# 4TH GCC ORGAN TRANSPLANTATION & NEPHROLOGY CONGRESS

**22-25 JAN 2025**

**AL HASHEMI BALLROOM,RADISSON BLU - KUWAIT**

**Title** **ANCA Associated Vasculitis:**

**Management of critically sick patients**

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**Speaker** **Muriel Ghosn, MD**

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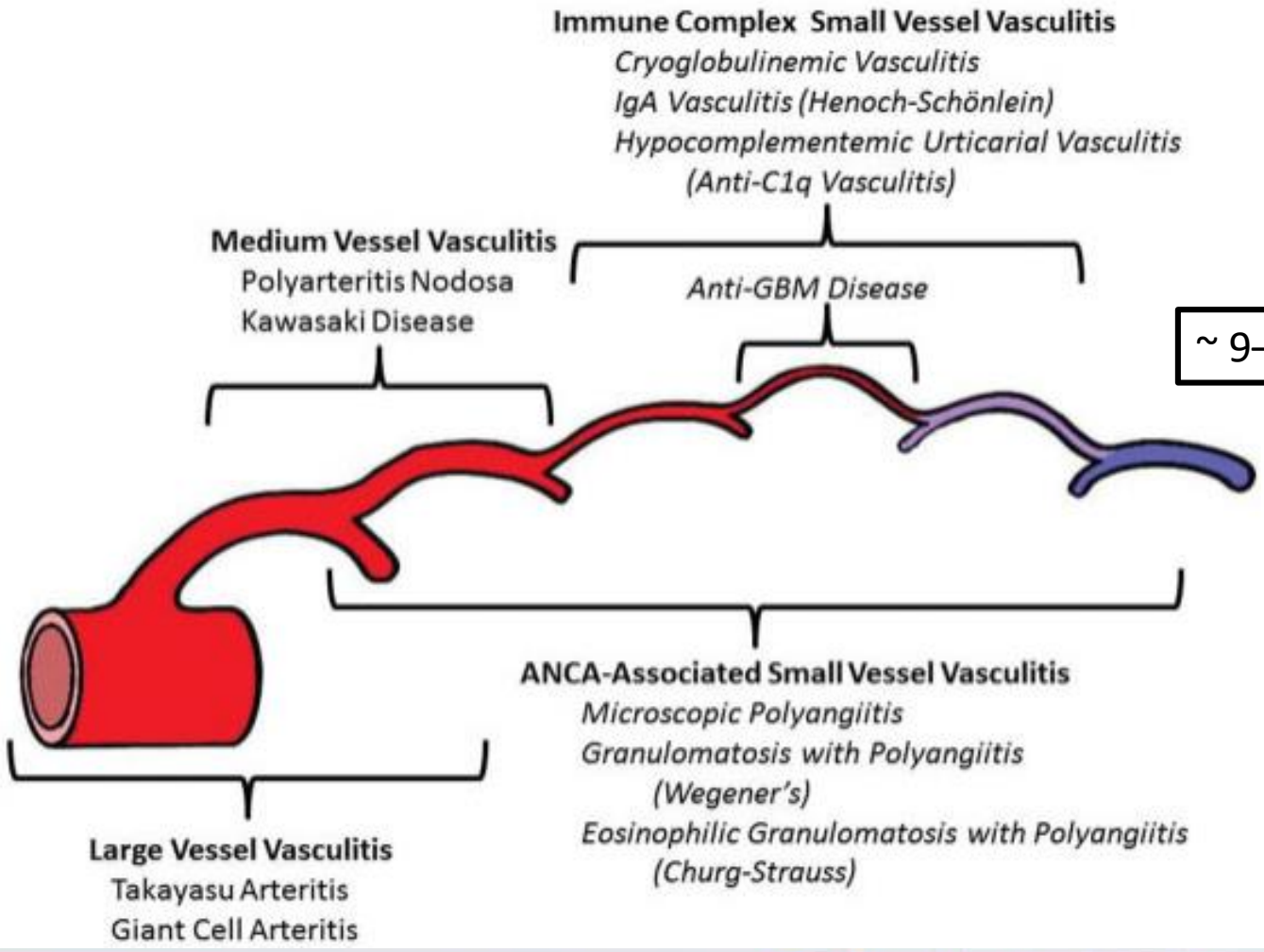
# Disclosures

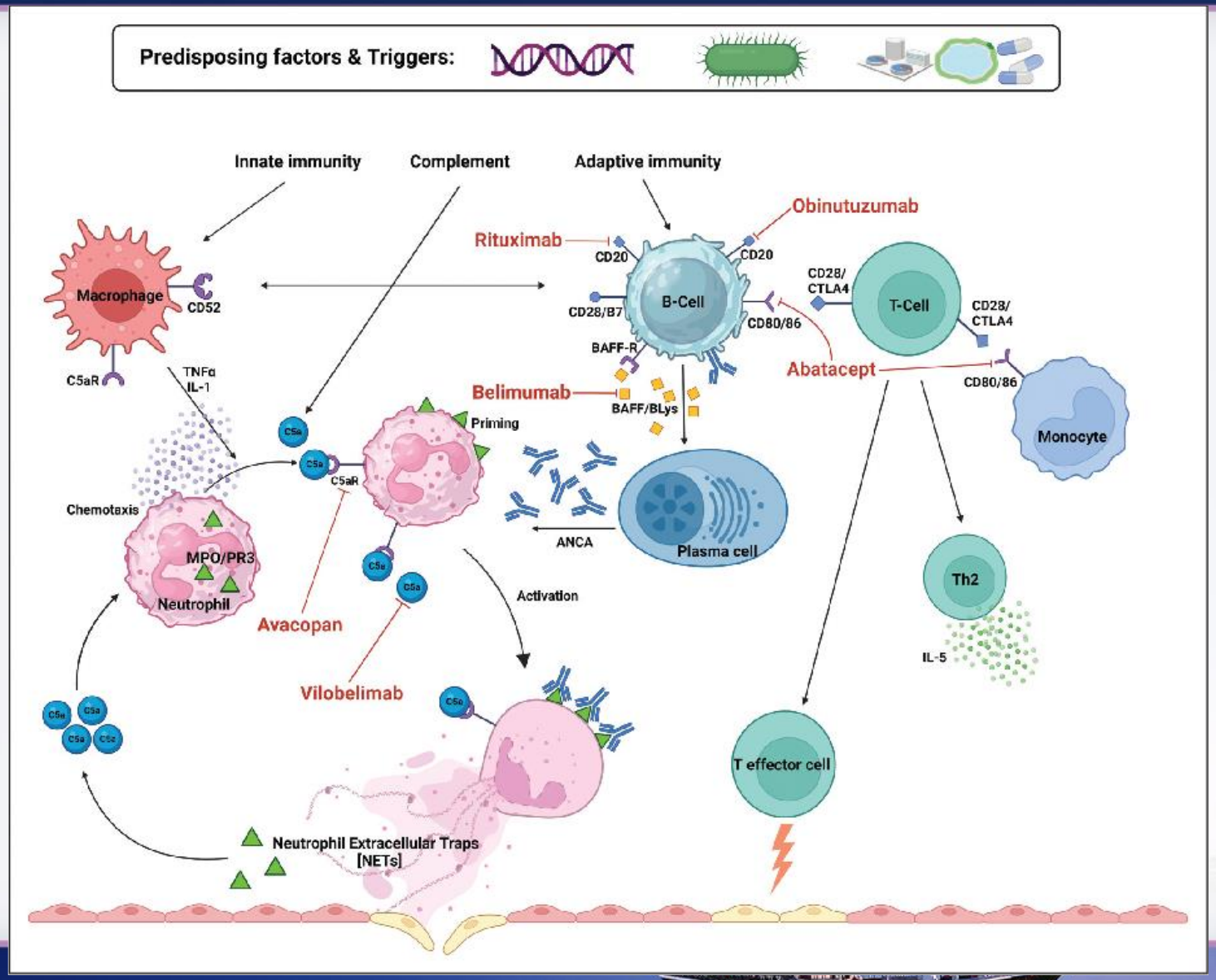
- None

# Outline

- ❑ Introduction
- ❑ Induction of remission
- ❑ Maintenance of remission
- ❑ The role of plasmapheresis
- ❑ Minimizing steroid use




~ 9–16% of AAVs are ANCA negative

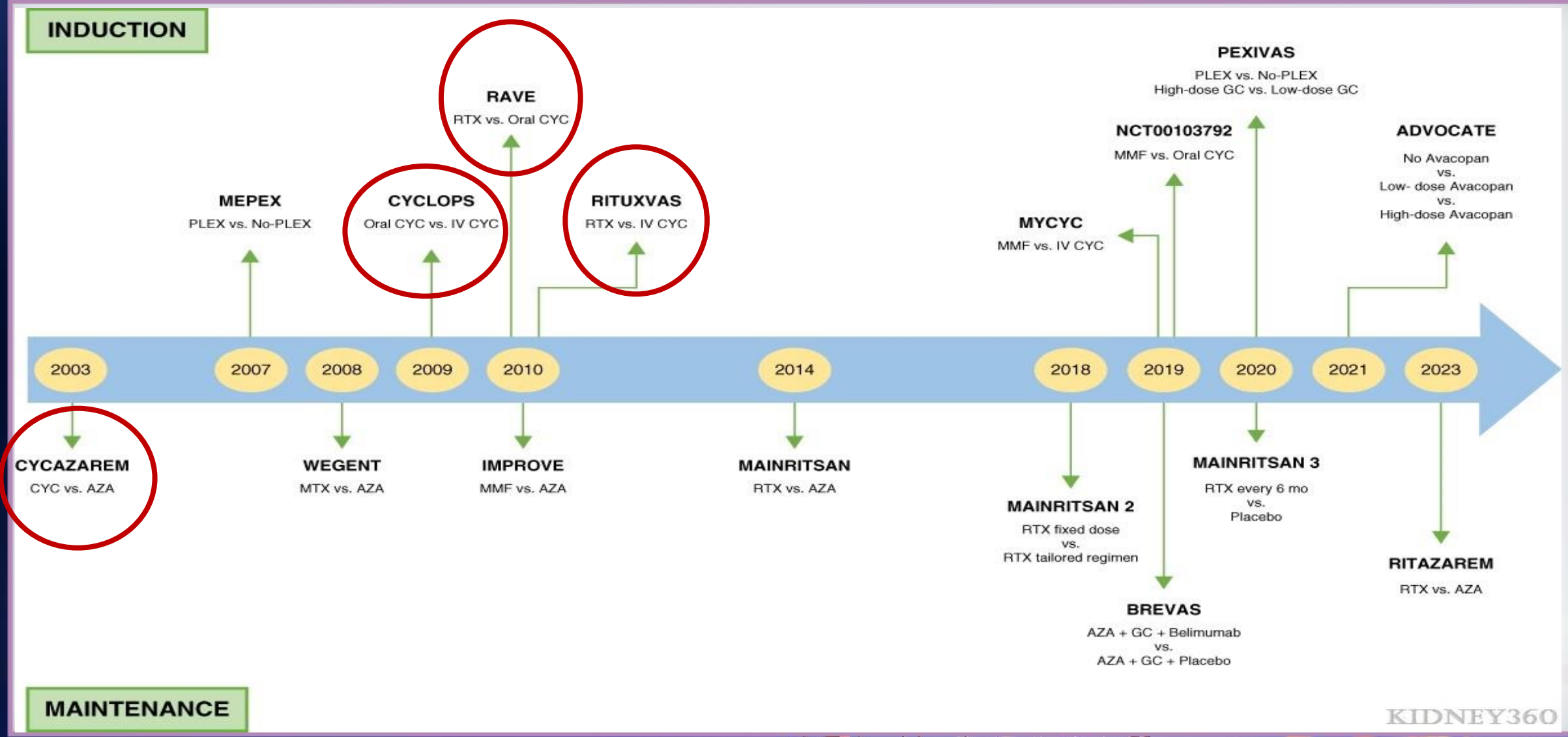

Predisposing factors & Triggers:
Innate immunity
Complement
Adaptive immunity
Macrophage
CD52
C5aR
TNFα
IL-1
Chemotaxis
MPO/PR3
Neutrophil
C5a
C5aR
Priming
Avacopan
Vilobelimab
Activation
Rituximab
Obinutuzumab
CD20
CD20
B-Cell
CD28/B7
CD80/86
BAFF-R
Belimumab
BAFF/BLys
ANCA
Plasma cell
CD28/
CTLA4
T-Cell
CD28/
CTLA4
Abatacept
CD80/86
Monocyte
Th2
IL-5
T effector cell
Neutrophil Extracellular Traps
[NETs]

# Introduction

- Kidney involvement occurs in 18% of AAV patients at initial presentation but in up to 77–85% within 2 years of diagnosis
- Up to 20%–25% of patients progress to kidney failure within a few years after diagnosis. Initial presentation and severity of kidney dysfunction are important predictors of mortality
- Before treatment with immunosuppressive regimens, mortality of patients with severe AAV approached 80% within 1 year of diagnosis.
- Currently, the estimated 5-year survival is 74%–91% for GPA and 45%–76% for MPA.

