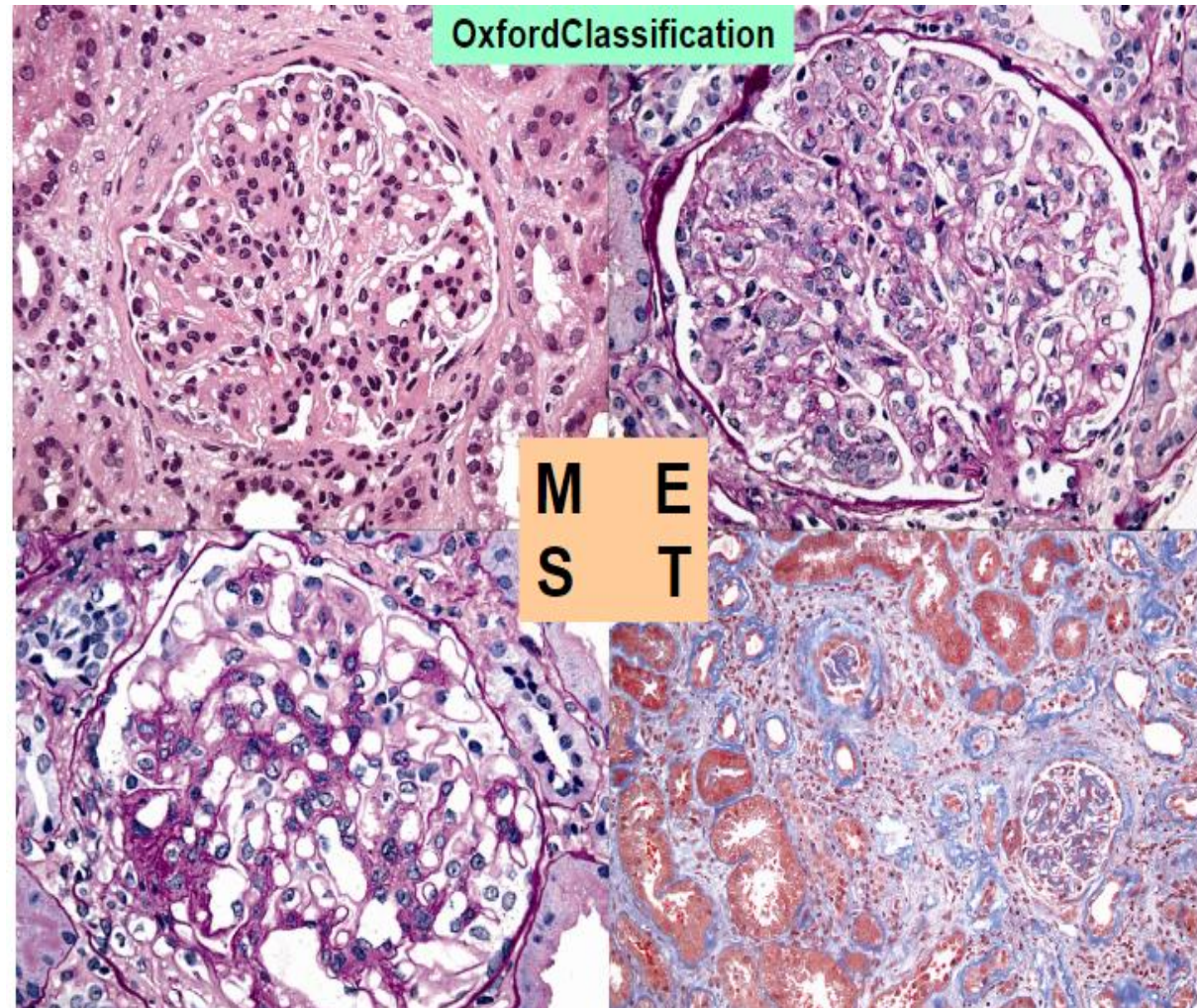
Lafayette R et al. Lancet 402: 859-870, 2023

KDIGO 2025 - Diagnosis of IgA Nephropathy

- 1) Diagnosis of IgA N requires a kidney Biopsy.
- 2) All patients with > 0.5 g proteinuria daily without a clear diagnosis and who may have IgAN should get a biopsy.
Consider Therapy.
- 3) R/O secondary causes : IgA V , viral infections (HIV, Hepatitis) , Inflammatory bowel disease, Autoimmune disease, Liver disease, IgA dominant infectious GN.
- 4) Evaluate the Bx by the Oxford classification (MEST-C score) – Does not tell you which **specific med** to use!!!
- 5) Evaluate Progression Risk – Int IgAN prediction Tool.

MESTC-Oxford Classification

- **Mesangial hypercellularity**
0 = <50%;
1 = >50% glomeruli involved
- **Endocapillary proliferation**
0 = Absent 1 = Present
- **Segmental glomerulosclerosis**
0 = Absent 1 = Present
- **Tubulo-Interstitial fibrosis**
0 = <25%
1 = 25-50%
2 = >50%
- **Crescents**
C0 – absent
C1-0-24%
C2 = or > 25%



Evaluating a New International Risk-Prediction Tool in IgA Nephropathy

JAMA Intern Med. 2019;179(7):942-952

Sean J. Barbour, MD, MSc; Rosanna Coppo, MD, FERA; Hong Zhang, MD, PhD; Zhi-Hong Liu, MD; Yusuke Suzuki, MD, PhD; Keiichi Matsuzaki, MD, PhD; Ritsuko Katafuchi, MD, PhD; Lee Er, MSc; Gabriela Espino-Hernandez, MSc; S. Joseph Kim, MD, PhD; Heather N. Reich, MD, PhD; John Feehally, FRCP; Daniel C. Cattran, MD, FRCPC; for the International IgA Nephropathy Network

AT&T LTE 10:12 AM 100%

< International IgAN Pr... ☆ ☰ ↗

Questions

Estimated GFR at biopsy 30 ml/min/1.73m² >

Systolic blood pressure at biopsy 190 mmHg >

Diastolic blood pressure at biopsy 90 mmHg >

Proteinuria at biopsy 6.9 g/day >

Age at biopsy 54 Years >

Race Caucasian >

Use of ACE inhibitor or ARB at the time of biopsy Yes >

MEST M-score 1 >

MEST E-score 1 >

MEST S-score 0 >

AT&T LTE 10:12 AM 100%

< International IgAN Pr... ☆ ☰ ↗

MEST S-score 0 >

MEST T-score 1 >

Immunosuppression use at or prior to biopsy No >

At how many months after renal biopsy would you like to determine risk of renal progression? 48 Months >

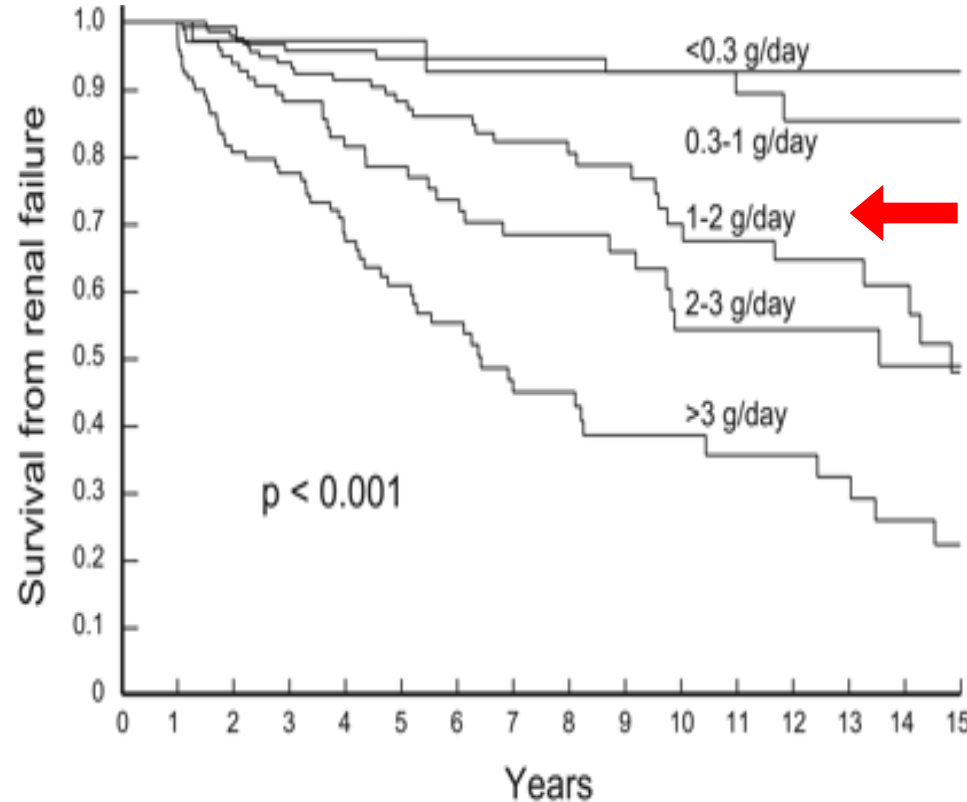
Results

Risk of Progression

The risk of a 50% decline in estimated GFR or progression to end-stage renal disease 4.0 years after renal biopsy is 56.66%

Reduction of Proteinuria Improves Prognosis in IgAN

- 542 pts with IgAN from Toronto registry
- Followed for 78 mos
- GFR declined at -4.5 ml/min/1.73 m²/yr
- 30% reached ESRD



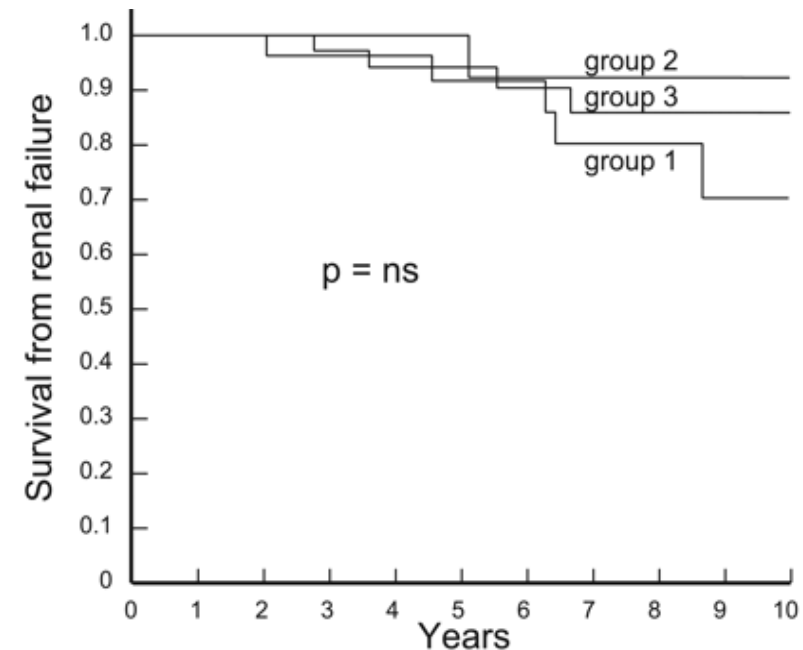
Regardless of peak proteinuria, attaining partial remission (<1 g/d)

leads to similarly good outcomes.

Group 1: 1-2 g/d peak proteinuria

Group 2: 2-3 g/d peak proteinuria

Group 3: >3 g/d peak proteinuria

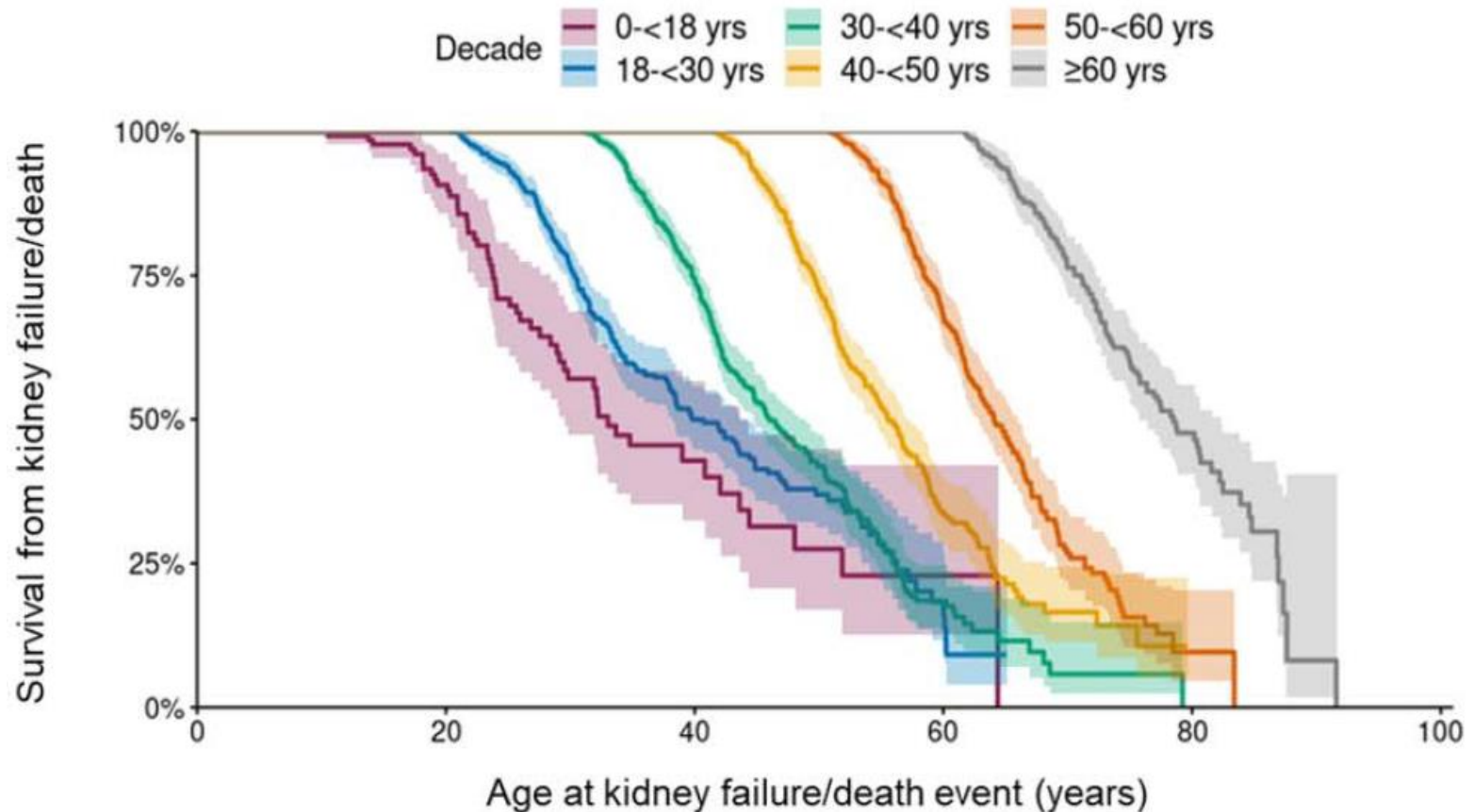


UK Registry Data: Most Patients With IgA Nephropathy Progressed to Kidney Failure Within 10 to 15 Years of Diagnosis

RaDaR IgA nephropathy cohort¹

- Retrospective study (n=2299 adults; n=140 children)
- Biopsy-proven IgA nephropathy plus proteinuria >0.5 g/day or eGFR <60 mL/min/1.73 m² at any time in their disease history

- 50% of patients reached kidney failure* or died during the study (median follow: 5.9 years)
- Median (95% CI) kidney survival: 11.4 (10.5-12.5) years
- Mean (SD) age at kidney failure/death*: 48 years



