UNIVERSITY ABOUBEKR BELKAID

FACULTY OF MEDICINE BENAOUDA BENZERDJEB

INTERNAL MEDICINE DEPARTMENT

LABORATORY OF RESEARCH ON DIABETES

مخبر بحث سكري

« LAREDIAB » Code ATRSS/DGRST N° W0417700

https://larediab.univ-tlemcen.dz

Mobile : 0770 218 100/ E-mail: ali.lounici@univ-tlemcen.dz

ACADEMIC HOSPITAL TIDJANI DAMERDJI

DEPARTMENT OF INTERNAL MEDICINE

5th Séminary of LAREDIAB

11th Congress OF AMIWIT

ANCA associated Vasculitis

How To treat

Bestaoui MH, Lounici A

Internal Medicine Department – Tlemcen university hospital center

Diabetes Research Laboratory – University of Tlemcen

December 10, 2022 Tlemcen

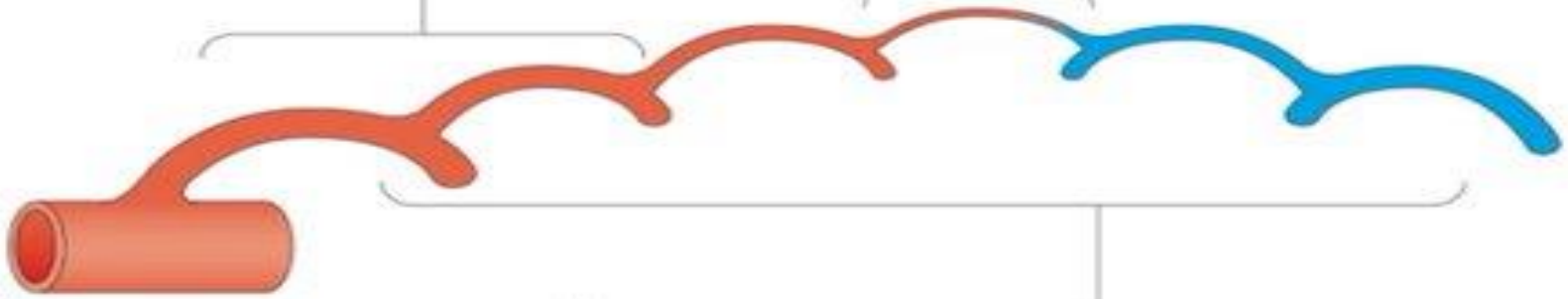
Chapel Hill 2012 Nomenclature

a

Medium vessel vasculitis
- Polyarteritis nodosa
- Kawasaki disease

Immune complex small vessel vasculitis
- Cryoglobulinaemic vasculitis
- IgA vasculitis (Henoch–Schönlein purpura)
- Hypocomplementemic urticarial vasculitis (Anti-C1q vasculitis)

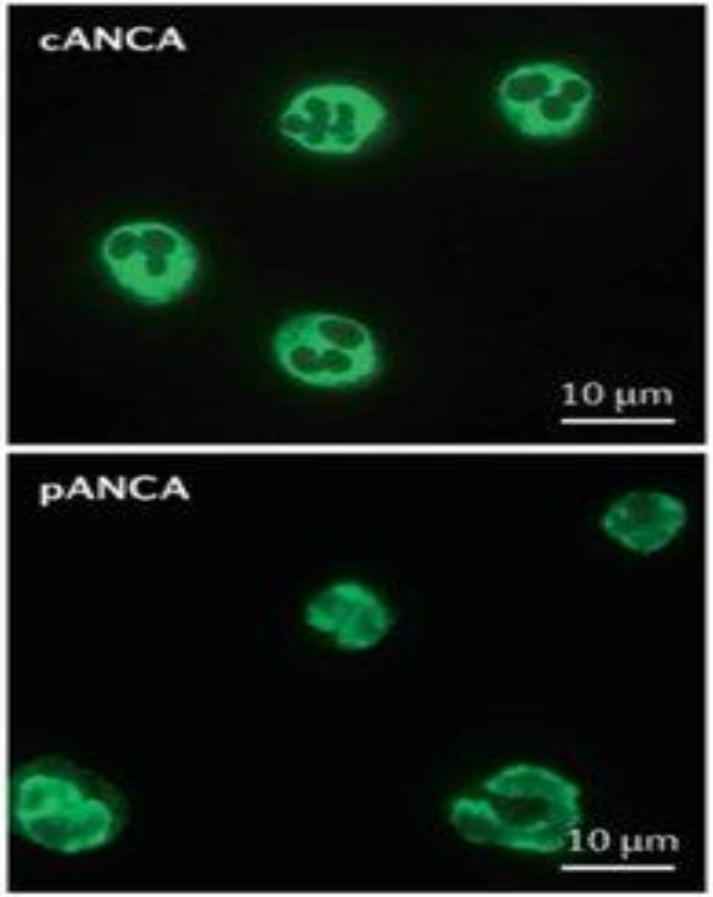
Anti-GBM disease



Large vessel vasculitis
- Takayasu arteritis
- Giant cell arteritis

ANCA-associated small vessel vasculitis
- Microscopic polyangiitis
- Granulomatosis with polyangiitis
- Eosinophilic granulomatosis with polyangiitis

b



nature reviews
disease primers

ANCA associated Vasculitis

Granulomatosis with polyangiitis

« Wegener Granumatosis »

Eosinophilic granulomatosis with polyangiitis

« Churg- Strauss Sd »

Microscopic Polyangiitis

C ANCA

Anti-Protéinase 3
« PR3 »

P ANCA

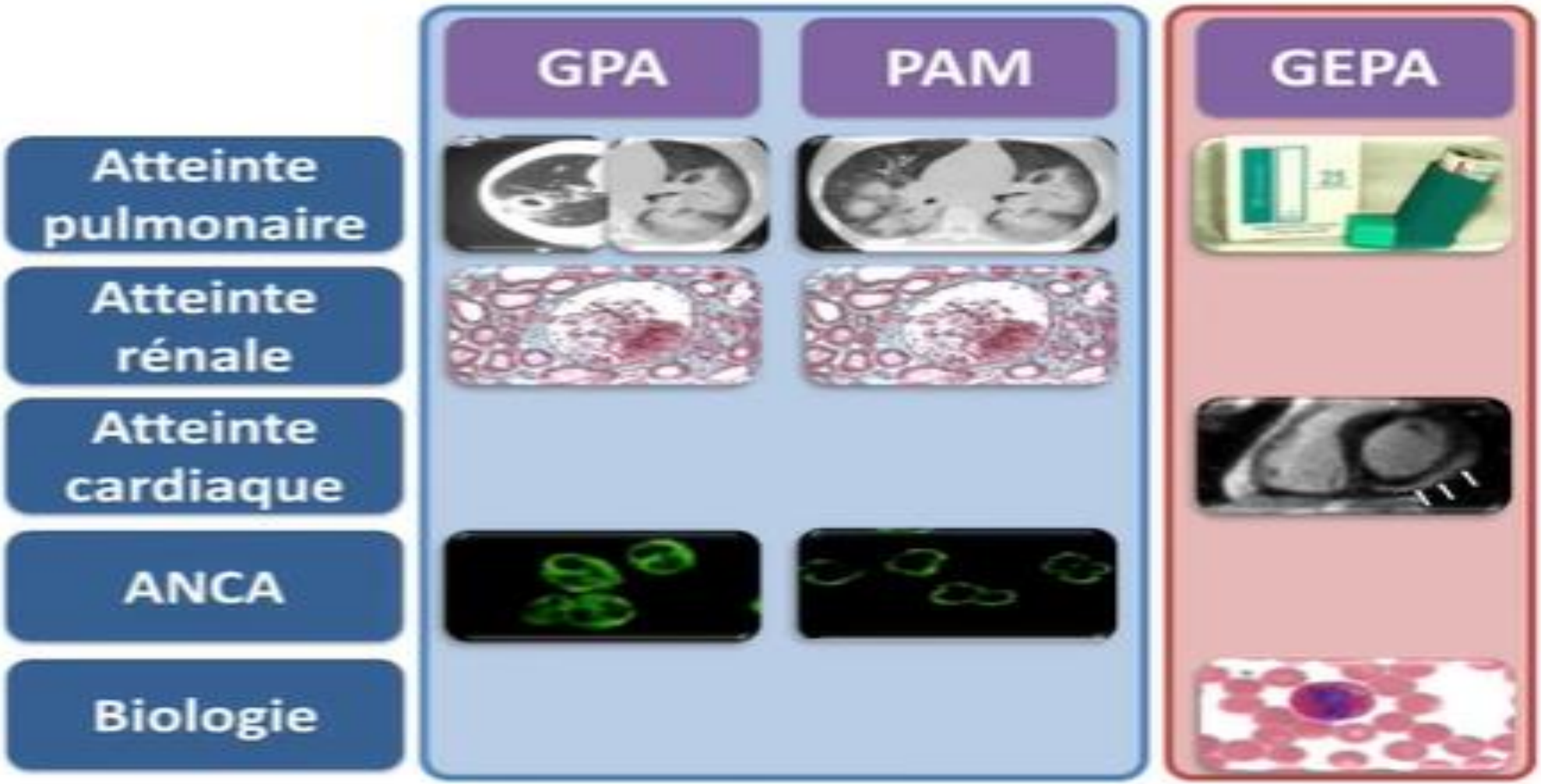
Antimyéloperoxydase
« MPO »

	Anti PR3	Anti MPO
GPA	**82,2%**	8,1%
MPA	2,1%	**95,9%**
EGPA	3,1%	**43,3%**

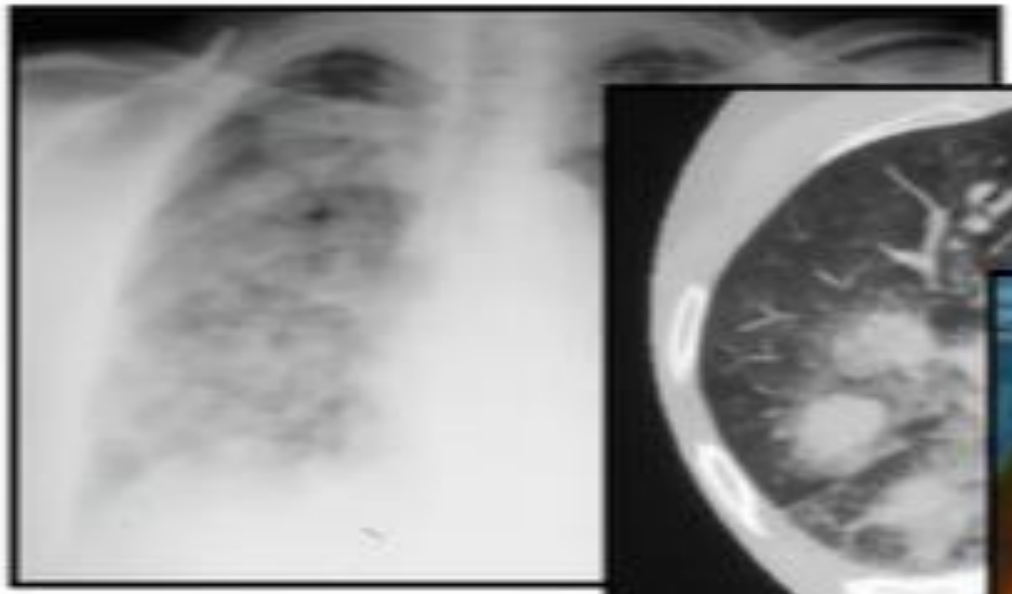
DCVAS study

+/- **histological evidence of vasculitis**

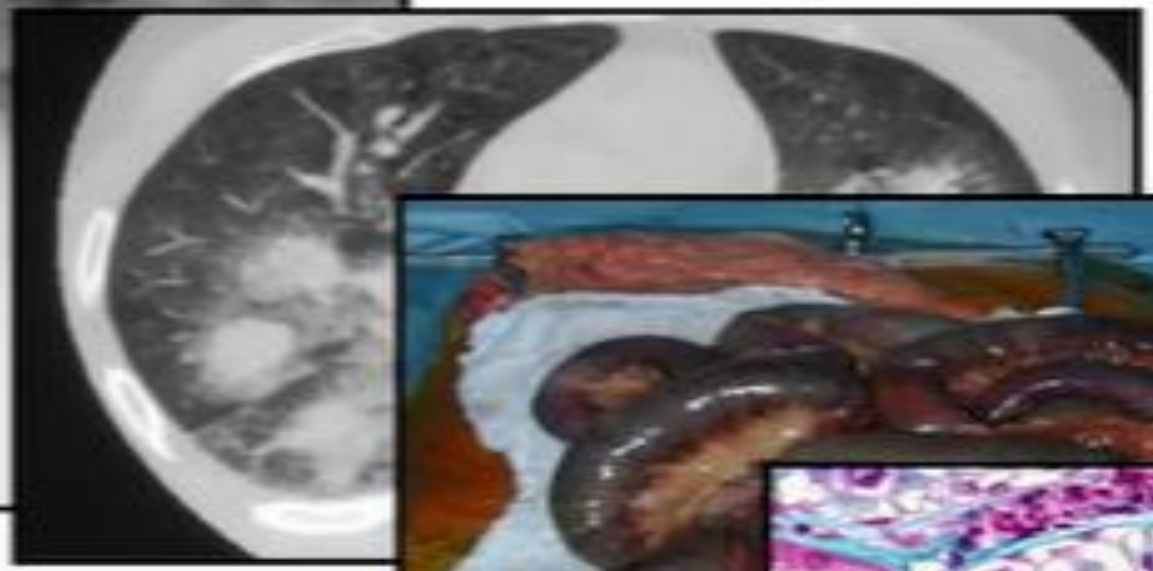
GPA/PAM vs. GEPA: Phénotypes distincts



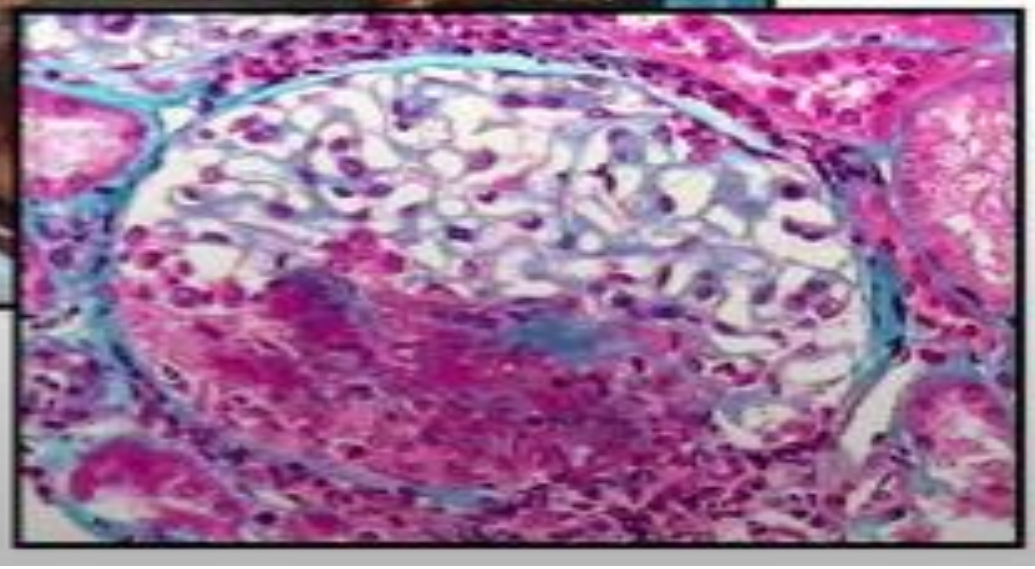
Formes fulminantes de VAA



Hémorragie intra-alvéolaire



Vascularite digestive



Insuffisance rénale
rapidement progressive

Presentation outline

- EULAR recommendations for the management of AAV – 2022 update*
- Focus on induction of remission with RTX, PLEX, and avacopan versus SOC in ANCA⊕ GPA and MPA