*Rizk DV et al. Evolution of Therapy for ANCA-Associated Vasculitis with Kidney Involvement. KIDNEY360 4: 1794–1805, 2023*
*Rizk DV et al. Antineutrophil cytoplasmic antibody-associated vasculitis . Curr Opin Nephrol Hypertens 2024, 33:503–511*

# Remission Induction


INDUCTION
RAVE
RTX vs. Oral CYC
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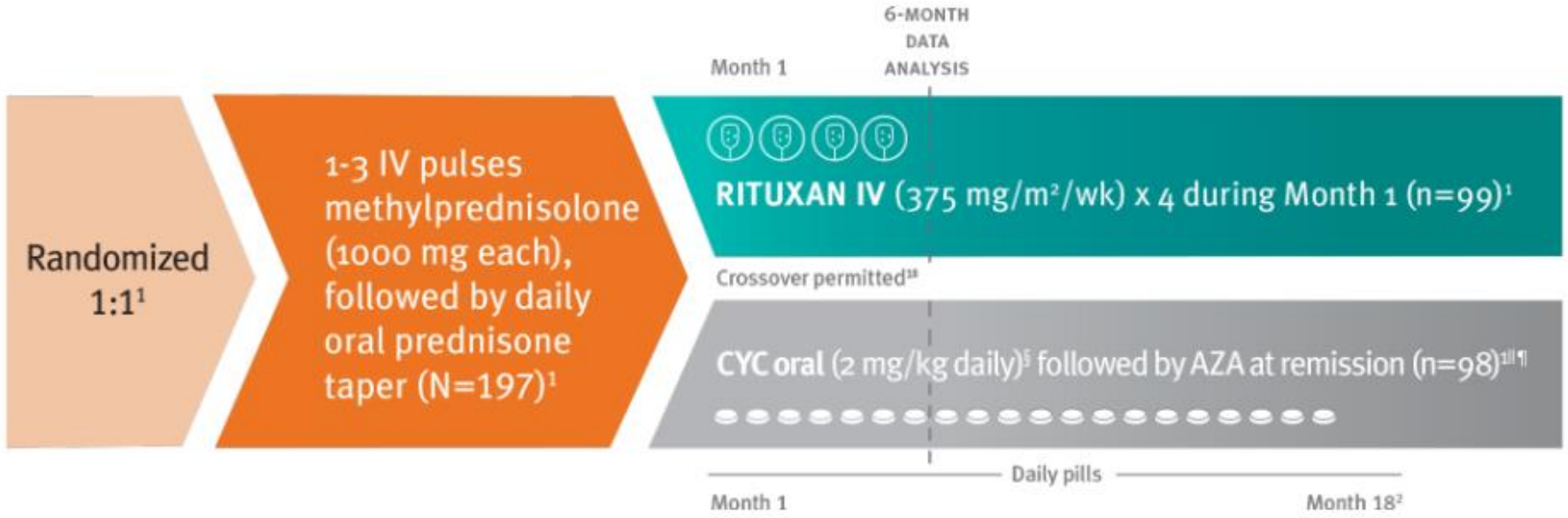
## STUDY DESIGN

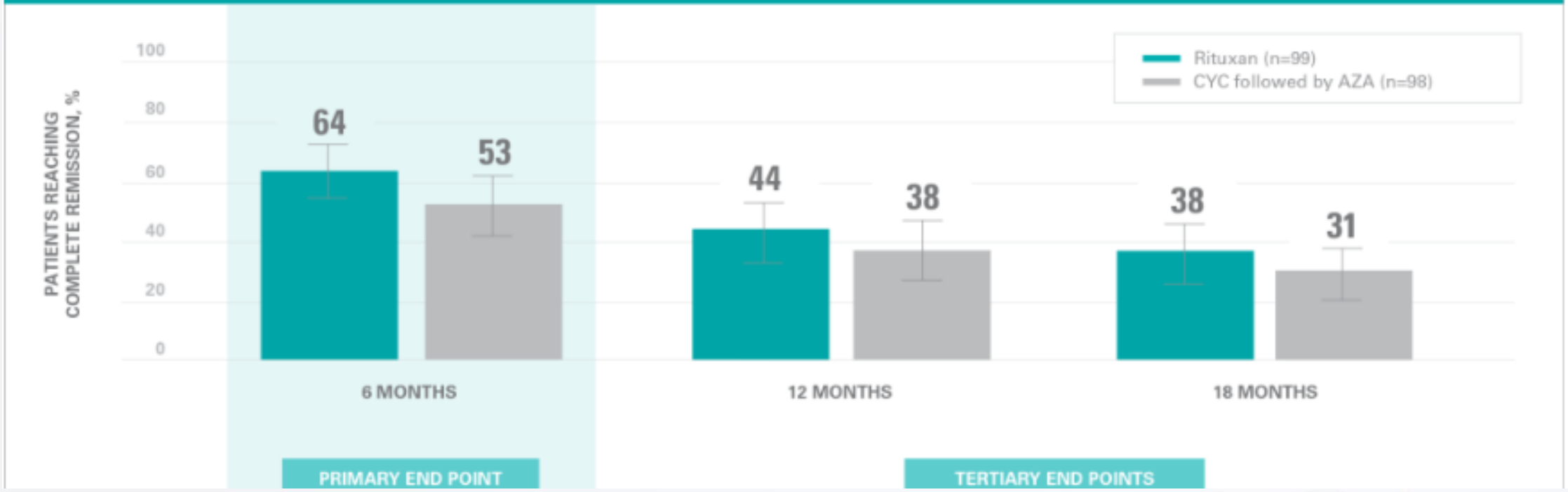



**Primary end point[3]:**
- Complete remission at 6 months

Nancy B. Allen, M.D., Fernando C. Fervenza, M.D., Ph.D., Duvuru Geetha, M.D., Karina A. Keogh, M.D., Eugene Y. Kissin, M.D., Paul A. Monach, M.D., Ph.D., Tobias Peikert, M.D., Coen Stegeman, M.D., Ph.D., Steven R. Ytterberg, M.D., and Ulrich Specks, M.D., for the RAVE–ITN Research Group*

## Complete remission rates at 6, 12, and 18 months[1,2,7]

Complete remission is defined as BVAS/GPA**=0 and prednisone dose of 0 mg




- Rituximab was non inferior to CYC in inducing remission at 6 months
- Rituximab may be superior in patients with relapsing disease
- No difference in overall adverse events but severe leukopenia was more common with CYC
- Patients with severe alveolar hemorrhage and those with Scr > 4 mg/dl were excluded
- This regimen allowed rapid steroid taper

# Treatment response among patients with PR3-AAV who received RTX vs. patients with PR3-AAV who received CYC/AZA

| | OR[1] | 95% CI | P-value |
|---|---|---|---|
| All patients with PR3-AAV (n = 131) [2] | | | |
| CR at 6 months | 2.11 | 1.04 – 4.30 | 0.04 |
| CR at 12 months | 1.96 | 0.95 – 4.05 | 0.07 |
| CR at 18 months | 1.44 | 0.68 – 3.05 | 0.34 |
| Patients with PR3-AAV with relapsing disease at baseline (n = 81)[3] | | | |
| CR at 6 months | 3.57 | 1.43 – 8.93 | <0.01 |
| CR at 12 months | 4.32 | 1.53 – 12.15 | <0.01 |
| CR at 18 months | 3.06 | 1.05 – 8.97 | 0.04 |

The NEW ENGLAND JOURNAL of MEDICINE

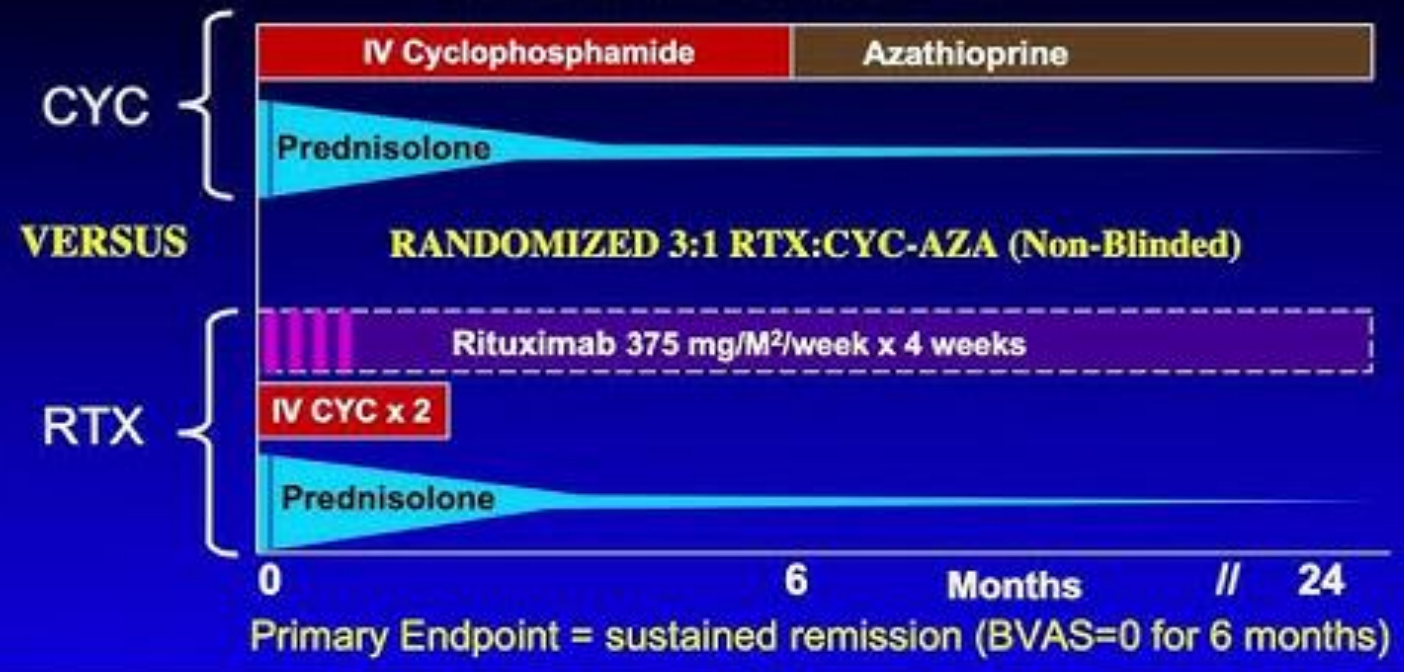
ESTABLISHED IN 1812 JULY 15, 2010 VOL. 363 NO. 3

# Rituximab versus Cyclophosphamide in ANCA-Associated Renal Vasculitis

Rachel B. Jones, M.R.C.P., M.D., Jan Willem Cohen Tervaert, M.D., Ph.D., Thomas Hauser, M.D., Raashid Luqmani, D.M., F.R.C.P., F.R.C.P.(E.), Matthew D. Morgan, M.R.C.P., Ph.D., Chen Au Peh, F.R.A.C.P., Ph.D., Caroline O. Savage, Ph.D., F.R.C.P., F.Med.Sci., Mårten Segelmark, M.D., Ph.D., Vladimir Tesar, M.D., Ph.D., Pieter van Paassen, M.D., Ph.D., Dorothy Walsh, B.S.C.N., Michael Walsh, M.D., F.R.C.P.(C.), Kerstin Westman, M.D., Ph.D., and David R.W. Jayne, M.D., F.R.C.P., for the European Vasculitis Study Group

# Cyclophosphamide vs Rituximab for Remission Induction (RITUXVAS)

*Jones et al. NEJM 2010; 363:211*



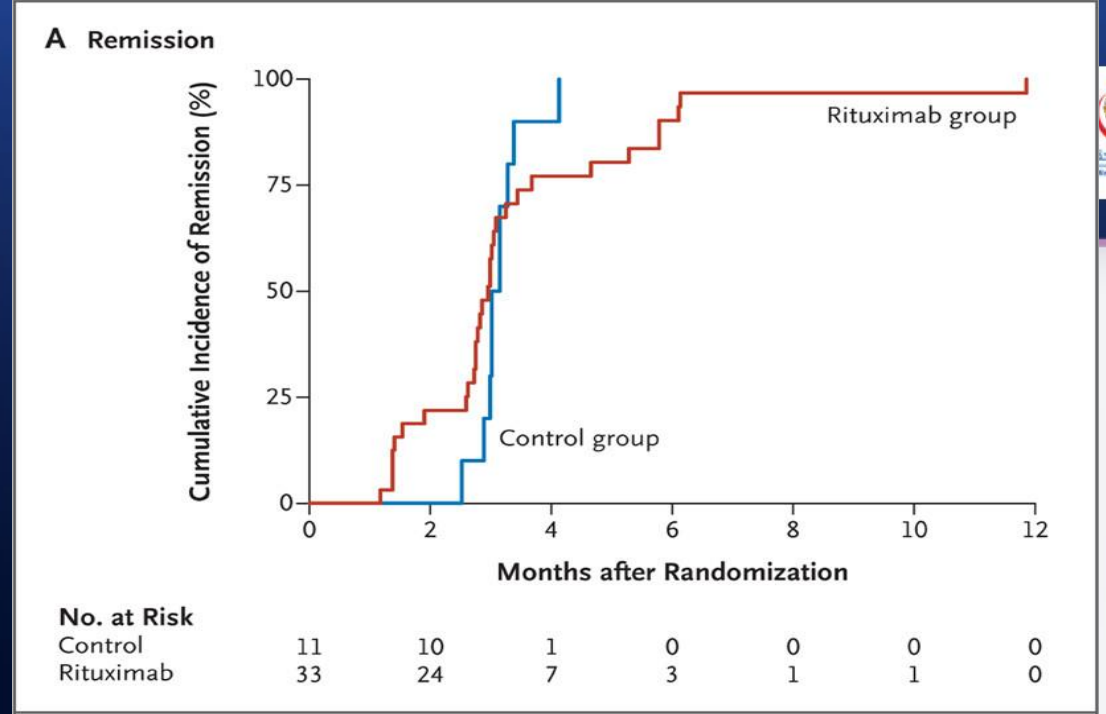

Primary Endpoint = sustained remission (BVAS=0 for 6 months)

