

# IgA-Nephropathie

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**RWTHAACHEN**

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# Darlegung potentieller Interessenskonflikte

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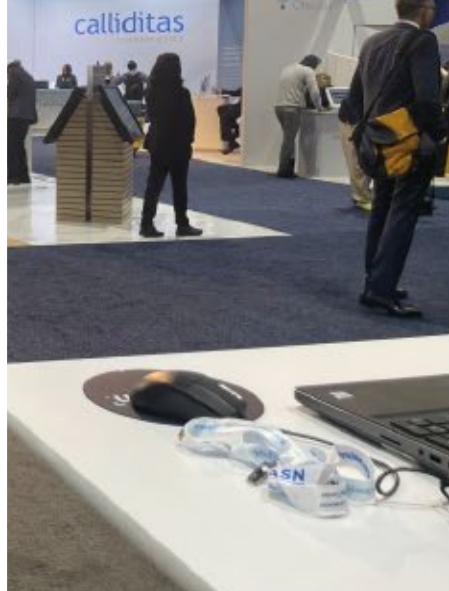
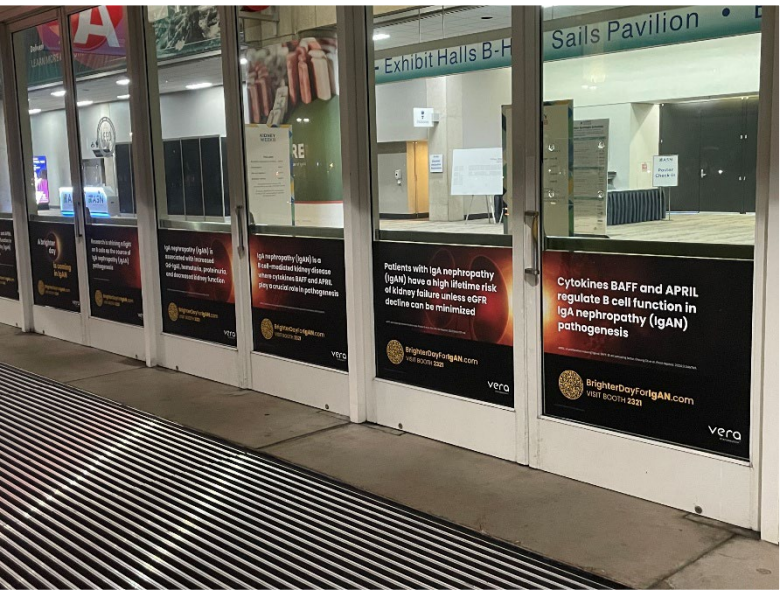
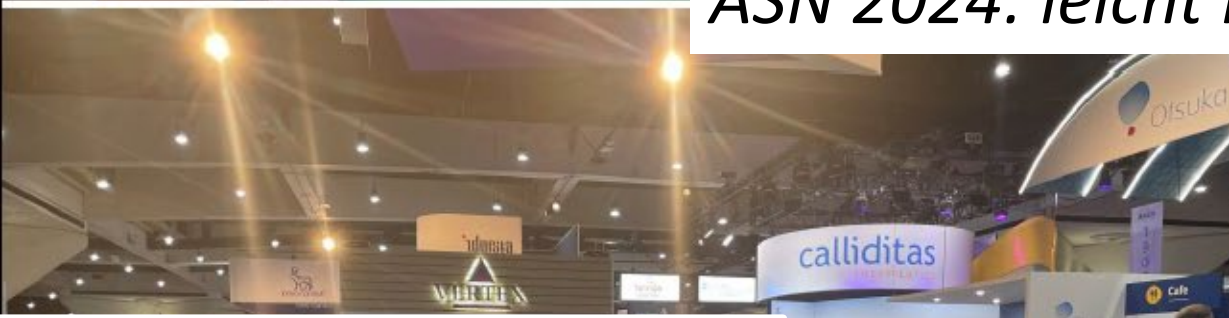
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**Data Safety Monitoring Boards:** AstraZeneca, NovoNordisk



ASN 2024: leicht IgAN-lastig.....



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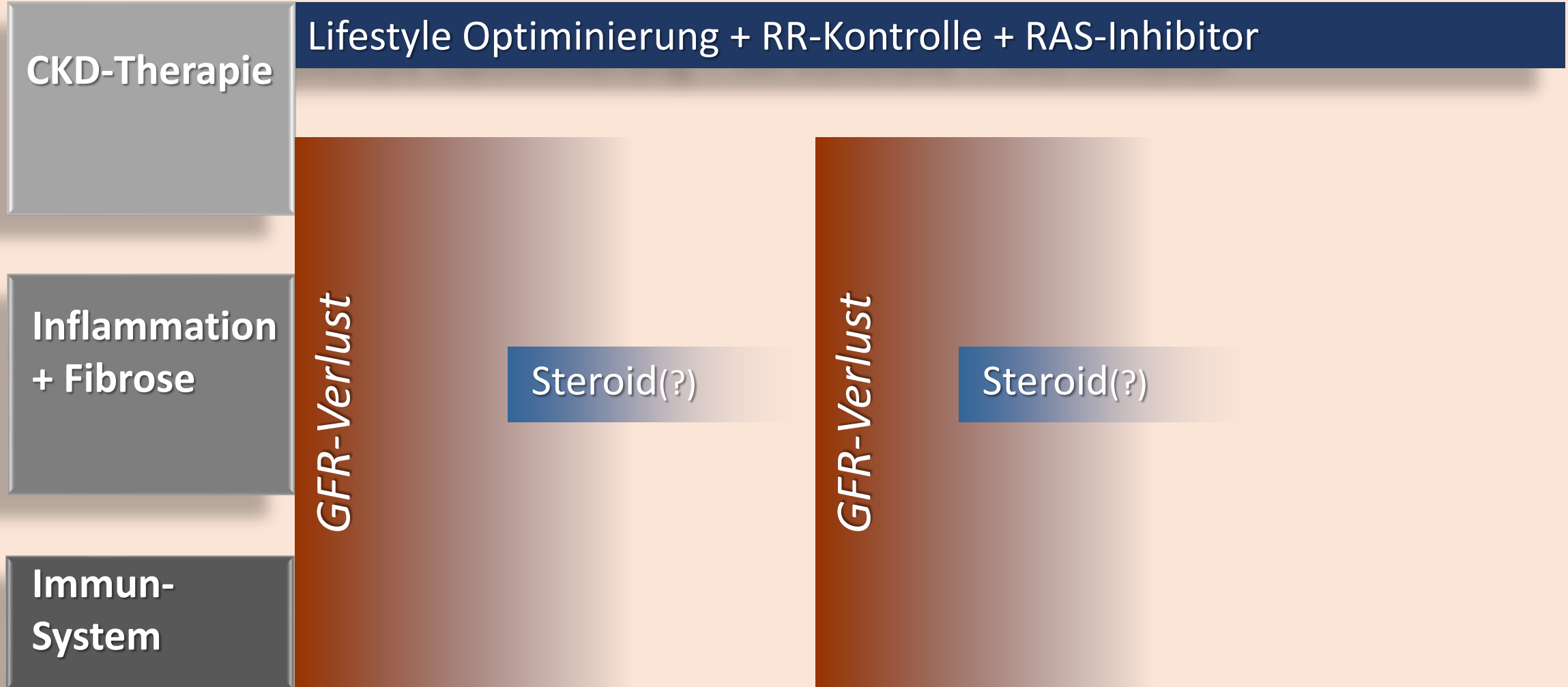