*Hellmich et al.
EULAR recommendations
AAV management – 2022 update
EULAR Congress
June 01st, 2022

GPA & MPA – Induction of remission

EULAR Recommendations – 2022 update	Organ- or life-threatening disease	Non-organ- or non-life-threatening disease
Recommended	• Combination of GC with either RTX or CYC • RTX preferred in relapse	
	• GC starting dose 50 – 75 mg pred.-equivalent/day; taper to 5 mg by 4 – 5 months	

Hellmich et al.
EULAR recommendations
AAV management – 2022 update
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GPA & MPA – Induction of remission

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Recommended	• Combination of GC with either RTX or CYC • RTX preferred in relapse	
	• GC starting dose 50 – 75 mg pred.-equivalent/day; taper to 5 mg by 4 – 5 months	
May be considered	• PLEX for creatinine >300 µmol/l due to active glomer-ulonephritis; not for routine use in alveolar hemorrhage	
	• Avacopan in combination with RTX or CYC as part of GC-reducing strategy	

Hellmich et al.
EULAR recommendations
AAV management – 2022 update
EULAR Congress
June 01st, 2022

GPA & MPA – Induction of remission

EULAR Recommendations – 2022 update	Organ- or life-threatening disease	Non-organ- or non-life-threatening disease
Recommended	• Combination of GC with either RTX or CYC • RTX preferred in relapse	• Combination of GC with RTX
	• GC starting dose 50 – 75 mg pred.-equivalent/day; taper to 5 mg by 4 – 5 months	
May be considered	• PLEX for creatinine >300 µmol/l due to active glomerulonephritis; not for routine use in alveolar hemorrhage	• Alternatives to RTX: MTX or MMF (*…can be considered…*)
	• Avacopan in combination with RTX or CYC as part of GC-reducing strategy	

Hellmich et al.
EULAR recommendations
AAV management – 2022 update
EULAR Congress
June 01st, 2022

Etude RAVE

- Etude randomisée internationale de non-infériorité en double aveugle avec double placebo

- Critères d'inclusion
  - Vascularites à ANCA avec BVAS >3
  - Première poussée ou rechute

- Critère de jugement principal
  - Rémission complète à 6 mois sans corticoïdes

Stone , N Engl J Med, 2010

RAVE

197 patients

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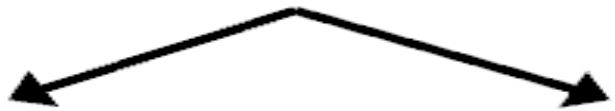
1 à 3 pulse methylprednisolone



Prednisone +

CYC oral

+ placebo RTX

Prednisone +

Placebo CYC

+ RTX

375 mg/m2 X 4

Azathioprine

12-15 mois

Placebo

Stone, N Engl J Med, 2010

Etude RAVE

Efficacité globale

Bras Rituximab: **60.4%**

Bras Cyclophosphamide: 64.6%

ont un BVAS = 0 à 6 mois sans corticothérapie

P<0.001 pour la non-infériorité

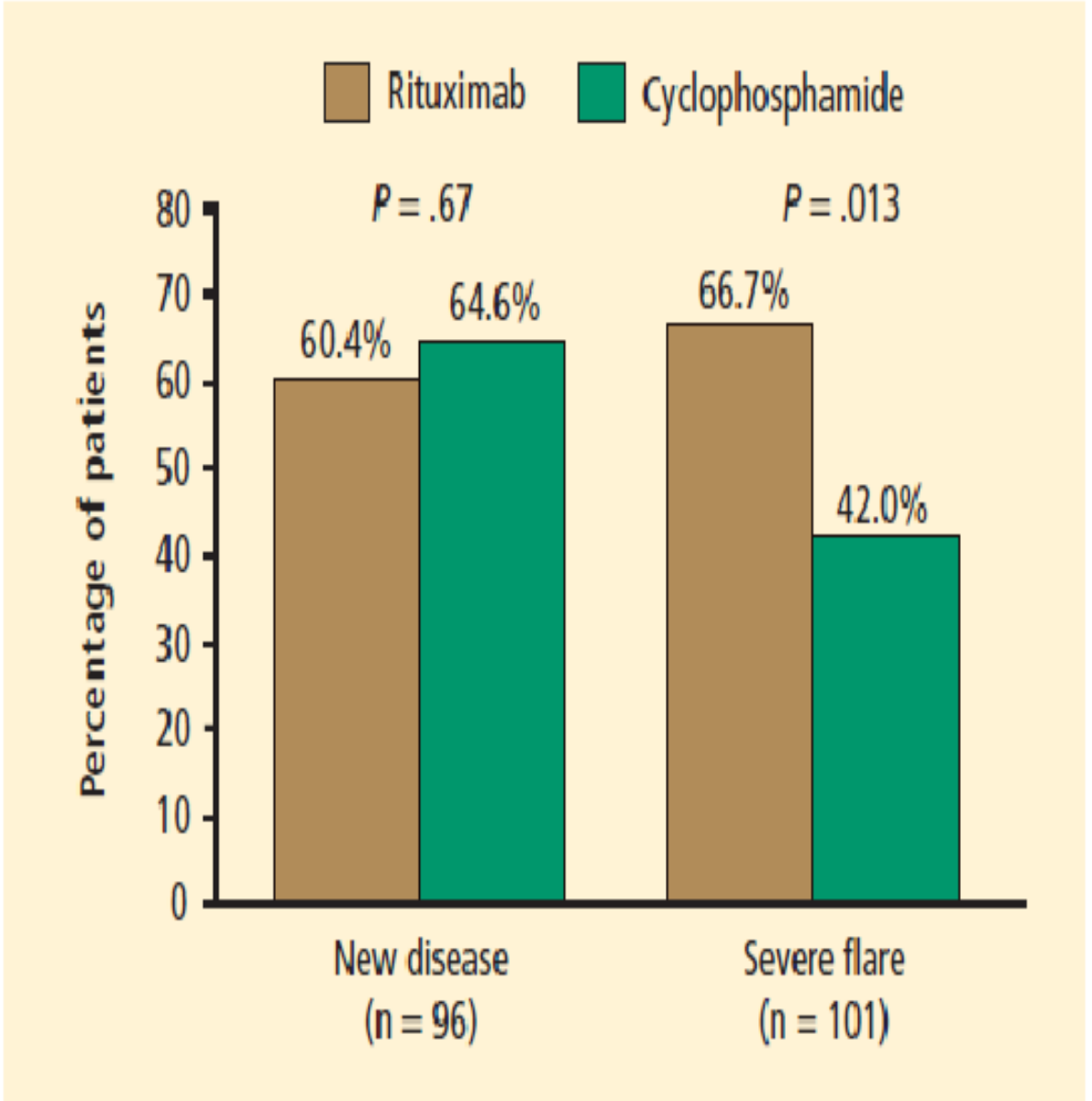
P=0.09 pour la supériorité

Sous-groupe des patients rechuteurs :

Bras Rituximab: **67%**

Bras Cyclophosphamide : 42%

P=0.01 pour la supériorité



RAVE – Treatment outcomes based on ANCA type

	PR3-AAV			MPO-AAV		
	RTX (n=66)	CYC/AZA (n=65)	P	RTX (n=33)	CYC/AZA (n=33)	P
CR at 6 months	43 (65)	31(48)	0.04	20 (61)	21 (64)	0.80
CR at 12 months	31 (47)	21 (32)	0.09	16 (49)	17 (52)	0.81
CR at 18 months	24 (36)	19 (29)	0.39	15 (46)	13 (39)	0.62

Unizony et al.
Ann Rheum Dis 2016

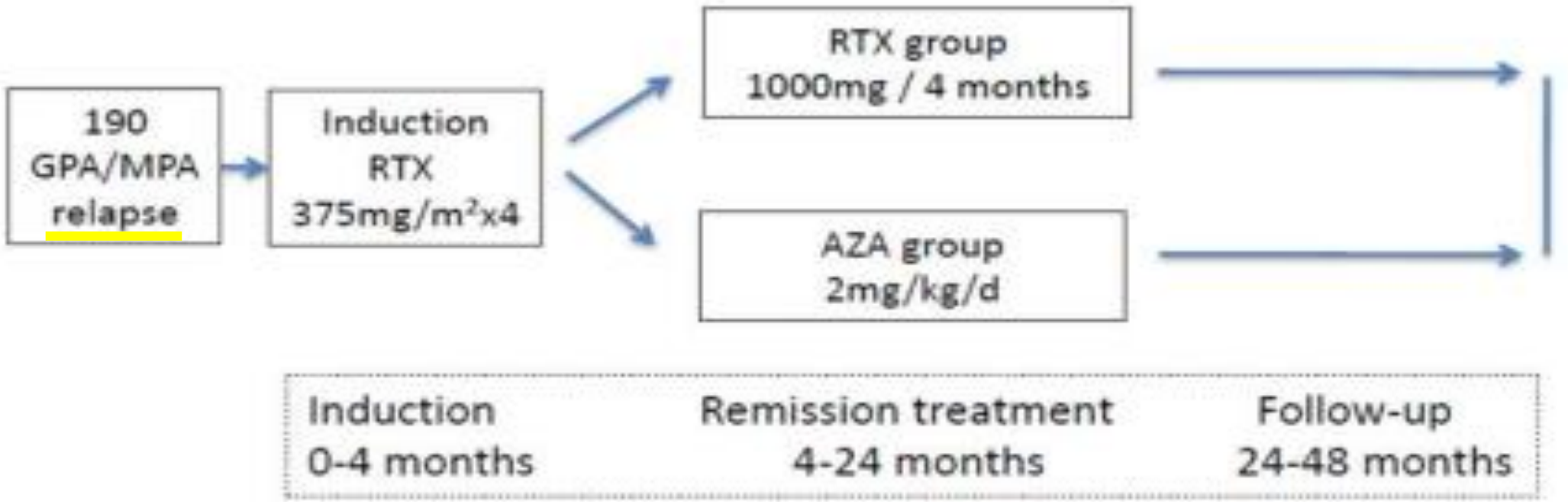
RAVE trial – Adverse events

Variable	Rituximab (N=99)	Cyclophosphamide–Azathioprine (N=98)	Total (N=197)	P Value
Total no. of participant-months	1371.5	1331.9	2703.4	
Adverse events				
Total no. of events	1399	1420	2819	
Participants with ≥1 event — no. (%)	98 (99)	98 (100)	196 (99)	>0.99
Events/participant-mo	1.02	1.07	1.04	0.24
Serious adverse events				
Total no. of events	59	63	122	
Participants with ≥1 event — no. (%)	42 (42)	37 (38)	79 (40)	0.50
Events/participant-mo	0.04	0.05	0.05	0.63
Deaths — no. (%)†	2 (2)	2 (2)	4 (2)	
Participants with ≥1 episode of leukopenia of grade 2 or higher — no. (%)	5 (5)	23 (23)	28 (14)	<0.001
Participants with ≥1 episode of infection of grade 3 or higher — no. (%)	12 (12)	11 (11)	23 (12)	>0.99
Pneumonia-related adverse events				
Total no. of events	4	11	15	
Participants with ≥1 episode of pneumonia — no. (%)	3 (3)	11 (11)	14 (7)	0.03
Pneumonia-related adverse events/participant-mo	0.0029	0.0083	0.0055	0.08