Patients With Low Proteinuria Levels Can Progress to Kidney Failure

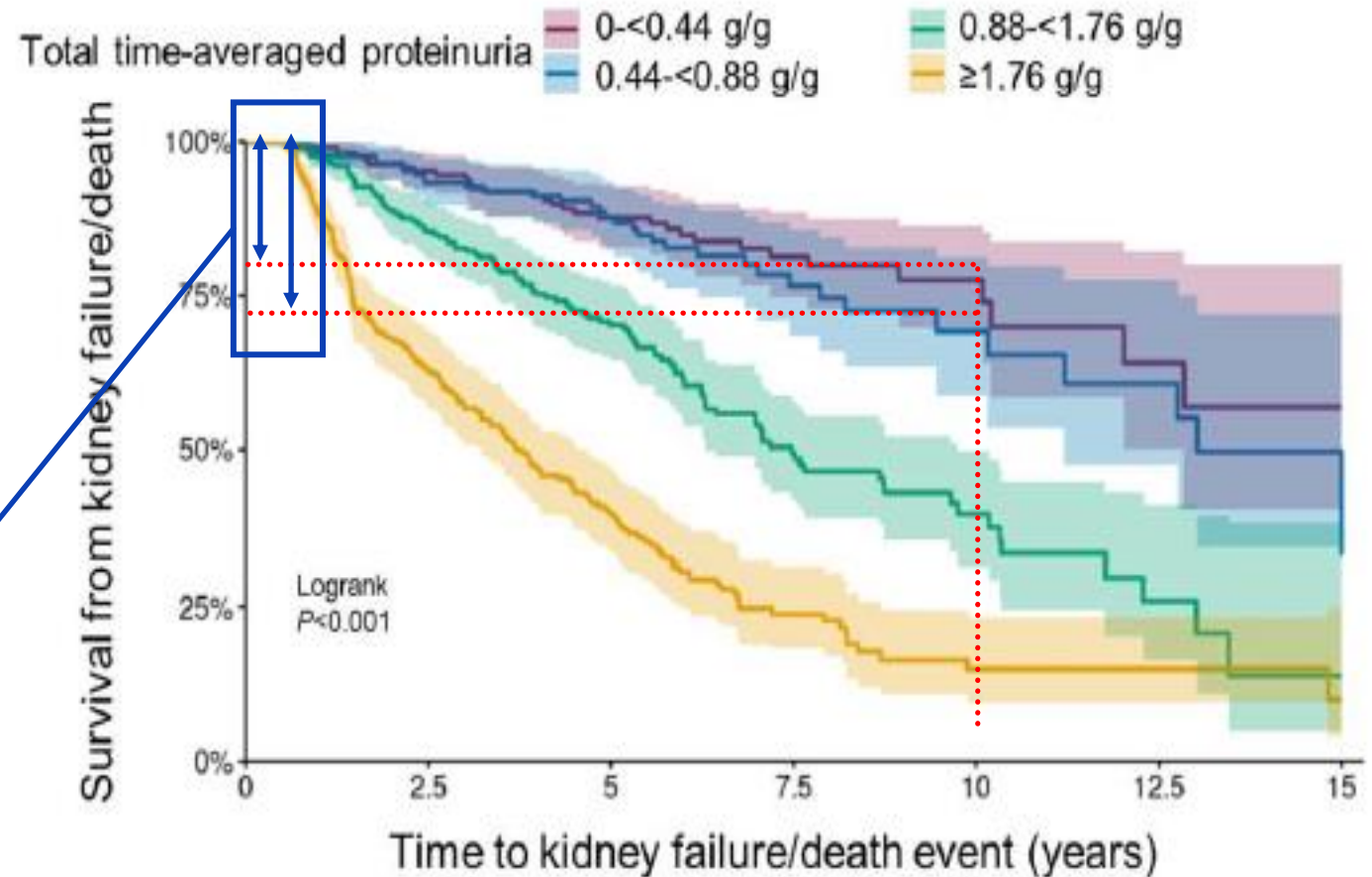
RaDaR IgA nephropathy cohort (2299 adults and 140 children) – proteinuria findings¹

Time-averaged proteinuria was significantly associated with worse kidney survival (and more rapid eGFR loss)

However, the 10-year risk of kidney failure/death was also relatively high in patients typically perceived to be “low-risk”:

~30% of patients with time-averaged
UPCR 0.44-<0.88 g/g

~20% of patients with time-averaged
UPCR <0.44 g/g

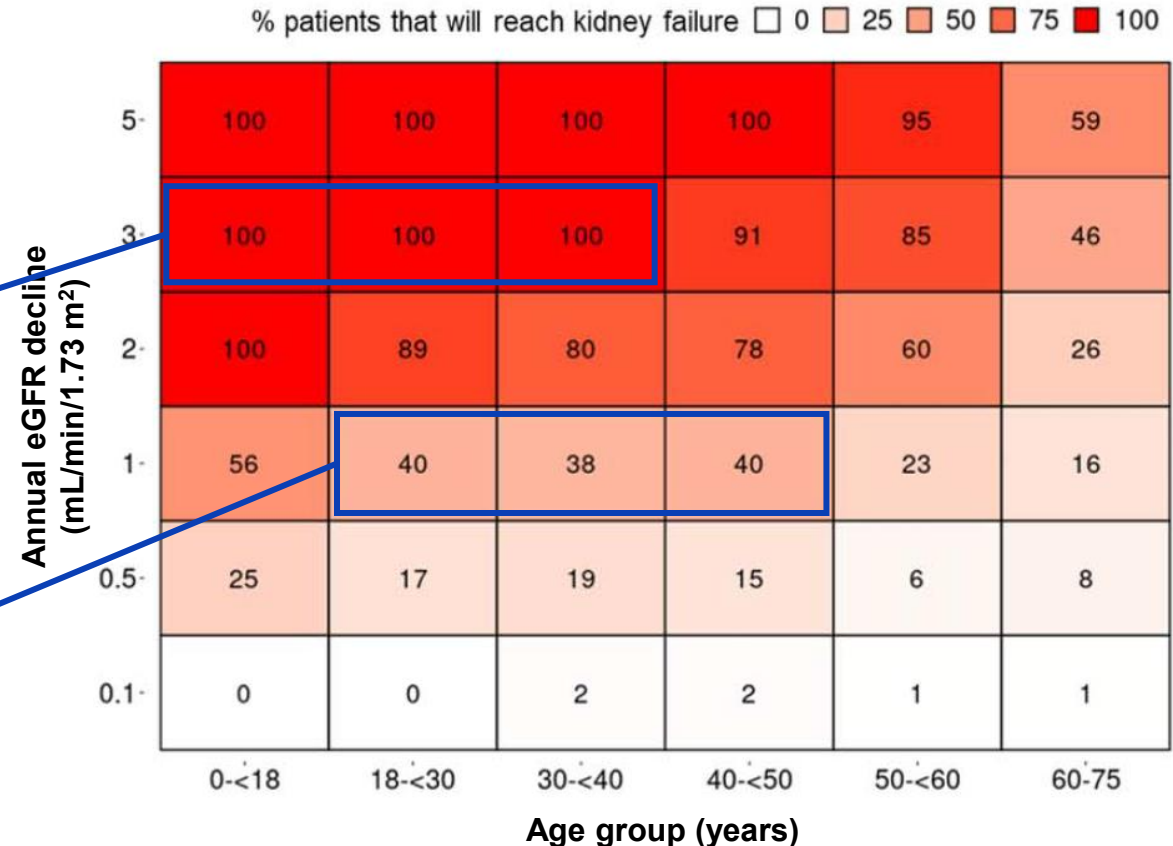


A Faster Rate of eGFR Decline in IgA Nephropathy = A Shorter Time to Kidney Failure

RaDaR (UK registry) IgA nephropathy cohort (2299 adults and 140 children)¹

eGFR decline of 3 mL/min/1.73 m²/year = 100% of patients <40 years old at diagnosis reaching kidney failure within expected lifetime

eGFR decline of 1 mL/min/1.73 m²/year of ~40% of adult patients <50 years old at diagnosis reaching kidney failure within expected lifetime



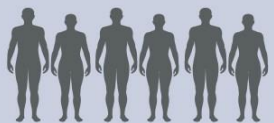
“To achieve the aspiration that no patient with IgAN should progress to kidney failure, the current approach to patient care needs to be re-evaluated.”

Pitcher D, Braddon F, Hendry B... Barratt J. CJASN 18:1-12, 2023

CKD progression, kidney failure, and mortality among US patients with IgA nephropathy

We evaluated kidney outcomes among a racially, ethnically, and socioeconomically diverse IgAN population in the USA.

Methods



655 adults with primary IgAN
(31% Asian/Pacific Islander, 3% Black,
40% Hispanic/Latino, 24% White)
2000–2022



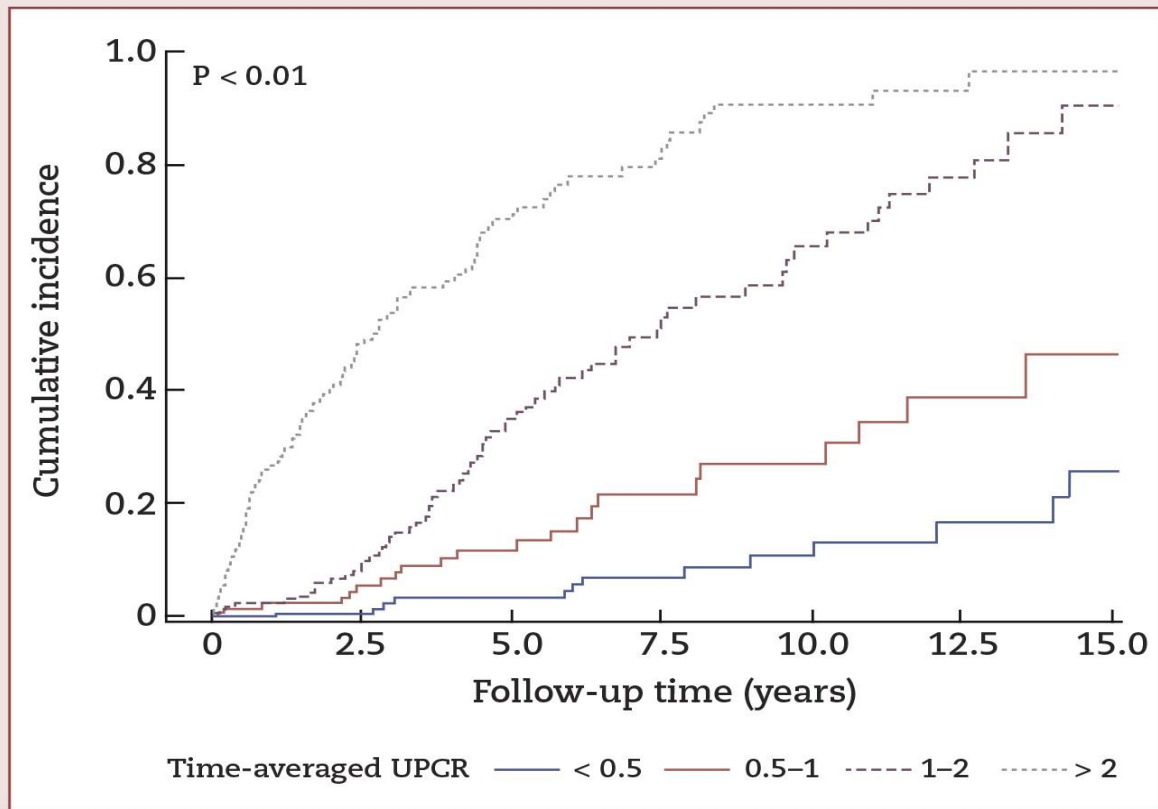
Composite endpoint
1. $\geq 50\%$ eGFR decline
2. Kidney failure
or 3. Mortality



234 (36%)
**reached composite
kidney endpoint**

Incidence rate
79.4 events
per 1000 patient-years
(95% CI 69.6, 90.7)

Results



Kidney Function Loss in Control Pts with Optimized Supportive Care In IgAN Trials						
Baseline characteristics	Manno et al. ¹ (Active control [ramipril])	TESTING ² (Placebo + RAS inhibition)	STOP-IgAN 10-year results ^{3,4} (RAS inhibition)	PROTECT ⁵ (Active control [irbesartan])	DAPA-CKD ⁶ (Placebo + RAS inhibition)	NeflgArd ⁷ (Placebo + RAS inhibition)
N in PBO ARM	49	246	80	202	133	182
Age, years*	35 (11)	37 (29-46)	45 (12) [†]	45 (12)	50 (13)	42 (34-49)
Systolic blood pressure, mmHg*	123 (8)	125 (116-131)	126 (10) [†]	130 (12)	127 (14)	124 (117-130)
Diastolic blood pressure, mmHg*	82 (7)	80 (74-86)	78 (8) [†]	83 (11)	80 (10)	79 (74-84)
Median proteinuria, g/24 h (IQR)	1.5 (1.4-2.3)	1.9 (1.4-2.9)	1.7 (0.8) [†]	1.8 (1.3-2.6)	N/A	2.2 (1.5-3.4)
eGFR, mL/min/1.73 m ² *	98 (28)	59 (42-78)	59 (27) [†]	57 (24)	43 (12)	55 (46-68)
Median time since IgAN diagnosis, years (IQR)	≤1 year before randomization	0.4 (0.3-1.2)	N/A	4.0 (1.0-10.0)	N/A	2.6 (0.6-6.5)
Total eGFR slope, mL/min/1.73 m ² per year [§]	−6.2	−5.0	−2.7	−3.9	−4.7	−5.4

KDIGO IGA N Guidelines 2025 Kidney Int. Oct 2025

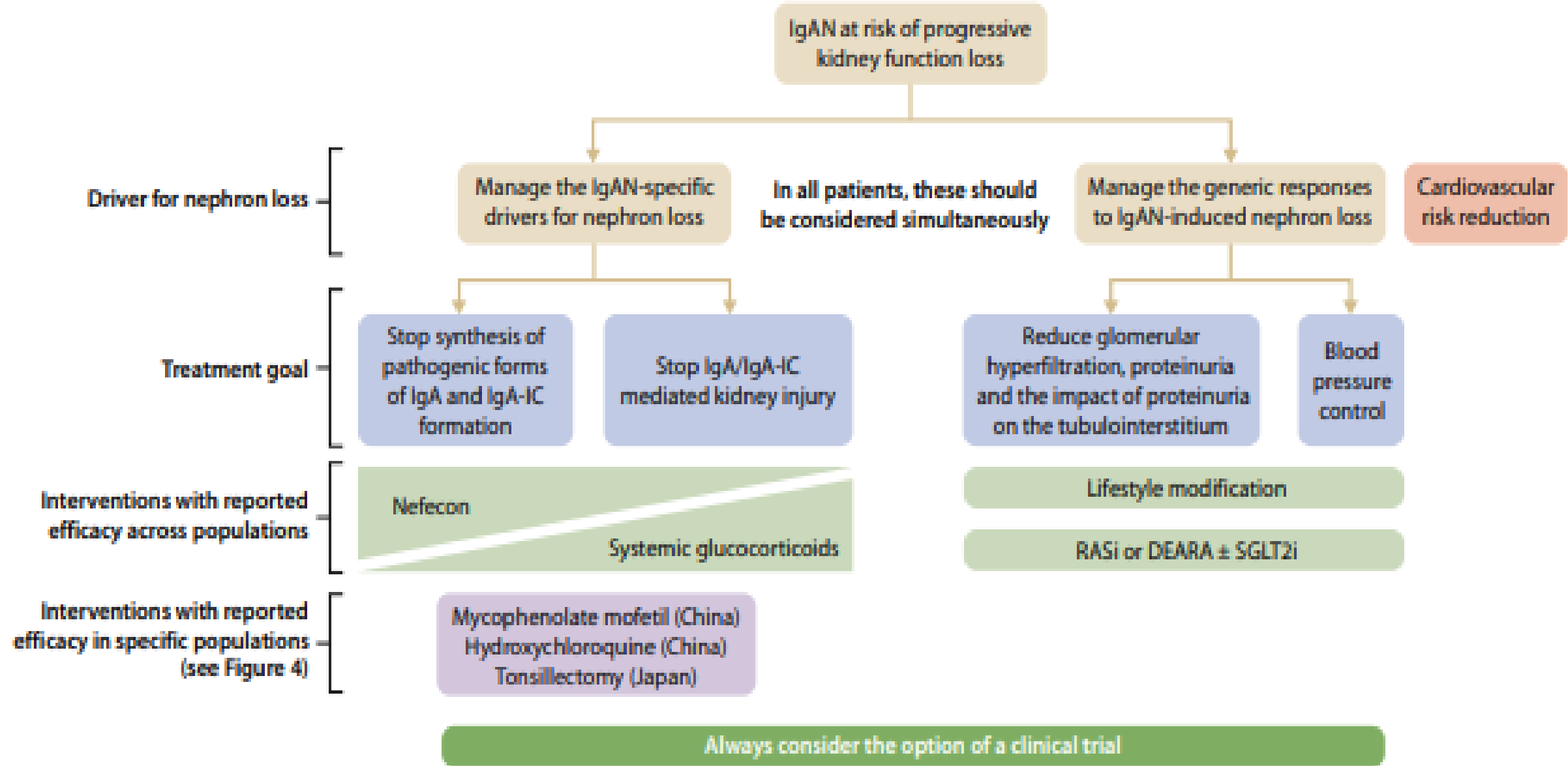


Figure 3 | Treatment targets in immunoglobulin A nephropathy (IgAN) and the positioning of drugs included in this guideline.