Novartis



# IgA-Nephropathie

*- Therapie bisher*



# Supportive Therapie der IgA-Nephropathie



## Practice Point 2.3.1. Considerations for treatment of all patients with IgAN

- The primary focus of management should be optimized supportive care.
- Assess cardiovascular risk and commence appropriate interventions as necessary.
- Give lifestyle advice including information on dietary sodium restriction, smoking cessation, weight control, and exercise as appropriate.

### Level 1 Empfehlungen

- Blutdruck-Kontrolle (**syst. RR im Sitzen in den 120ern**)
- **ACEI oder ARB**, Dosis hochtitrieren!
- Dihydropyridin Calcium-Kanalblocker als Erstlinien-Therapie meiden
- **SGLT2-Inhibitor**
- Proteinzufuhr kontrollieren

**ALLE**

### Level 2 Empfehlungen

- **NaCl-Zufuhr reduzieren**, Trinkmenge 1,5-2L/d, Diuretikum
- Non-Dihydropyridine Calcium-Kanalblocker Therapie
- **Alle Komponenten des metabolischen Syndroms korrigieren**
- Aldosteron-Antagonist,  $\beta$ -Blocker
- **Nikotin-Konsum einstellen**

**So viele Maßnahmen wie möglich**

# Jährlicher eGFR Verlust bei IgA-Nephropathie: die Kontroll-Arme

Studie	Vergleichsarm	Jährl. eGFR Verlust [ml/min]	Quelle
STOP-IgAN (Steroide)	Optimiert supportiv	-1,5	Rauen, NEJM 2015
TESTING (Steroide)	Plazebo	-5,0	Lv, JAMA 2022
PROTECT (Sparsentan)	Irbesartan 300 mg	-3,8	Rovin, Lancet 2023
NEFIGARD (Nefecon)	Plazebo	-6,0	Lafayette, Lancet 2023
DAPA-CKD (Dapagliflozin)	Plazebo	-4,7	Wheeler, Kidney Int 2021
Iptacopan Phase II	Plazebo	-6,6 (extrapoliert von -3,3 nach 6 Monaten)	Zhang, Kidney Int 2023
Telitacicept Phase II	Plazebo	-10,0 (extrapoliert von -5 nach 6 Monaten)	Lv, Kidney Int Rep 2023
MMF	Losartan	-3,8	Hou, JAMA Netw Open 2023

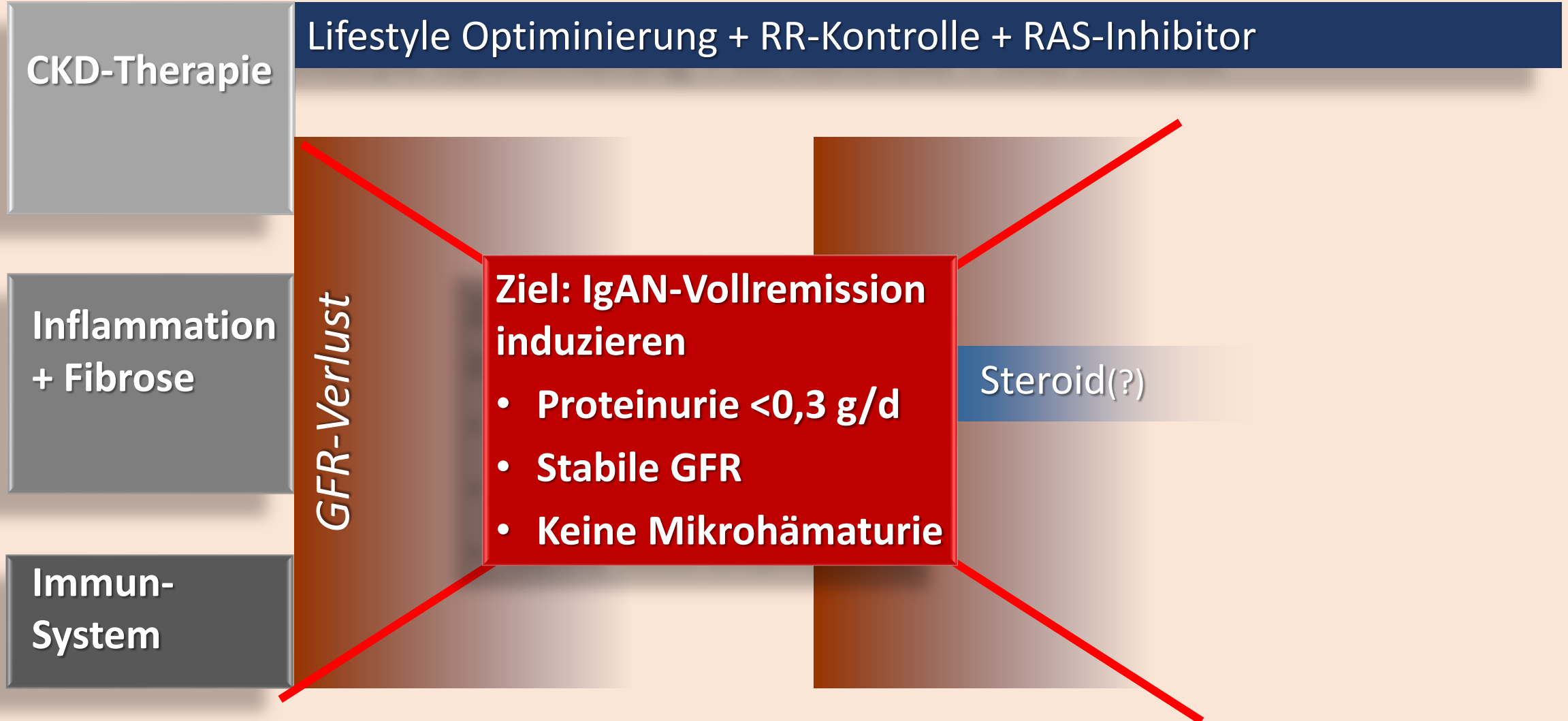
# Systemische (Hochdosis) Kortikosteroide bei IgAN: jüngere Studien