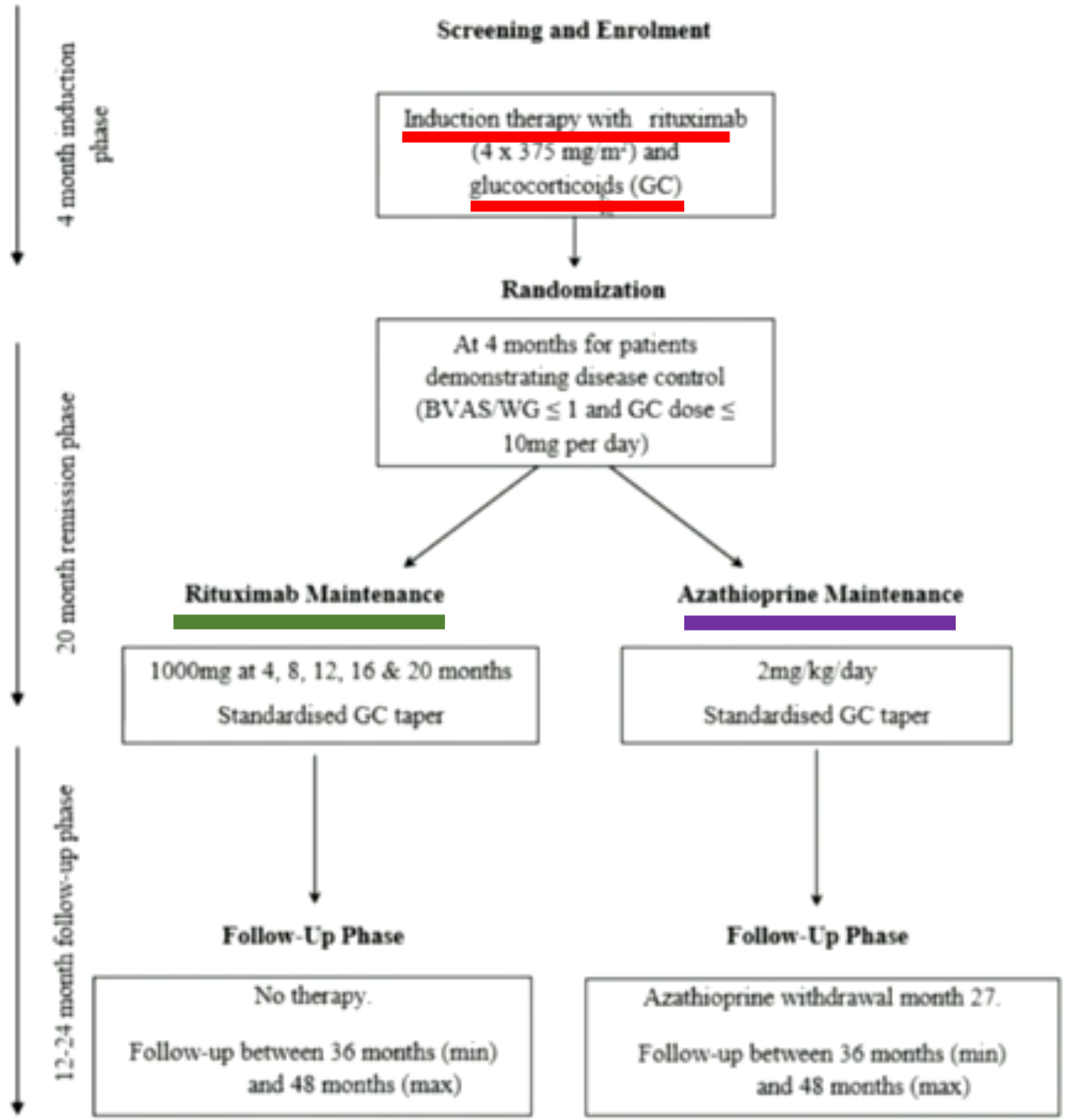
Specks et al.
New Engl J Med 2013

RITAZAREM

rituximab (RTX) or azathioprine (AZA) for remission after RTX induction

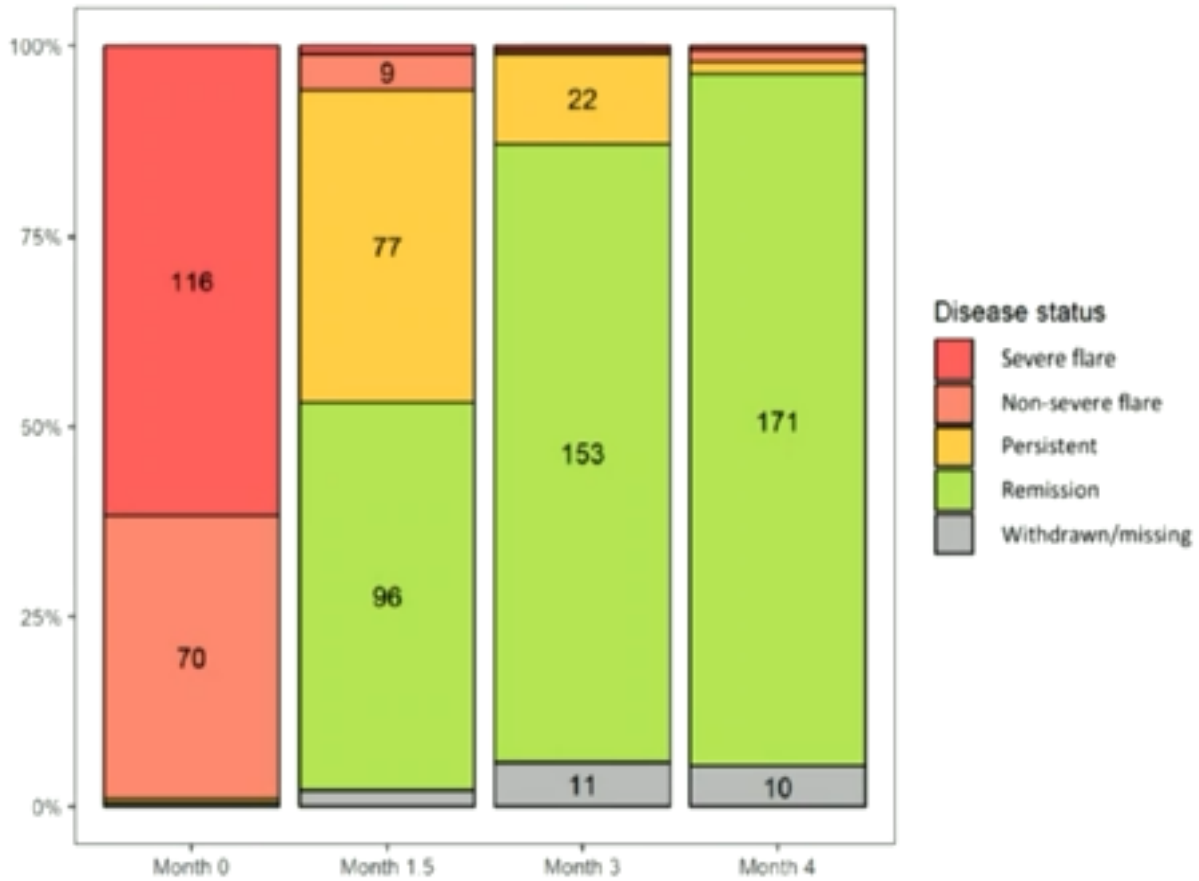


RITAZAREM trial design



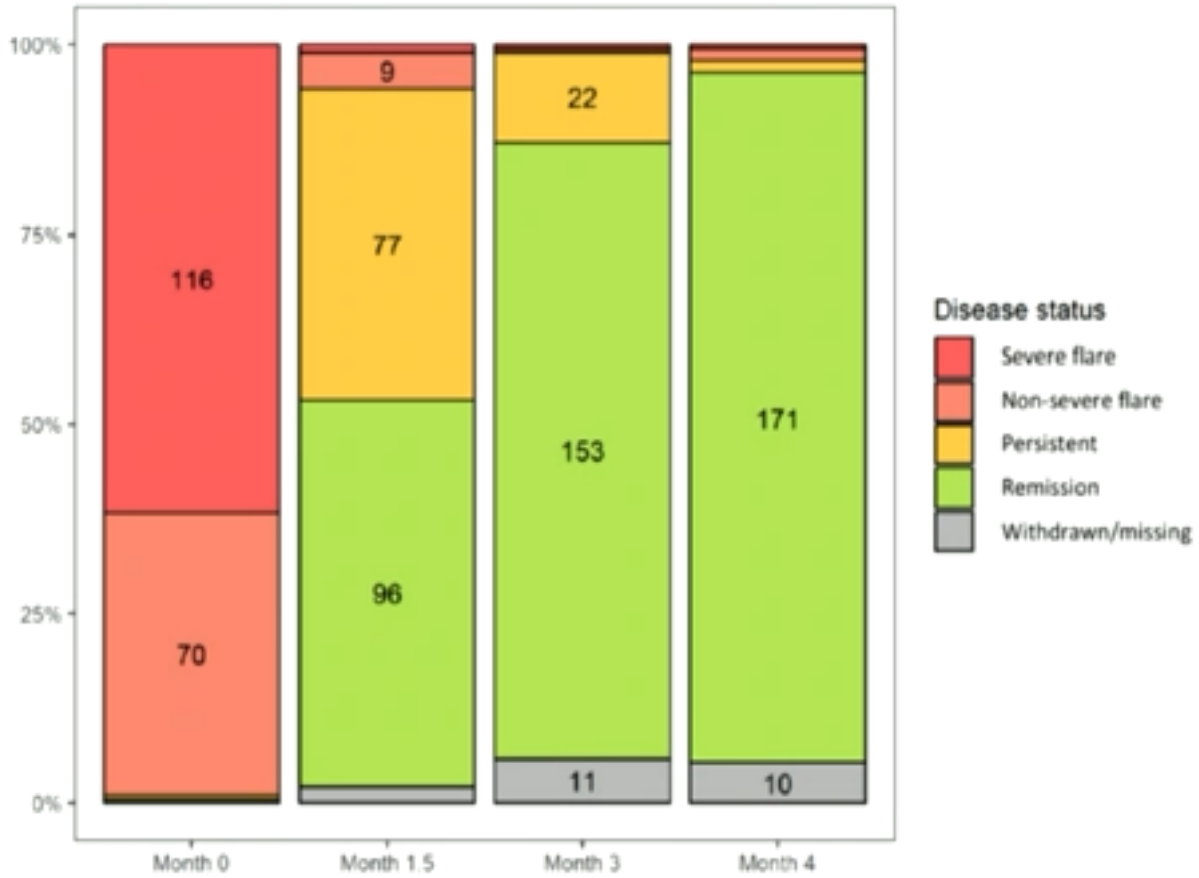
Gopaluni et al. Trials 2017

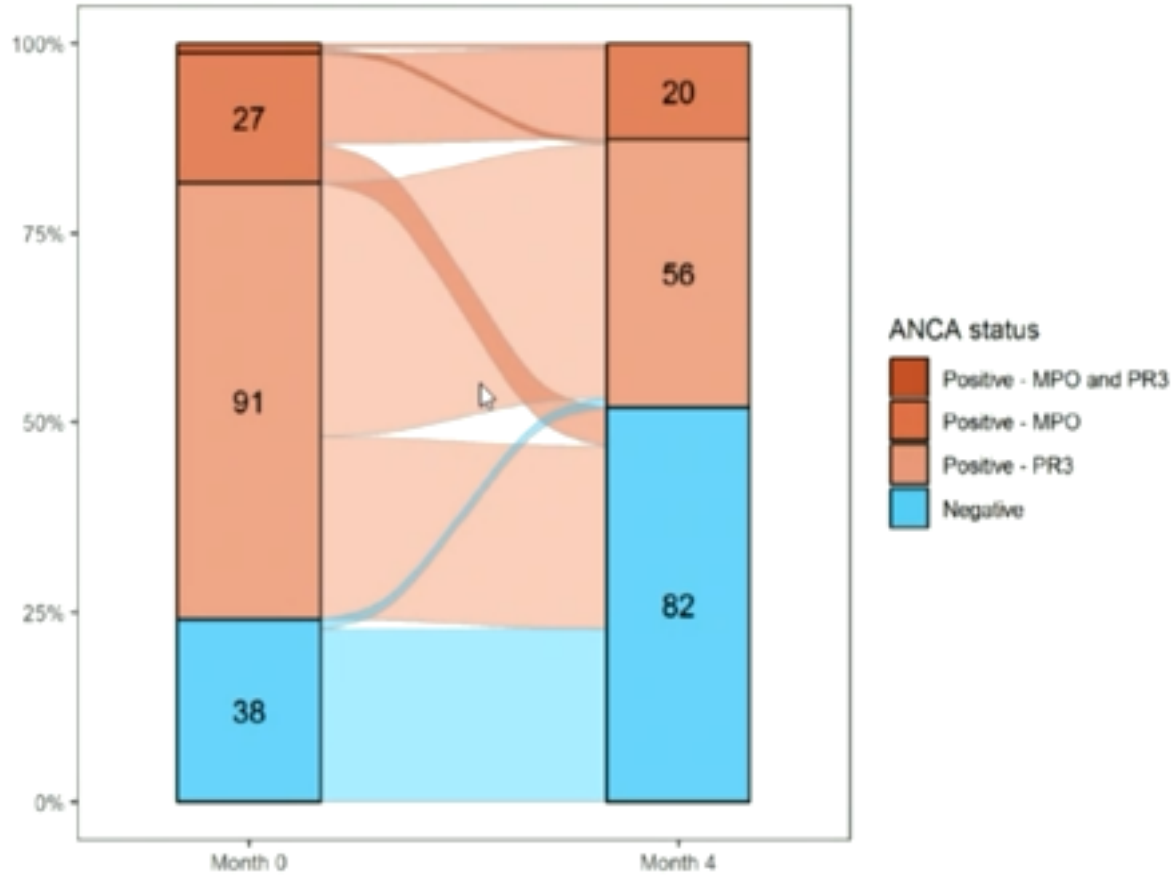
RITAZAREM – Disease response



Smith et al.
Ann Rheum Dis 2020

RITAZAREM – Disease response & change in ANCA

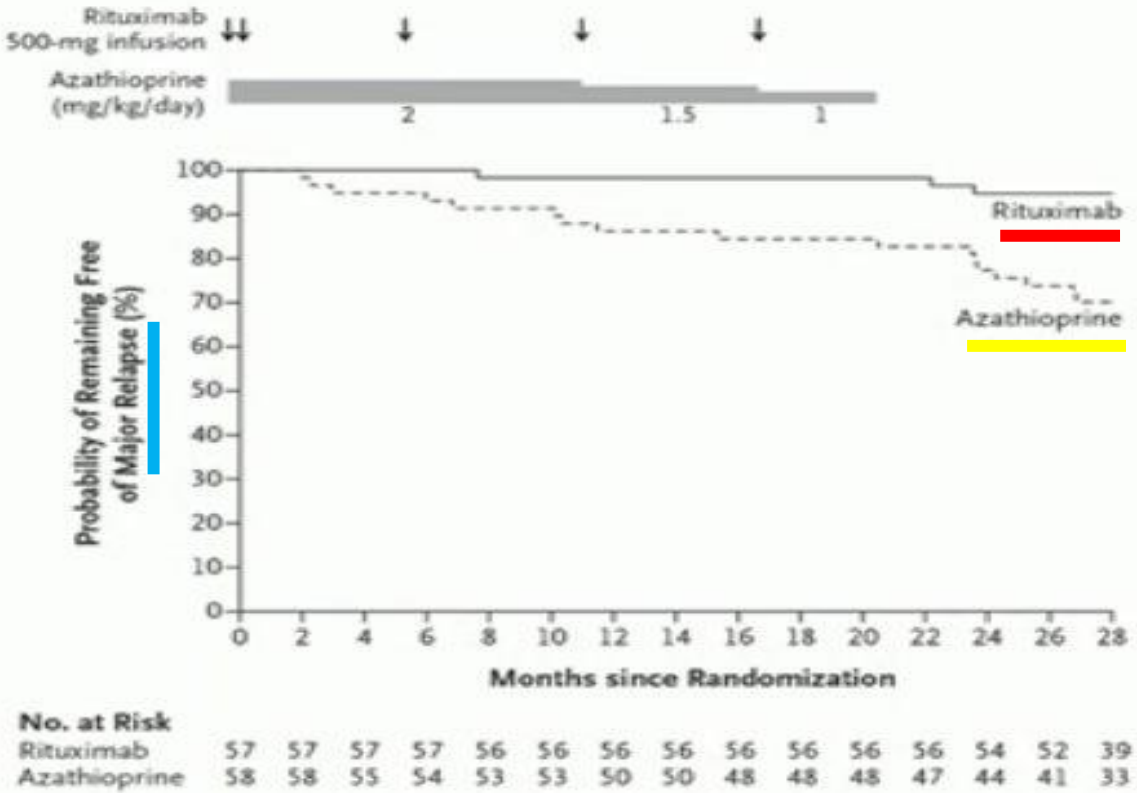




Smith et al.
Ann Rheum Dis 2020

RITAZAREM

Rituximab as a maintenance agent in AAV

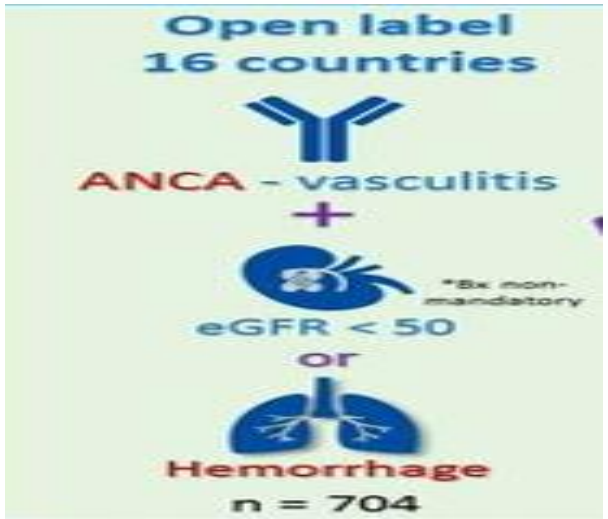


115 mainly newly diagnosed patients who had all received cyclophosphamide induction therapy

HR 6.61 (95% CI, 1.56 to 27.96; P=0.002)