Current and Future Meds for IgA Nephropathy therapy

For Glomerular Inflammation steroids and MMF work

TR Budesonide – FDA approved

Sparsentan – FDA Approved -combined ETA antagonist + ARB

Dapagliflozin, Empagliflozin – FDA approved for CKD

Iptacopan – FDA accelerated FDA approval - complement blocker

Atrasentan - FDA accelerated FDA approval - endothelin antagonist

Sibeprenlimab – FDA accelerated approval - anti-APRIL inhibitor

Atacicept – FDA accelerated approval – -anti-BAFF/ anti-April inhibitors

Telitacicept in China , Povetacicept later this year ?, zigakibart -anti-April

Felzartamab - anti CD 38 -like daratumumab.

Effect of Oral Methylprednisolone on Decline in Kidney Function/Kidney Failure in IgA N - TESTING STUDY

LV J, Wong MG, Hladunewich M, et al JAMA 327: 188-1898,2022

	Full Dose (n=262)	Reduced Dose (n=241)
Regimen	• MP 0.6-0.8 mg/kg/d (max 48 mg) x2mo • Tapering 8 mg/mo over additional 4-6mo	• MP 0.4 mg/kg/d (24-32 mg) x2mo • Tapering 4 mg/mo over additional 4-6mo • antibiotic prophylaxis x12 wks
Follow-up	5.7 yr	2.5 yr
Primary composite outcome	0.58 (95%CI 0.41-0.81)	0.27 (95%CI 0.11-0.65)
Serious Adverse Events	30 vs 5 in placebo	7 vs 3 in placebo
• Hospitalized infection	• 11 vs 1 ($p=0.006$)	• 5 vs 2 ($p= 0.45$)
• Death	• 3 vs 0	• 1 vs 0

Role of Systemic Glucocorticoids in Reducing IgA and Galactose-Deficient IgA1 Levels in IgA Nephropathy



TESTING Trial
China Cohort (N=137)



Serum samples
collected at baseline,
6 and 12 months



Levels of Total IgA and
Gd-IgA1 measured



Association between
markers and proteinuria
reduction was analyzed

Timepoints	Reduced Dose (95% CI)		Full Dose (95% CI)	
	IgA (%)	Gd-IgA1 (%)	IgA (%)	Gd-IgA1 (%)
6 months	27.2 (16.4-36.6)	21.2 (10.6-30.6)	34.0 (25.7-41.4)	42.0 (36.1-48.6)
12 months	20.4 (8.7-30.7)	4.6 (-8.3-15.9)	10.8 (-0.47-20.8)	25.4 (16.8-33.1)
	similar to placebo (p=0.47)		significant reduction (p<0.001)	



Changes in Total IgA,
Gd-IgA1 and proteinuria
reduction

Positive correlation
for methylprednisolone
groups

No significant
correlation
for placebo group



Reduction in Gd-IgA1 levels
at 6 months was not
associated with long-term
kidney progression events
(p=0.49)

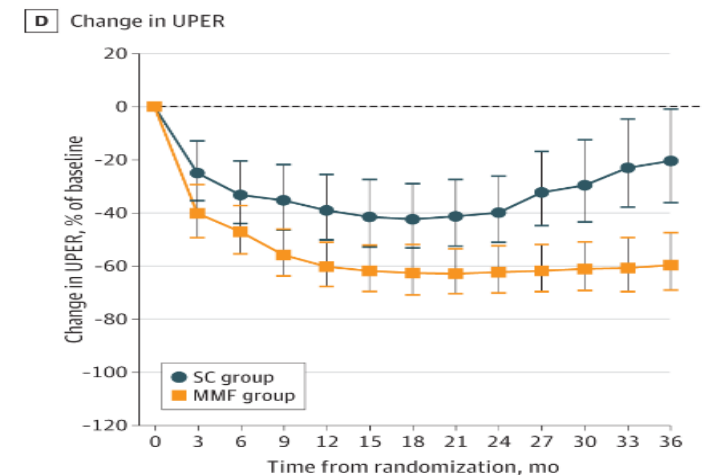
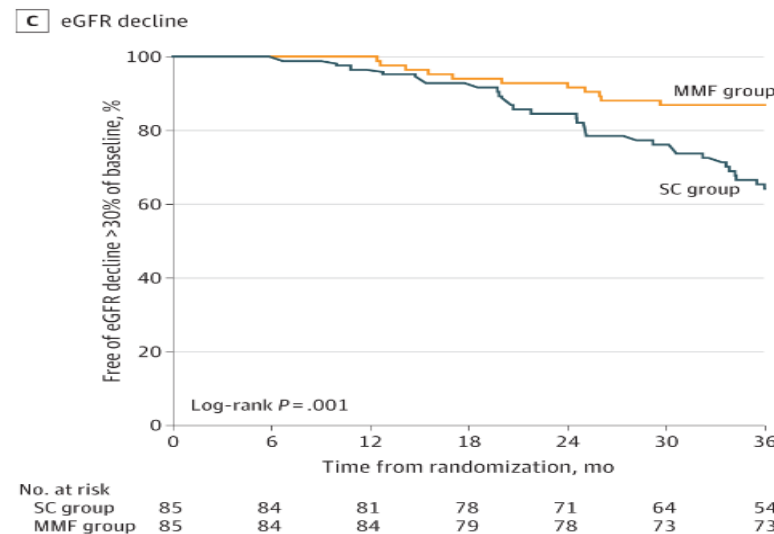
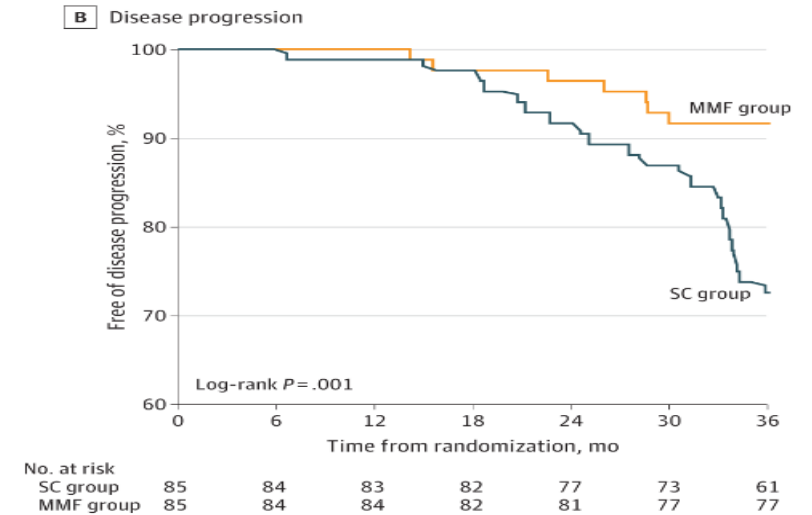
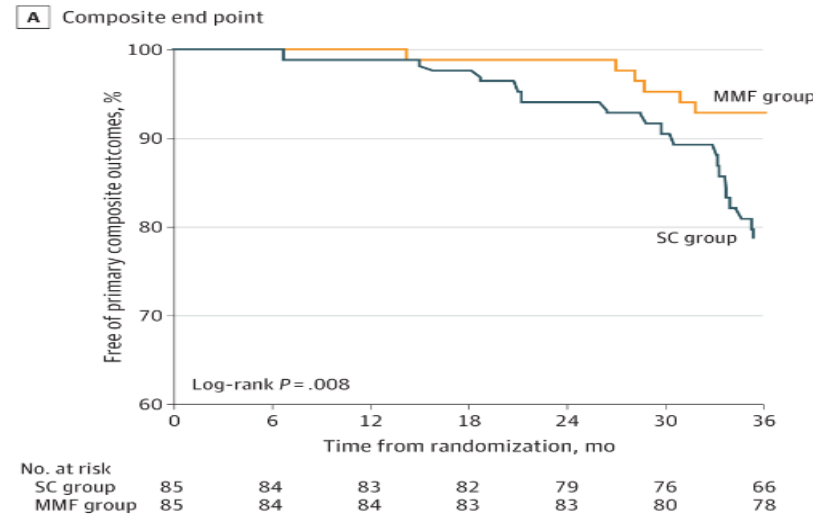
Conclusions: Systemic glucocorticoids significantly reduce total IgA and Gd-IgA1 levels in IgAN compared to placebo, however the treatment effects may diminish over time.

Jincan Zan, Jingyi Li, Muh Geot Wong et al. Role of Systemic Glucocorticoids in Reducing IgA and Gd-IgA1 Levels in IgA Nephropathy. CJASN, DOI: 10.2215/CJN.0000000816
Visual Abstract by Carlo Trinidad, MD

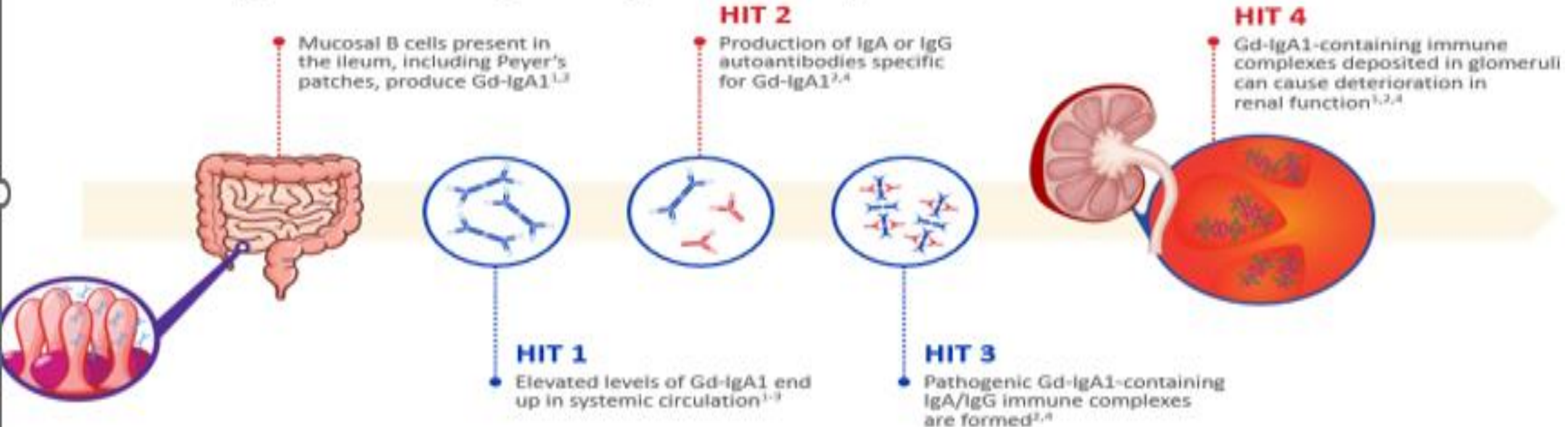
MAIN Trial : Effectiveness of Mycophenolate Mofetil Among Patients With Progressive IgA Nephropathy: A Randomized Clinical Trial

JAMA Network Open. 2023;6(2):e2254054. Feb 6,2023

- MMF 1.5 g/d x 12 months + 0.75-1.0 g for at least 6 months
- vs placebo
- N=170



"4-Hit" Hypothesis: A Widely Accepted Model for Understanding the Pathogenesis of IgA Nephropathy



Block autimmune mech of IgAN

Block formation of Gd IgA1
Block IgA1 immune Complexes

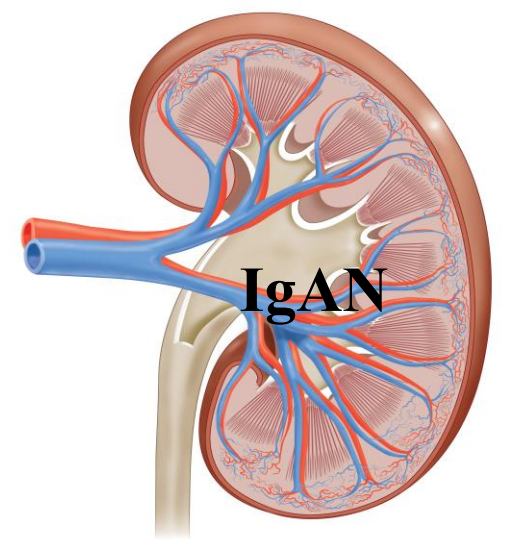
Block nonspecific - CGN

ACE inhib/ARBs
SGLT2inhibs
Sparsentan

Block Glom inflammation /scarring

Steroids, MMF, other immune meds

KDIGO 2025 IgA N - UpToDate 2026



1) Biopsy early - for proteinuria ≥ 0.5 g/d

Risk of progressive loss of kidney function if proteinuria ≥ 0.5 g/d on or off treatment. Start treatment/additional treatment .

2) Goal – Reduce proteinuria < 0.5 g ,reduce loss of function ($< 1\text{cc/min/yr}$)

3) Focus on “simultaneously”:

- Reducing IgA IC formation and IC- mediated glomerular injury
- Manage existing IgAN-induced nephron loss – ACE inhib/ARB, endothelin blockers, SGLT2inhibs
- Manage Glomerular inflammation.

4) Cannot use MEST score to pick specific medication. General guide to Therapy

Current and Future Meds for IgA Nephropathy therapy

For Glomerular Inflammation steroids and MMF work

TR Budesonide – FDA approved

Sparsentan – FDA Approved -combined ETA antagonist + ARB

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Felzartamab - anti CD 38 -like daratumumab.

Efficay and Safety of TR Budesonide in Primary IgA N (NefigArd)Lafayette R, Kristensen J, Stone A et al. The Lancet 402: 859-870, 2023

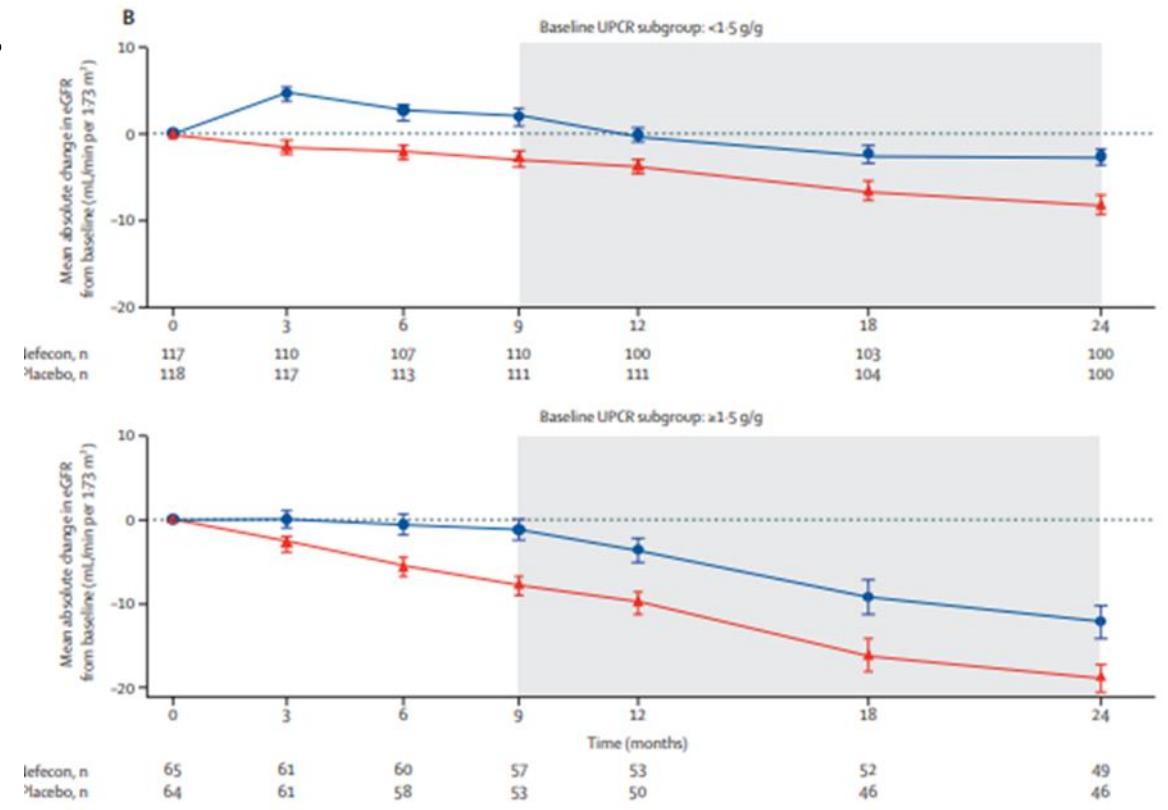
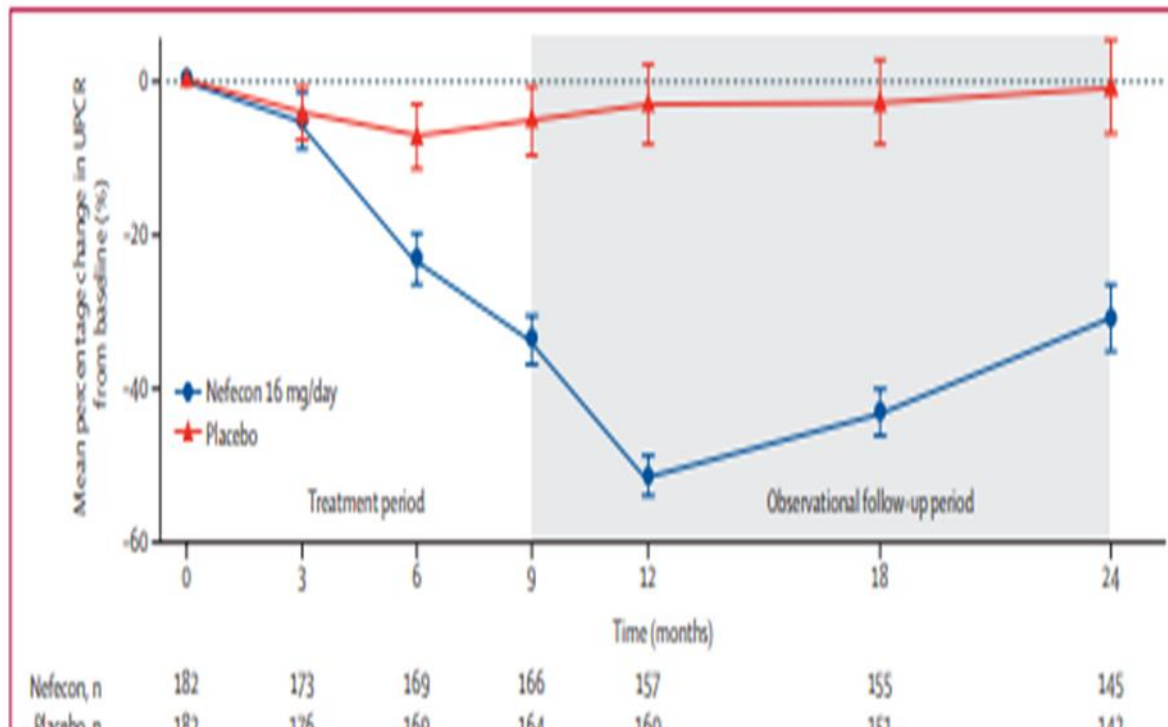
364 Pts w IgAN , eGFR 35-90cc/min Uprot/Ucreat >0.8g/g
or Uprot >1 g/D

16 mg TR budesonide for 9 mo vs PBO All Optimized support.