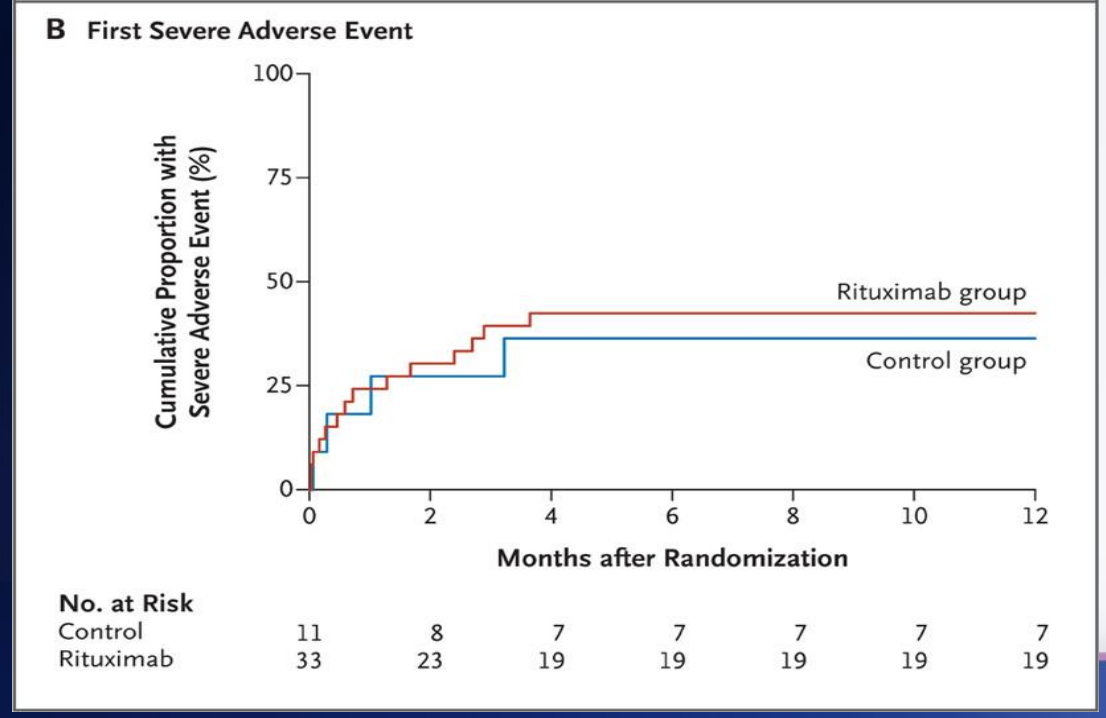
44 ANCA (+) GPA or MPA, new dx

Hypothesis: RTX better than CYC
Primary endpoint: RTX 76%, CYC 82%

Rate of adverse events: RTX = CYC

Mortality rate: 18% (6 RTX, 2 CYC)
- Median age 68, 20% dialysis
- GFR: RTX 20, CYC 12 ml/min




- High remission rate and high rate of adverse events in both groups
- Rituximab non inferior to CYC, allowed reduced exposure to CYC
- Included patients with more severe renal disease

# Remission Induction Summary

| Rituximab preferred | Cyclophosphamide preferred |
|---|---|
| ▪ Children and adolescents<br>▪ Premenoposal women and men concerned about their fertility<br>▪ Frail older adults<br>▪ Glucocorticoid-sparing especially important<br>▪ Relapsing disease<br>▪ PR3-ANCA disease<br>▪ Azathioprine allergy | ▪ Severe GN (SCr >4mg/dl [354 µmol/l]). Combination of 2 intravenous pulses of cyclophosphamide with rituximab can be considered<br>▪ Low baseline IgG < 300mg/dl<br>▪ Rituximab difficult to access |

# Remission Maintenance

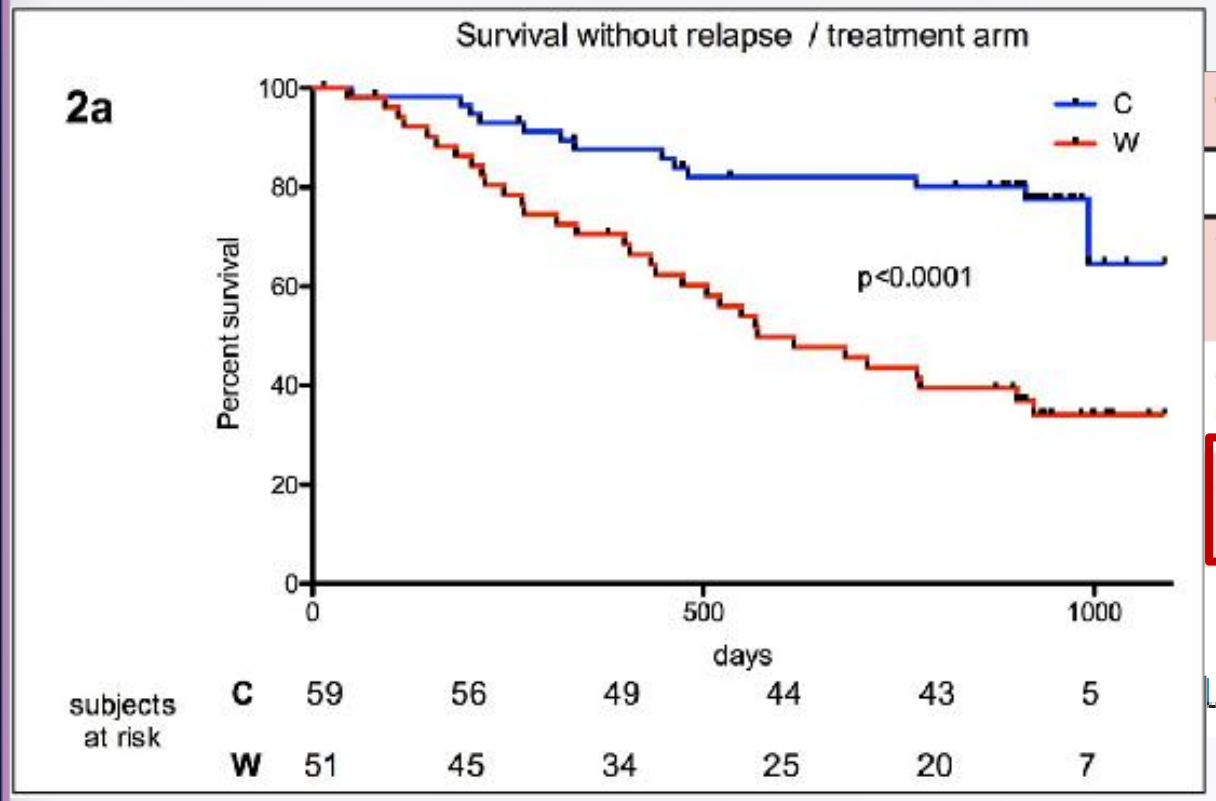
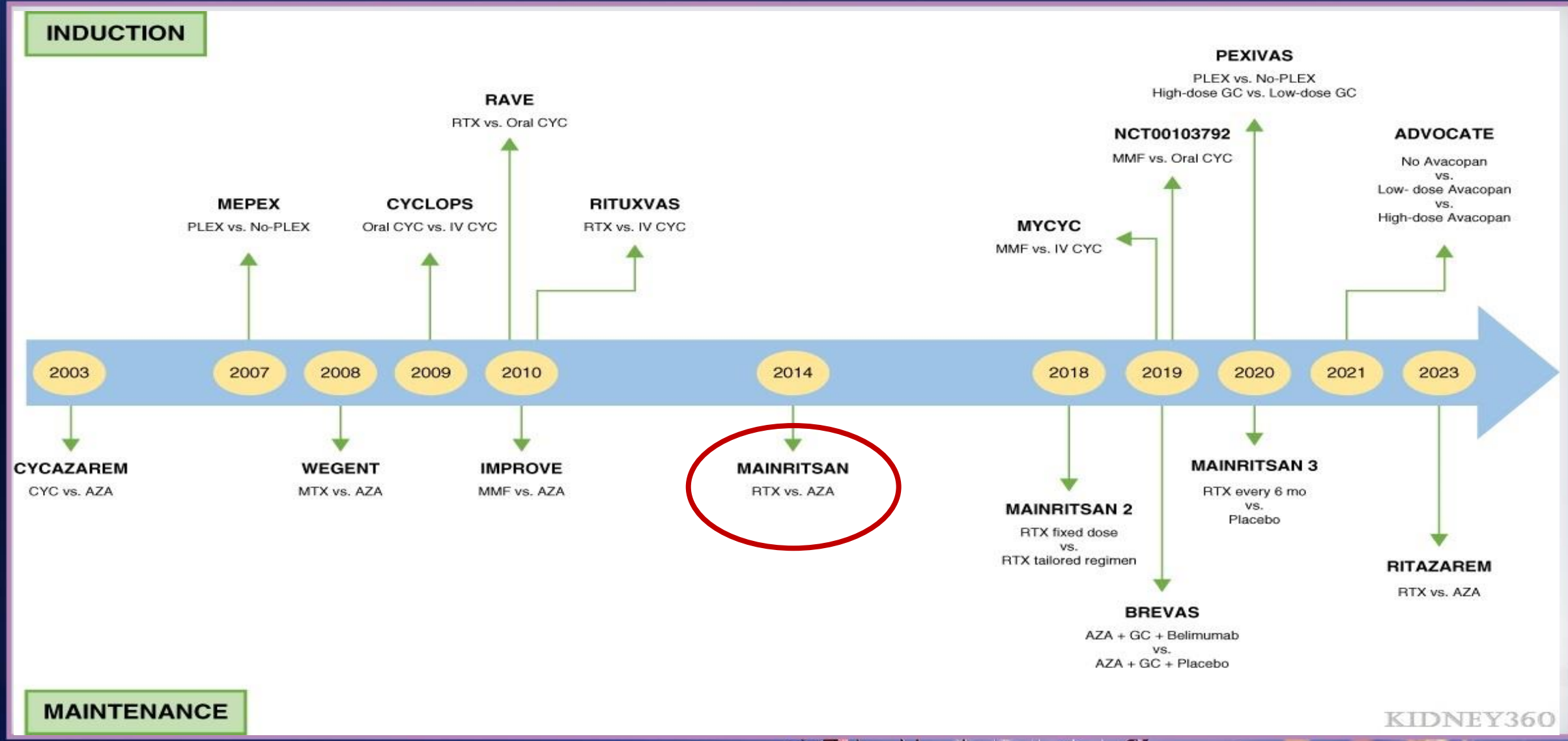



**Table 3** Risk factors associated with AAV relapse

| | Subgroup | Relapse risk | p Value | OR (95% CI) |
|---|---|---|---|---|
| Treatment arm | W | 32/51 (63%) | <0.0001 | 5.96 (2.58 to 13.77) |
| | C | 13/59 (22%) | | |
| ANCA specificity at diagnosis | PR3 | 28/57 (49%) | 0.13 | 1.82 (0.83 to 3.98) |
| | MPO | 17/49 (35%) | | |
| ANCA testing at randomisation | Positive | 30/58 (51%) | 0.017 | 2.57 (1.16 to 5.68) |
| | Negative | 15/51 (29%) | | |
| Disease | MPA | 22/58 (38%) | 0.5 | 0.77 (0.36 to 1.65) |
| | GPA | 23/52 (44%) | | |