Studie	Design	Primärer Endpunkt	Nebenwirkungen	Ethnizität
<b>STOP-IgAN</b> NEJM 2015, KI 2020	Prospektiv (N=162)	Kein Benefit	Verdopplung infektiöse NW	Europäer
<b>TESTING</b> JAMA 2017 + 2022	Prospektiv (N= 503)	2,5 Jahre Verzögerung Nierenversagen	Deutl. mehr (5x letale) infektiöse NW	Asiaten
<b>Rumänien</b> Medicine 2022	Retrospektiv (N=83)	Kein Benefit	?	Europäer
<b>UK</b> PLOSone 2022	Retrospektiv (N=401)	Kein Benefit	?	Europäer
<b>Norwegen</b> BMC Nephrol 2024	Retrospektiv (N=151)	Kein Benefit	NW ↑ ↑	Europäer
<b>China</b> CJASN 2023	Retrospektiv (N=3946)	40% Risiko Redukt. Nierenversagen	Schwere NW ↑ ↑	Chinesen (55% mit RASi)



# IgA-Nephropathie

## - Therapie bisher



# IgA-Nephropathie

## - Therapie heute und zukünftig

CKD-Therapie

Lifestyle Optimierung + RR Kontrolle + RAS-Inhibitor

+ SGLT2 Inhibitor; zusätzlich Mineralokortikoid Antagonist?

Inflammation  
+ Fibrose

Immun-  
System

# IgA-Nephropathie

## - Therapie heute und zukünftig

### CKD-Therapie

Lifestyle Optimierung + RR Kontrolle + RAS-Inhibitor

+ SGLT2 Inhibitor; zusätzlich Mineralokortikoid Antagonist?

Endothelin-1 Hemmung (DEARA oder selektiver Antagonist)

Inflammation  
+ Fibrose

Immun-  
System

# Efficacy and safety of sparsentan vs irbesartan in patients with IgAN 2-year results from PROTECT, a phase 3 randomized controlled trial

	Sparsentan (n=202)	Irbesartan (n=202)	Between group difference
Rate of change in eGFR mL/min/1.73 m <sup>2</sup>			
Week 6 to week 110 (chronic slope)	-2.9 (-3.6 to -2.2)	-3.8 97% reached target dose 300 mg daily	1.1 (0.1-2.1) <b>p=0.037</b>
Day 1 to week 110 (total slope)	-2.9 (-3.6 to -2.2)	-3.9 (-4.6 to -3.1)	1.0 (-0.03 to 1.9) <b>p=0.058</b>
	Least square (LS) mean (95% CI)		Difference (95% CI)

• Nur anstelle von RAS-Blocker (NICHT zusätzlich!)  
 • Zugelassen für primäre IgAN mit Proteinurie >1 g/Tag  
 • jährliche Behandlungskosten knapp 60.000 €

ORIGINAL ARTICLE

## Atrasentan in Patients with IgA Nephropathy

Hiddo J.L. Heerspink, Ph.D., Meg Jardine, M.B., B.S., Ph.D.,  
Donald E. Kohan, M.D., Ph.D., Richard A. Lafayette, M.D., Adeera Levin, M.D.,  
Adrian Liew, M.D., Hong Zhang, Ph.D., Amit Lodha, M.B., B.S.,  
Todd Gray, M.S.P.H., Yi Wang, Ph.D., Ronny Renfurm, M.D.,  
and Jonathan Barratt, M.D., for the ALIGN Study Investigators\*

### ALIGN Phase III Studie

- **Teil A = Proteinurie nach 9 Monaten**  
(=> ausreichend für vorläufige Zulassung)
- **Teil B = eGFR slope nach 2 Jahren**  
(nötig für definitive Zulassung)

ORIGINAL ARTICLE

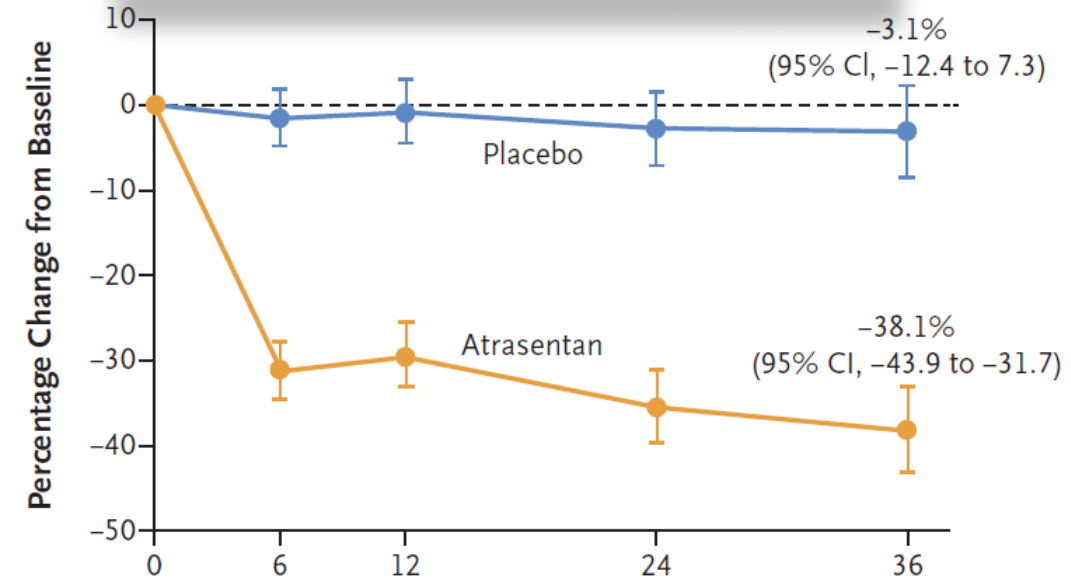
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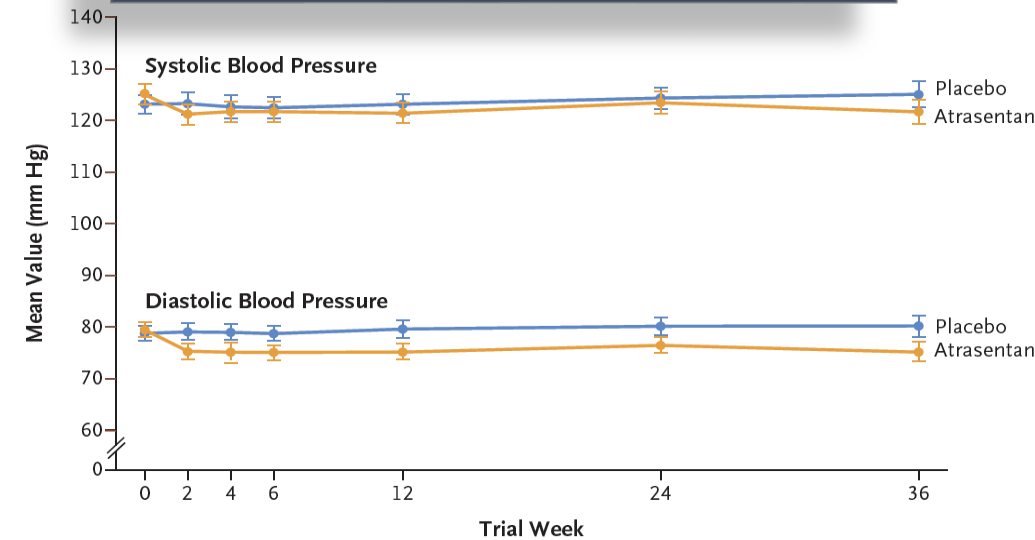
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### Protein/Krea Ratio im 24h Urin