Most common side effects edema (17%), HBP(12%) acne 11%

No increase infections, 7 DM all pre-DM or prior DM

No deaths



ire 1: Mean absolute change in eGFR from baseline to 24 months (full analysis set)

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

Kidney int. 2024 105:381-388

David Wimbury^{1,8}, Masahiro Muto^{2,8}, Jasraj S. Bhachu¹, Katrin Scionti¹, Jeremy Brown¹, Karen Molyneux³, Claudia Seikrit³, Dita Maixnerová⁴, Laura Pérez-Alós⁵, Peter Garred⁵, Jürgen Floege³, Vladimír Tesar⁴, Bengt Fellstrom^{6,8}, Rosanna Coppo⁷ and Jonathan Barratt¹

¹Mayer IgA Nephropathy Laboratories, Department of Cardiovascular Sciences, University of Leicester, Leicester, UK; ²Department of Nephrology, Juntendo University Faculty of Medicine, Tokyo, Japan; ³Division of Nephrology and Clinical Immunology, Rheinisch-Westfälische Technische Hochschule Aachen University, Aachen, Germany; ⁴Department of Nephrology, 1st Faculty of Medicine, General University Hospital, Charles University, Prague, Czech Republic; ⁵Laboratory of Molecular Medicine, Department of Clinical Immunology, Rigshospitalet, Copenhagen, Denmark; ⁶Department of Medical Sciences, Uppsala University, Uppsala University Hospital, Uppsala, Sweden; and ⁷Fondazione Ricerca Molinette, Regina Margherita Hospital, Turin, Italy

Kidney International (2024) 105, 381–388; <https://doi.org/10.1016/j.kint.2023.11.003>

KEYWORDS: chronic kidney disease; complement; cytokines; glomerulus; IgA nephropathy; proteinuria

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Nefecon is the first approved treatment for patients with immunoglobulin A nephropathy (IgAN) at high risk of progression to kidney failure (accelerated approval by US Food and Drug Administration; conditional approval by European Medicines Agency).^{1–3} Nefecon delivers budesonide, in a targeted formulation, to the gut-associated

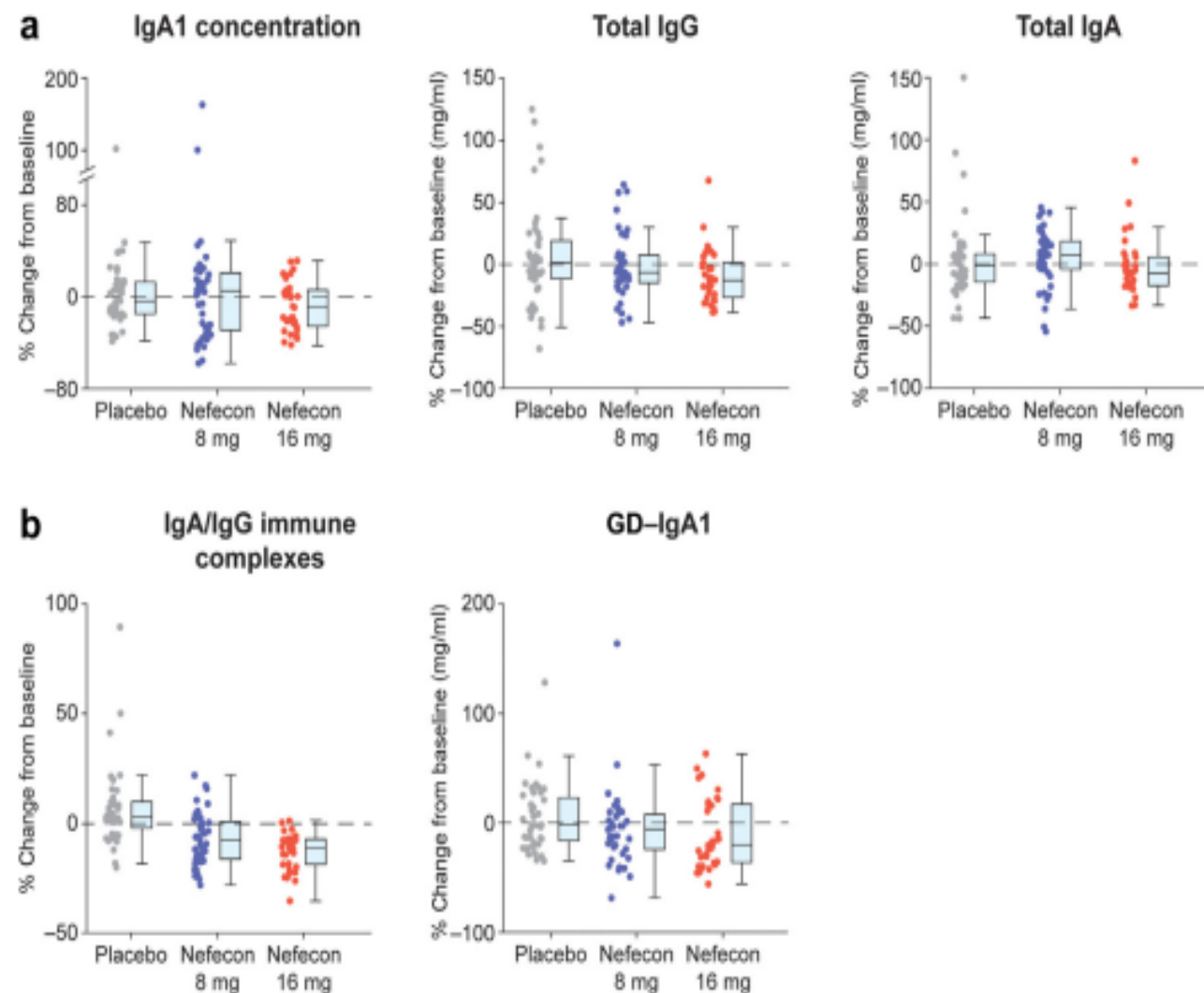
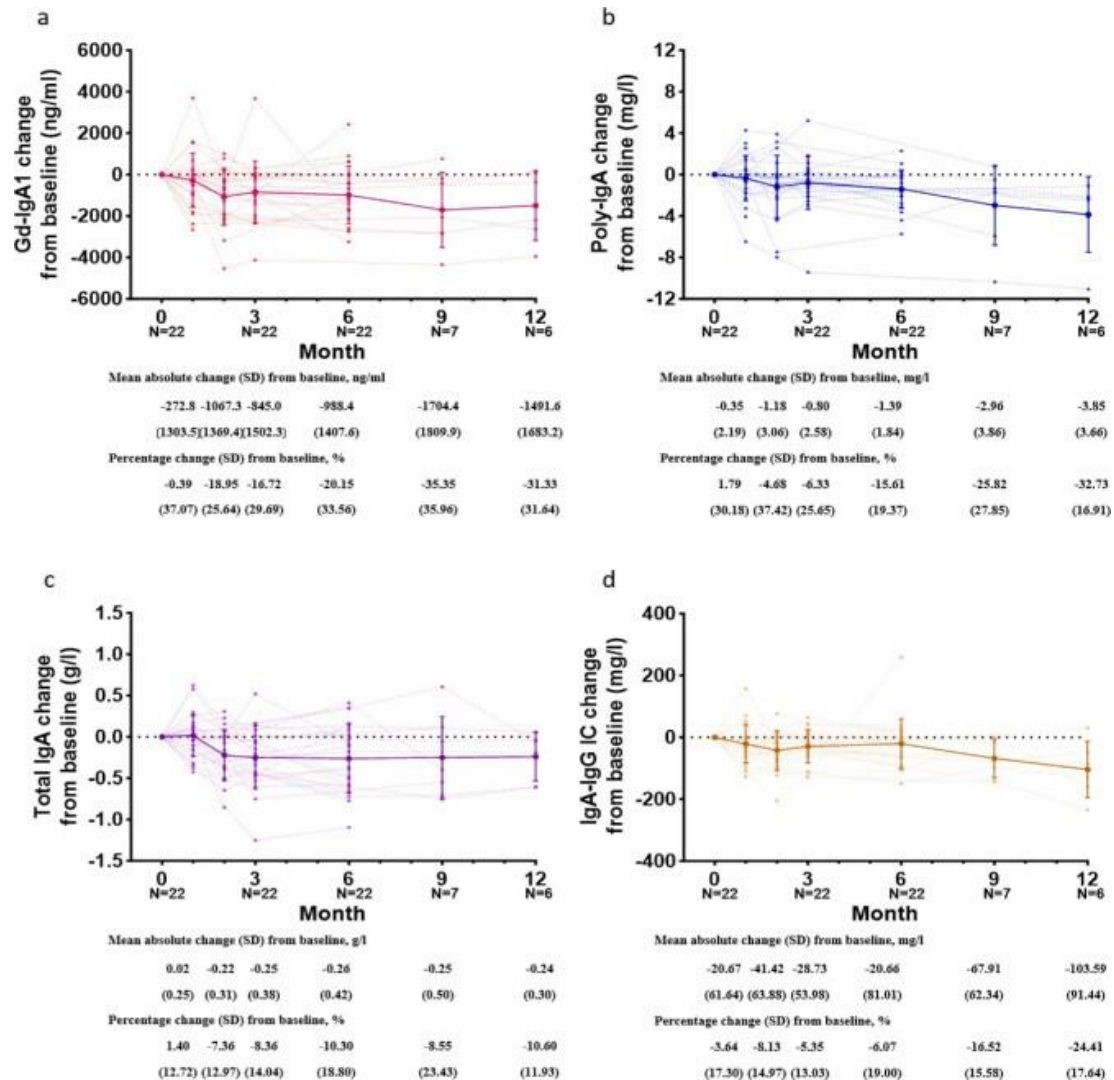
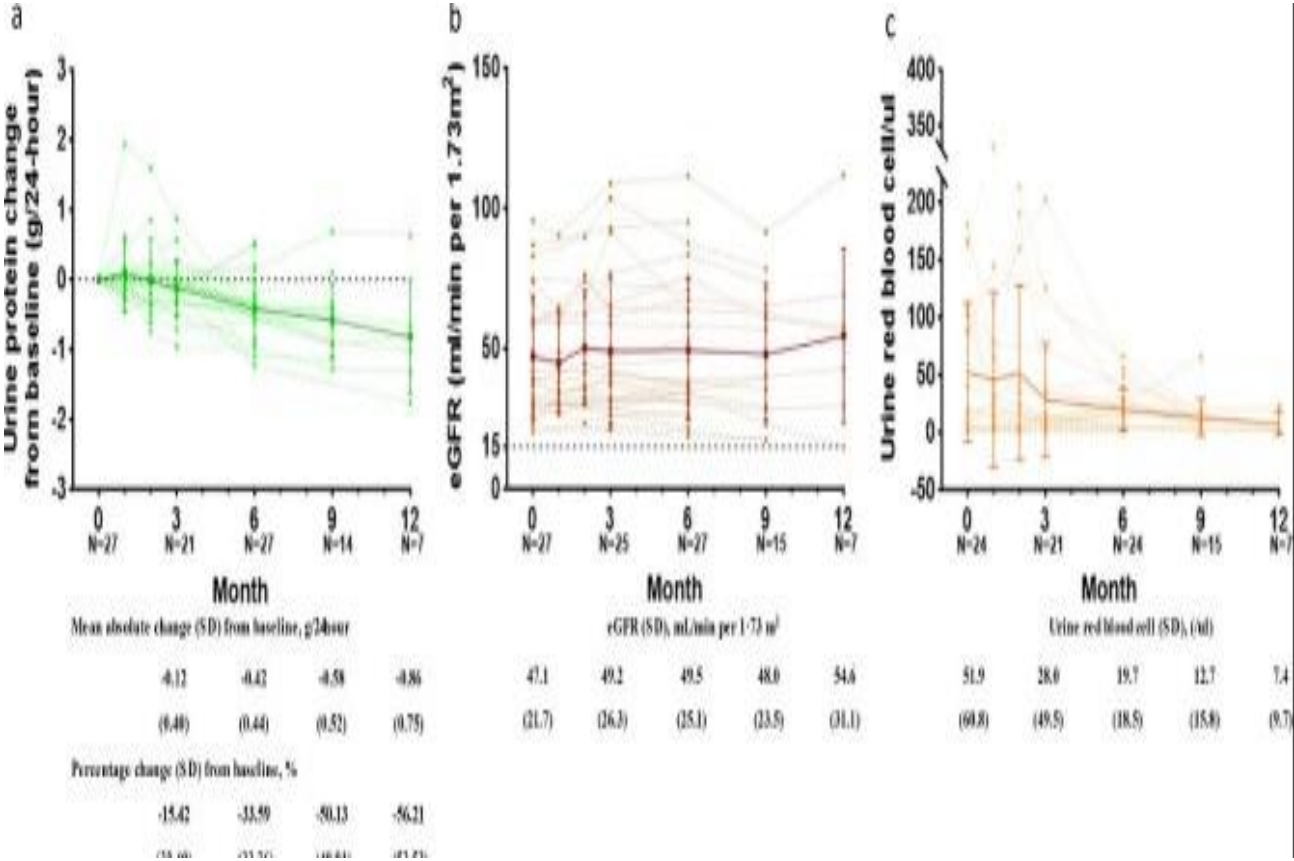


Figure 1 | Change from baseline by treatment group in biomarkers demonstrating the disease-modifying effect of Nefecon at 9 months. (a) IgA1 concentration ($p = 0.0656$), total IgG ($p = 0.2491$), total IgA ($p = 0.3955$). (b) IgA/IgG immune complexes ($p < 0.0001$).