uropean Vasculitis Society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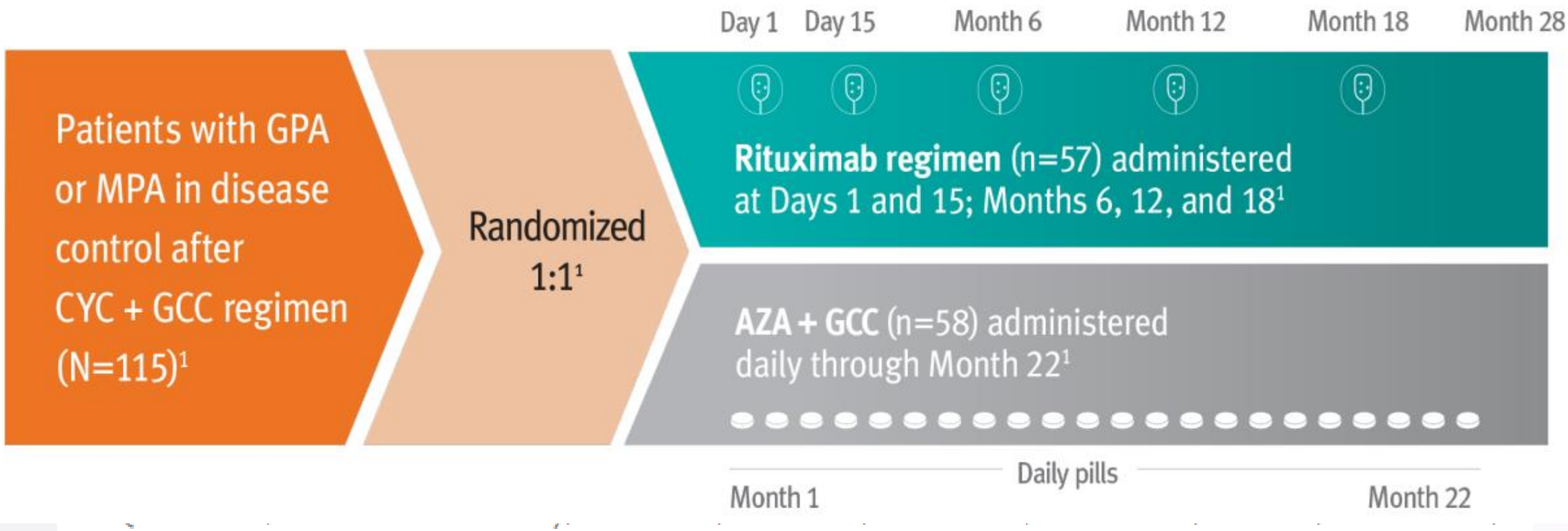
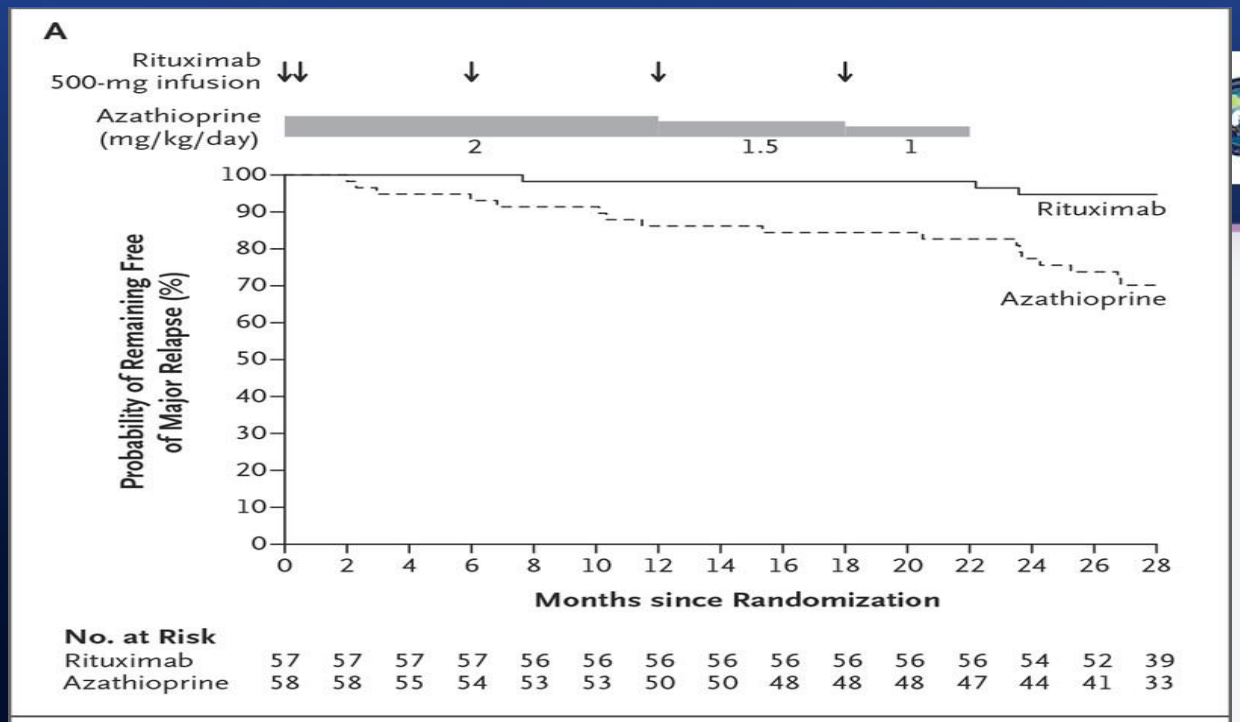
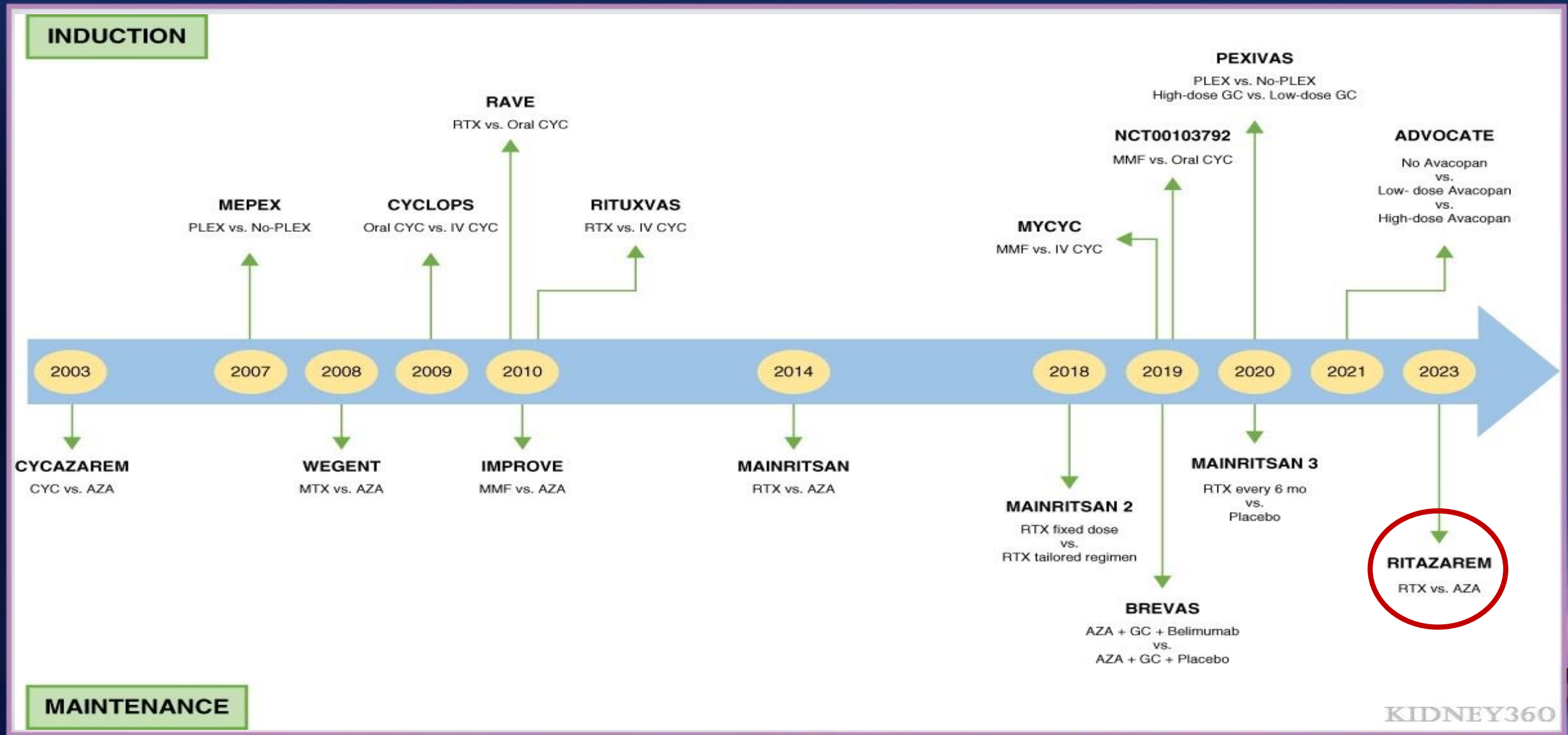



M. Ducret, E. Daugas, T. Papo, B. Bonnotte, A. Mahr, P. Ravaud, and L. Mouthon, for the French Vasculitis Study Group*




Rate of major relapse at 28 months: 29 % in the AZA group vs 5 % in the rituximab group (P=0.002)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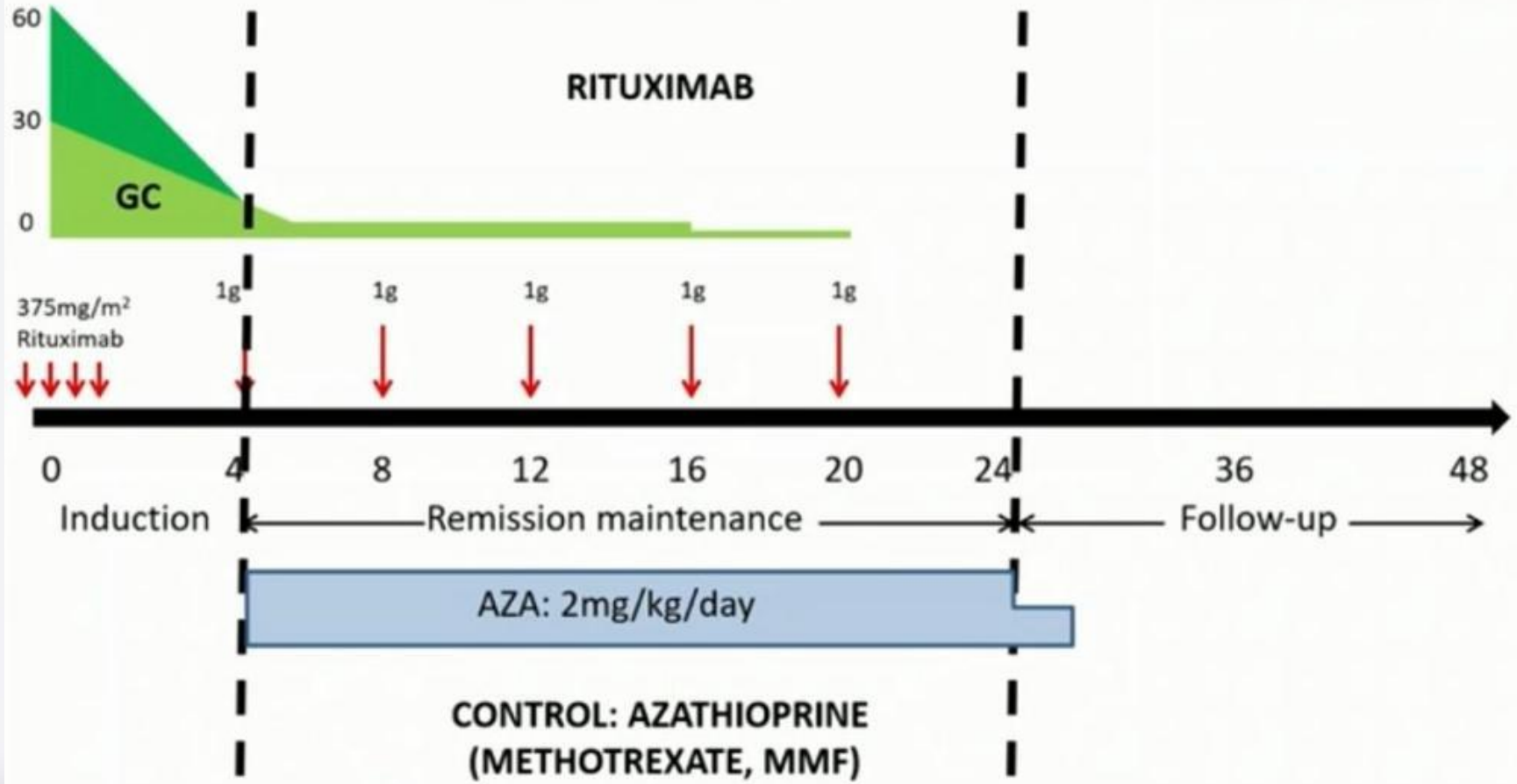
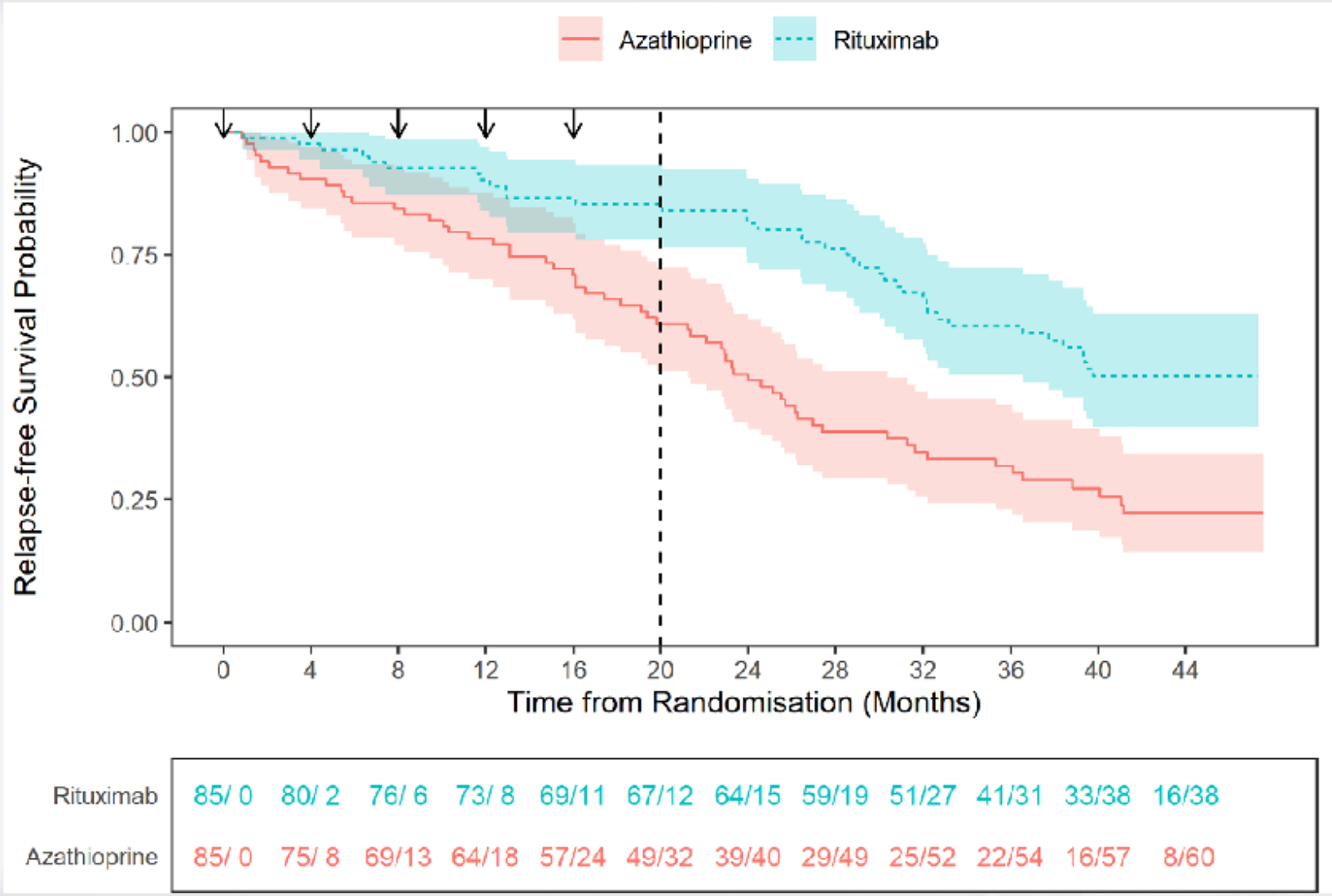
RITAZAREM