### Blutdruck

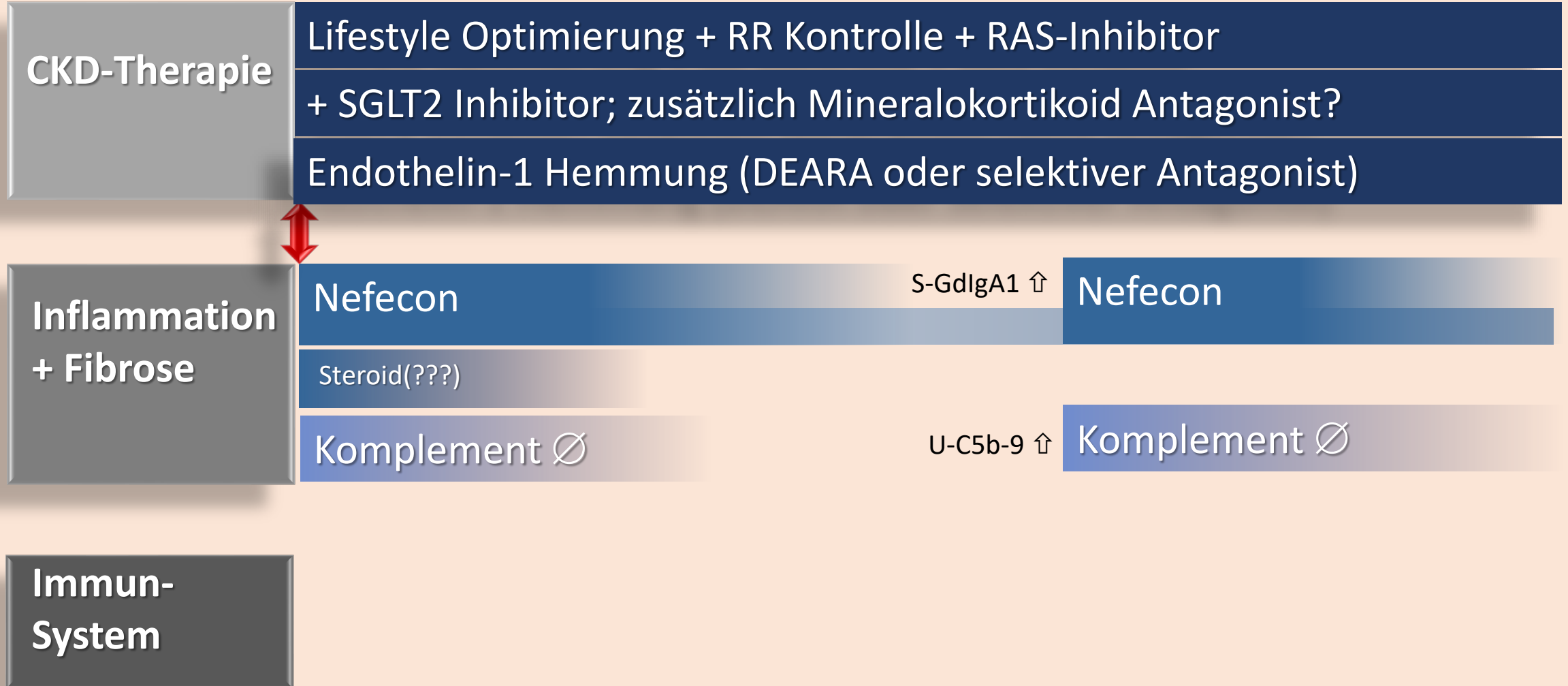


No. of Patients

Placebo	170	165	161	167	166	157	123
Atrasentan	169	162	164	165	161	154	129

# IgA-Nephropathie

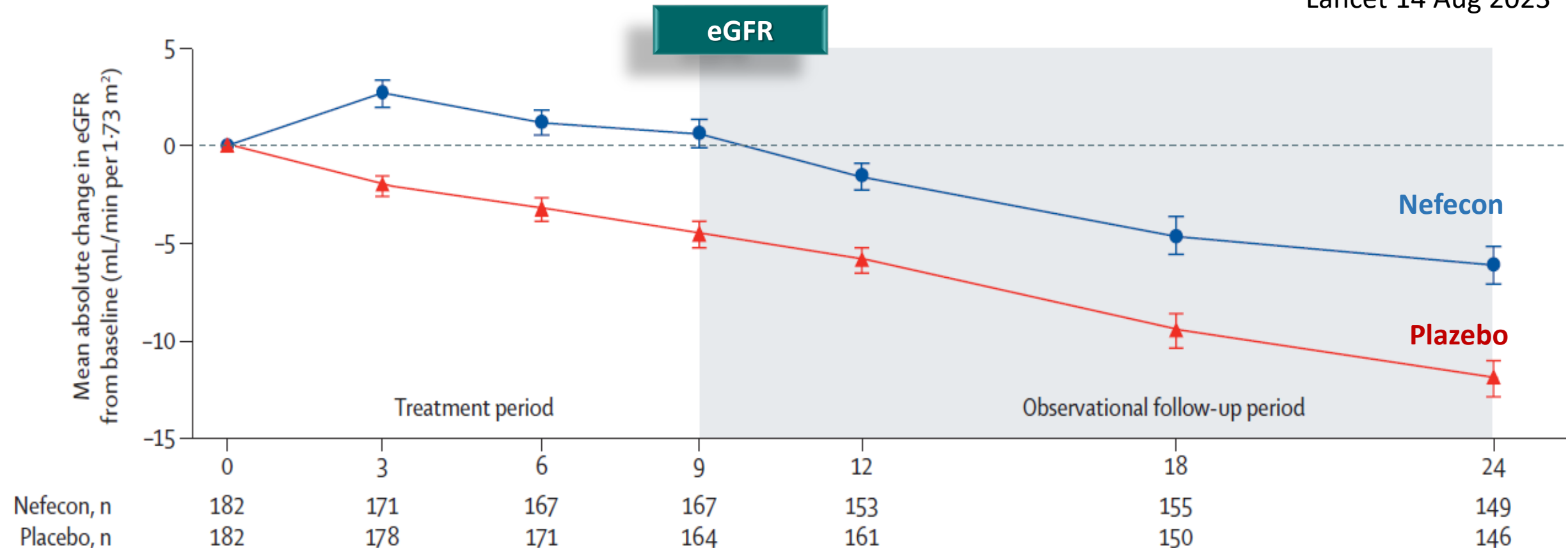
## - Therapie heute und zukünftig



# Efficacy and safety of a targeted-release formulation of budesonide in patients with primary IgA-nephropathy (NeflgArd): 2-year results from a randomized phase 3 trial

*Richard Lafayette, Jens