Predictive value Of Gd-IgA1, poly-IgA in treatment of IgAN with TR Budesonide

Chen Q , Chen P, He R et al. Clin Kidney Journal Jul 2025



Efficacy and Safety of Sparsentan vs Irbesartan in IgA nephropathy

(Protect Study 2 yr blinded Phase 3 Trial Lancet 402:2077 2023

- N=404 randomized
- 29% Asian
- Age at IgAN dx = ~40y
- Age at enrollment = 46y
- UPE = 1.8 g/d
- eGFR = 57 ml/min/1.73m²

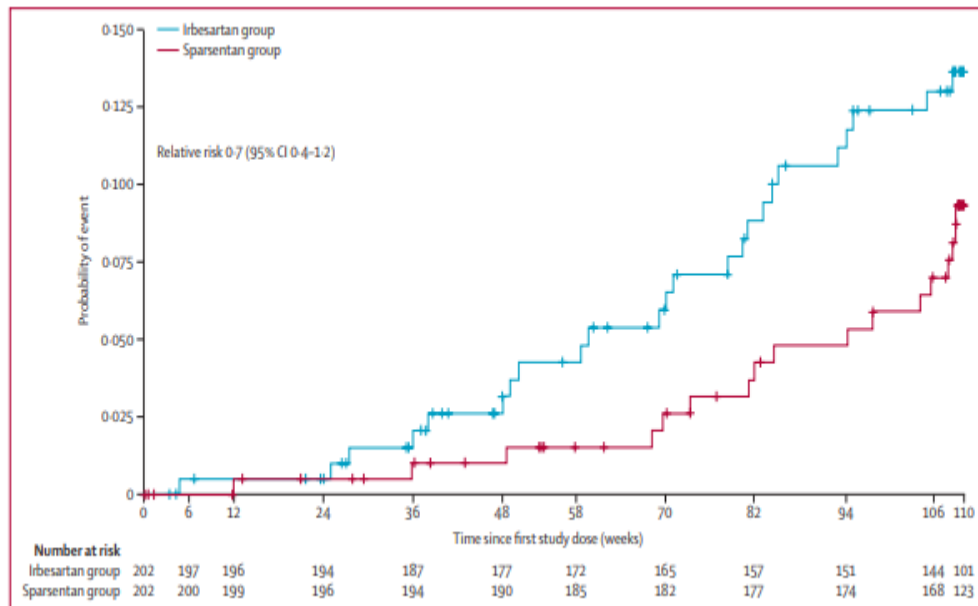
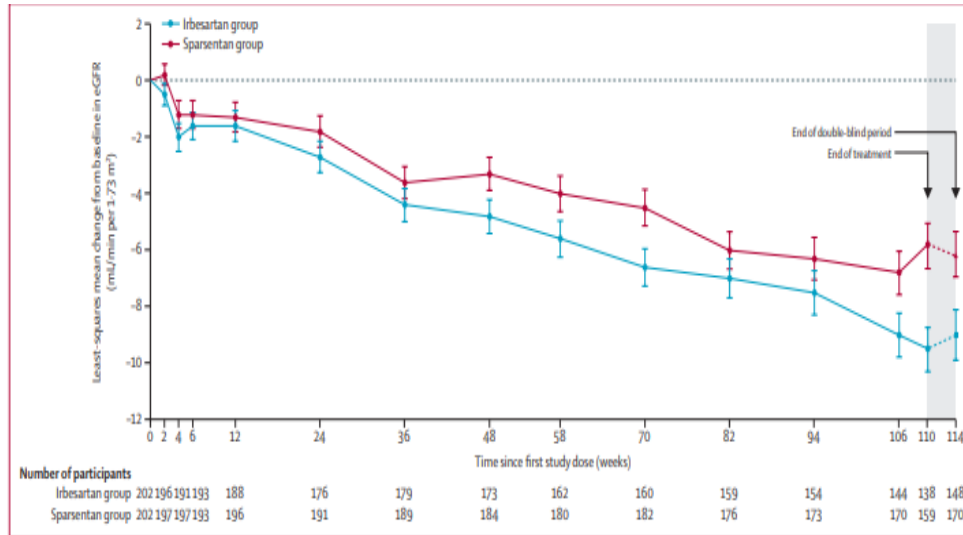


Figure 4: Time to reach the composite kidney failure endpoint of confirmed 40% eGFR reduction, end-stage kidney disease, or all-cause mortality

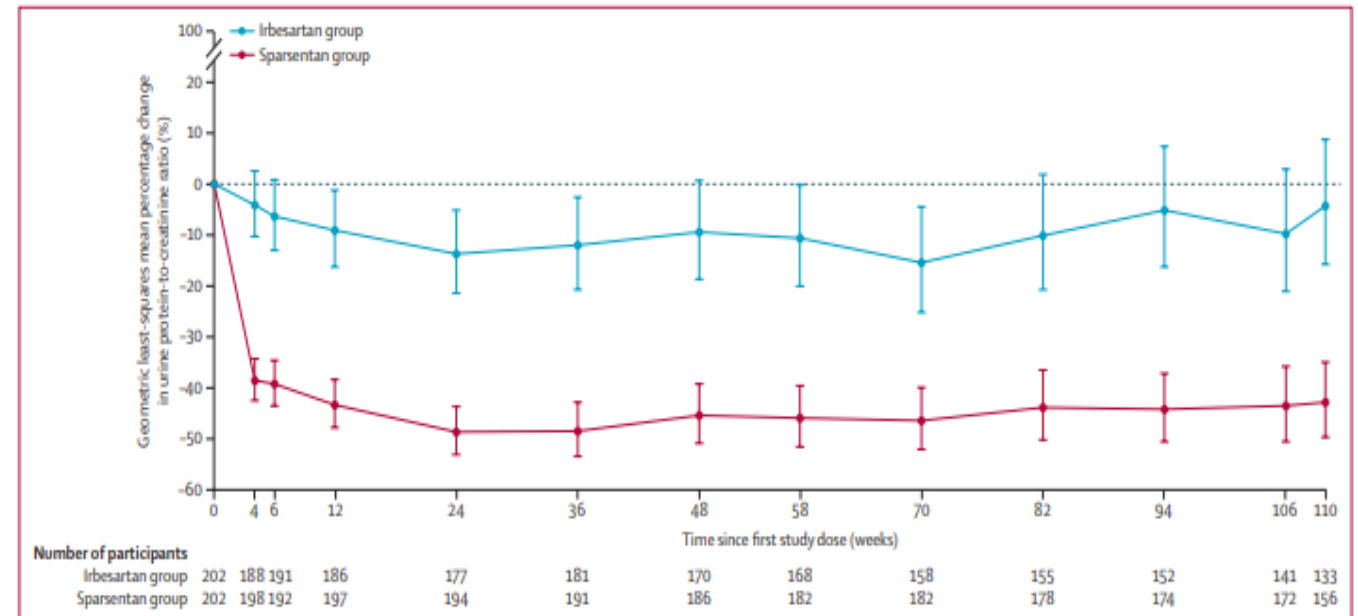
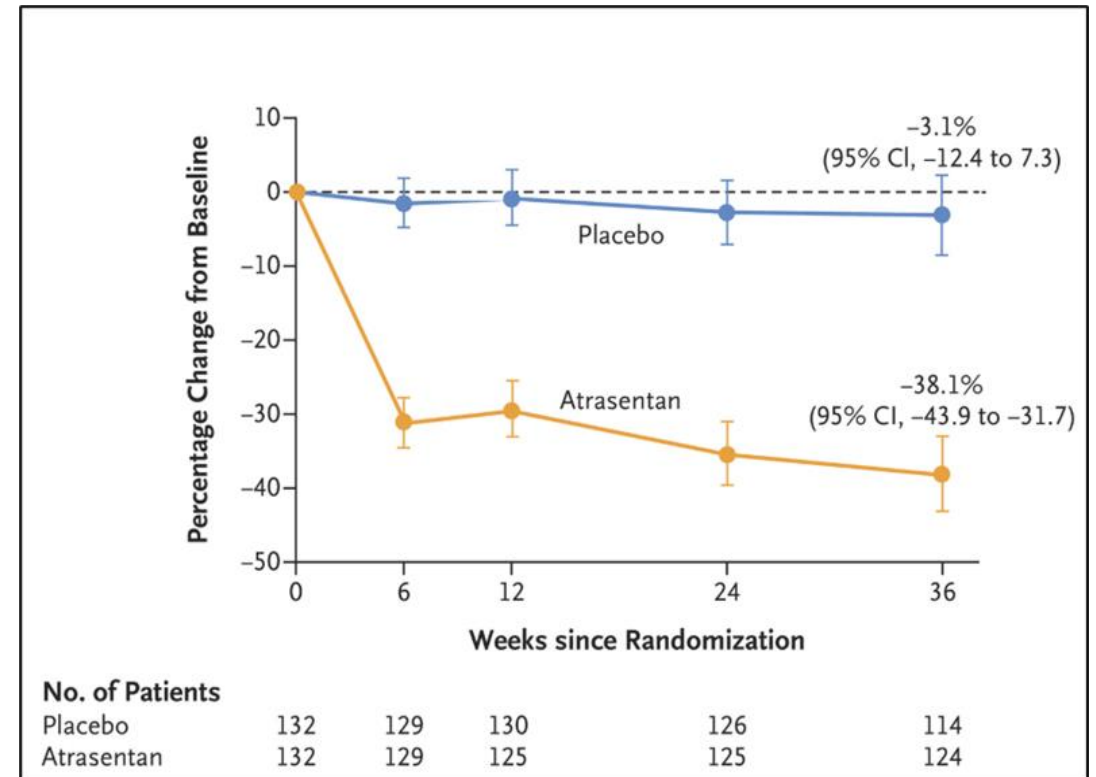


Figure 5: Geometric least-squares mean percentage change from baseline in the urine protein-to-creatinine ratio at each visit up to week 110

ALIGN Trial: Atrasentan vs Placebo in Patients with IgAN

- 264 IgAN Pts
- eGFR ≥ 30 ml/min
- UPCR ≥ 1 g/g
- Max tolerated ACE inhib/ ARB for ≥ 12 weeks

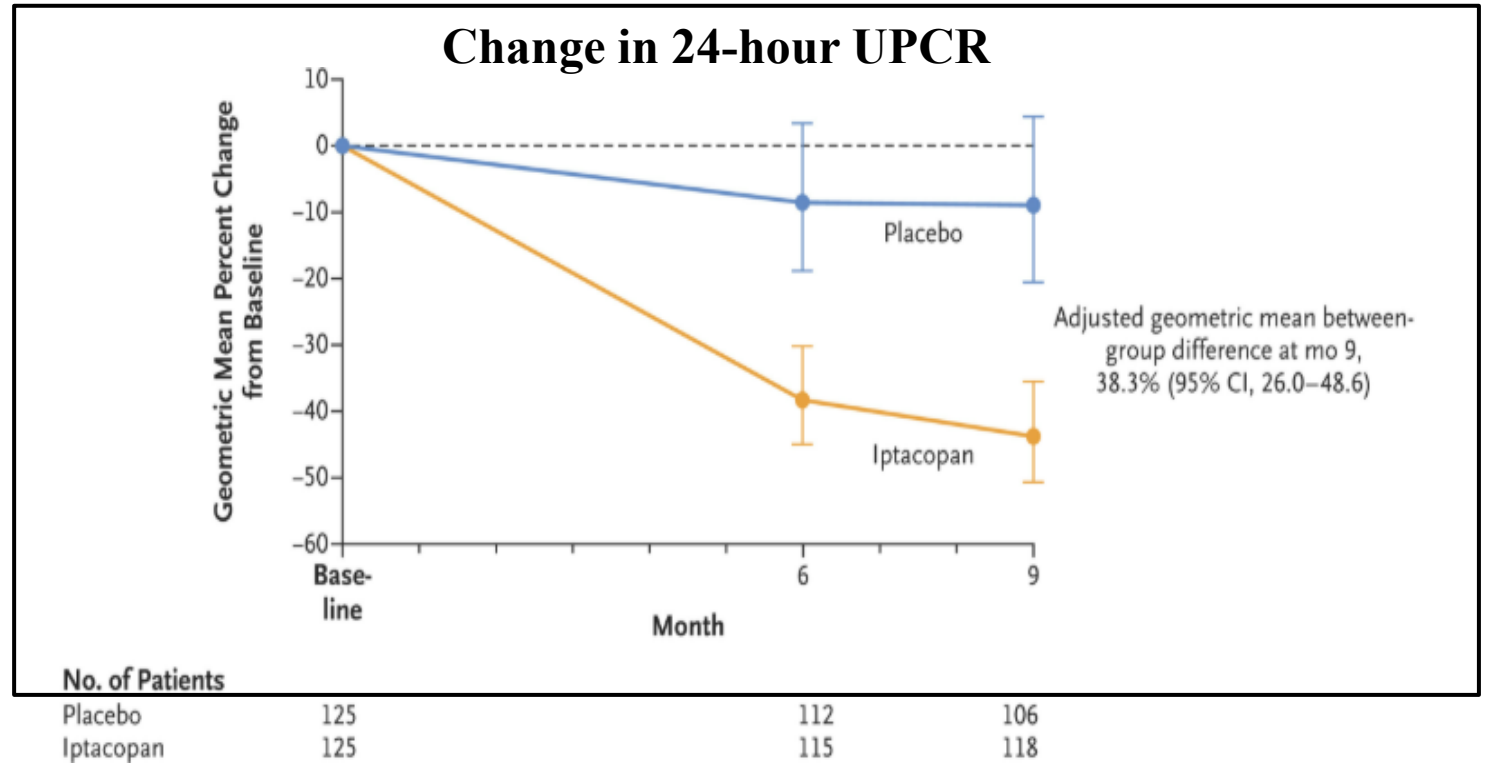
Atrasentan reduced proteinuria at 36 weeks vs PBO



Phase 3 APPLAUSE-IgAN: Iptacopan vs Placebo in Patients with IgAN

Study Patients

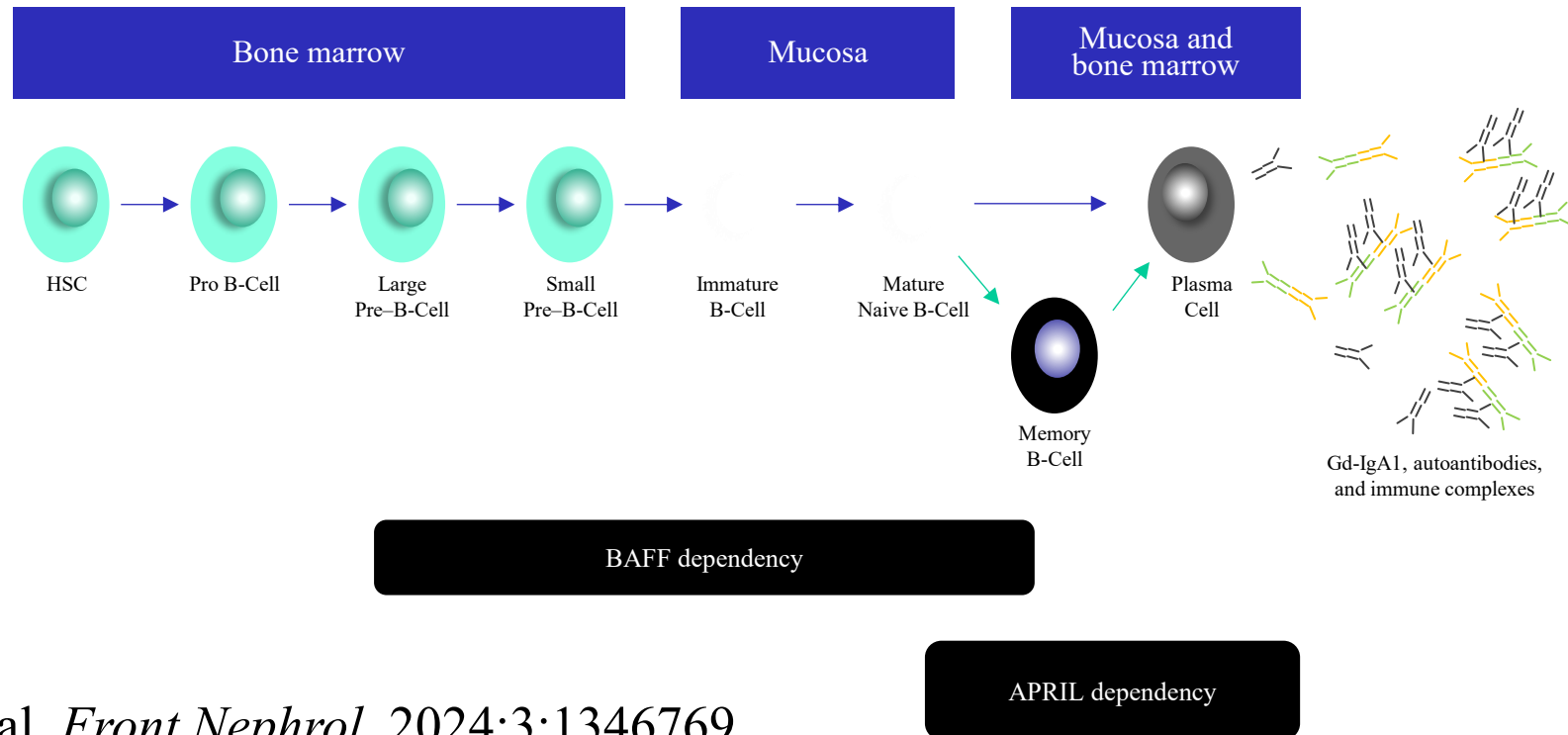
- Biopsy-proven IgAN
- eGFR ≥ 30 ml/min
- UPCR ≥ 1 g/g
- Stable dose of ACE inhibitor or ARB for ≥ 90 days w or w/o SGLT2inhibitor
- 200mg PO daily
- End point 2 yrs eGFR slope vs PBO