# RITAZAREM Trial treatments

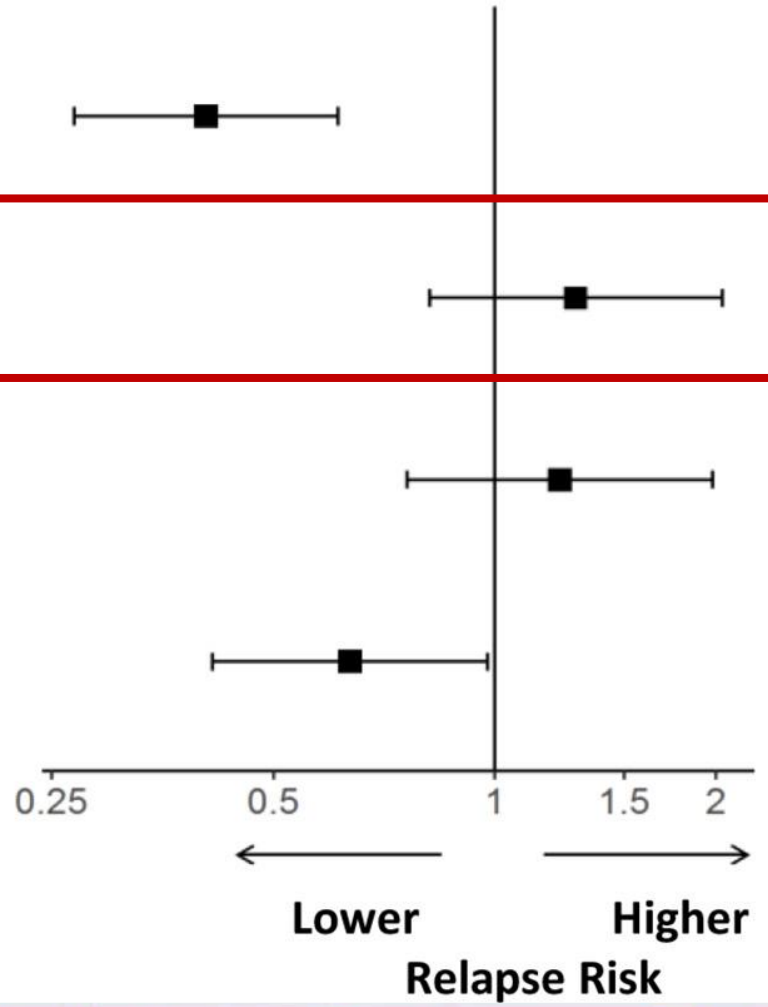





| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Rituximab | 85/ 0 | 80/ 2 | 76/ 6 | 73/ 8 | 69/11 | 67/12 | 64/15 | 59/19 | 51/27 | 41/31 | 33/38 | 16/38 |
| Azathioprine | 85/ 0 | 75/ 8 | 69/13 | 64/18 | 57/24 | 49/32 | 39/40 | 29/49 | 25/52 | 22/54 | 16/57 | 8/60 |

At month 24: relapse rate was 15 % vs 38 %
At month 48: relapse rate was 50 % vs 78 %

| | Contrasts | | | Conditional HR (95% CI) | p-value |
|---|---|---|---|---|---|
| **Treatment Group** | Rituximab (N=85) | vs | Azathioprine (N=85) | 0.41 (0.27 - 0.61) | <0.001 |
| **Induction Regimen** | 1A (N=48) | vs | 1B (N=122) | 1.29 (0.82 - 2.04) | 0.277 |
| **ANCA Type** | anti-PR3 (N=123) | vs | anti-MPO (N=47) | 1.23 (0.76 - 1.98) | 0.402 |
| **Type of Relapse** | Severe (N=106) | vs | Non-Severe (N=64) | 0.64 (0.41 - 0.98) | 0.040 |



## Vasculitis

**Table 2** Adverse events according to treatment regimen in the RITAZAREM trial

| | Total (N=188) | Rituximab (N=85) | Azathioprine (N=85) | Not randomised (N=18) |
|---|---|---|---|---|
| Number (%) of patients with a serious adverse event | 92 (49%) | 37 (44%) | 48 (56%) | 7 (39%) |
| Number (%) of patients with a serious infection | 39 (21%) | 15 (18%) | 19 (22%) | 5 (28%) |
| Number (%) of patients with a non-serious infection | 119 (63%) | 54 (64%) | 62 (73%) | 3 (17%) |
| Number (%) of patients with plasma IgG<5 g/L | 66 (35%) | 36 (42%) | 26 (31%) | 4 (22%) |
| Number (%) of patients with plasma IgG<3 g/L | 17 (9%) | 8 (9%) | 6 (7%) | 3 (17%) |

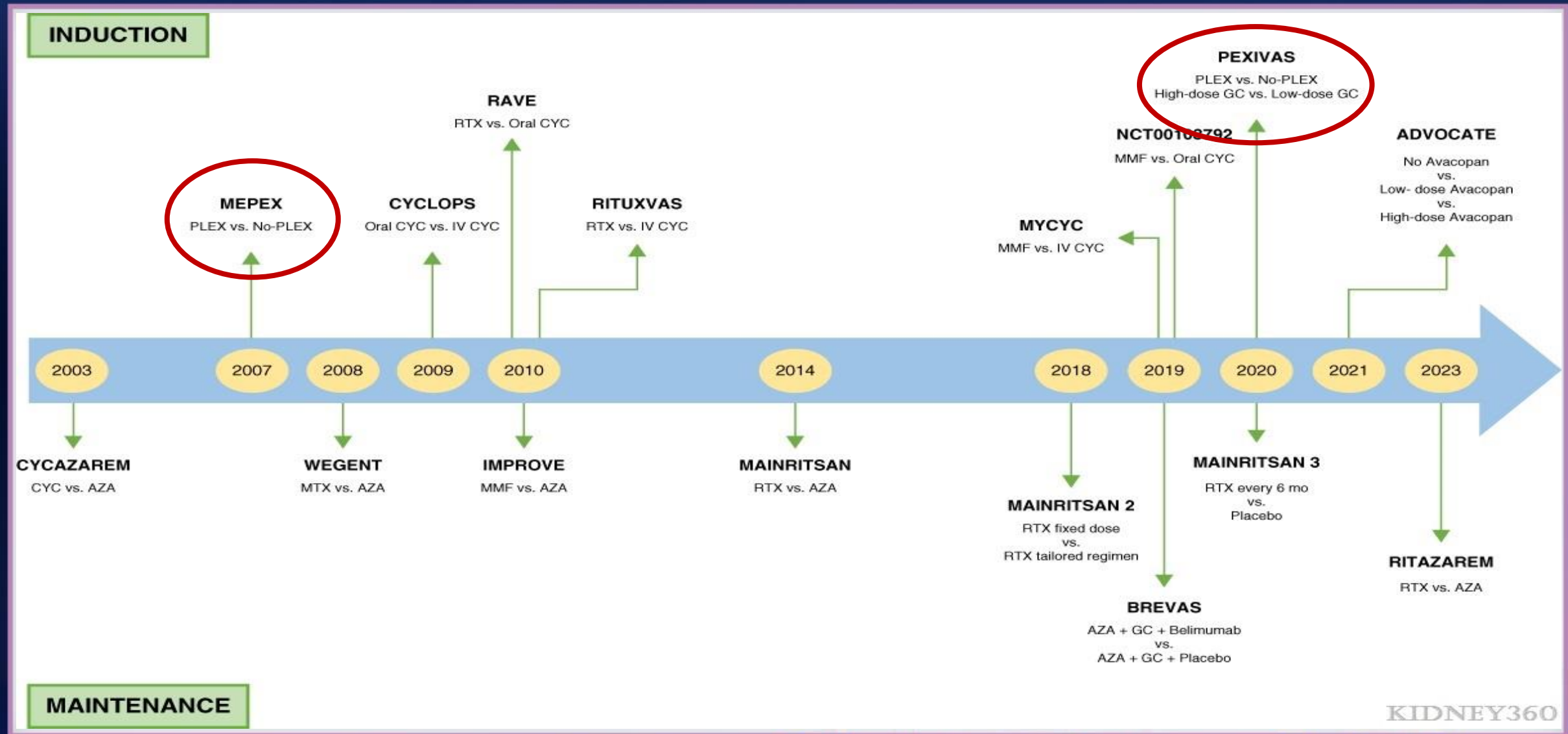
- Despite higher doses rituximab, 15 % relapse rate during the maintenance phase and almost 50 % during the follow up phase
- Hypogammaglobulinemia remains a problem
- Supports reduction in glucocorticoid exposure (70 % used low dose steroids)

# Remission maintenance
## Summary

- **Rituximab superior to AZA**
- **Minimum duration of maintenance: weak evidence**. **The EULAR and KDIGO guidelines advise maintenance therapy for at least 24–48 months following induction.** Relapse risk factors should be taken into consideration.
- ANCA serologies can help but should not replace clinical judgement
- IgG levels should be monitored every 6 months if using rituximab for maintenance
- Glucocorticoids should not be withdrawn early if using AZA (or MMF or MTX) for maintenance

| Baseline factors | Factors after diagnosis |
|---|---|
| • Diagnosis of granulomatosis with polyangiitis<br>• PR3–ANCA subgroup<br>• Higher serum creatinine<br>• More extensive disease<br>• Ear, nose, and throat disease | • History of relapse<br>• ANCA positive at the end of induction<br>• Rise in ANCA |

# The role of Plasmapheresis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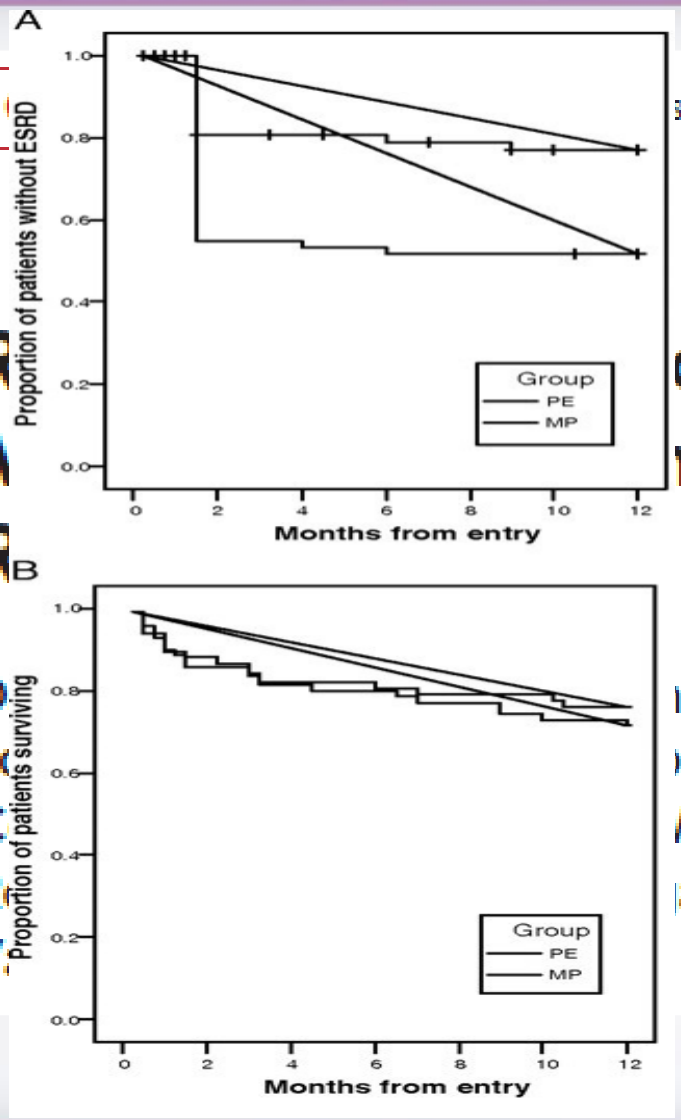


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# R of Plasma Exchange or High-Dosage M e as Adjunctive Therapy for Severe R

Severe or life threatening events occurred in ~ 50 % of the patients with leukopenia and infections being the most common