Guillevin et al. NEJM, 2014

PEXIVAS trial design



Severe AAV

Standard Therapy with Cyclophosphamide or Rituximab

Adjunctive Plasma Exchange

No Plasma Exchange

Standard-Dose Glucocorticoids

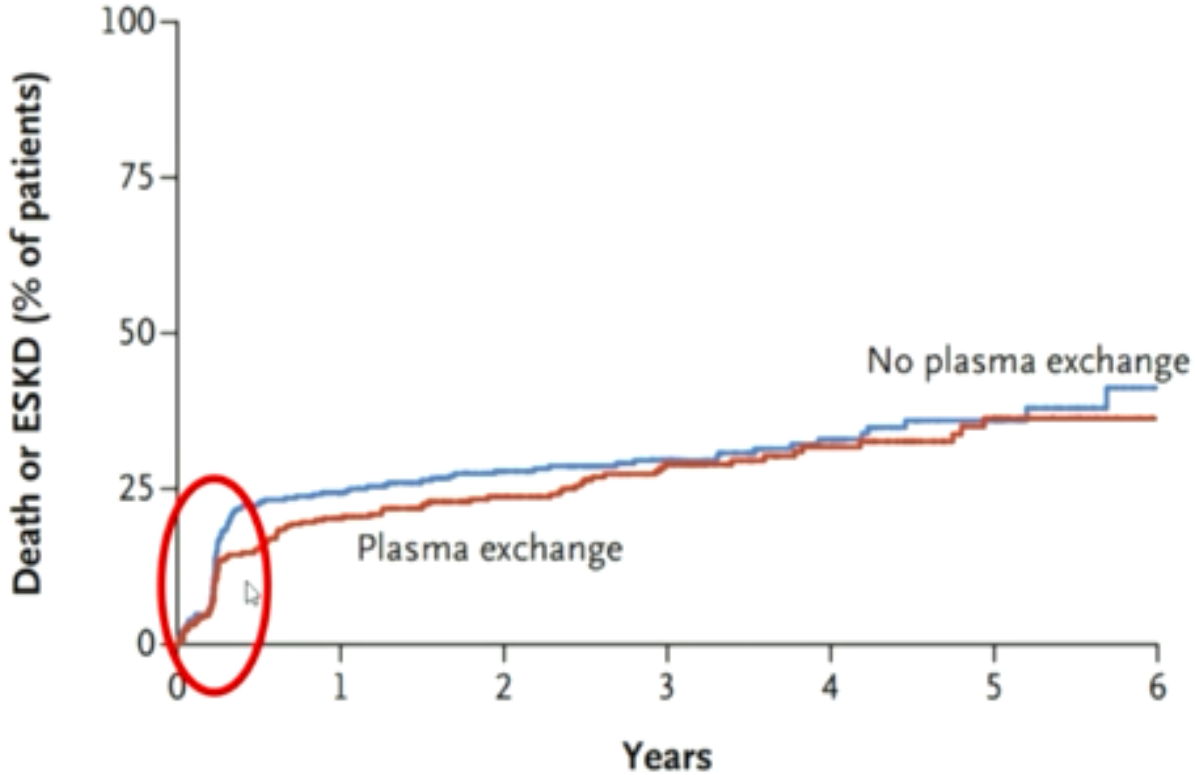
Reduced-Dose Glucocorticoids

Standard-Dose Glucocorticoids

Reduced-Dose Glucocorticoids

Walsh et al.
New Engl J Med 2020

PEXIVAS – Death or ESKD according to PLEX Y/N

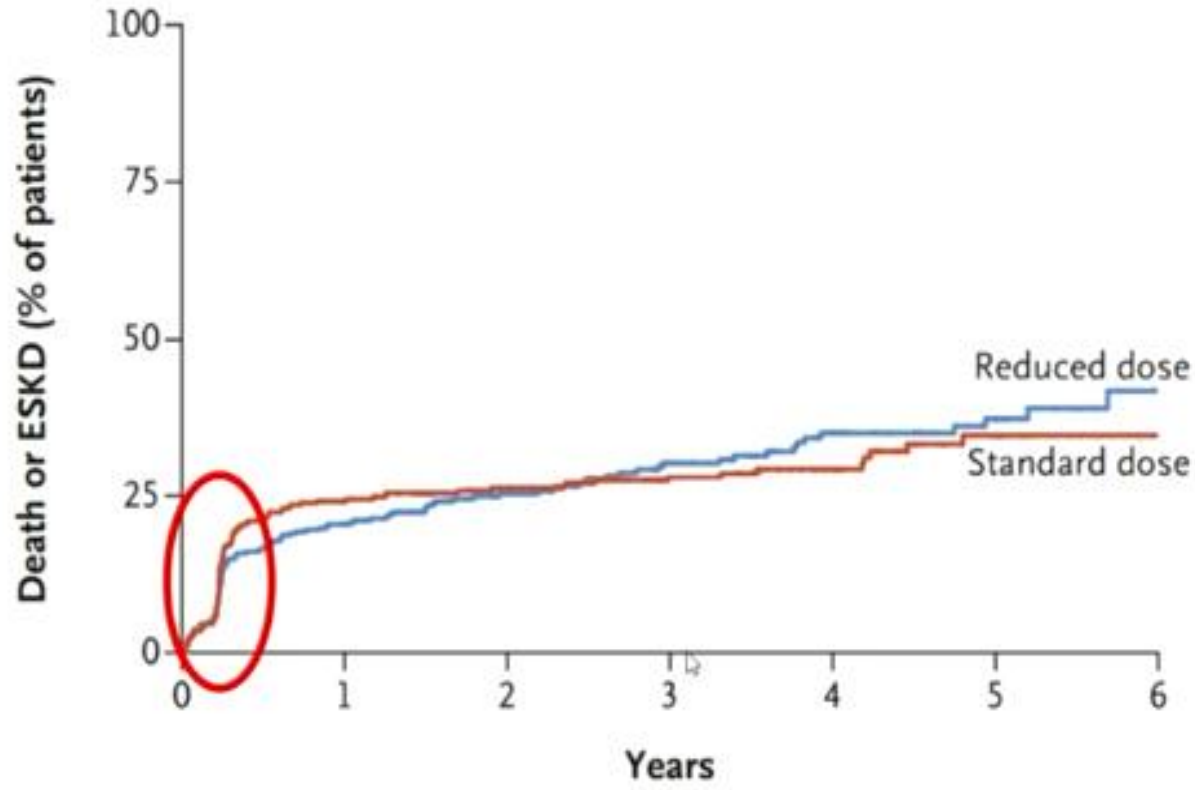


No. at Risk							
No plasma exchange	352	244	183	136	82	44	10
Plasma exchange	352	252	186	135	82	43	10

Walsh et al.
New Engl J Med 2020

PEXIVAS – Death or ESKD according to GC regimen

Week	Standard			Reduced-dose		
	<50 kg	50-75 kg	>75 kg	<50 kg	50-75 kg	>75 kg
	pulse	pulse	pulse	pulse	pulse	pulse
1	50	60	75	50	60	75
2	50	60	75	25	30	40
3-4	40	50	60	20	25	30
5-6	30	40	50	15	20	25
7-8	25	30	40	12.5	15	20
9-10	20	25	30	10	12.5	15
11-12	15	20	25	7.5	10	12.5
13-14	12.5	15	20	6	7.5	10
15-16	10	10	15	5	5	7.5
17-18	10	10	15	5	5	7.5
19-20	7.5	7.5	10	5	5	5
21-22	7.5	7.5	7.5	5	5	5
23-52	5	5	5	5	5	5
>52	Investigators' Local Practice			Investigators' Local Practice		



No. at Risk							
Reduced dose	353	256	185	133	80	48	9
Standard dose	351	240	184	138	84	39	11

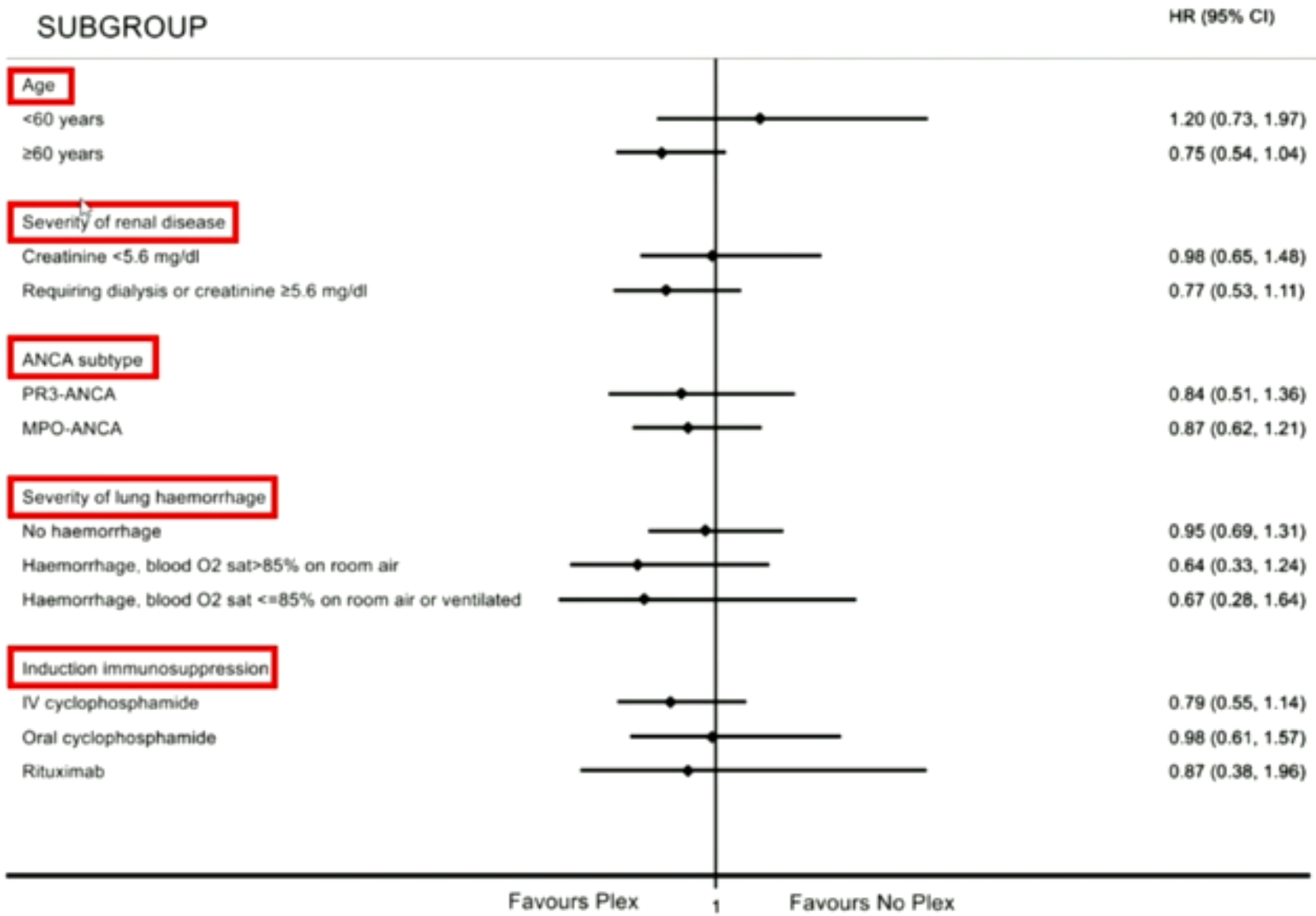
Walsh et al.
New Engl J Med 2020

PEXIVAS – Secondary outcomes

Secondary Outcome	Reduced-Dose vs. Standard-Dose Glucocorticoid Regimen *effect size (95% CI)*
Death from any cause	0.78 (0.53–1.17)
End-stage kidney disease	0.96 (0.68–1.34)
Sustained remission	1.04 (0.92–1.19)
Serious adverse events	0.95 (0.75–1.20)
Serious infections at 1 year	0.69 (0.52–0.93)

Walsh et al.
New Engl J Med 2020

PEXIVAS – Death or ESKD according to subgroup



Walsh et al.
New Engl J Med 2020

PEXIVAS

Plasma exchange and glucocorticoids in severe ANCA-associated vasculitis

#NephJC

Design

Open label
16 countries

ANCA - vasculitis

+

eGFR < 50

*Bx non-mandatory

or

Hemorrhage

n = 704

Randomization

All: CYC or Rituximab

PLEX x 7
n = 352

No PLEX
n = 352

Standard steroids
n = 351

Reduced steroids
n = 353

Median follow up: 3 years

Primary outcome: death + ESKD

28 % = CI = 0.6, 1.1 = 31 %

25 % = CI = -3.4, 8 = 28 %

Severe infections

33 % > CI = 0.52, 0.93 27 %

Conclusions: Among patients with severe ANCA-associated vasculitis, PLEX did not reduce the incidence of death or ESKD. A reduced-dose regimen of steroids was noninferior to a standard-dose regimen with respect to death or ESKD.

M. Walsh, P.A. Merkel, C.-A. Peh et. al. Plasma Exchange and Glucocorticoids in Severe ANCA-Associated Vasculitis. NEJM 2020;382:622-31.

@NephroGuy

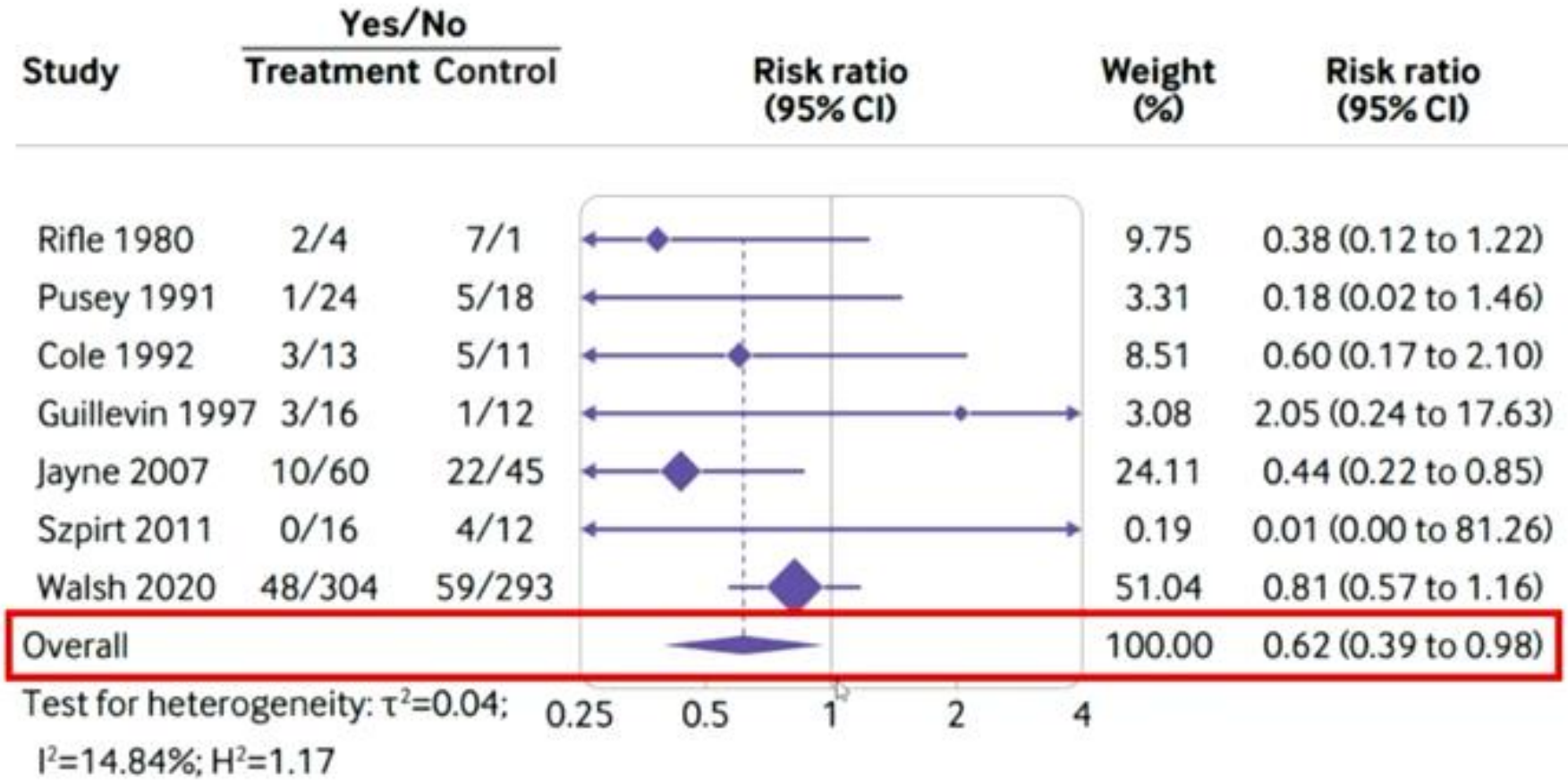
PLEX meta-analysis – Characteristics of trials

Study	Follow-up (months)	Plasma exchange: Method	Plasma exchange: No of treatments	Plasma exchange: Volume/ treatment	Participants: No	Mean age (years): wPLEX	Mean age (years): Ctrl	Female (%): PLEX	Female (%): Ctrl	Baseline creatinine (µmol/L): PLEX	Baseline creatinine (µmol/L): Ctrl	Baseline dialysis (%): PLEX	Baseline dialysis (%): Ctrl	Lung haem
Rifle 1980	22	Centrifuge	5 in 5 days + additional for non-response	1.5 plasma volumes	14	41	52	50	25	893	1140	67	88	No
Mauri 1985	36	Centrifuge and filter	6 in 12 days + additional for non-response	3.5 L	22	NR	NR	NR	NR	1193	1158	50	50	NR
Pusey 1991	58	Centrifuge	5 in 7 days + additional for non-response	4 L	48	52	51	36	39	793	637	44	34	Yes
Cole 1992	12	Centrifuge	≥10 in 16 days	1 plasma volume	32	NR	NR	NR	NR	634	769	25	43	NR
Guillevin 1997	12	Centrifuge and filter	9 or 12 at 3 times/week	60 mL/kg	32	47	62	47	38	439	287	32	15	NR
Zauner 2002	127	NR	3 + <9 for non-response	40 mL/kg	39	55	56	29	22	NR	NR	NR	NR	Yes
Jayne 2007, Walsh 2013	12, 47	Centrifuge and filter	7 in 14 days	60 mL/kg	137	67	66	41	36	701	732	67	71	Yes
Szpirt 2010	60	Filter	6 + 3-6 for persistent ANCA	4 L	32	58	56	25	19	262	250	13	25	Yes
Walsh 2020	35	Centrifuge and filter	7 in 14 days	60 mL/kg	704	63	64	42	45	327	336	19	21	Yes

Lung haem = Presence of lung haemorrhage at baseline. PLEX = Plasma exchange. Ctrl = Control. NR = Not reported.