Iptacopan reduced proteinuria at 9 months by 38.3% compared to placebo

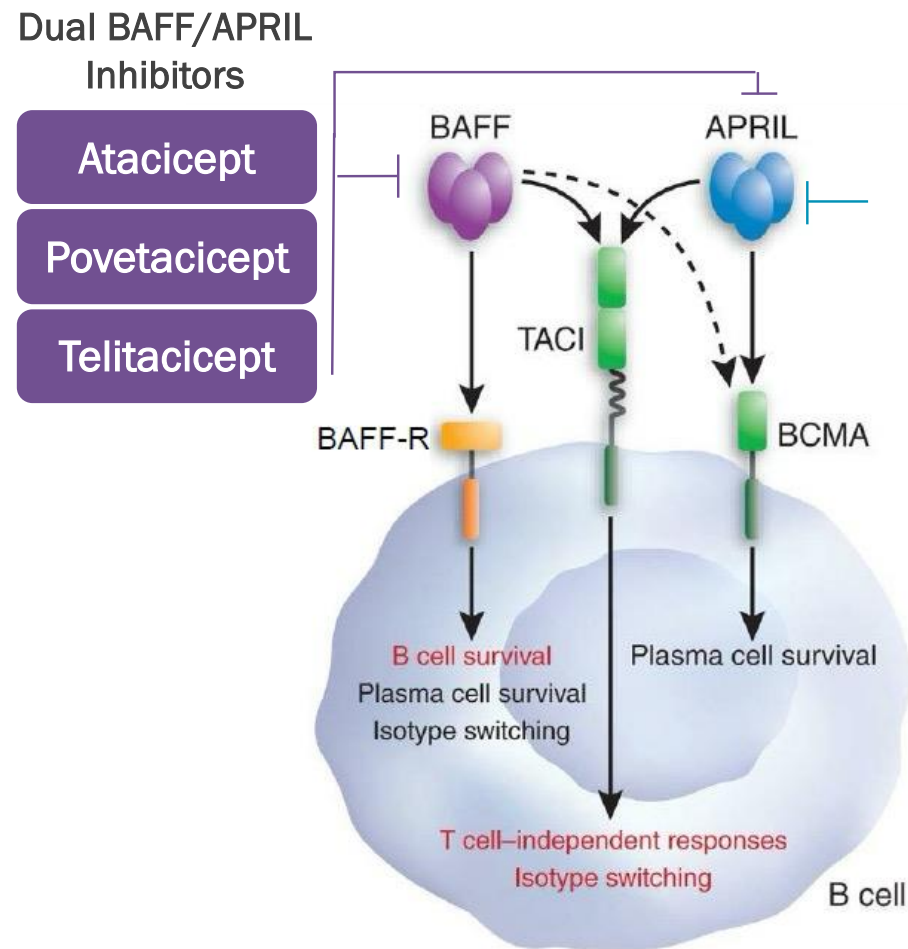
B-Cell Activating Factor (BAFF) and A Proliferation-Inducing Ligand (APRIL)

play a critical role in the production of IgA⁺ B-cells



Cheung CK, et al. *Front Nephrol.* 2024;3:1346769.

BAFF and APRIL Inhibitors in IgAN



Sibeprenlimab is a monoclonal antibody that works by targeting and neutralizing the cytokine A Proliferation-Inducing Ligand (APRIL)

VISIONARY: A Phase 3 Trial of Sibeprenlimab in IgAN

V Perkovic H trimarchi, V Tesar et al NEJM 11/8/2025

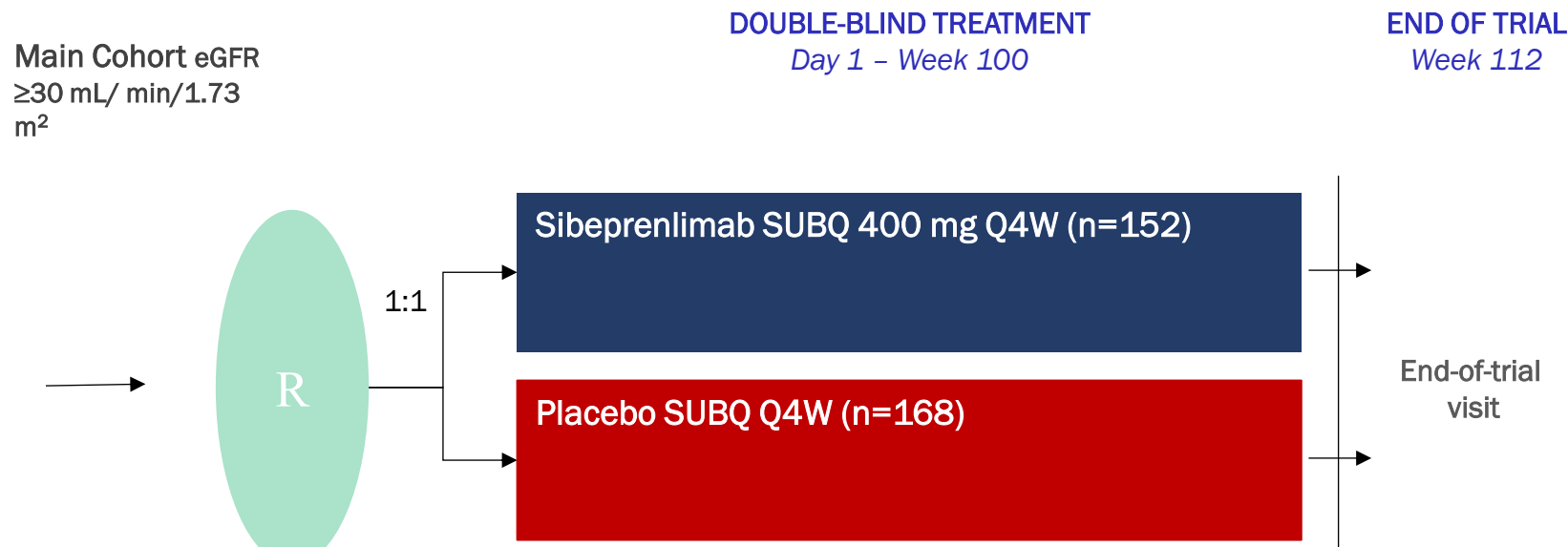
Multicenter, Double-Blind,
Randomized, Placebo-
Controlled

- Bx confirmed IgAN
- Proteinuria ≥ 1.0 g/day or uPCR ≥ 0.75 g/g
- eGFR ≥ 30 mL/min/1.73 m²

ENDPOINTS

Primary: Change in 24-h uPCR
at month 9

Secondary: Annualized slope
eGFR over 24 mo.



	Sibeprenlimab	PBO
Median (range) uPCR-24 h, g/g	1.2 (0.5-6.7)	1.3 (0.5-5.5)
eGFR, mean mL/min/ 1.73/m2	63.5 (24.4)	63.4 (25.3)
Median time from biopsy to randomization (range), years	1.3 (0.1-23.7)	1.9 (0-34.0)
SGLT2i use at baseline n (%)	56 (36.9)	72 (42.9)

VISIONARY: A Phase 3 Trial of Sibeprenlimab in IgAN

V Perkovic, H Trimarchi, V Tesar et al NEJM 11/8/2025

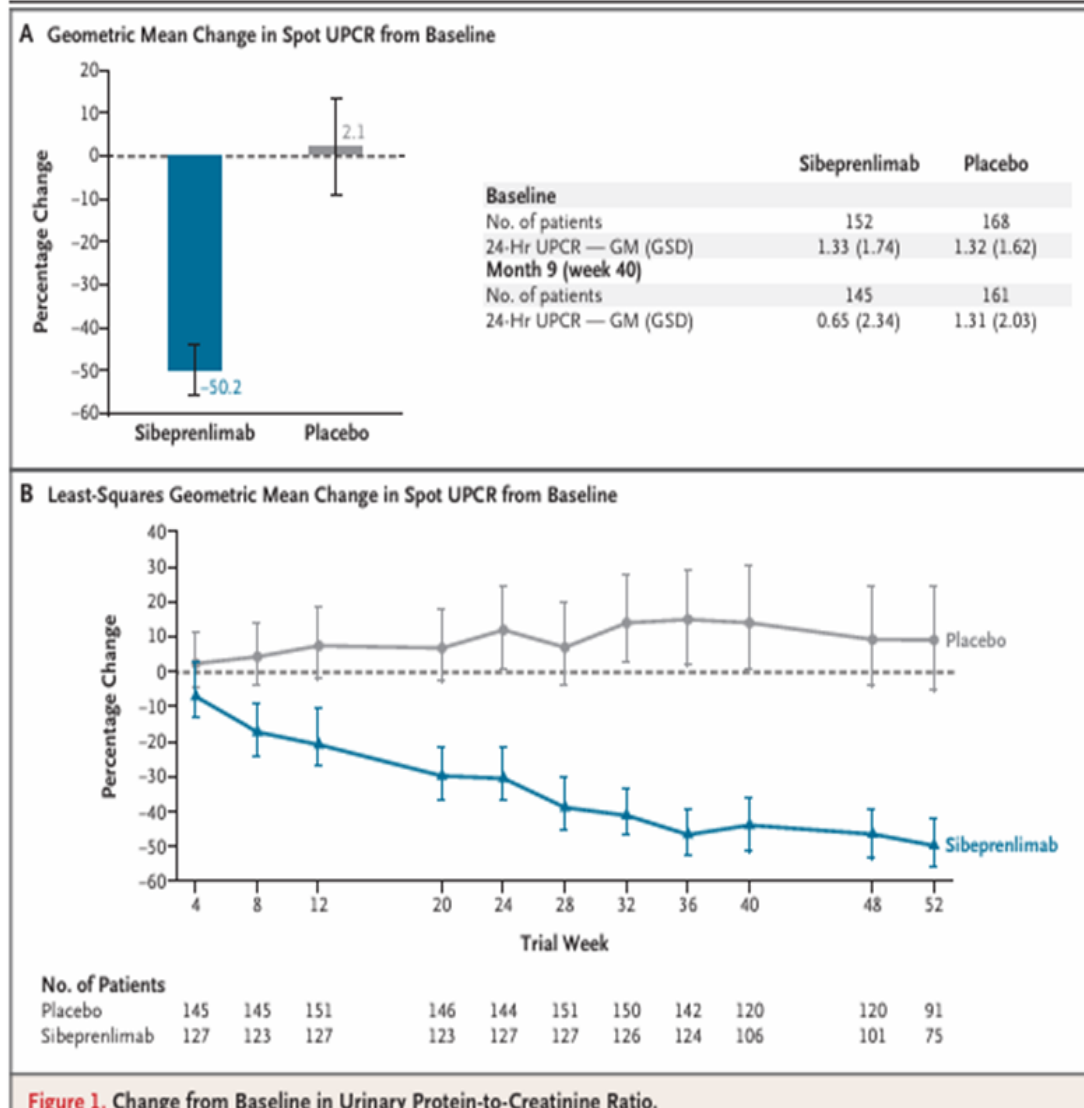
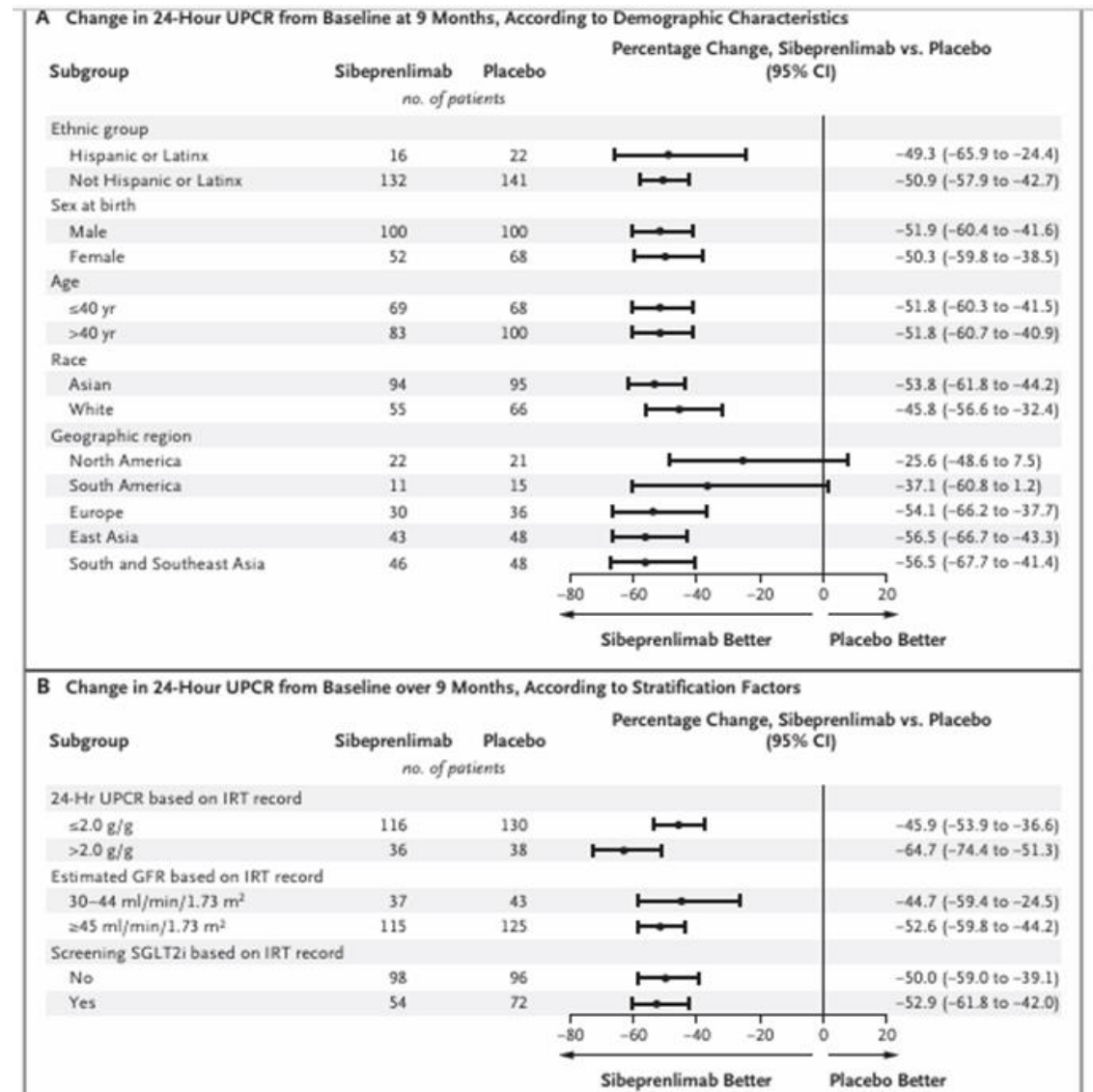


Figure 1. Change from Baseline in Urinary Protein-to-Creatinine Ratio.