D , † Niels Rasmussen, ‡ Daniel Abramowicz, § Franco Ferrario, ‖
L eix, ** Caroline O.S. Savage, †† Renato A. Sinico, ‖
C N. Westman, §§ Fokko J. van der Woude, ‖‖
R aarden, ¶¶ and Charles D. Pusey; on behalf of the European
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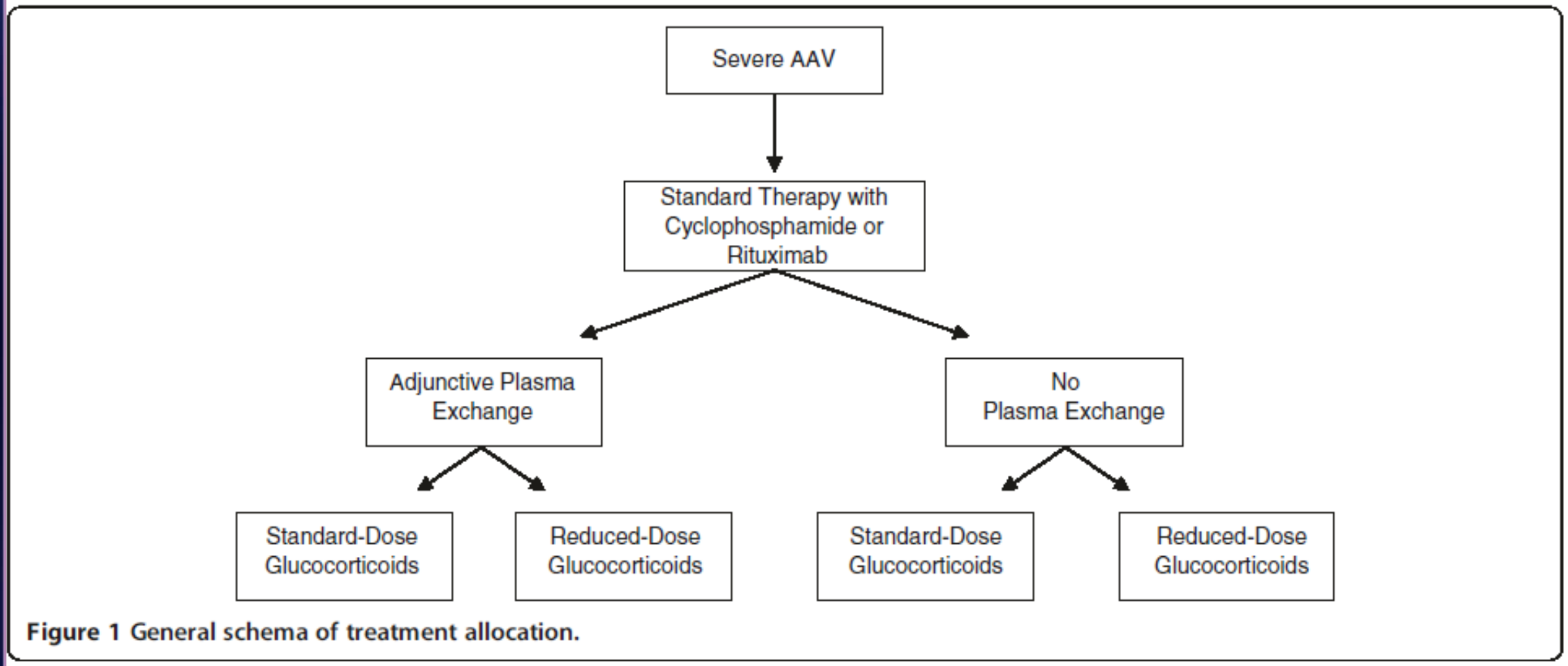
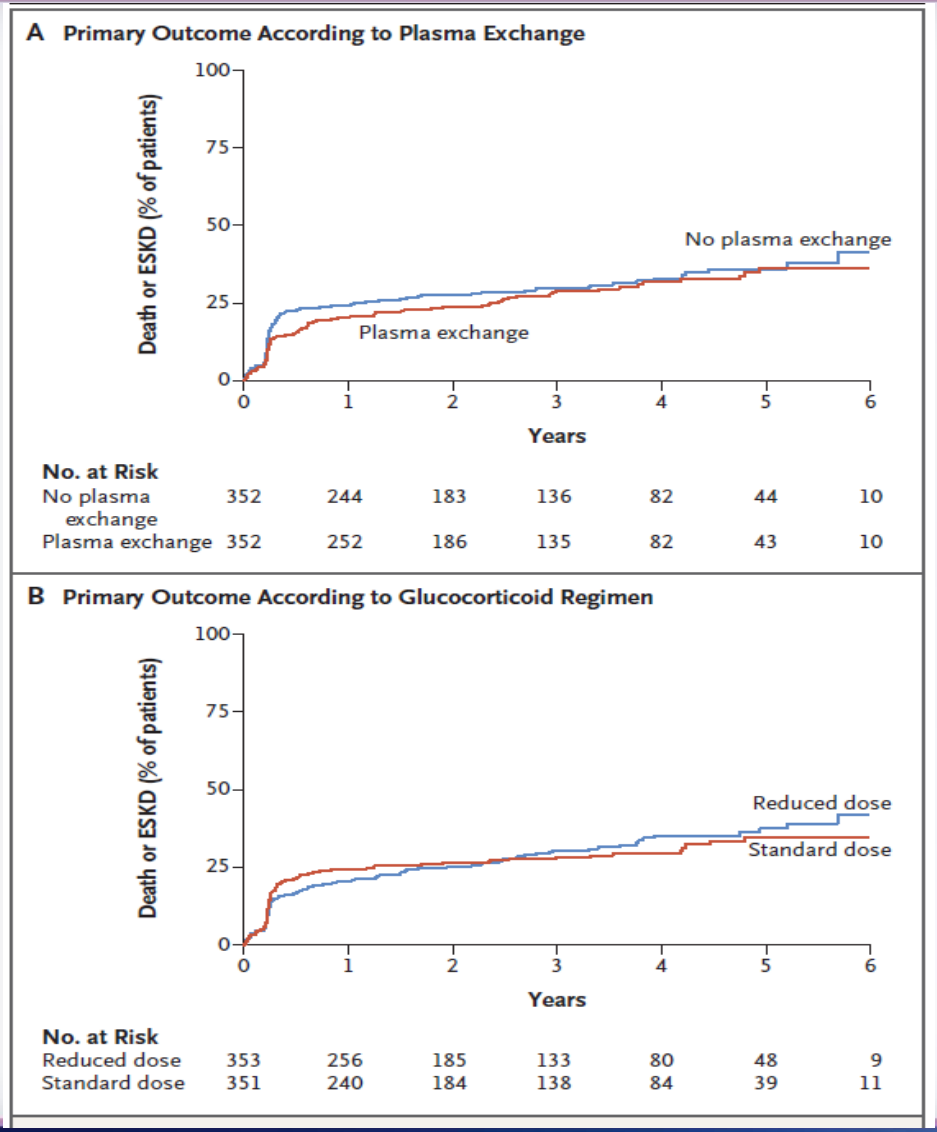



**Figure 1** General schema of treatment allocation.




Serious infections at 1 year were less common in the reduced-dose steroids group than in the standard- dose group (incidence rate ratio, 0.69; 95% CI (0.52 to 0.93)

RESEARCH

OPEN ACCESS

Check for updates

# The effects of plasma exchange in patients with ANCA-associated vasculitis: an updated systematic review and meta-analysis

Michael Walsh,[1,2,3] David Collister,[3,4] Linan Zeng,[2,5] Peter A Merkel,[6] Charles D Pusey,[7] Gordon Guyatt,[1,2] Chen Au Peh,[8,9] Wladimir Szpirt,[10] Toshiko Ito-Hara,[11,12] David R W Jayne,[13] on behalf of the Plasma exchange and glucocorticoid dosing for patients with ANCA-associated vasculitis BMJ Rapid Recommendations Group*

## INTERPRETATION

For the treatment of AAV, plasma exchange has no important effect on mortality, reduces the 12 month risk of ESKD, but increases the risk of serious infections.

Use of Plasma exchange is supported by The KDIGO and The American Society of Apheresis 2020 guidelines for patients with SCr >3.4 mg/dl (>300 mmol/l), patients requiring dialysis or with rapidly increasing SCr, and patients with diffuse alveolar hemorrhage who have hypoxemia

- Infections rather than active vasculitis have become the major cause of mortality in the first treatment year.
- In a review of four of the randomized controlled trials performed by The European Vasculitis Study Group, mortality was 11 % in the first year. Infection was the direct cause of death in 50% of the cases while active vasculitic disease was the sole cause in only 14% of patients.
- In a retrospective review of 113 patients with WG, Cyclophosphamide and corticosteroids were independently associated with significantly higher risk of major infection.

*Turnbull J, et al. Adverse effects of therapy for ANCA-associated vasculitis Best Pract Res Clin Rheumatol. 2009*

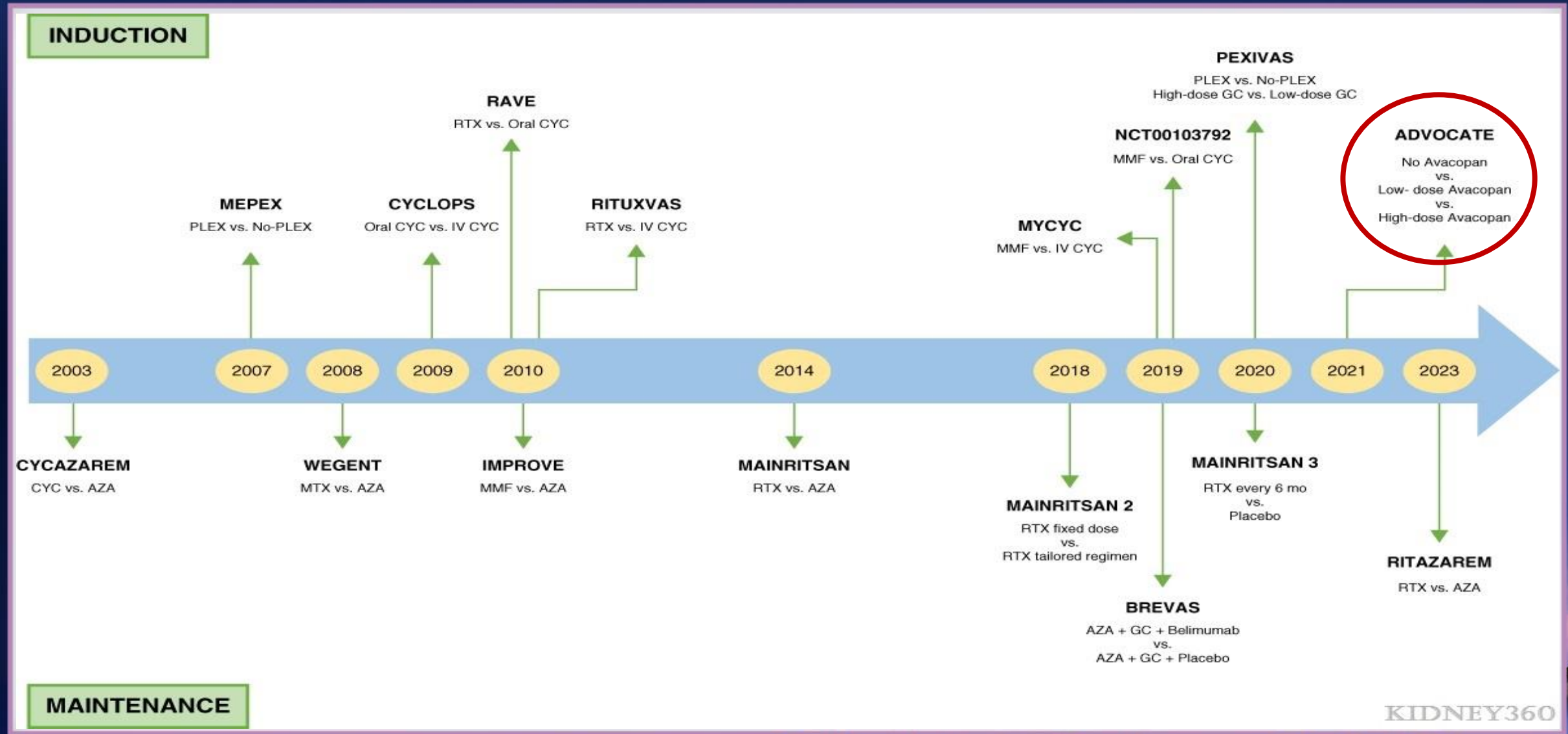
*Charlier C et al. Risk factors for major infections in Wegener's granulomatosis: analysis of 113 patients. Ann Rheum Dis 2009;68:658–663.*

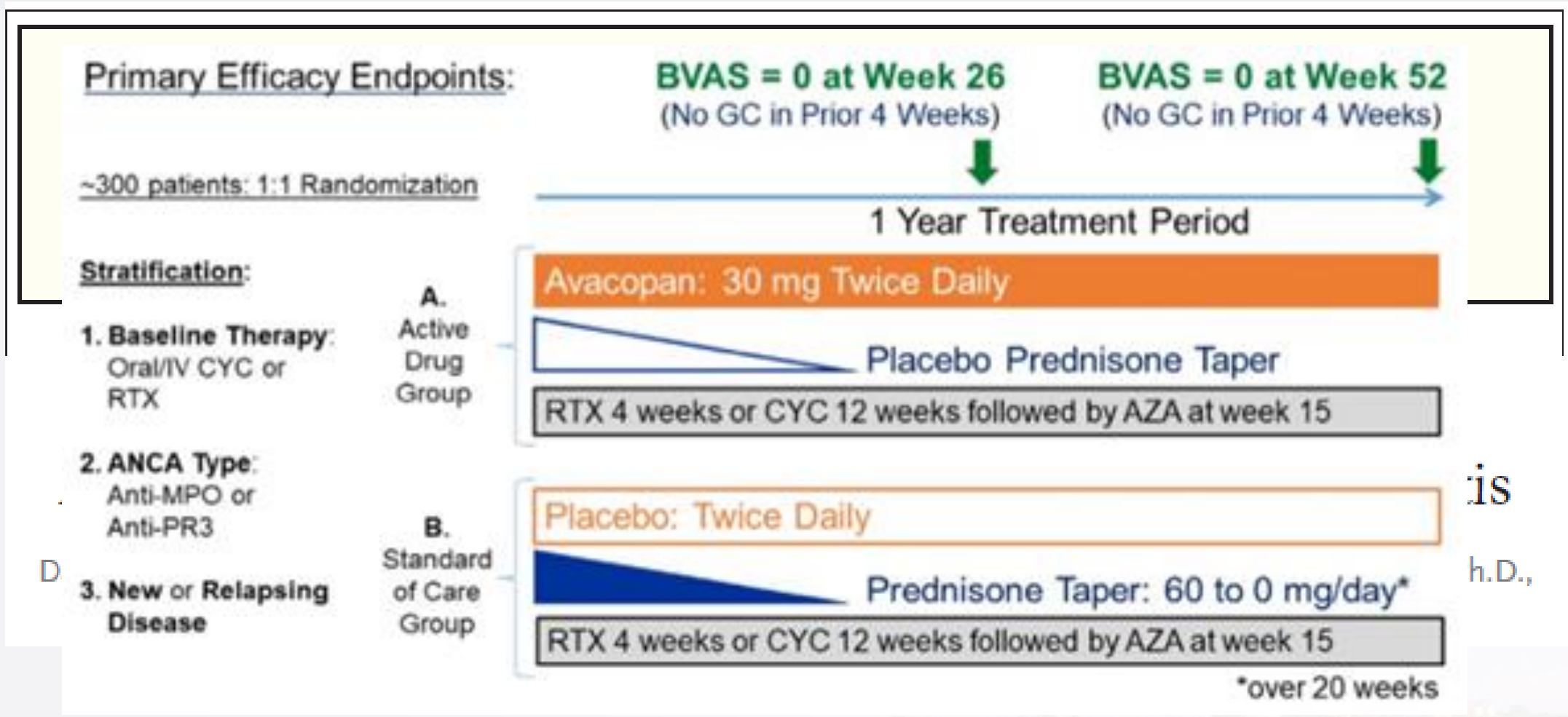
*Walsh M et al. Effects of duration of glucocorticoid therapy on relapse rate in antineutrophil cytoplasmic antibody associated vasculitis: a meta-analysis. Arthritis Care Res (Hoboken). 2010;62:1166–1173*