Walsh et al. BMJ 2022

PLEX meta-analysis – 1-year ESKD



Study	Yes/No Treatment	Yes/No Control	Risk ratio (95% CI)	Weight (%)	Risk ratio (95% CI)
Rifle 1980	2/4	7/1		9.75	0.38 (0.12 to 1.22)
Pusey 1991	1/24	5/18		3.31	0.18 (0.02 to 1.46)
Cole 1992	3/13	5/11		8.51	0.60 (0.17 to 2.10)
Guillevin 1997	3/16	1/12		3.08	2.05 (0.24 to 17.63)
Jayne 2007	10/60	22/45		24.11	0.44 (0.22 to 0.85)
Szpirt 2011	0/16	4/12		0.19	0.01 (0.00 to 81.26)
Walsh 2020	48/304	59/293		51.04	0.81 (0.57 to 1.16)
Overall				100.00	0.62 (0.39 to 0.98)

Test for heterogeneity: τ^2=0.04; I^2=14.84%; H^2=1.17

Walsh et al.
BMJ 2022

PLEX meta-analysis – 1-year ESKD

Outcome	Risk group	Estimated risk reduction	Risk ratio (95% CI)
ESKD	Low Creatinine ≤200 µmol/l	0.08% (0.02% - 0.12%)	0.62 (0.39 – 0.98)
	Low-moderate Creatinine >200 – 300 µmol/l	2.1% (0.6% - 3.1%)	
	Moderate-high Creatinine >300 – 500 µmol/l	4.6% (1.2% - 6.8%)	
	High Creatinine >500 µmol/l	16.0% (4.2% - 23.6%)	

Walsh et al.
BMJ 2022

PLEX meta-analysis – 1-year ESKD

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	Moderate-high Creatinine >300 – 500 µmol/l	4.6% (1.2% - 6.8%)	
	High Creatinine >500 µmol/l	16.0% (4.2% - 23.6%)	
Outcome	**Risk group**	**Estimated risk increase**	**Risk ratio (95% CI)**
Infection	Low Creatinine ≤200 µmol/l	2.7% (0.3% - 5.6%)	1.27 (1.08 – 1.49)
	Low-moderate Creatinine >200 – 300 µmol/l	4.9% (0.5% - 10.1%)	
	Moderate-high Creatinine >300 – 500 µmol/l	8.6% (1.0% - 17.9%)	
	High Creatinine >500 µmol/l	13.5% (1.5% - 28%)	

Walsh et al.
BMJ 2022

PLEX meta-analysis – 1-year ESKD

Outcome	Risk group	Estimated risk reduction		Risk ratio (95% CI)
ESKD	Low Creatinine ≤200 µmol/l	0.08% (0.02% - 0.12%)		0.62 (0.39 – 0.98)
	Low-moderate Creatinine >200 – 300 µmol/l	2.1% (0.6% - 3.1%)		
	Moderate-high Creatinine >300 – 500 µmol/l	4.6% (1.2% - 6.8%)	NNT 24	
	High Creatinine >500 µmol/l	16.0% (4.2% - 23.6%)	NNT 7	
Outcome	**Risk group**	**Estimated risk increase**		**Risk ratio (95% CI)**
Infection	Low Creatinine ≤200 µmol/l	2.7% (0.3% - 5.6%)		1.27 (1.08 – 1.49)
	Low-moderate Creatinine >200 – 300 µmol/l	4.9% (0.5% - 10.1%)		
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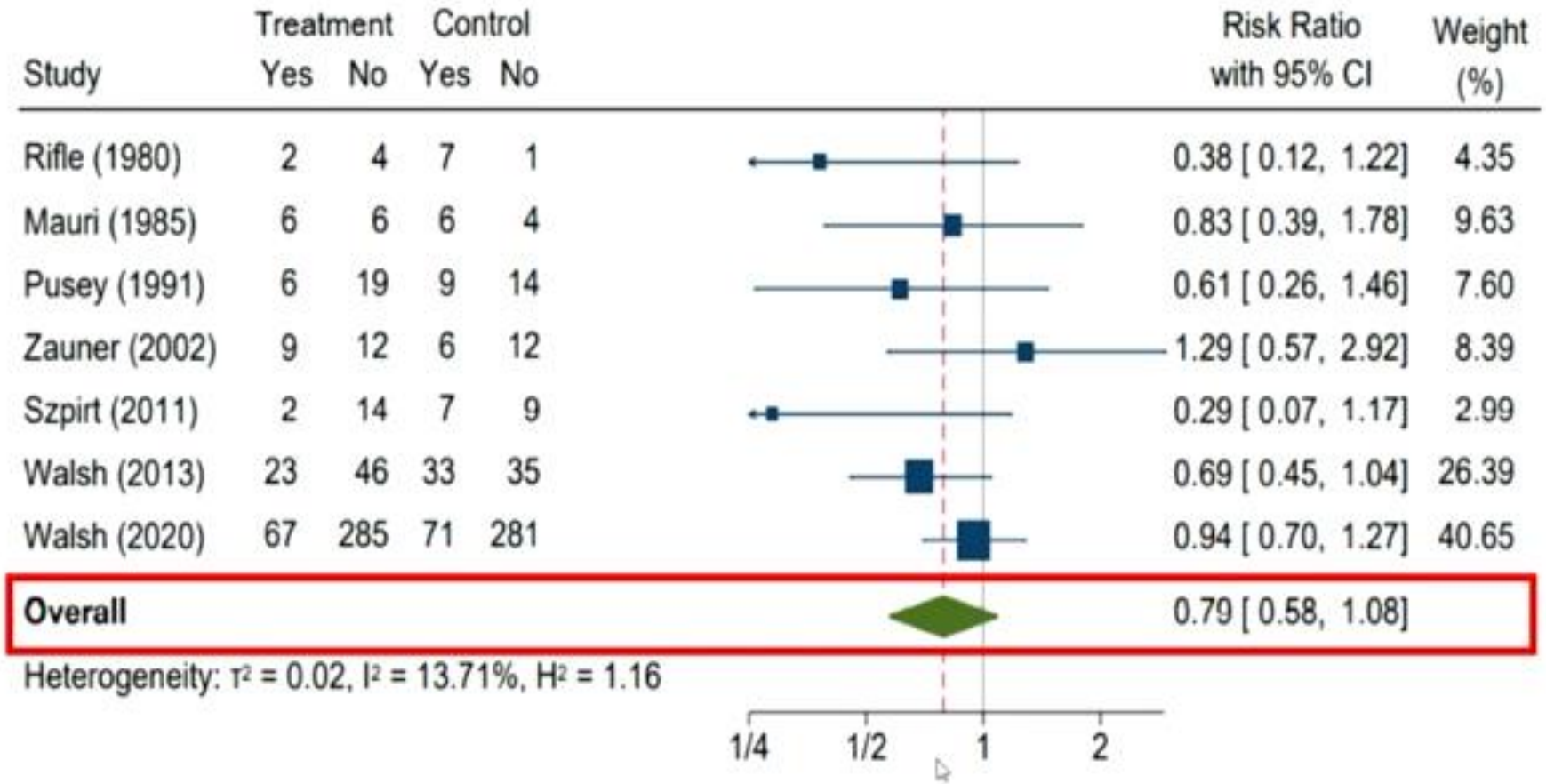
	High Creatinine >500 µmol/l	13.5% (1.5% - 28%)		

Walsh et al.
BMJ 2022

PLEX meta-analysis – Long-term follow-up ESKD



Walsh et al.
BMJ 2022

Could PLEX be a game-changer in the treatment of ANCA - associated vasculitis?

#NephJC

Systematic review & meta-analysis

Systematic reviews updated to July 2020

9 randomized trials

1060 AAV participants

AAV: ANCA associated vasculitis

PLEX EFFECT

12 months follow up

Reduced risk of ESKD

RR 0.62
(95% CI 0.39 - 0.98)

Increased infection risk

RR 1.27
(95% CI 1.08 - 1.49)

All-cause mortality no significant effect

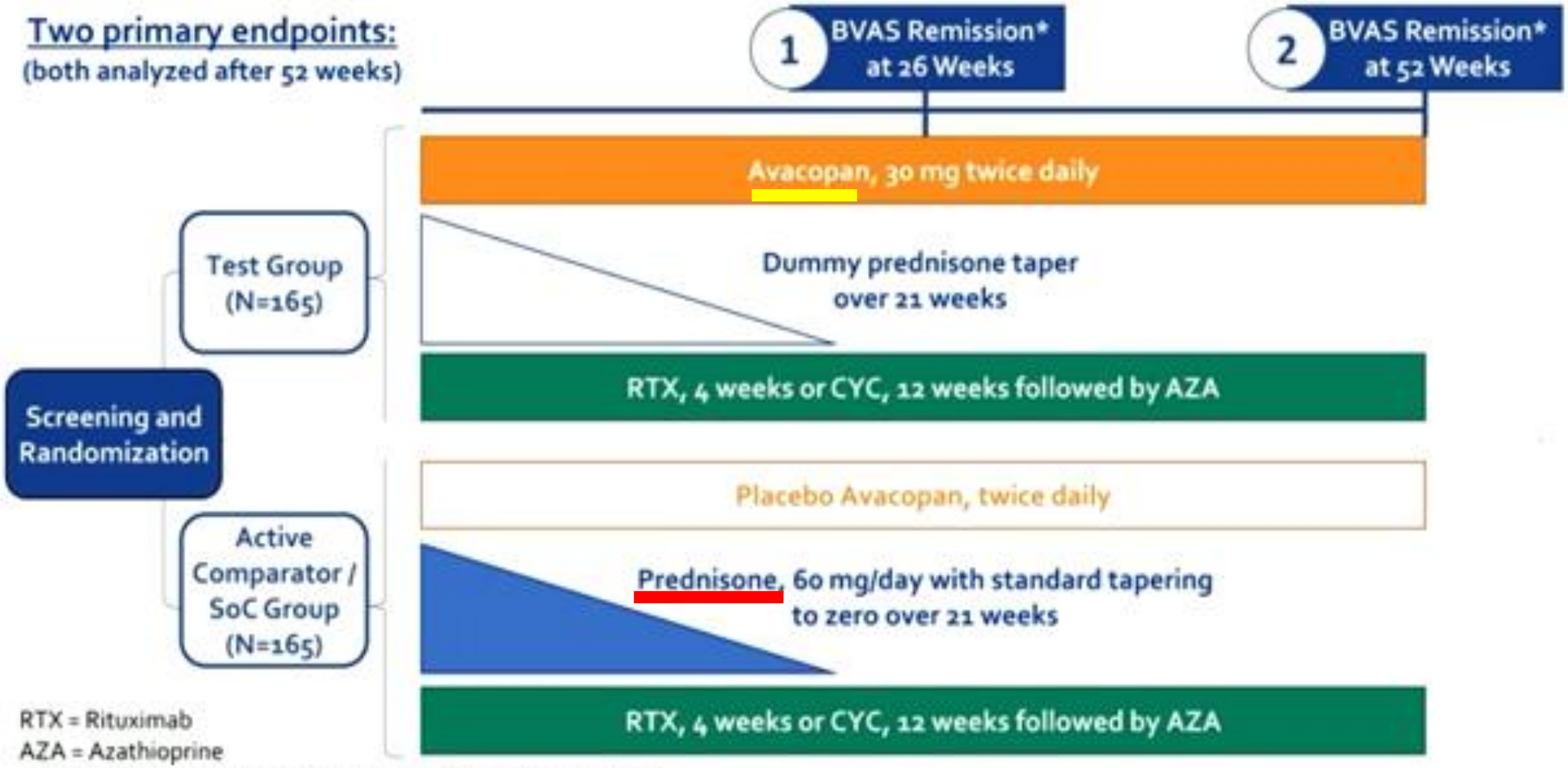
RR 0.90
(95% CI 0.64 to 1.27)

CONCLUSION: Current evidence does not demonstrate a strong role for PLEX in addition to standard care in preventing death. PLEX may delay the need for dialysis, which could improve a patient's quality of life, but it has serious adverse effects.

Walsh M, Collister D, Zeng L, et al. ***The effects of plasma exchange in patients with ANCA-associated vasculitis: an updated systematic review and meta-analysis.*** BMJ. 2022 doi: 10.1136/bmj-2021-064604.