VISIONARY: A Phase 3 Trial of Sibeprenlimab in IgAN

V Perkovic Htrimarchi, V Tesar et al NEJM 11/8/2025

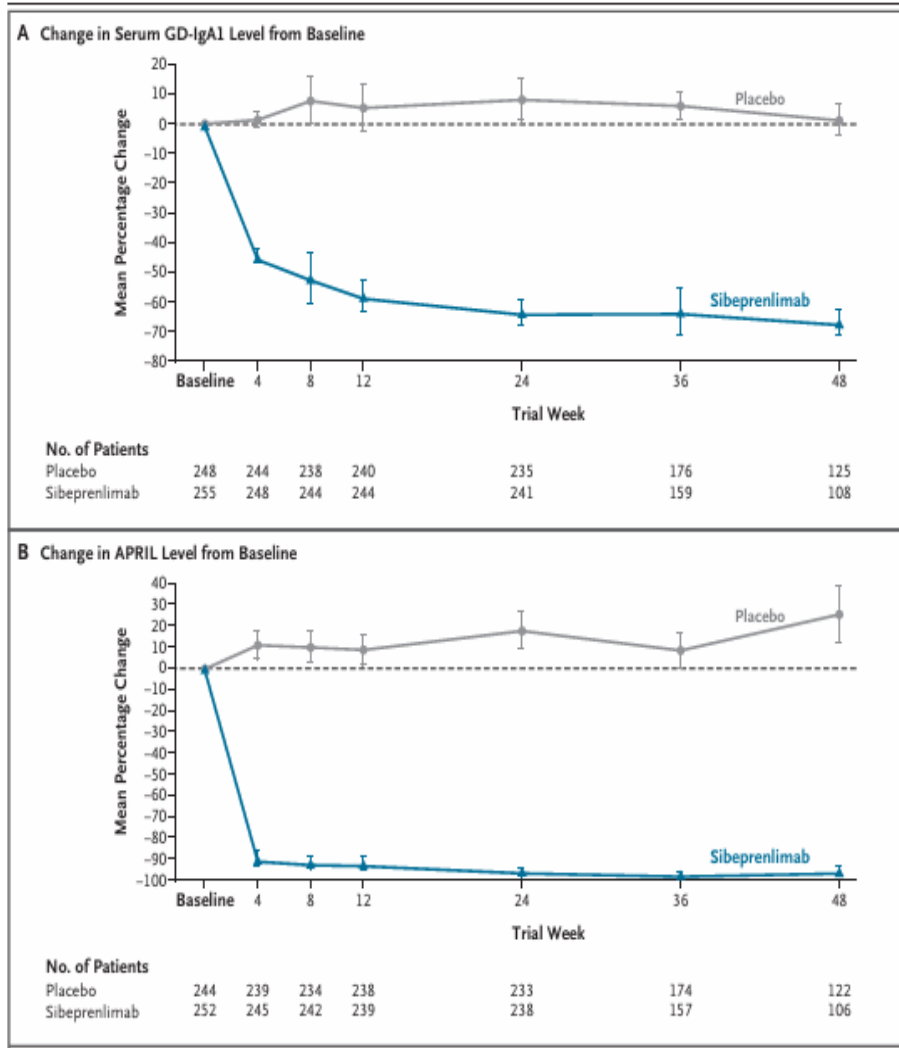


Table 2. Adverse Events Occurring during the Treatment Period in the Safety Population.*

Event	Sibeprenlimab (N = 259)	Placebo (N = 251)
	no. of patients (%)	
Any adverse event occurring during treatment period†	192 (74.1)	206 (82.1)
Adverse event related to sibeprenlimab or placebo	75 (29.0)	67 (26.7)
Event occurring in ≥5% of patients in either trial group		
Injection-site erythema	34 (13.1)	30 (12.0)
Injection-site pain	26 (10.0)	23 (9.2)
Injection-site swelling	16 (6.2)	13 (5.2)
Pyrexia	14 (5.4)	10 (4.0)
Coronavirus disease 2019	25 (9.7)	17 (6.8)
Influenza	21 (8.1)	16 (6.4)
Nasopharyngitis	32 (12.4)	25 (10.0)
Upper respiratory tract infection	38 (14.7)	35 (13.9)
Back pain	17 (6.6)	14 (5.6)
Any serious adverse event occurring during treatment period‡	9 (3.5)	11 (4.4)
Any serious adverse event related to sibeprenlimab or placebo	1 (0.4)	1 (0.4)
Any severe adverse event occurring during treatment period	4 (1.5)	8 (3.2)
Any adverse event leading to discontinuation of sibeprenlimab or placebo	1 (0.4)	4 (1.6)
Death	0	0

Newer IgAN Agents Acting on BAFF and APRIL

Atacicept

Human TACI-IgG1 fusion protein

Binds to BLyS/BAFF and APRIL
Inhibits B cell activation and
Ig production

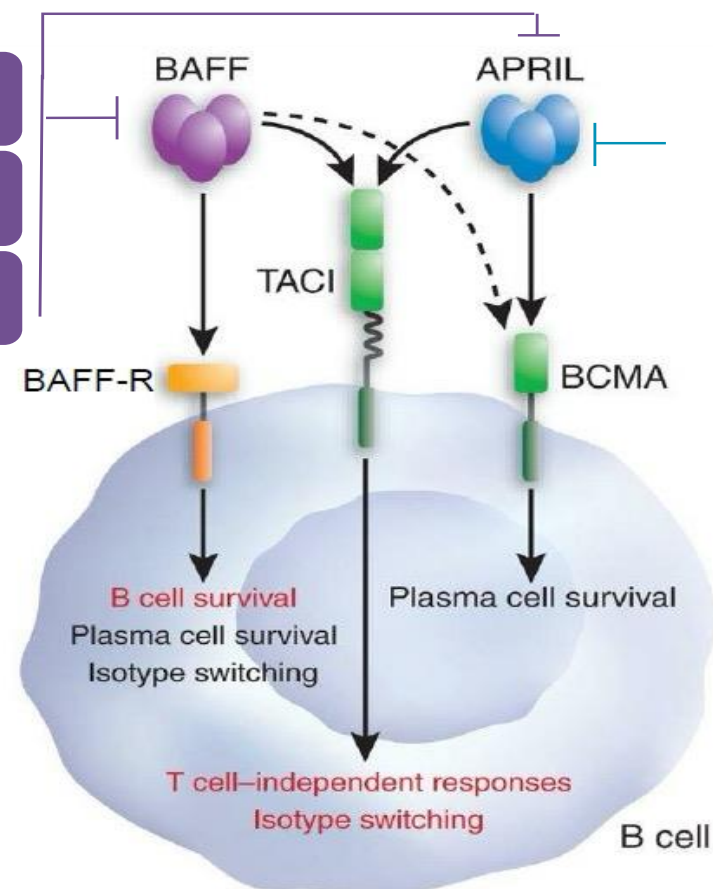
Dual BAFF/APRIL
Inhibitors

Atacicept

Povetacicept

Telitacicept

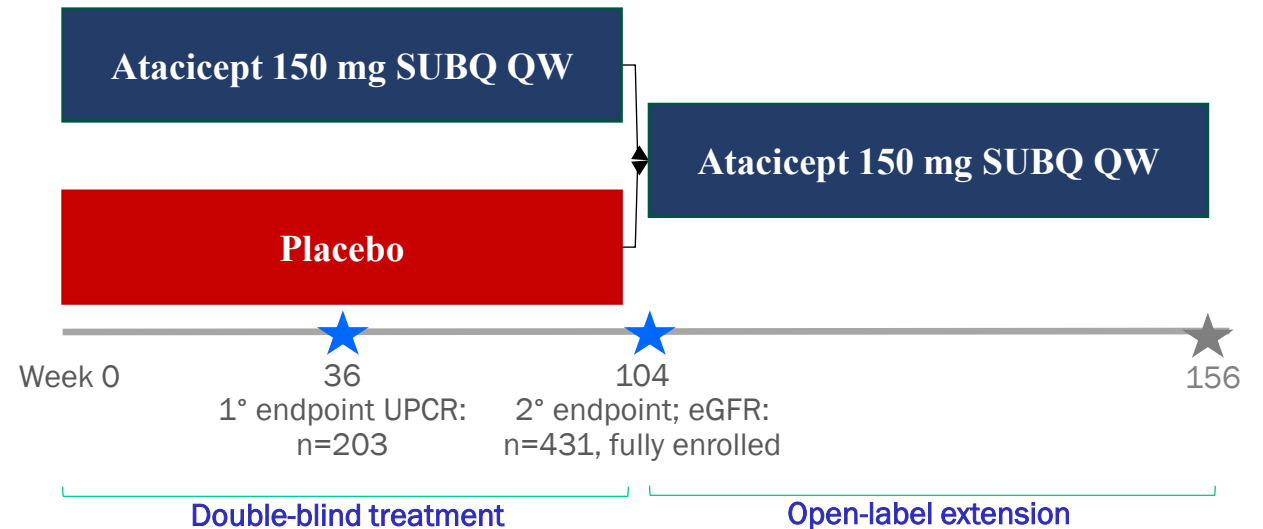
APRIL
Inhibitors



ORIGIN 3: Phase 3 IgAN Study of Atacicept

Multinational, Randomized, Placebo-Controlled Trial

- Bx-proven IgAN and high risk of disease progression
- UPCR ≥ 1 g/g or UP ≥ 1 g/24 hours
- eGFR ≥ 30 mL/min/1.73 m²/year
- Stable and optimized RAASi for ≥ 12 weeks,



Primary endpoint: 24-hour UPCR at week 36

Key secondary endpoint: eGFR up to week 104

Participants received blinded treatment with atacicept 150 mg, or placebo, self-administered at home by subcutaneous injection once per week

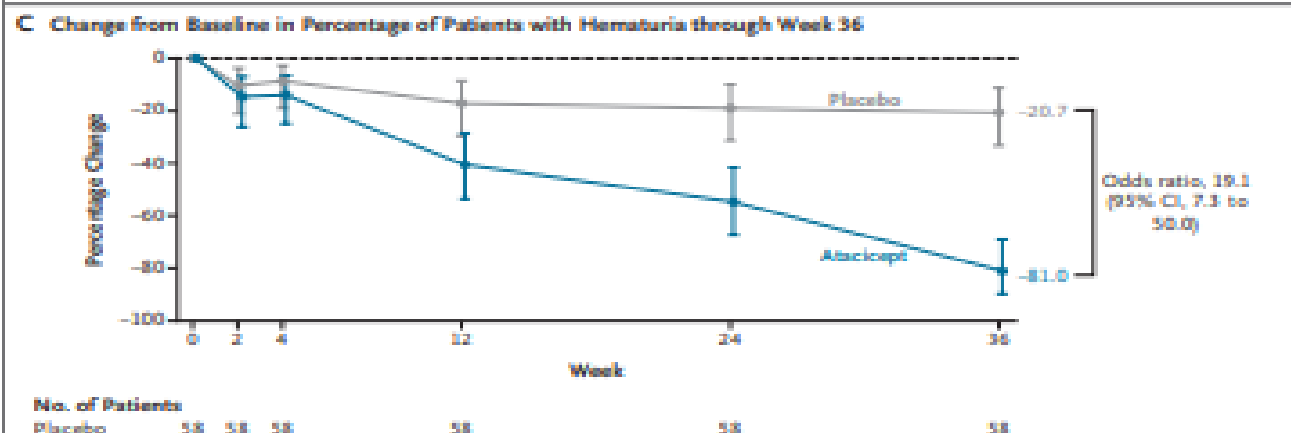
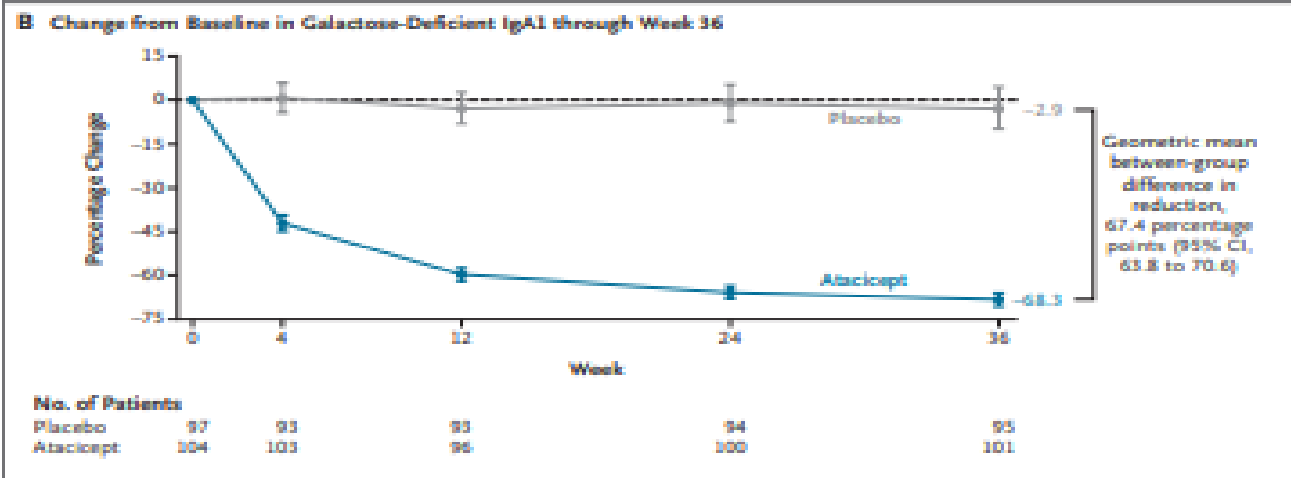
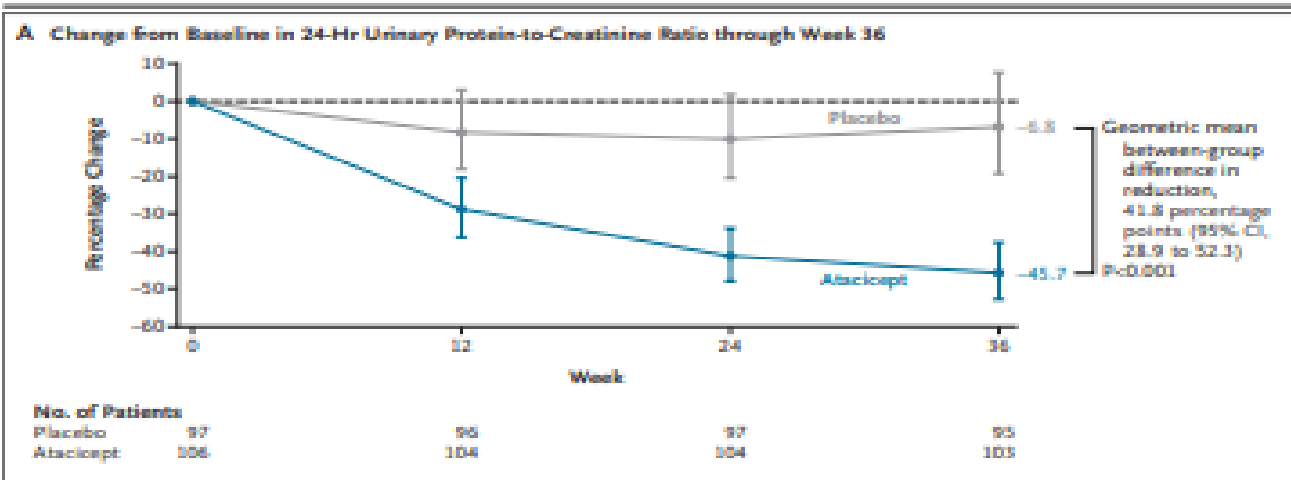
ORIGIN 3: Phase 3 IgAN Study of Atacicept – 36 week interim analysis

Characteristics	Atacicept (n=106)	Placebo (n=97)	Total (N=203)
Median age (range), years	40 (18-72)	40 (19-70)	40 (18-72)
Male sex, n (%)	57 (54)	58 (60)	115 (57)
Race, n (%)			
White	46 (43)	42 (43)	88 (43)
Asian	59 (56)	52 (54)	111 (55)
Black or African American	0	1 (1)	1 (0.5)
Native Hawaiian or Other Pacific Islander	0	1 (1)	1 (0.5)
Hispanic/Latino ethnicity, n (%)	14 (13)	6 (6)	20 (10)
UPCR by 24-hour urine, mean $\pm$ SD, g/g	1.7 $\pm$ 0.9	1.8 $\pm$ 1.2	1.7 $\pm$ 1.0
eGFR, mean $\pm$ SD, mL/min/1.73 m²/year	65 $\pm$ 28	65 $\pm$ 29	65 $\pm$ 28
Time since biopsy, mean $\pm$ SD, y	2.5 $\pm$ 2.6	2.5 $\pm$ 2.4	2.5 $\pm$ 2.5
SGLT2i use, n (%)	59 (56)	49 (51)	108 (53)