Kristensen, Andrew Stone, Jürgen Floege, Vladimir Tesar, Hernán Trimarchi, Hong Zhang, Necmi Eren, Alexander Paliege, Heather N Reich, Brad H Rovin, Jonathan Barratt, on behalf on the NeflgArd trial investigators*

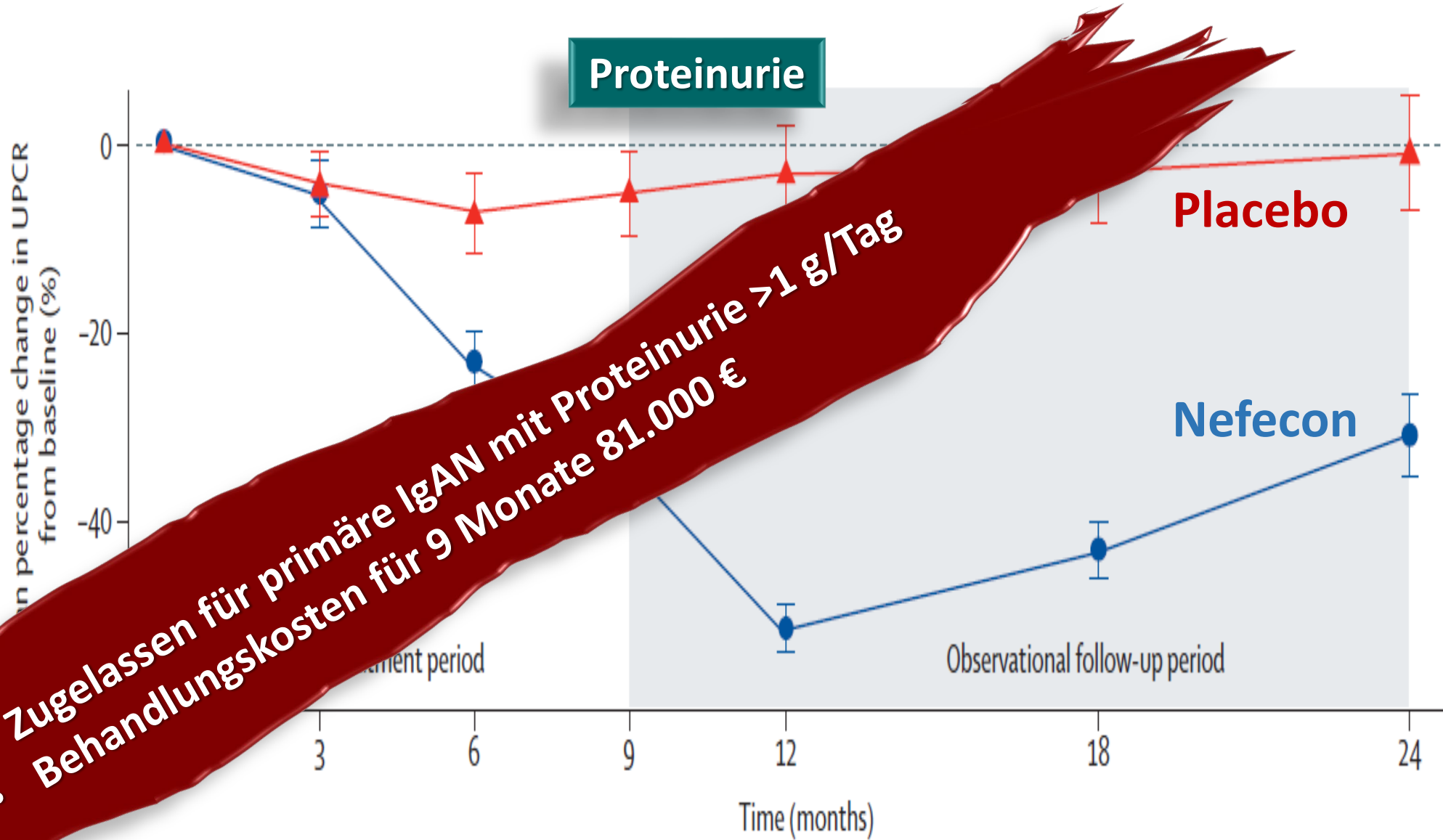
Lancet 14 Aug 2023





**Targeted release budesonide (Nefecon) in IgAN: Nefigard phase III trial**

- Zugelassen für primäre IgAN mit Proteinurie >1 g/Tag
- Behandlungskosten für 9 Monate 81.000 €