Visual abstract by Cristina Popa, MD @NephroSeeker

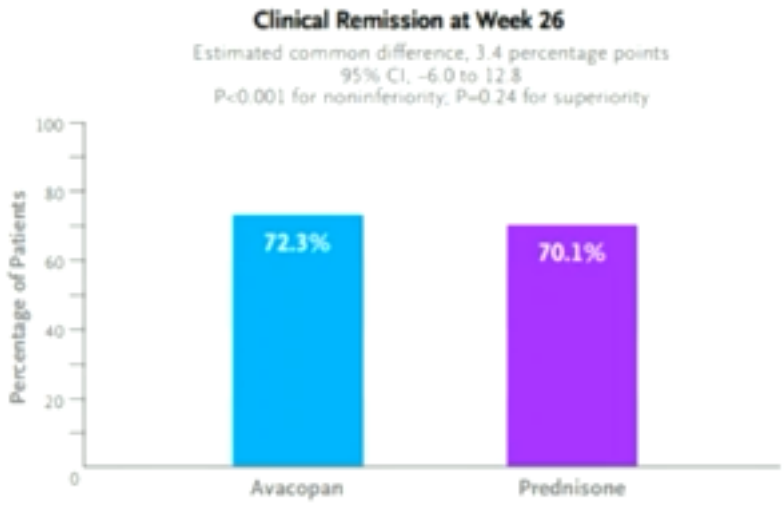
ADVOCATE trial design

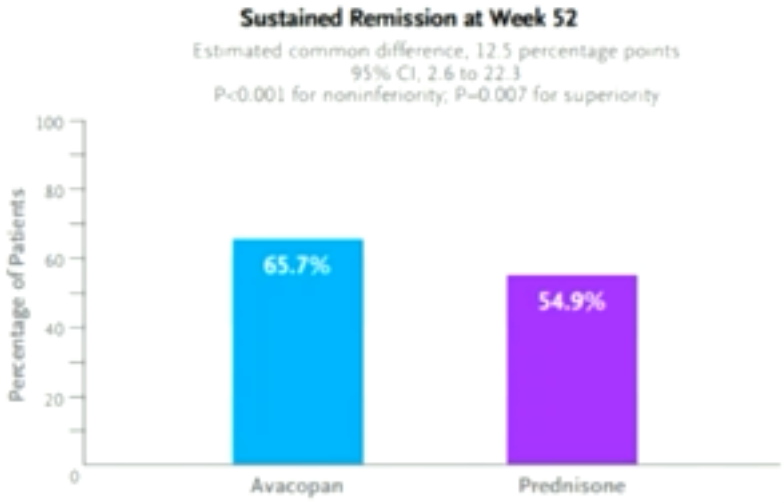


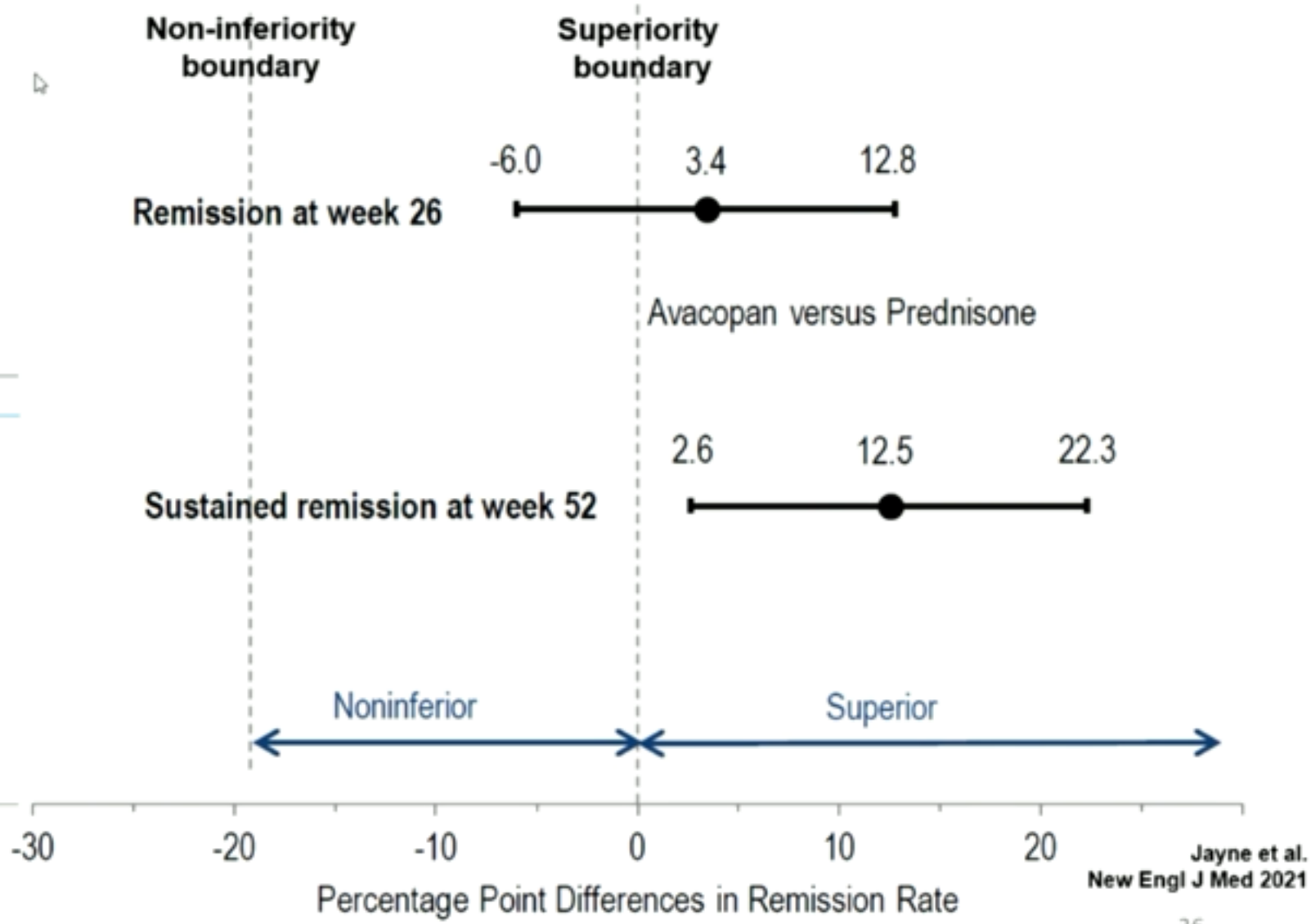
RTX = Rituximab
AZA = Azathioprine
*BVAS Remission: BVAS of zero and no steroids for ≥4 weeks

Merkel et al.
JMIR Res Protoc 2020

ADVOCATE – Remission at week 26 & 52

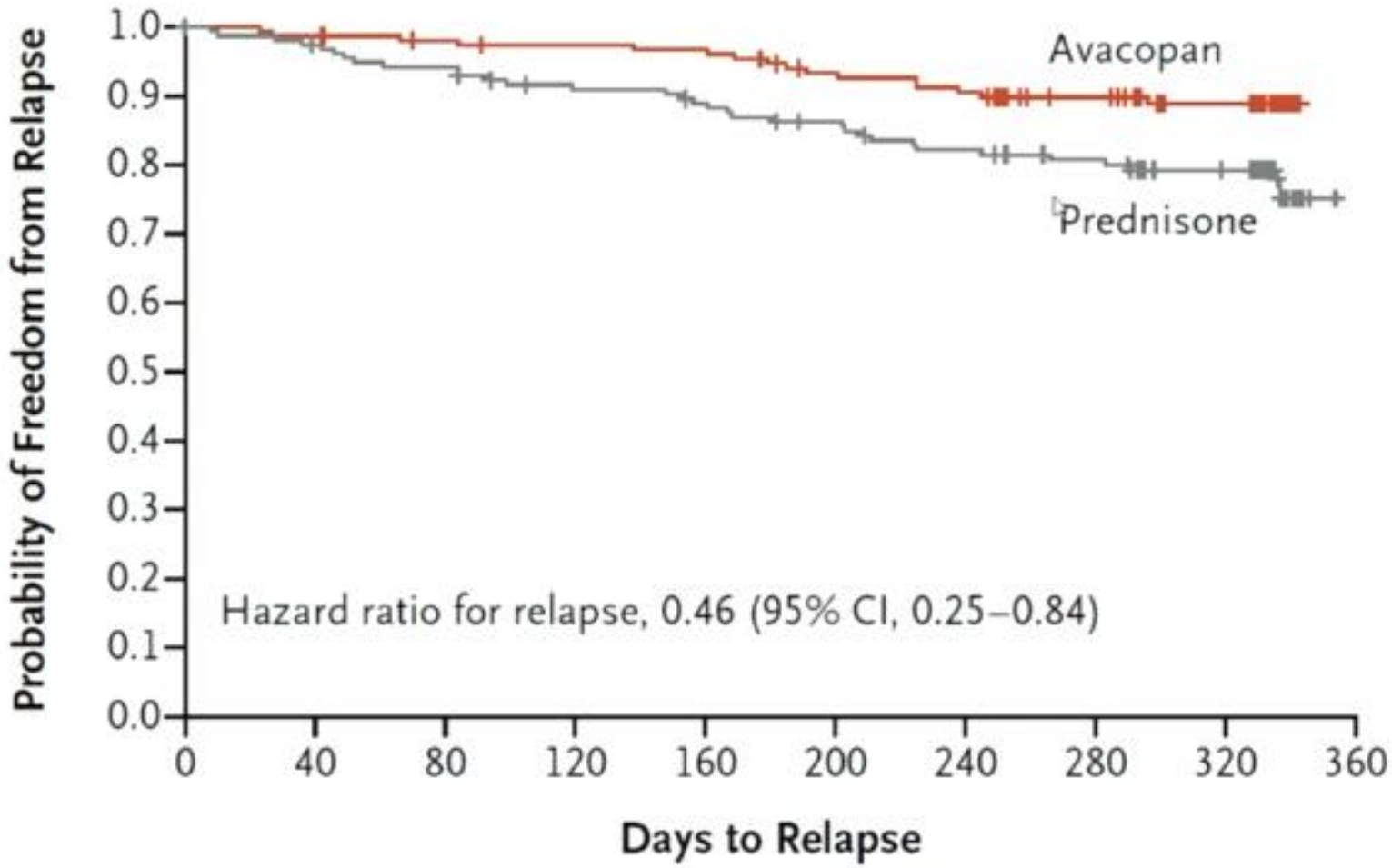






Jayne et al.
New Engl J Med 2021

ADVOCATE – Relapse-free survival

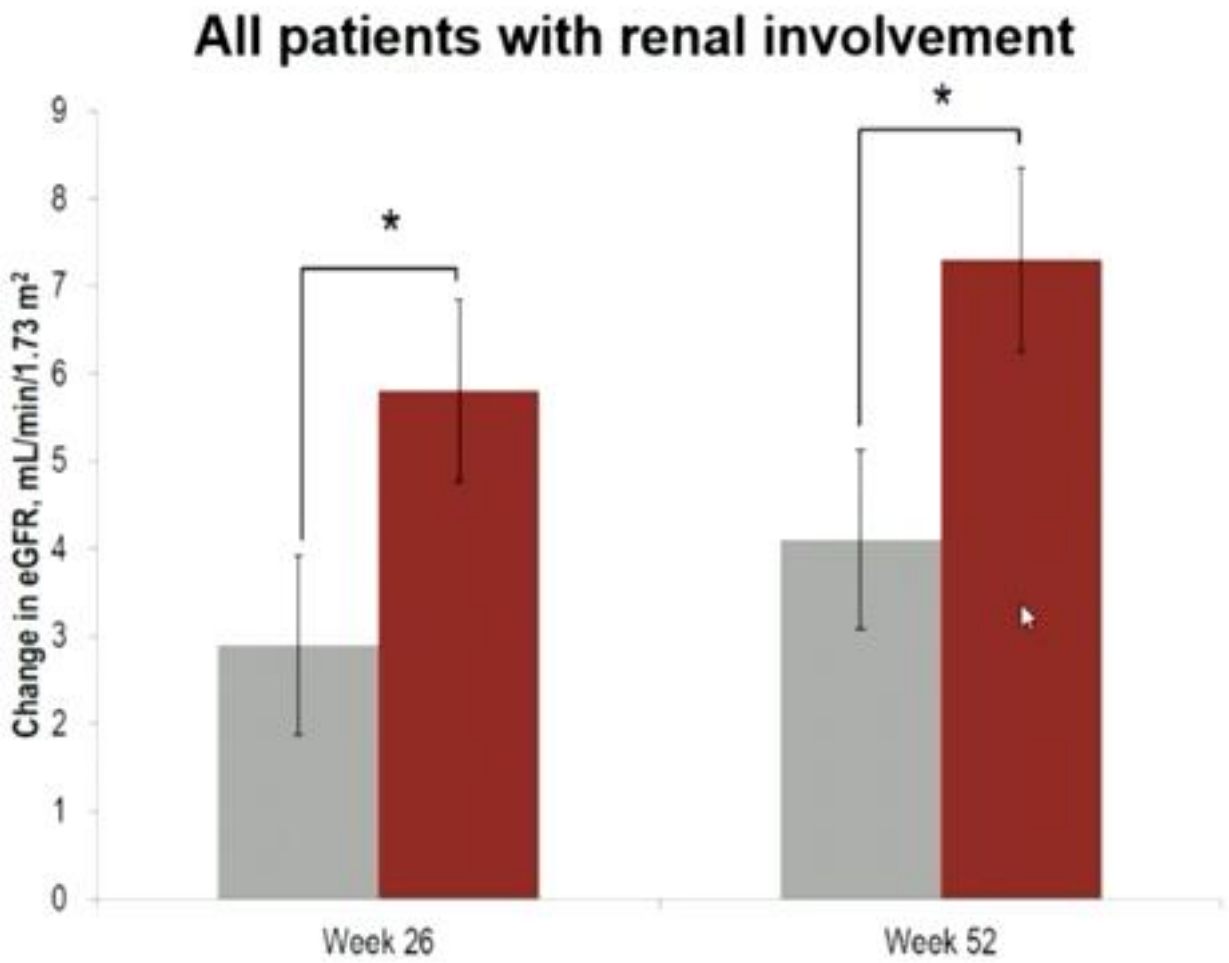


No. at Risk

Avacopan	158	153	149	146	145	133	129	115	92	0
Prednisone	157	151	146	137	133	126	119	111	90	0

Jayne et al.
New Engl J Med 2021

ADVOCATE – eGFR recovery



Jayne et al.
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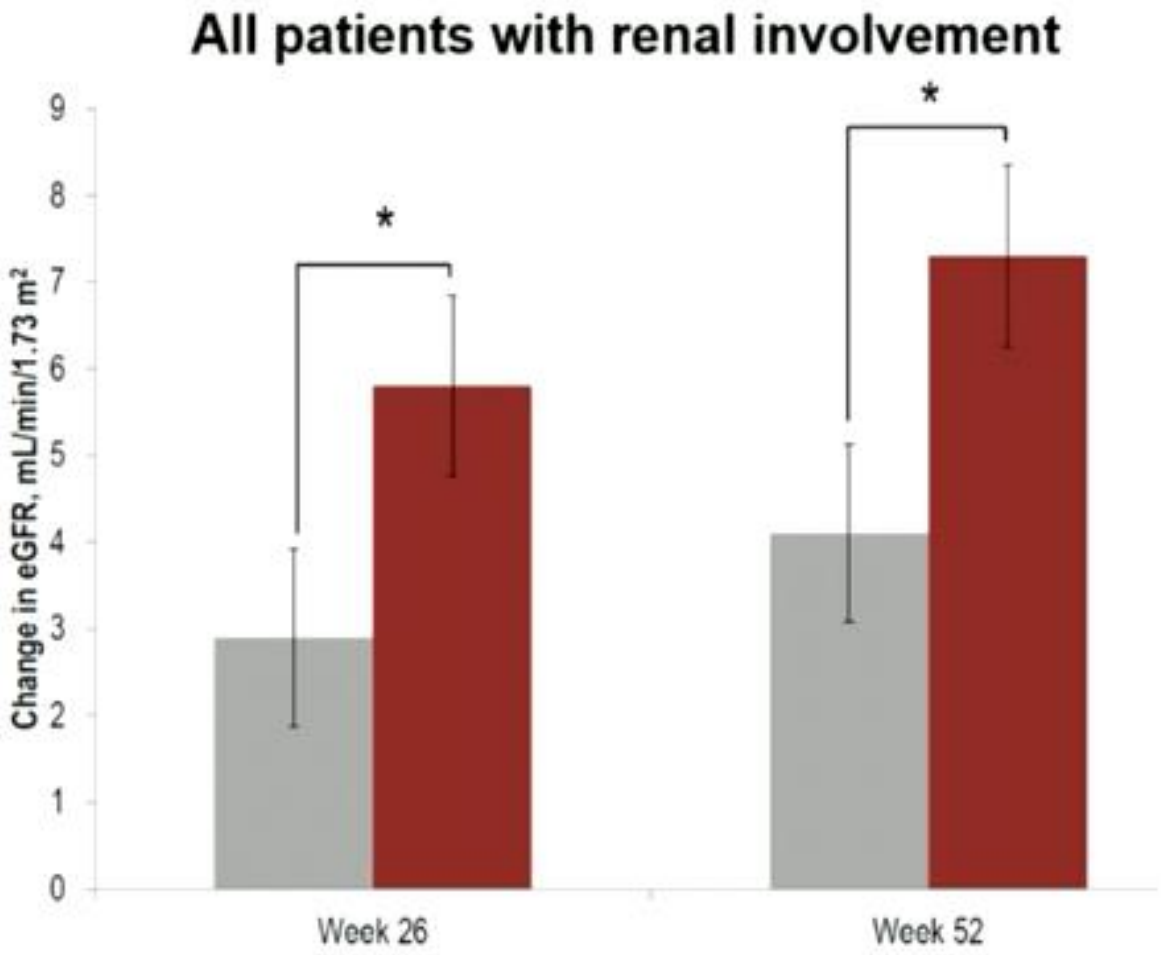