Atacicept Phase 3 Origin Study

- 36 week Interim Analysis

Lafayette R, Barbour SJ, Brenner RM et al
NEJM Nov 6 2025



1:1 multicenter, double blind randomized ,
PBO controlled

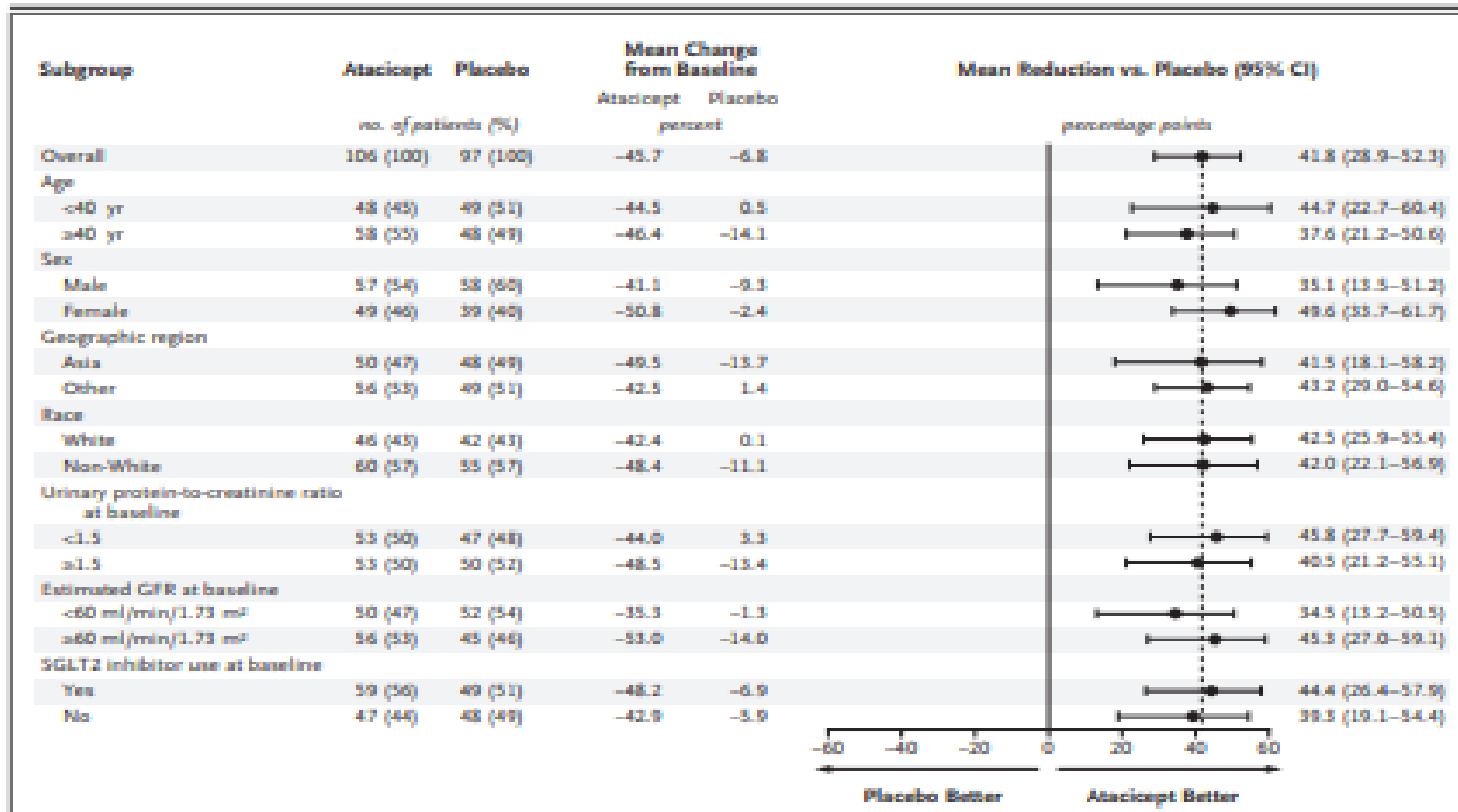
150 mg sq at home vs PBO

203 pts in interim analysis

At 36 weeks 42% greater reduction UpUcr w Ataci
GdIgA1 67% difference in reduction
Resolution hematuria 81%

Adverse events mild and 59% Ataci and 50% PBO

ORIGIN 3: Phase 3 IgAN Study of Atacicept – 36 week interim analysis

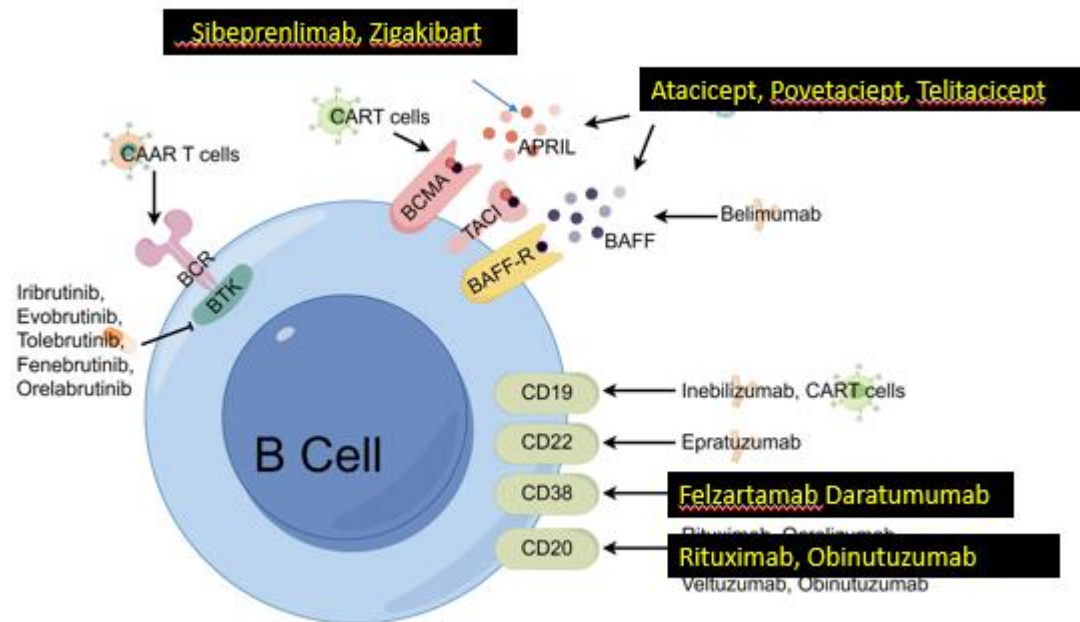


ORIGIN 3: Safety Profile of Atacicept

Participants, n (%)	Atacicept (n=214)	Placebo (n=214)	Total (N=428)
AEs	127 (59)	107 (50)	234 (55)
Serious AEs	1 (0.5)	11 (5)	12 (3)
AEs leading to drug discontinuation	2 (1)	8 (4)	10 (2)
AEs of infections and infestations	68 (32)	60 (28)	128 (30)
Serious or severe infections	0	3 (1)	3 (1)
Opportunistic infections	0	0	0
Study drug-related AEs	63 (29)	22 (10)	85 (20)
AEs associated with injection site reactions	51 (24)	11 (5)	62 (14)
Hypersensitivity reactions	8 (4)	14 (7)	22 (5)
AEs leading to death	0	0	0

Some Other B cell Therapies being Studied for IgAN

- **Povetacicept – FDA approval this year?**
- **Telitacicept – Presented Chinese phase 3 trial Part A at ASN 2025**
- **Felzartamab – anti CD 38 monoclonal antibody being investigated in a number of disease including IgAN**



How do I treat IgAN in 2026?

Assess Patient: Proteinuria, GFR, Oxford Class, **Bx > 0.5 g prot/day + no Dx**

Therapy directed at CKD progression . More chronicity-MESTC the more important.

RAAS inhibition: ACE/ ARB + **Sparsentan** or Atrasentan or + **SGLT2 inhib.**

Therapy for Glomerular Inflammation

Glucocorticoids: Low dose regimen only, duration limited by toxicity. Can follow w **MMF**

OR

TR Budesonide Some steroid side effects. How long to treat? 9 mo or longer ?

OR

Iptacopan for bad inflammation, resistant to other Rx and ? espec if complement on Bx?

Therapy for Pathogenesis - -Sibeprenlimab , Atacicept , and other BAFF/APRIL and APRIL blockers

May be first line, but need more long term data , final GFR/ final FDA approval. and cost???



WE PROMISE TO BE A THIRSTY MAN
ONLY IN RIVERS VALLEY

**BONELESS
CHUCK
ROASTS**

\$1.37
LB.

WE'VE GOT IT ALL PACKAGED
RED RIVER VALLEY

**RED
POTATOES**

5.00 LBS.
**BUY ONE GET ONE
FREE**

Numbers
Go
Play
Now

WE GUARANTEE WHITE OR YELLOW
TO THE MAX

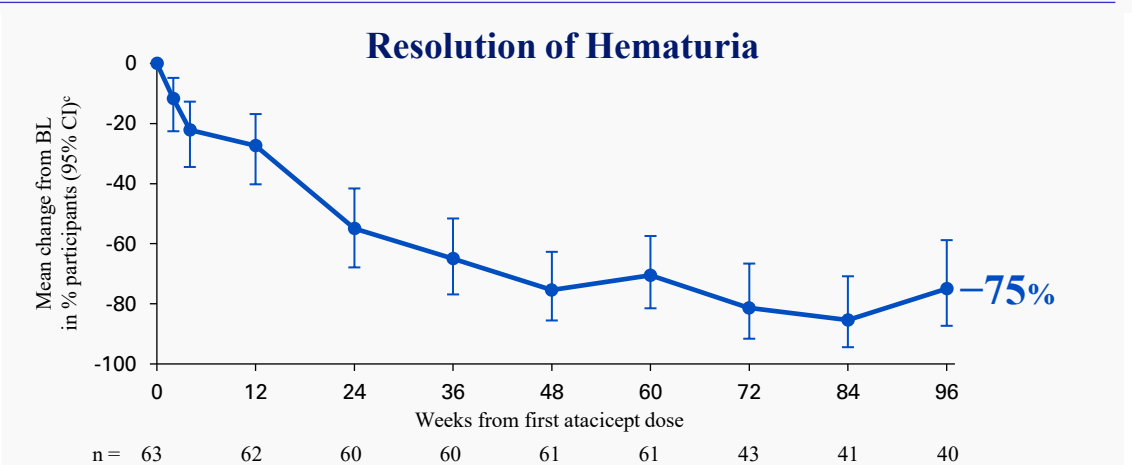
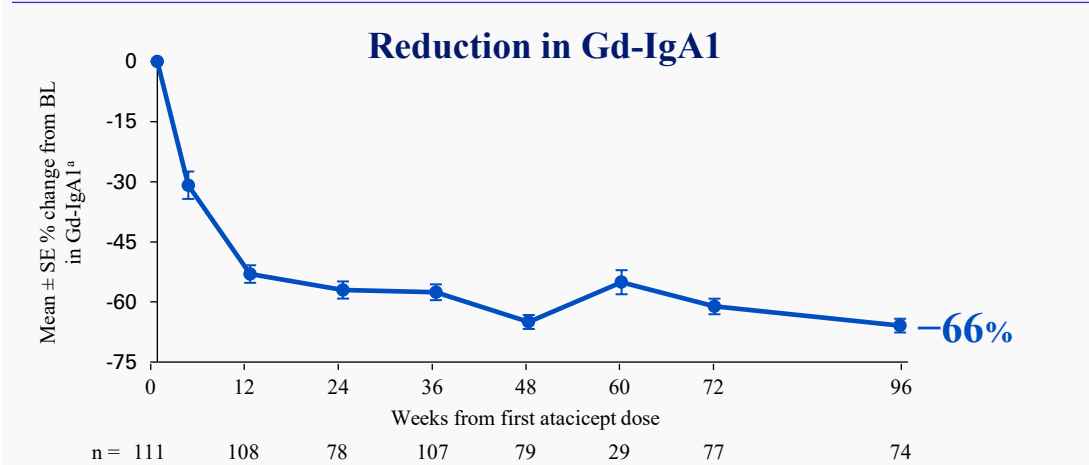
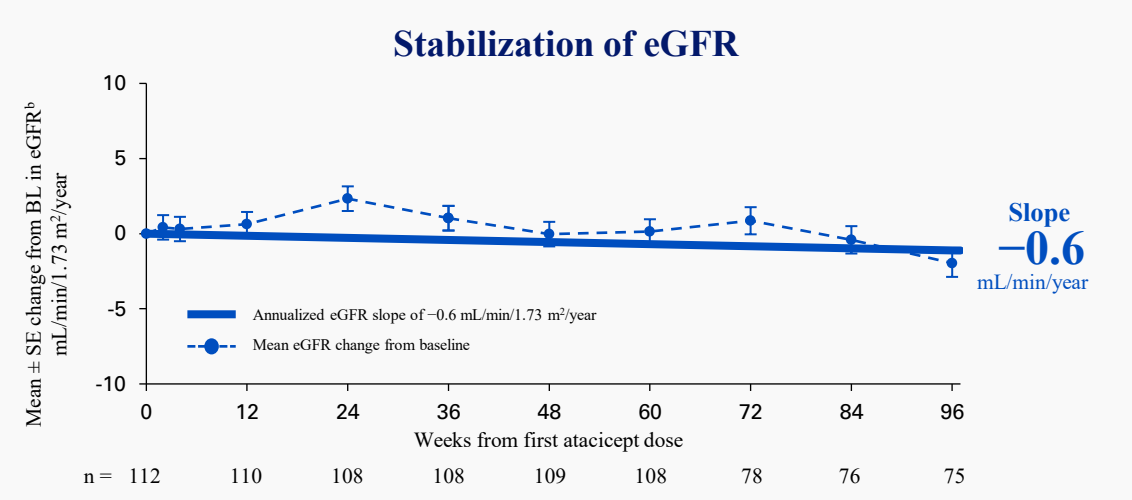
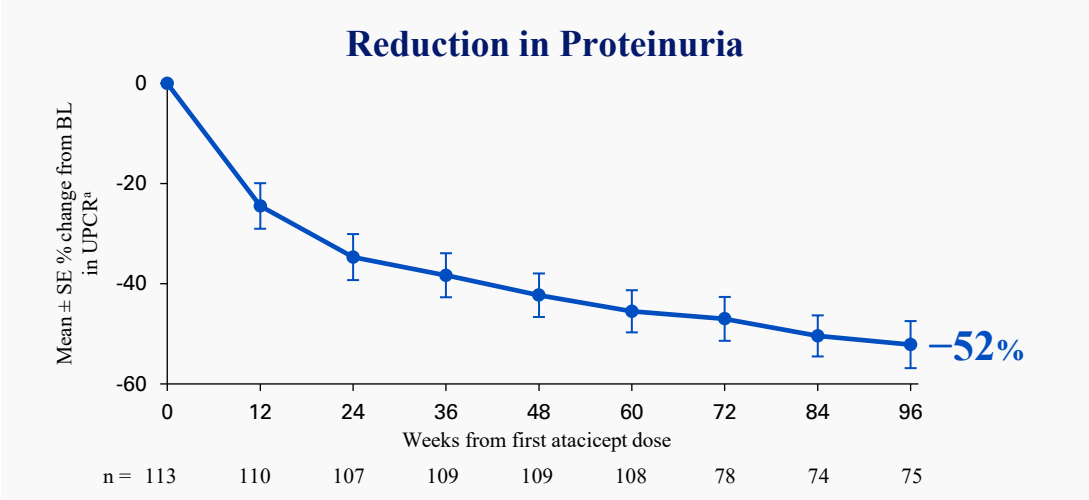
**IGA
CHEESE
SINGLES**

TO THE MAX
ONE GET ONE
FREE



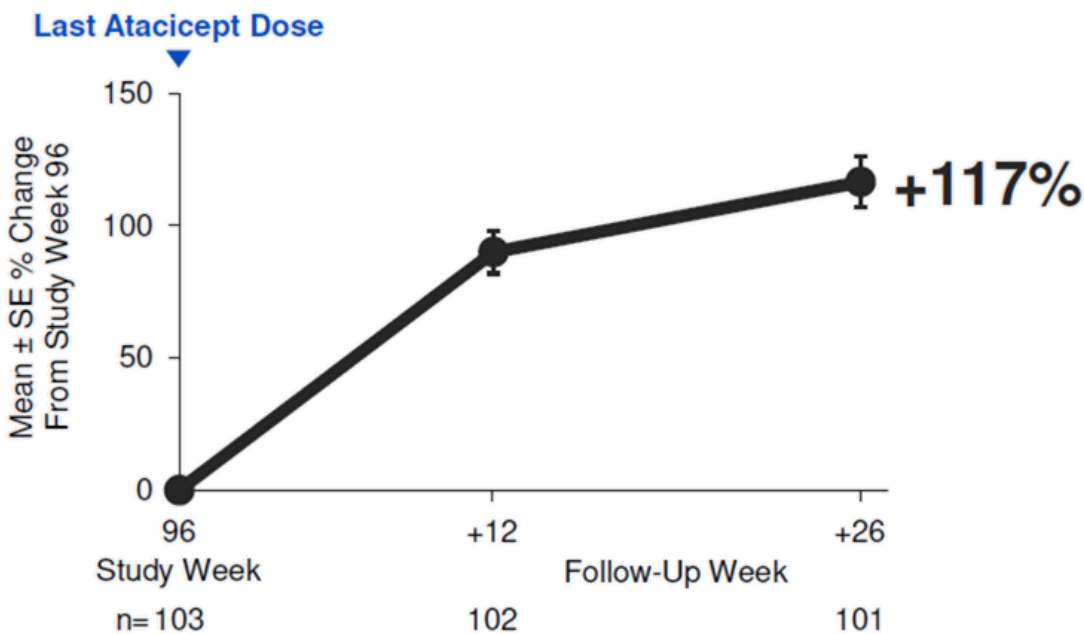
ORIGIN 2b: Phase 2b Endpoints at Week 96

Atacicept 150 mg



ORIGIN 2b: Phase 2b Changes in Key Markers During Off-Treatment Follow-Up

Gd-IgA1% Change From Study Week 96



eGFR Change From Study Week 96