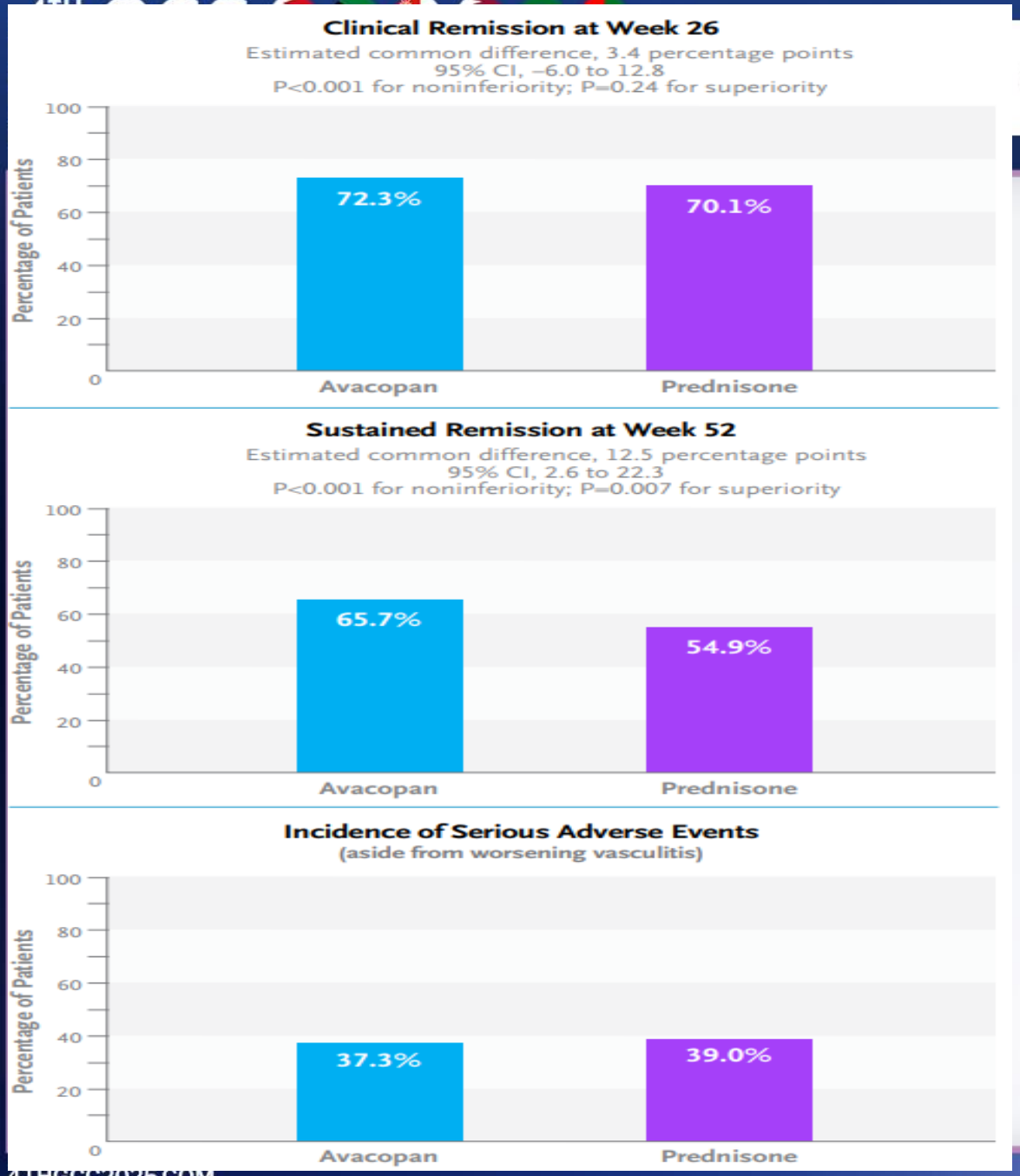
# Minimizing corticosteroids

| RAVE | LOVAS | RITAZAREM | PEXIVAS |
|---|---|---|---|
| **Induction** | | **Maintenance** | |
| ▪ Newly diagnosed and relapsing AAV equally<br>▪ Prednisone was stopped by 5 months | ▪ Newly diagnosed<br>▪ MPO – AAV<br>▪ Rituximab induction<br>▪ Excluded patients with DAH and GFR < 15 ml/min<br>▪ Less infections in the reduced steroid arm | ▪ Relapsing AAV<br>▪ 70 % of the patients used reduced dose steroids | ▪ Patients with severe disease (GFR < 50 ml/min or DAH)<br>▪ Majority treated with CYC<br>▪ Serious infections at one year were less common in the reduced dose steroid group |

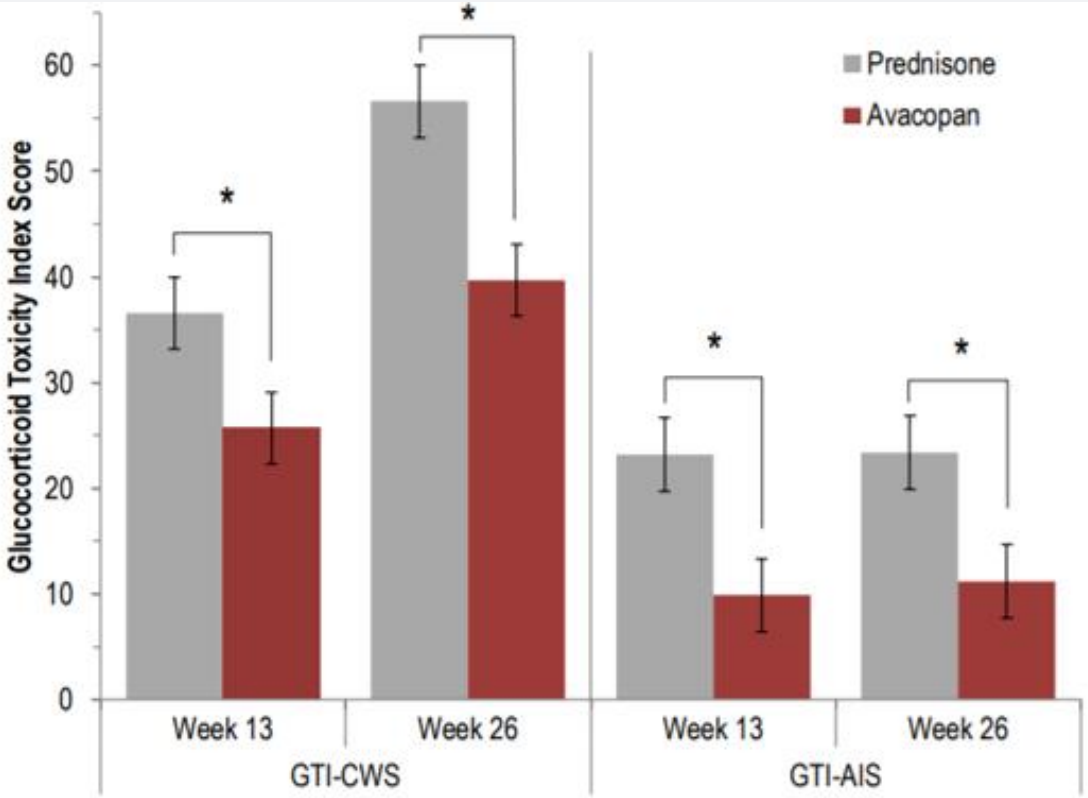
- **Avacopan for steroid sparing:** High cost, limited availability, and lack of long-term safety data are currently barriers to its wider application.


INDUCTION
RAVE
RTX vs. Oral CYC
PEXIVAS
PLEX vs. No-PLEX
High-dose GC vs. Low-dose GC
NCT00103792
MMF vs. Oral CYC
ADVOCATE
No Avacopan
vs.
Low- dose Avacopan
vs.
High-dose Avacopan
MEPEX
PLEX vs. No-PLEX
CYCLOPS
Oral CYC vs. IV CYC
RITUXVAS
RTX vs. IV CYC
MYCYC
MMF vs. IV CYC
2003
2007
2008
2009
2010
2014
2018
2019
2020
2021
2023
CYCAZAREM
CYC vs. AZA
WEGENT
MTX vs. AZA
IMPROVE
MMF vs. AZA
MAINRITSAN
RTX vs. AZA
MAINRITSAN 2
RTX fixed dose
vs.
RTX tailored regimen
MAINRITSAN 3
RTX every 6 mo
vs.
Placebo
RITAZAREM
RTX vs. AZA
BREVAS
AZA + GC + Belimumab
vs.
AZA + GC + Placebo
MAINTENANCE

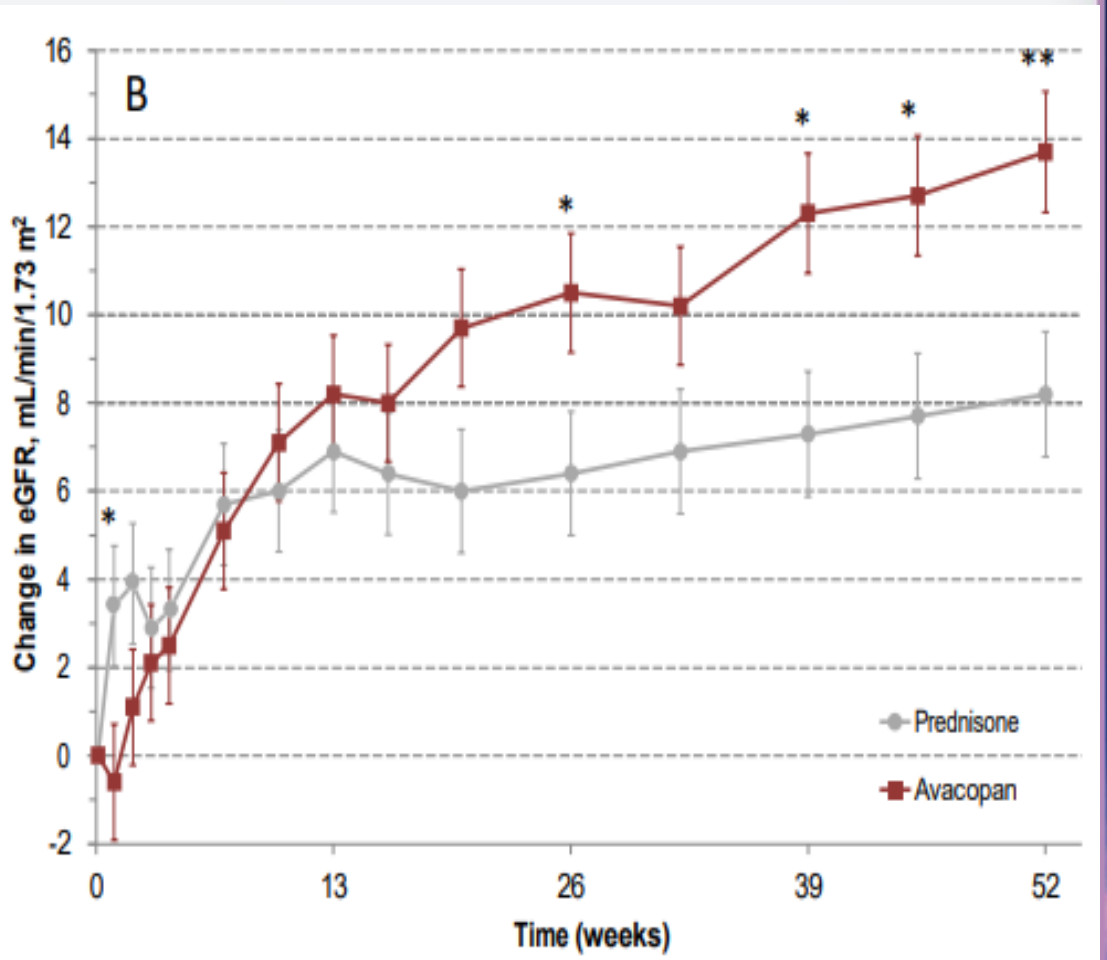

Primary Efficacy Endpoints:
BVAS = 0 at Week 26
(No GC in Prior 4 Weeks)
BVAS = 0 at Week 52
(No GC in Prior 4 Weeks)
~300 patients: 1:1 Randomization
1 Year Treatment Period
Stratification:
1. Baseline Therapy: Oral/IV CYC or RTX
2. ANCA Type: Anti-MPO or Anti-PR3
3. New or Relapsing Disease
A. Active Drug Group
Avacopan: 30 mg Twice Daily
Placebo Prednisone Taper
RTX 4 weeks or CYC 12 weeks followed by AZA at week 15
B. Standard of Care Group
Placebo: Twice Daily
Prednisone Taper: 60 to 0 mg/day*
RTX 4 weeks or CYC 12 weeks followed by AZA at week 15
*over 20 weeks

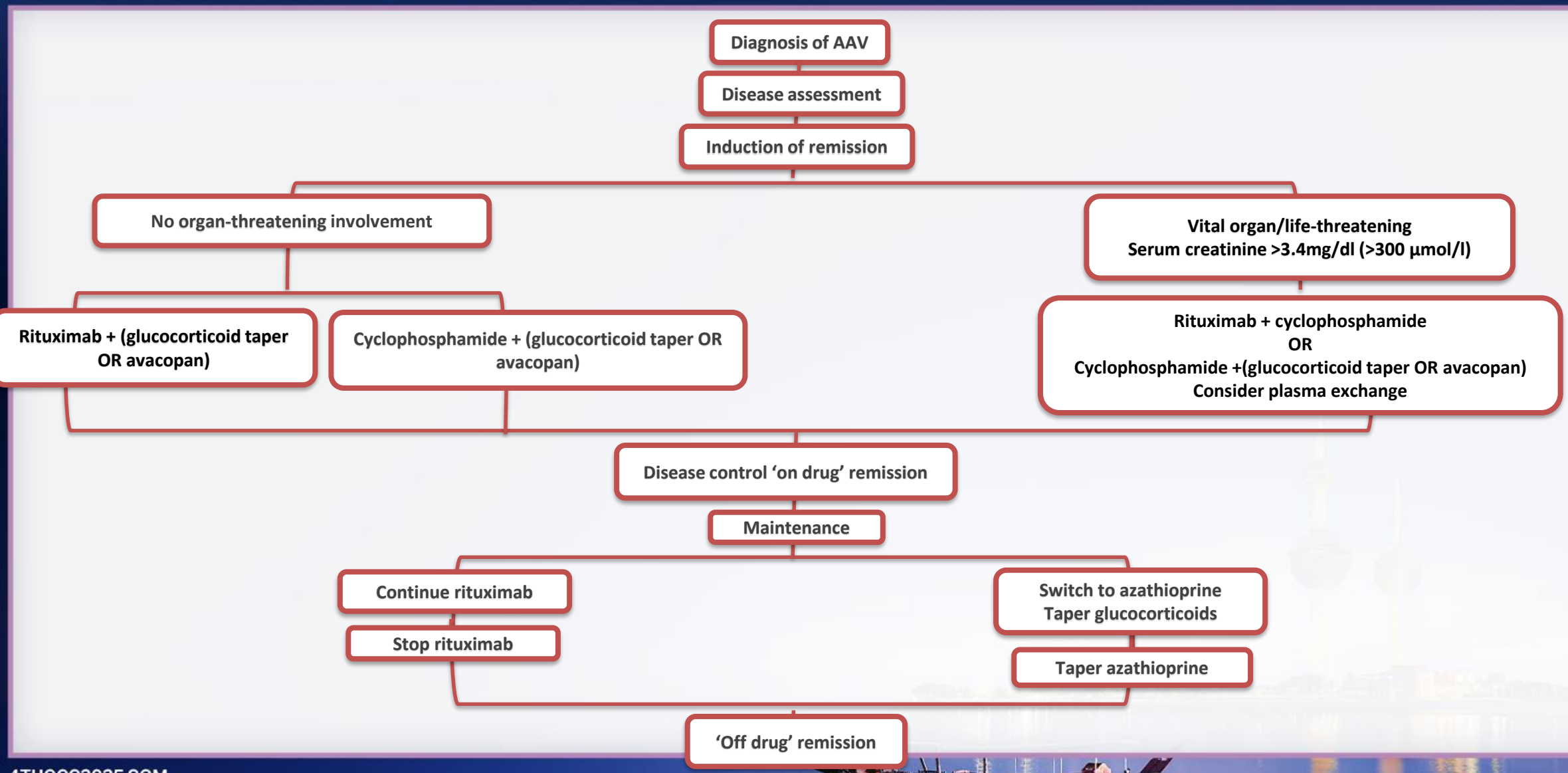



- No cases of N. Meningitidis
- LFTs abnormalities (5.4% vs 3.7%)