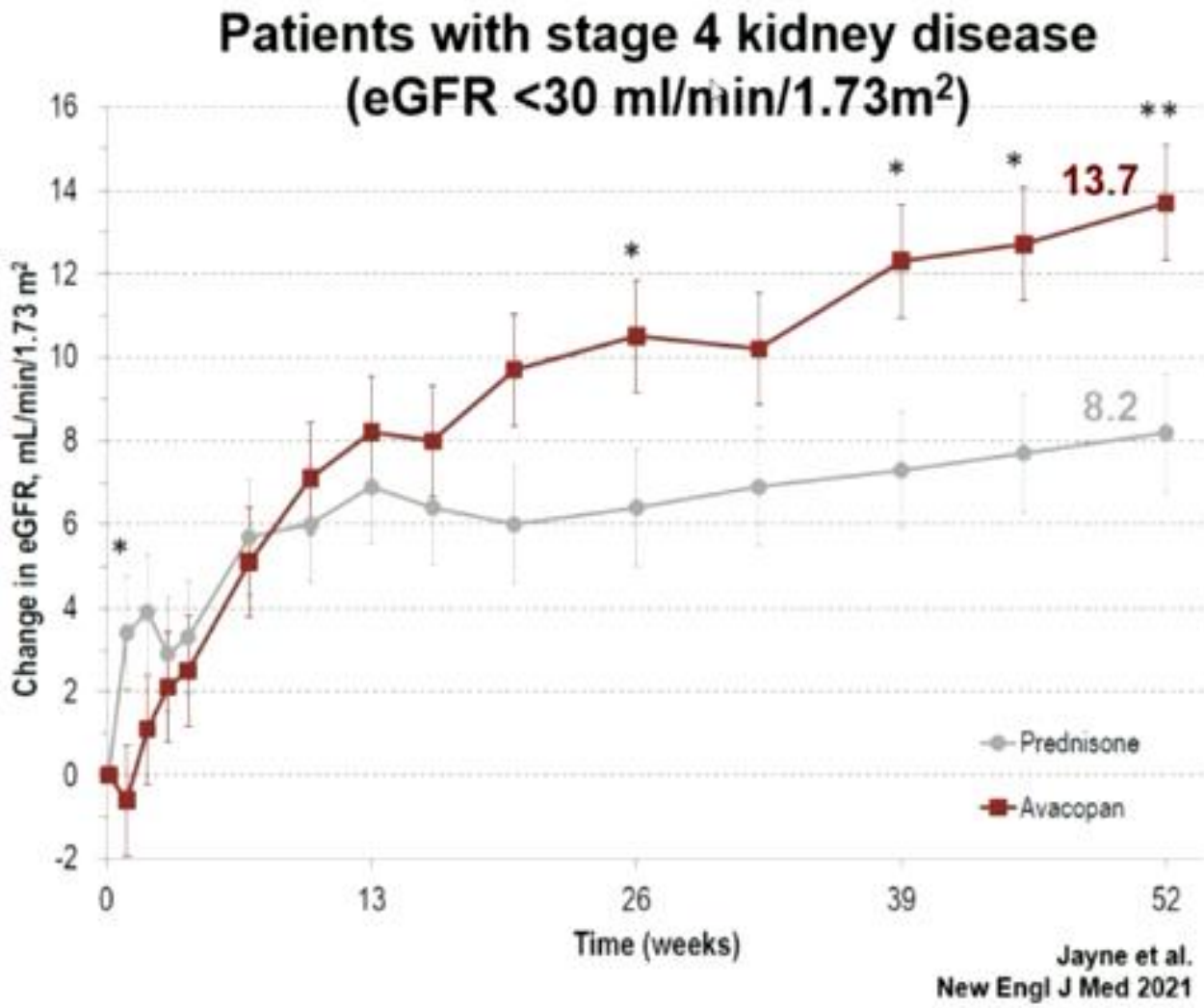

Jayne et al.
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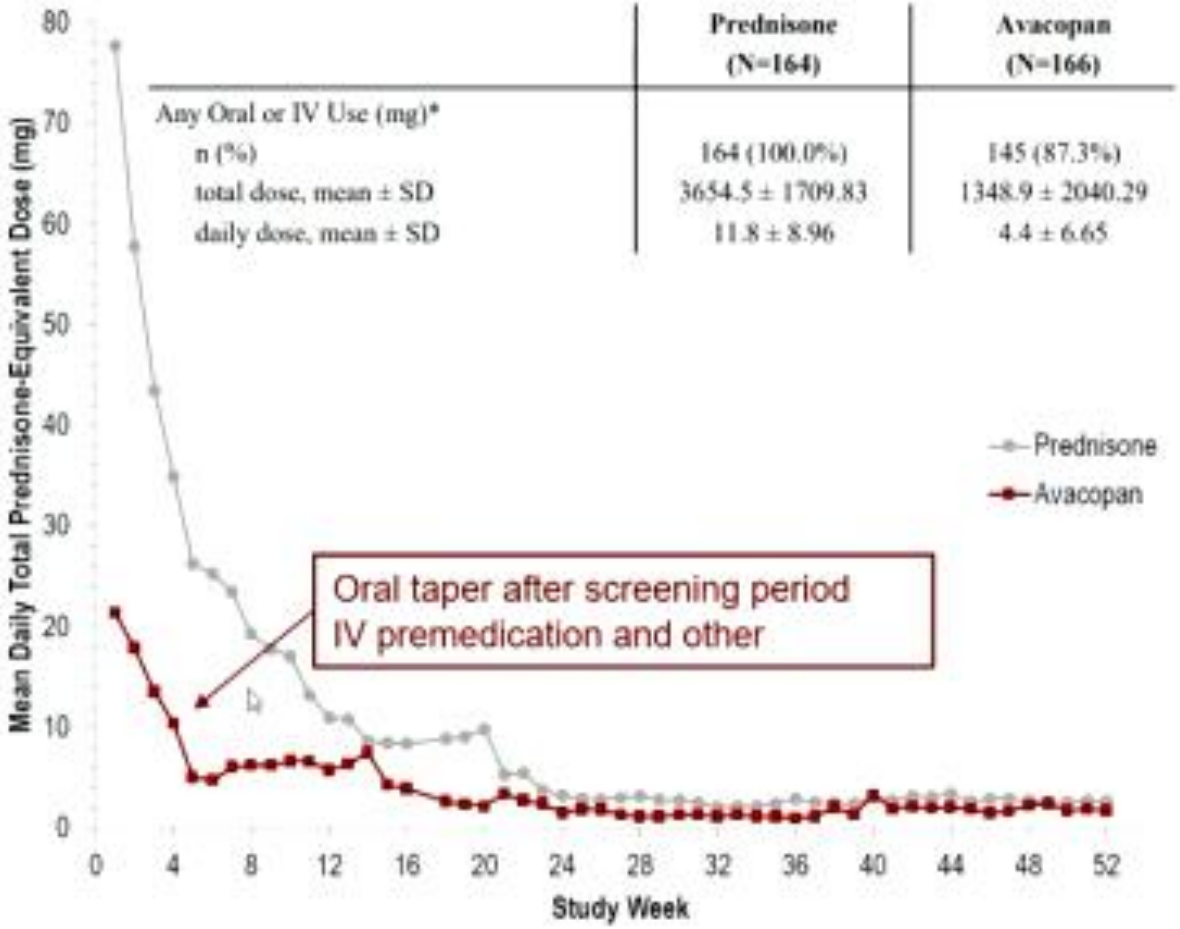
ADVOCATE – Glucocorticoid toxicity

	Prednisone (N=164)	Avacopan (N=166)
Any Oral or IV Use (mg)*		
n (%)	164 (100.0%)	145 (87.3%)
total dose, mean ± SD	3654.5 ± 1709.83	1348.9 ± 2040.29
daily dose, mean ± SD	11.8 ± 8.96	4.4 ± 6.65



Jayne et al.
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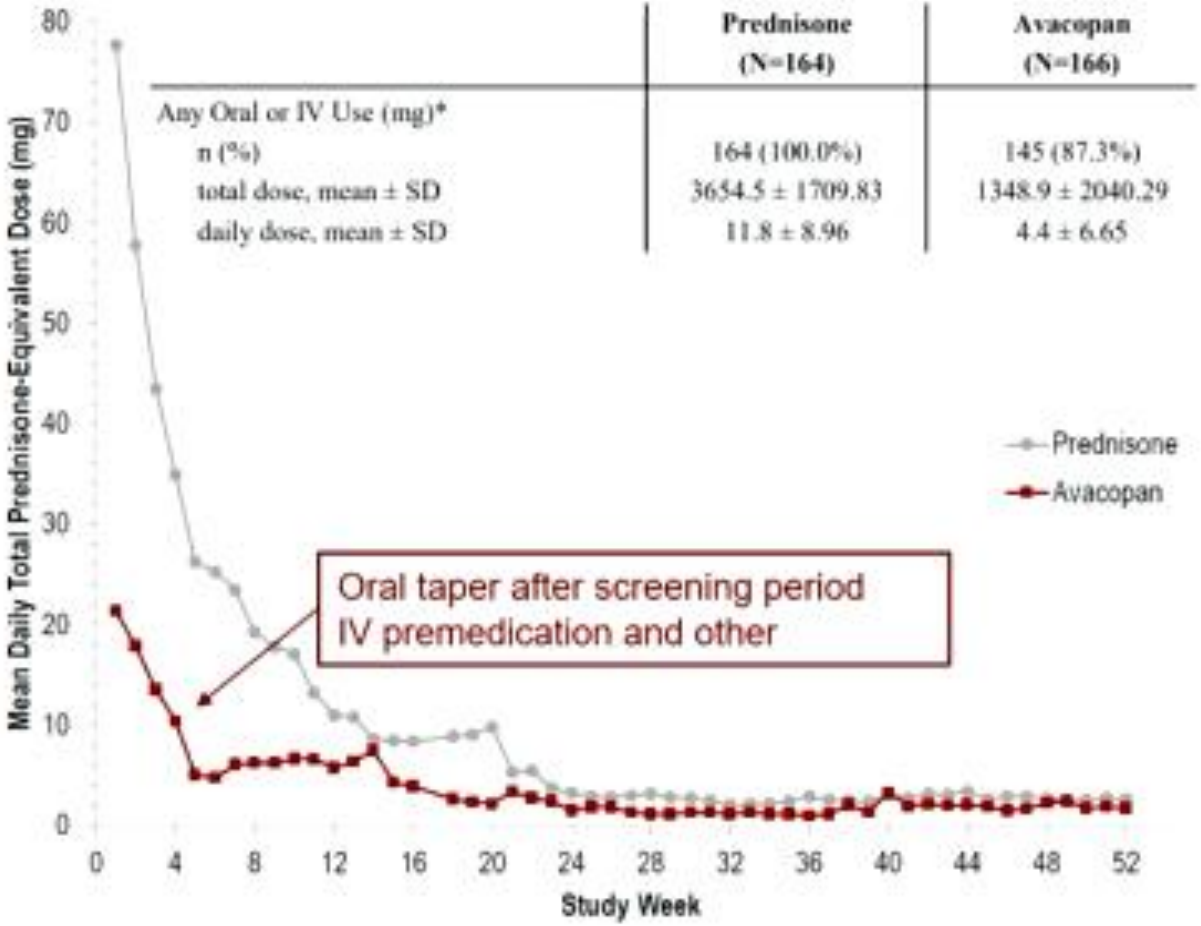
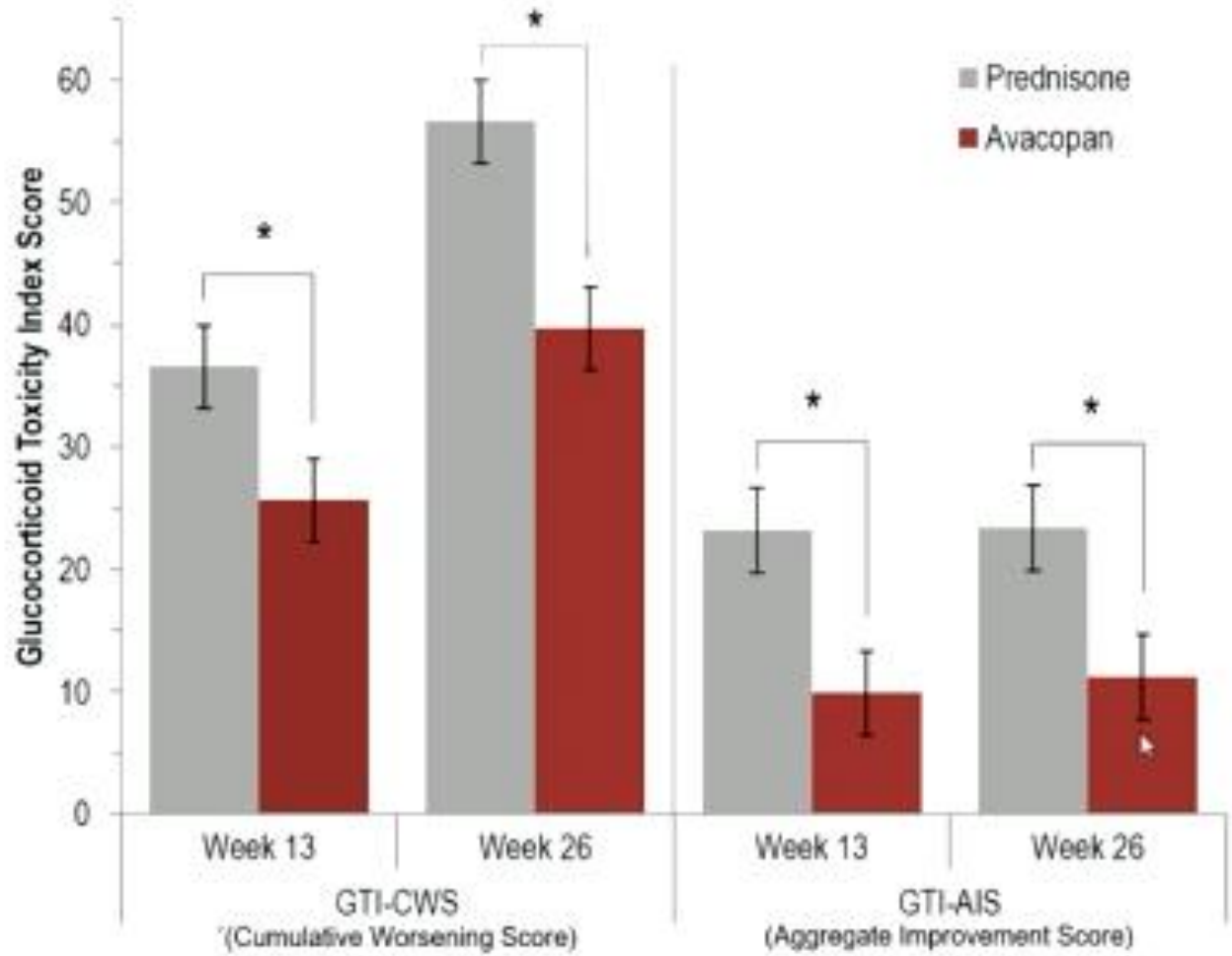




Jayne et al.
New Engl J Med 2021

ADVOCATE – Serious adverse events

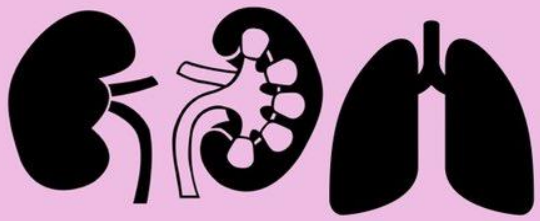
Event	Avacopan (N = 166)	Prednisone (N = 164)
Any serious adverse event‡		
No. of patients (%)	70 (42.2)	74 (45.1)
No. of events	116	166
Any serious event related to vasculitis worsening§		
No. of patients (%)	17 (10.2)	23 (14.0)
No. of events	18	36
Any serious event not related to vasculitis worsening		
No. of patients (%)	62 (37.3)	64 (39.0)
No. of events	98	130
Discontinuation of trial medication due to adverse event — no. (%)	26 (15.7)	29 (17.7)
Any infection		
No. of patients (%)	113 (68.1)	124 (75.6)
No. of events	233	291
Any serious infection¶		
No. of patients (%)	22 (13.3)	25 (15.2)
No. of events	25	31
Any serious opportunistic infection — no. (%)	6 (3.6)	11 (6.7)
Death due to infection — no. (%)	1 (0.6)	2 (1.2)
Life-threatening infection — no. (%)	1 (0.6)	2 (1.2)
Serious adverse event of abnormality on liver-function testing — no. (%)	9 (5.4)	6 (3.7)
Any adverse event potentially related to glucocorticoids — no. (%)**	110 (66.3)	132 (80.5)
Cardiovascular	72 (43.4)	85 (51.8)
Infectious	22 (13.3)	25 (15.2)
Gastrointestinal	3 (1.8)	4 (2.4)
Psychological	27 (16.3)	39 (23.8)
Endocrine or metabolic	23 (13.9)	48 (29.3)
Dermatologic	14 (8.4)	28 (17.1)
Musculoskeletal	19 (11.4)	21 (12.8)
Ophthalmologic	7 (4.2)	12 (7.3)