Nefecon, n	182	173	169	166	157	155	145
Placebo, n	182	176	169	164	160	151	142

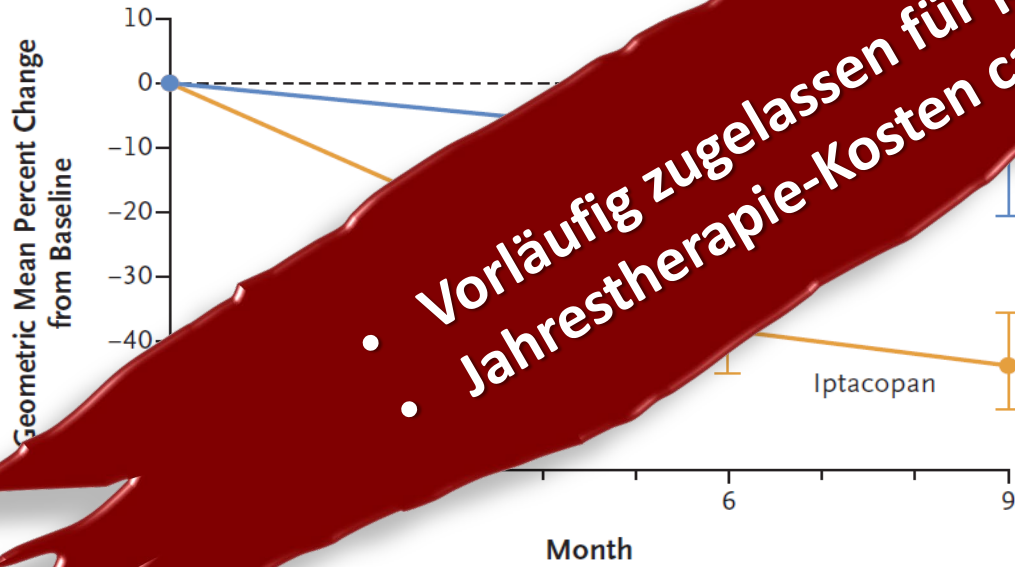
October 26, 2024

ORIGINAL ARTICLE

# Alternative Complement Pathway Inhibition with Iptacopan in IgA Nephropathy

V. Perkovic, J. Barratt, B. Rovin, N. Kashihara, B. Maes, H. Zhang, H. Trimarchi, D. Kollins, O. Papachristofi, S. Jacinto-Sanders, T. Merkel, N. Guerard, R. Renfurm, T. Hach, and D.V. Rizk

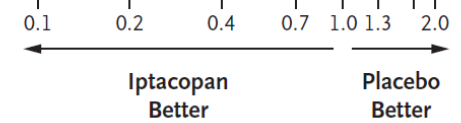
Change in 24-Hr Urinary Protein-to-Creatinine Ratio



No. of Patients	0	6	9
Placebo	125	112	106
Iptacopan	125	115	118

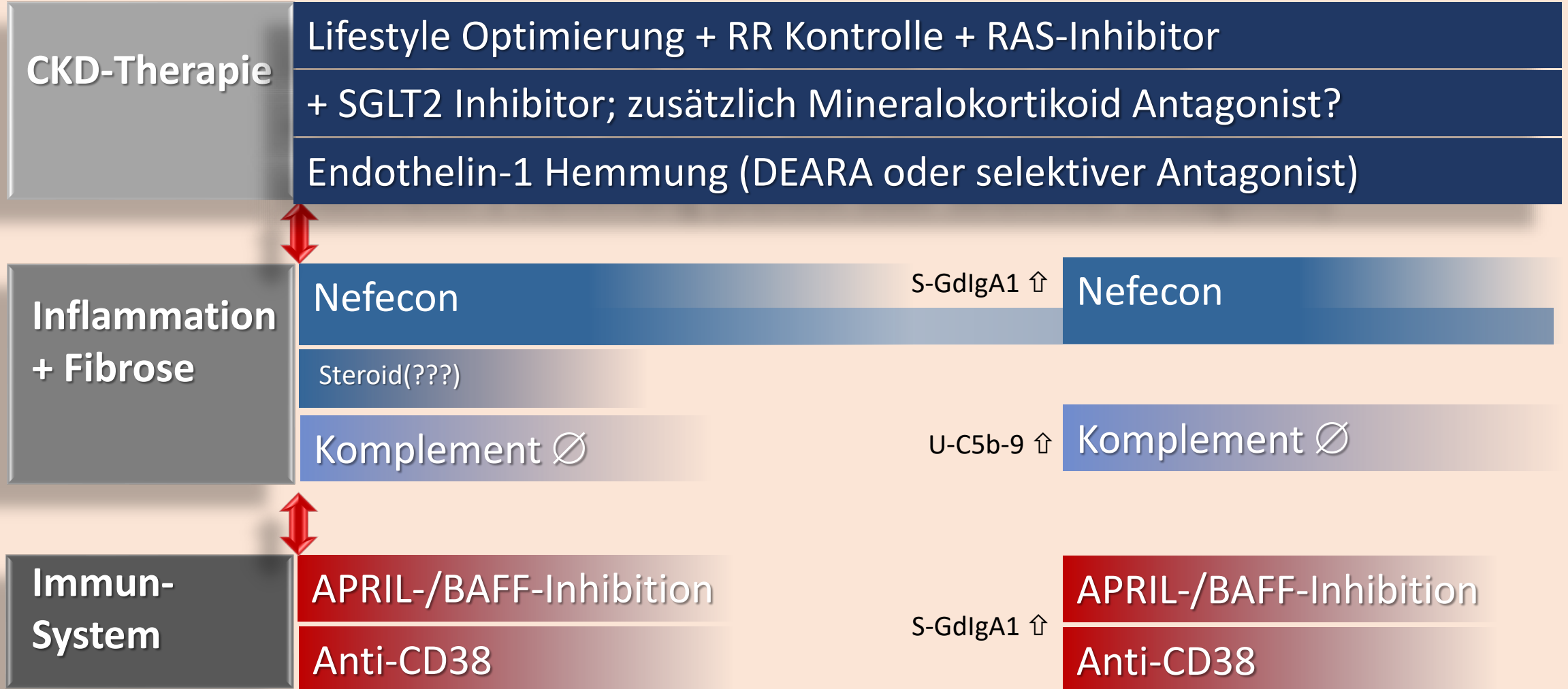
Subgroup	Iptacopan no. of patients/total no.	Placebo no. of patients/total no.	Geometric Mean Ratio (95% CI)
Overall	118/125	106/125	0.55 (0.48, 0.63)
Sex			
Male	68/71	66/80	0.55 (0.48, 0.63)
Female	50/54	40/40	0.55 (0.48, 0.63)
Geographic region			
Asia	32/36	27/34	0.55 (0.48, 0.63)
All other regions	86/89	79/91	0.55 (0.48, 0.63)
24-Hr urinary protein-to-creatinine ratio at baseline			
<1.5	30/34	27/34	0.55 (0.48, 0.63)
≥1.5	76/91	79/91	0.55 (0.48, 0.63)
<2	59/67	47/58	0.55 (0.48, 0.63)
≥2	32/36	27/34	0.55 (0.48, 0.63)
≥2	86/89	79/91	0.55 (0.48, 0.63)
≥2	16/18	12/14	0.55 (0.48, 0.63)
≥2	102/107	94/111	0.55 (0.48, 0.63)
≥2	93/97	74/90	0.55 (0.48, 0.63)
Negative or trace	20/23	28/30	0.55 (0.48, 0.63)
M score			
M1	69/76	66/80	0.55 (0.48, 0.63)
M0	40/40	35/39	0.55 (0.48, 0.63)
E score			
E1	32/36	30/36	0.55 (0.48, 0.63)
E0	76/79	69/81	0.55 (0.48, 0.63)
S score			
S1	81/87	81/89	0.55 (0.48, 0.63)
S0	27/28	19/29	0.55 (0.48, 0.63)
T score			
T1 or T2	46/48	44/53	0.55 (0.48, 0.63)
T0	63/68	58/67	0.55 (0.48, 0.63)
C score			
C1 or C2	32/35	17/22	0.55 (0.48, 0.63)
C0	72/76	72/85	0.55 (0.48, 0.63)

Vorläufig zugelassen für primäre IgAN in den USA  
 Jahrestherapie-Kosten ca. 500.000 \$










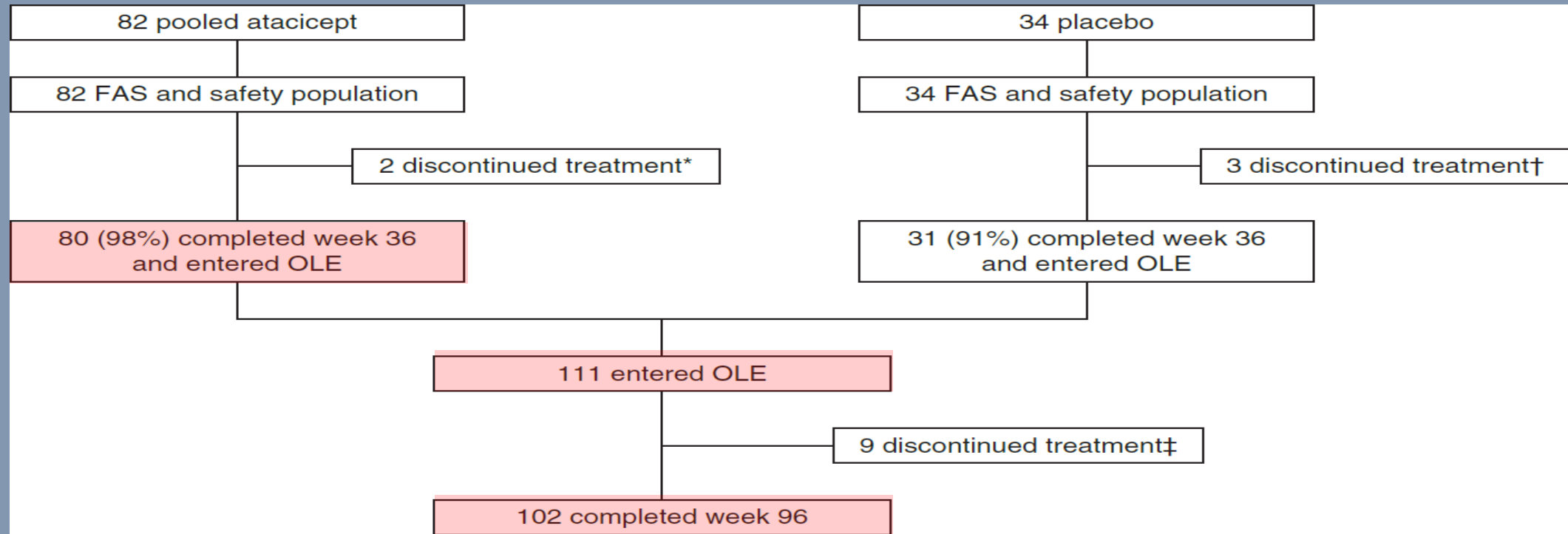
# IgA-Nephropathie

## - Therapie heute und zukünftig



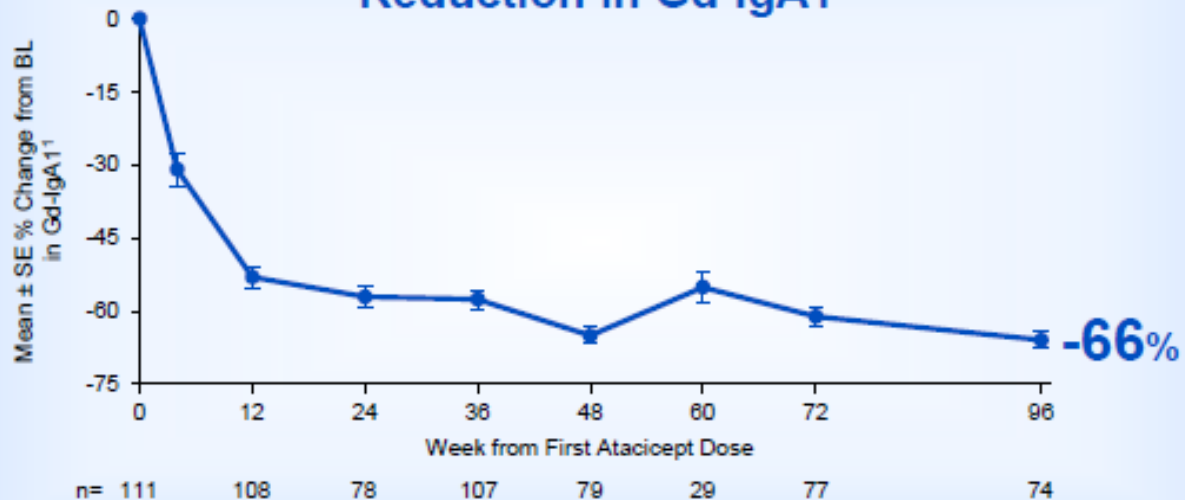
# Long-Term Results from an Open-Label Extension Study of Atacicept for the Treatment of IgA Nephropathy

Jonathan Barratt <sup>1</sup>, Sean Barbour,<sup>2</sup> Robert Brenner,<sup>3</sup> Kerry Cooper,<sup>3</sup> Xuelian Wei,<sup>3</sup> Necmi Eren,<sup>4</sup> Jürgen Floege,<sup>5</sup> Vivekanand Jha <sup>6,7,8</sup>, Sung Gyun Kim <sup>9</sup>, Bart Maes <sup>10</sup>, Richard K.S. Phoon <sup>11</sup>, Harmeet Singh,<sup>12</sup> Vladimír Tesář <sup>13</sup>, and Richard Lafayette <sup>14</sup> on behalf of the **ORIGIN Phase 2b Investigators\***