Jayne et al.
New Engl J Med 2021

Avacopan for the Treatment of ANCA-Associated Vasculitis: ADVOCATE trial

STUDY POPULATION

>12 yrs,
Newly diagnosed/relapsing GPA/MPA,
MPO/PR3 +ve, eGFR>15,



Induction Regimen
Rituximab/IV or oral
Cyclophosphamide f/b
Azathioprine maintenance

RANDOMISATION

INTERVENTION

Avocapan 30 mg BD — 166 patients

Prednisone weight based — 165 patients
tapered by wk 20 (no prednisone beyond wk 21)

OUTCOME

	Remission wk 26	Sustained Remission wk 52
Avocapan 30 mg BD	72.3%	65.7%
p(non inferiority) p(superiority)	p(ni):<0.001 p(s):0.24	p(ni):<0.001 p(s):0.007
Prednisone weight based	70.1%	54.9%

Remission was defined as a Birmingham Vasculitis Activity Score (BVAS) of 0 and no receipt of glucocorticoids for vasculitis within 4 weeks

Other inferences

	Mean daily steroid dose wk1-52	Severe Adverse Events
Avocapan 30 mg BD	4mg	25%
Prednisone weight based	12mg	23.5%

- Steroids were tapered too fast in the steroids arm, and Avocapan group was not completely steroid free, though glucocorticoid toxicity index was definitely higher in the steroid group
- Baseline cumulative and daily steroid use during screening period in prednisolone group was higher
- 80% patient had renal involvement, patients with DAH requiring mechanical ventilation >14 days were excluded
- cyclophosphamide was not given according to EUVAS protocol and no repeat doses of Rituximab was given

Jayne et al
DOI: 10.1056/NEJMoa2023386

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2021; 384:599-609

*Visual abstract. For illustration purpose only. We encourage you to read the full article

@EnvisionRheumat

GPA & MPA – Maintenance of remission

EULAR Recommendations – 2022 update	Following induction of remission with RTX or CYC
Recommended	• RTX
	• Duration of remission maintenance: 24 – 48 months following induction of remission in new-onset disease
Should be considered	• Longer duration in relapsing disease or those with an increased risk of relapse
May be considered	• Alternatives to RTX: AZA or MTX

Hellmich et al.
EULAR recommendations
AAV management – 2022 update
EULAR Congress
June 01st, 2022

EGPA – Induction of remission

EULAR Recommendations – 2022 update	New-onset or relapsing organ- or life-threatening disease	New-onset or relapsing non-organ- or non-life-threatening disease	Relapsing or refractory non-organ- or non-life-threatening disease
Recommended	• Combination of high-dose GC with CYC	• GC	• MEPO
May be considered	• Alternative to CYC: Combination of high-dose GC with RTX		

Hellmich et al.
EULAR recommendations
AAV management – 2022 update
EULAR Congress
June 01st, 2022

Mepolizumab Treatment In Relapsing or Refractory EGPA (MIRRA study)

- patients EGPA avec un antécédent de rechute ou une maladie réfractaire ET recevant une dose de Corticoïdes ≥ 7.5mg/j

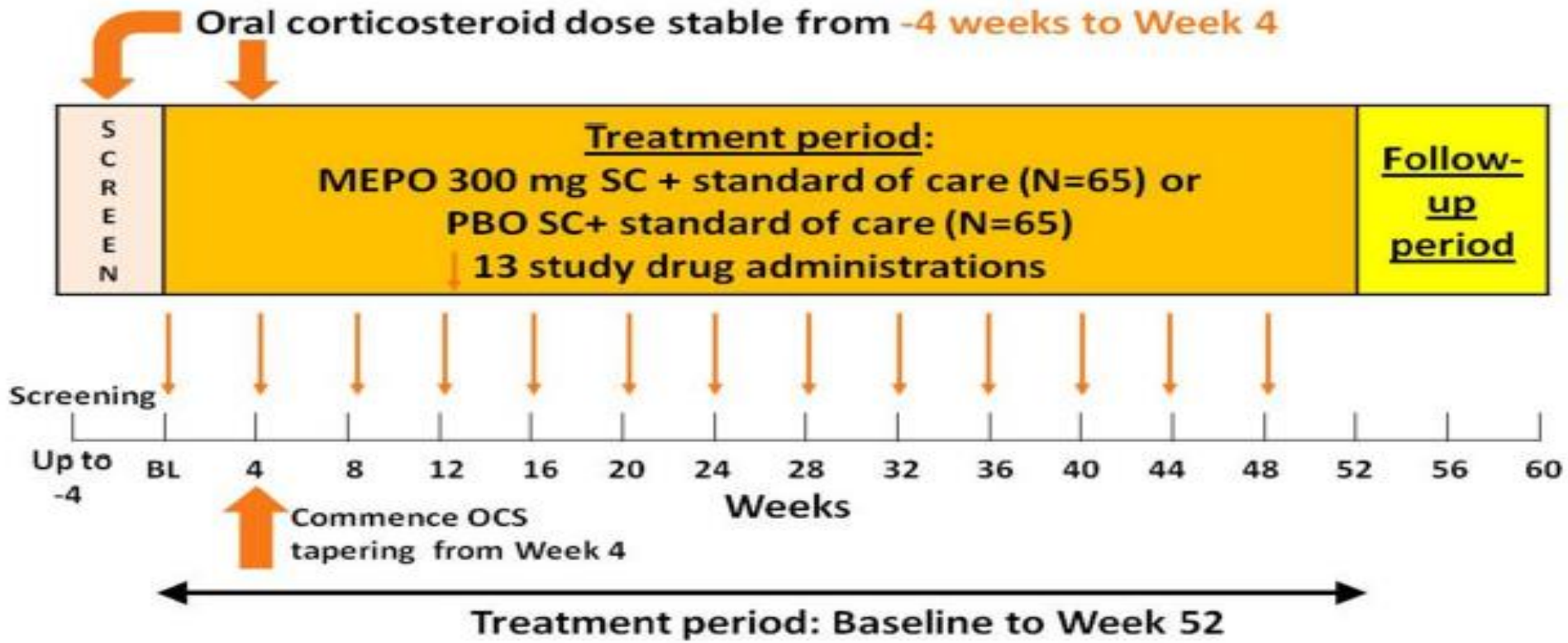
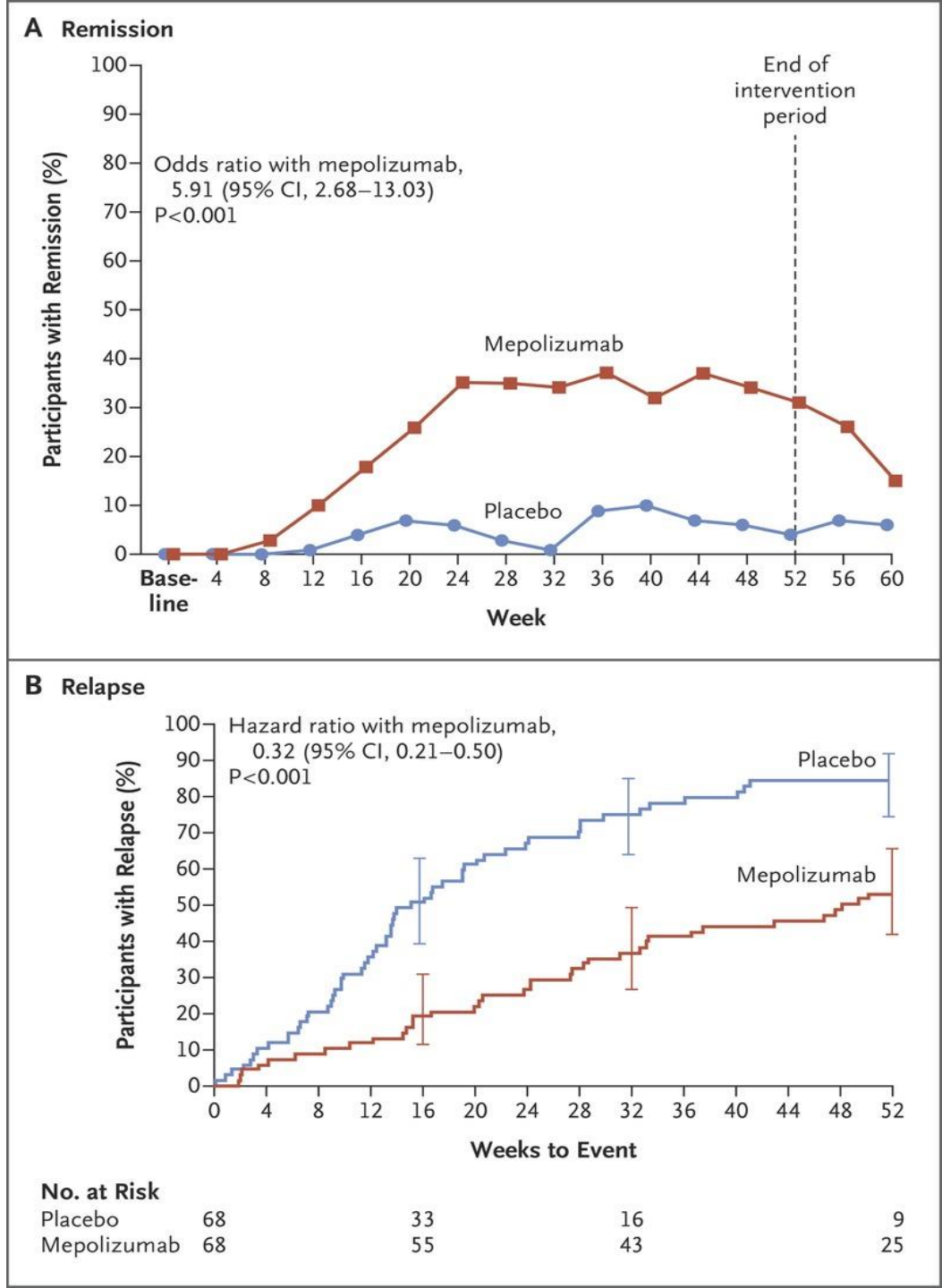


Table 2. Efficacy End Points in the Intention-to-Treat Population.*

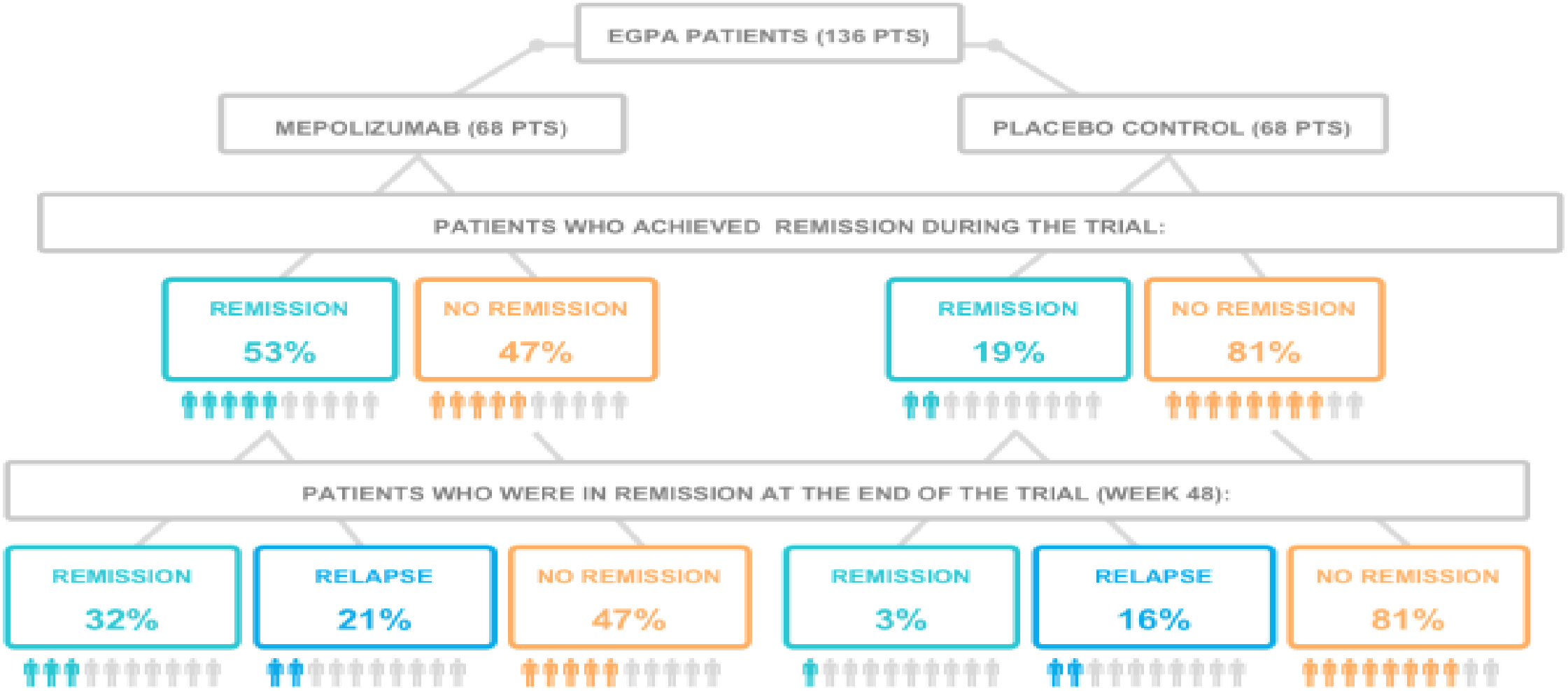
End Point	Mepolizumab (N=68)	Placebo (N=68)	Odds Ratio or Hazard Ratio (95% CI)	P Value
	no. of participants (%)			
Primary end points				
Accrued weeks of remission over 52-wk period			5.91 (2.68–13.03)	<0.001
0 wk	32 (47)	55 (81)		
>0 to <12 wk	8 (12)	8 (12)		
12 to <24 wk	9 (13)	3 (4)		
24 to <36 wk	10 (15)	0		
≥36 wk	9 (13)	2 (3)		
Remission at wk 36 and wk 48	22 (32)	2 (3)	16.74 (3.61–77.56)	<0.001
Other end points				
Remission within the first 24 wk that was sustained until wk 52	13 (19)	1 (1)	19.65 (2.30–167.93)	0.007
First EGPA relapse	38 (56)	56 (82)	0.32 (0.21–0.50)	<0.001

* Odds ratios are shown for the analyses of the two primary end points and for the secondary analysis of remission within the first 24 weeks that was sustained until week 52. For the analysis of accrued weeks in remission, the odds ratio is for 24 or more weeks of accrued remission. Remission was defined as a BVAS of 0 (on a scale from 0 to 63, with higher scores indicating greater disease activity) and a prednisolone or prednisone dose of 4.0 mg or less per day. For the time-to-event analysis of the first relapse of EPGA, the hazard ratio is shown. Participants with a first EGPA relapse were those who had a relapse before the completion of the planned trial period or who withdrew prematurely from the trial.



The MIRRA Trial: Mepolizumab vs. placebo for EGPA

Wechsler et al, N. Engl. J. Med., 2017



EGPA – Maintenance of remission

EULAR Recommendations – 2022 update	Following induction of remission for organ- or life-threatening disease	Following induction of remission for relapsing non-organ- or non-life-threatening disease
Should be considered	• MTX, AZA, MEPO, or RTX	
Recommended		• MEPO

Hellmich et al.
EULAR recommendations
AAV management – 2022 update
EULAR Congress
June 01st, 2022

Summary – GPA & MPA

- *EULAR recommendations 2022* update: Induction of remission with combination of GC with either RTX or CYC; RTX preferred in relapse
- Different treatment outcomes with respect to ANCA type (*RAVE trial*)
- PLEX may delay ESKD in patients with severe active glomerulonephritis, but also increases risk of infection (*PLEX meta-analysis*)
- Avacopan improves disease control and recovery of renal function and reduces glucocorticoid need and toxicity (*ADVOCATE trial*)