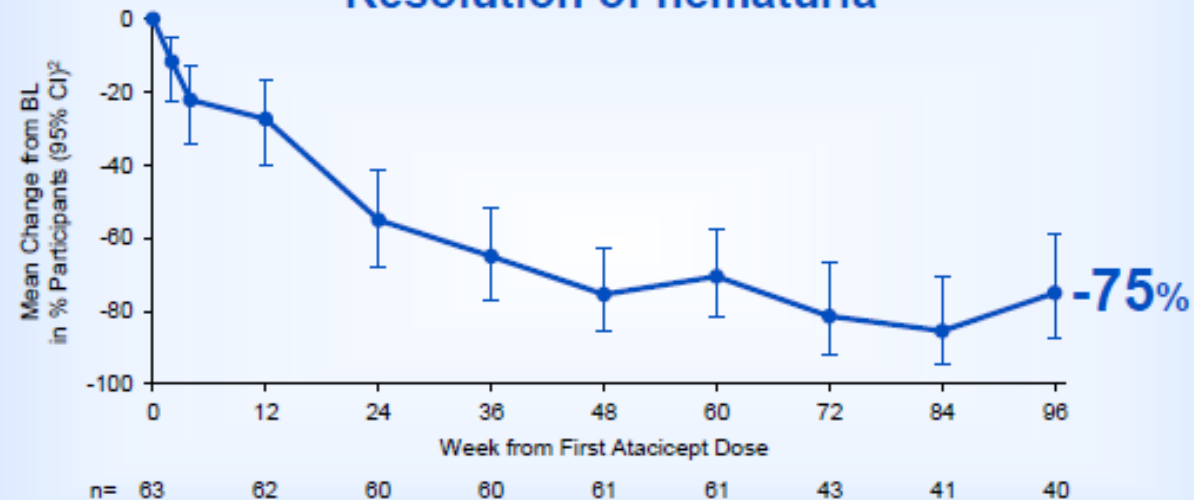


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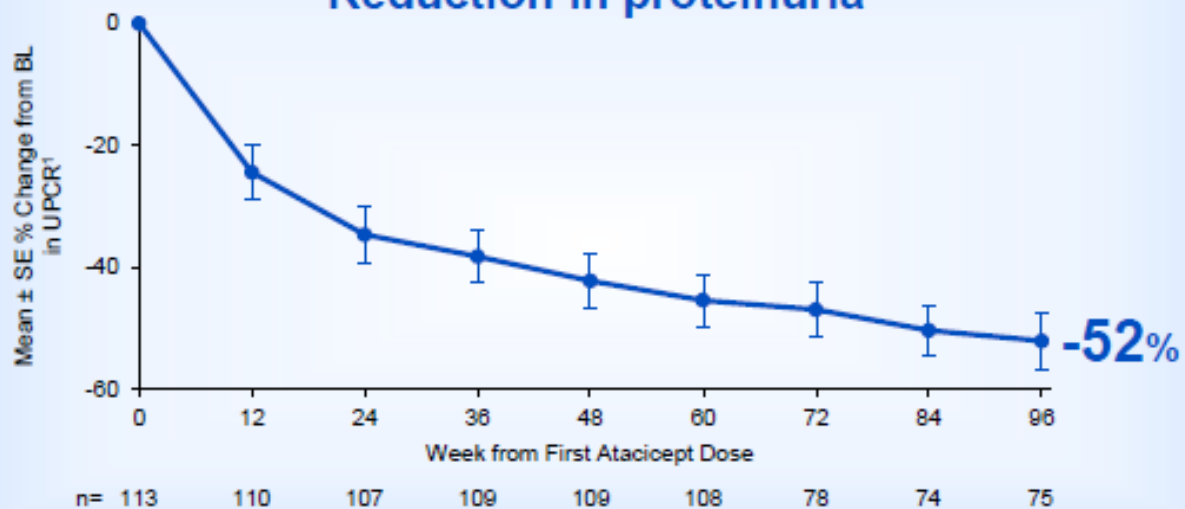
## Reduction in Gd-IgA1



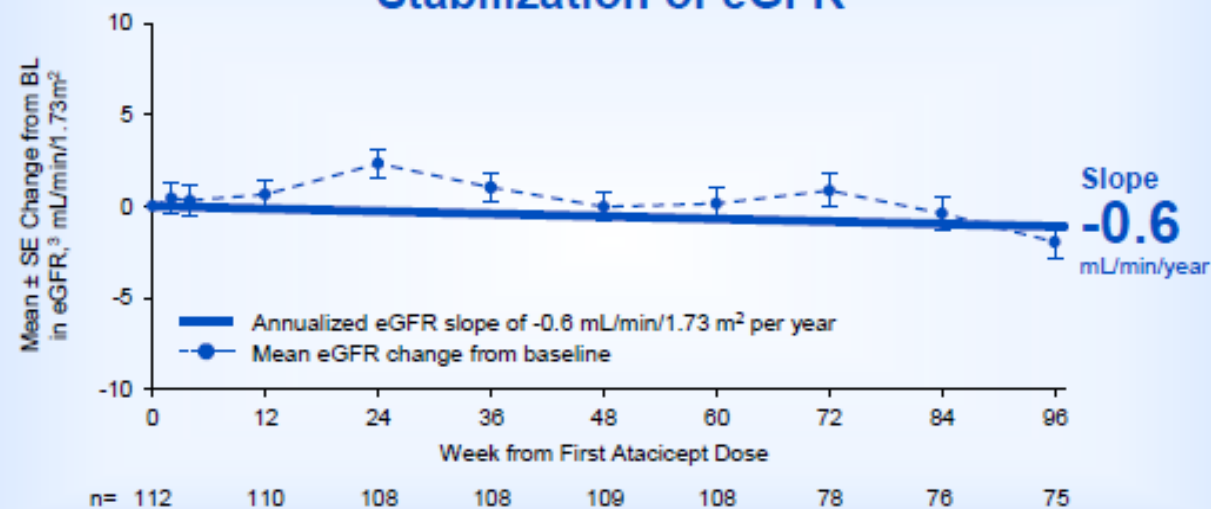
## Resolution of hematuria



## Reduction in proteinuria



## Stabilization of eGFR



# IgA-Nephropathie

## - Therapie heute und zukünftig