Glucocorticoid Toxicity Index Cumulative Worsening Score (GTI-CWS; range from 0 to 410; higher score indicates greater toxicity) and Aggregate Improvement Score (GTI-AIS; range from –317 to 410) by treatment group and study visit

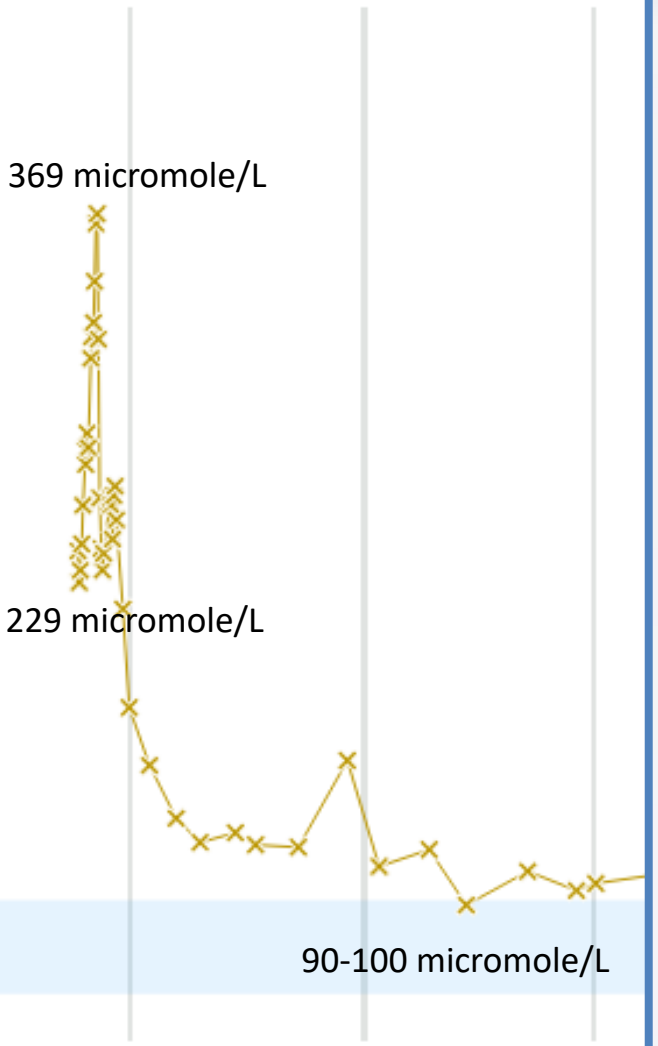



Diagnosis of AAV
Disease assessment
Induction of remission
No organ-threatening involvement
Vital organ/life-threatening
Serum creatinine >3.4mg/dl (>300 µmol/l)
Rituximab + (glucocorticoid taper OR avacopan)
Cyclophosphamide + (glucocorticoid taper OR avacopan)
Rituximab + cyclophosphamide
OR
Cyclophosphamide +(glucocorticoid taper OR avacopan)
Consider plasma exchange
Disease control 'on drug' remission
Maintenance
Continue rituximab
Stop rituximab
Switch to azathioprine
Taper glucocorticoids
Taper azathioprine
'Off drug' remission

# Clinical Cases

# Case 1

- 36 year old female patient with PMH significant for PFO status post closure in 2010
- Initially presented to an outside hospital with pain in the left gluteal region treated with multiple types of antibiotics. After discharge home, she was taking ibuprofen consistently for body aches. No joint pains or swelling, malar rash, photosensitivity or oral ulcers

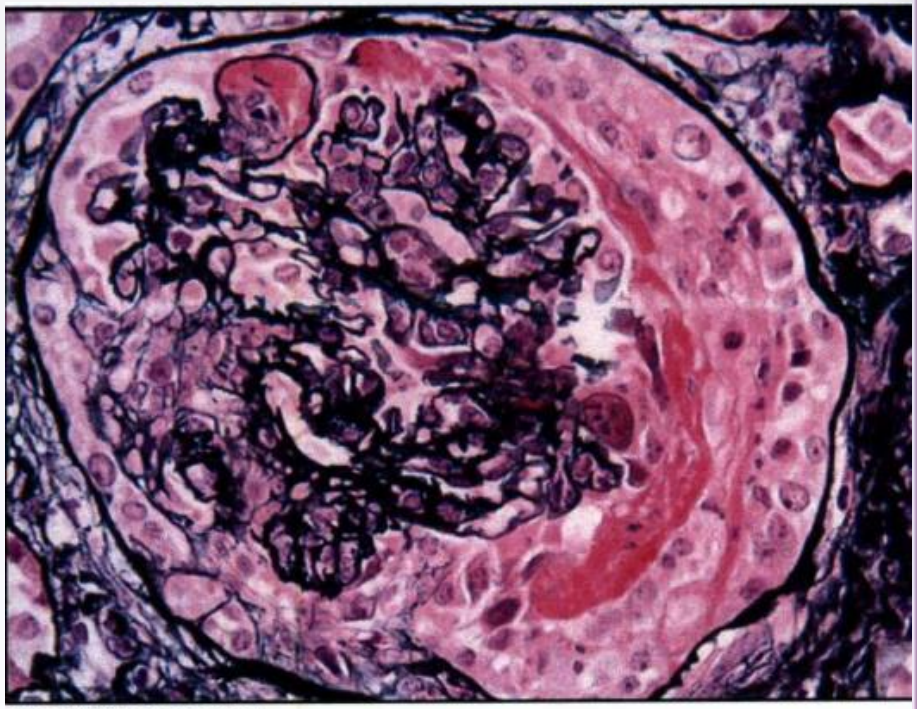



Urinalysis: 2 + protein, > 25 RBCs/hpf, no WBCs. UPCR 276 mg/mmole

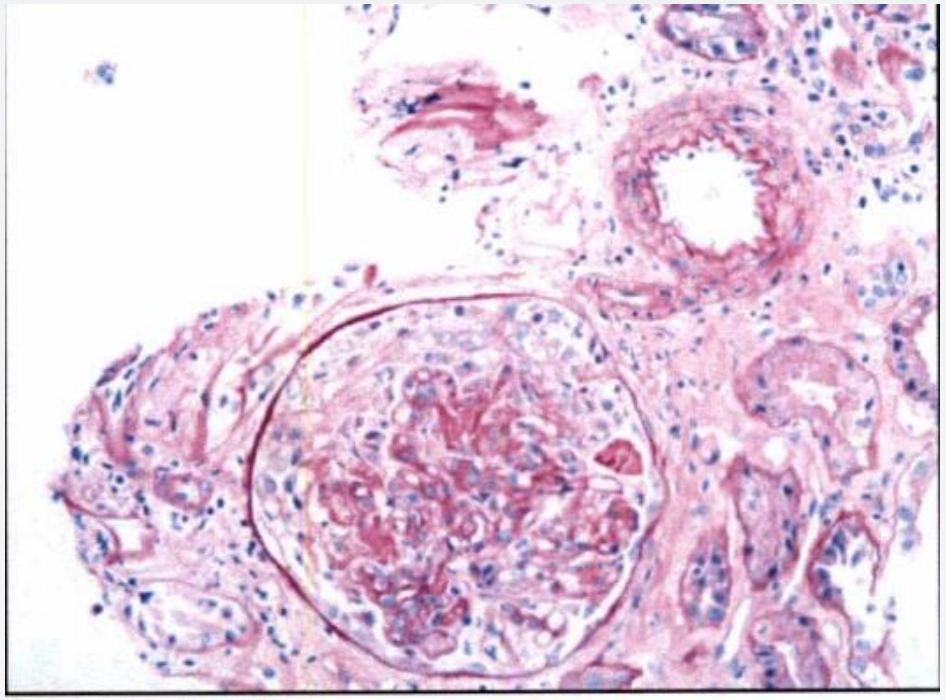
| AUTOIMMUNE | | | | | | | |
|---|---|---|---|---|---|---|---|
| Anticentromere B antibodies | | | | | | | <0.2 |
| Chromatin antibodies | | | | | | | <0.2 |
| DNA antibodies, double stranded | | | | | | | <1 |
| Glomerular basement membrane a... | see attached | | | | | | |
| Jo-1 antibodies | | | | | | | <0.2 |
| Myeloperoxidase antibodies | see attached | | | | | | |
| Proteinase 3 antibodies | see attached | | | | | | |
| Scleroderma (Scl) 70 antibodies | | | | | | | <0.2 |
| Antistreptolysin O (ASO) antibodies | | | | | | 34 | |
| Neutrophil cytoplasmic Abs (cAN... | <1:20 | | | | | | |
| Neutrophil cytoplasmic Abs (pAN... | 1:640 ▲ | | | | | | |
| Ribosomal Protein (Quant) | | | | | | | <0.2 |
| RNP antibodies | | | | | | | <0.2 |
| Sm / RNP antibodies | | | | | | | <0.2 |
| Smith antibodies | | | | | | | <0.2 |
| SS-A antibodies (Ro) | | | | | | | <0.2 |
| SS-B antibodies (La) | | | | | | | <0.2 |
| Complement C3 | | | | | | | 141 |
| Complement C4 | | | | | | | 26 |

| Test | Result | Units | Reference Range |
|---|---|---|---|
| Antiproteinase 3 (PR-3) Abs | <3.5 R | U/mL | 0.0-3.5 |
| R: Performed At: BN LabCorp Burlington 1447 York Court Burlington, NC 272153361 Nagendra Sanjai MD Ph:8007624344 | | | |
| Antimyeloperoxidase (MPO) Abs | 45.5 HIGH R | U/mL | 0.0-9.0 |
| R: Performed At: BN LabCorp Burlington 1447 York Court Burlington, NC 272153361 Nagendra Sanjai MD Ph:8007624344 | | | |
| Antiglomerular BM Ab | 3 R | units | 0-20 |
| R: Negative 0 - 20<br>Weak Positive 21 - 30<br>Moderate to Strong Positive >30<br><br>Performed At: BN LabCorp Burlington 1447 York Court Burlington, NC 272153361 Nagendra Sanjai MD Ph:8007624344 | | | |

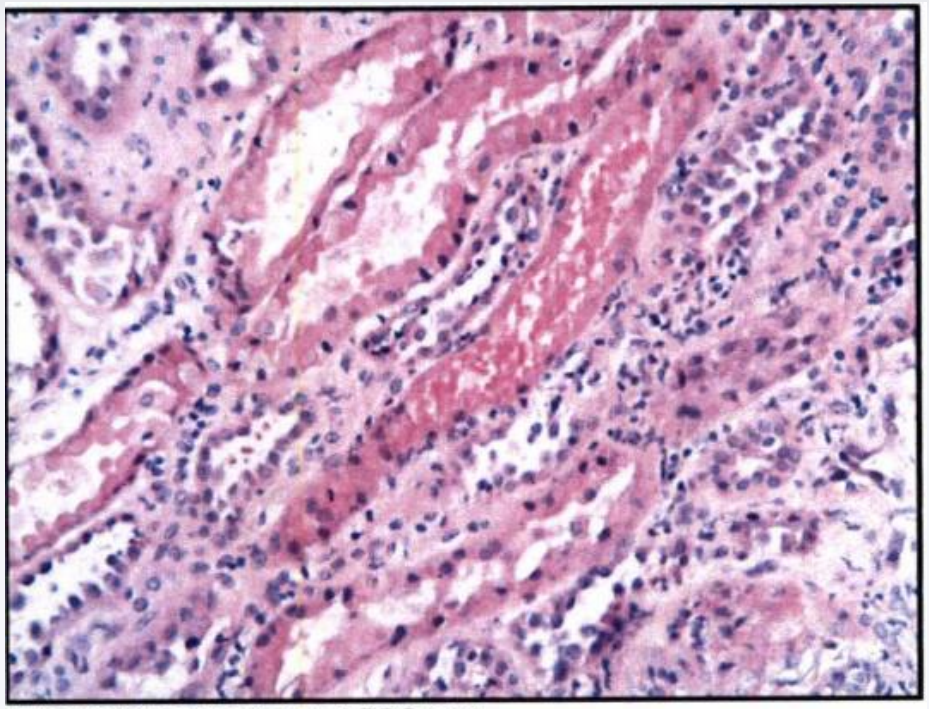
## Kidney Biopsy



Necrotizing crescent



Crescent, normal artery



Interstitial inflammation and RBC cast

## FINAL DIAGNOSIS

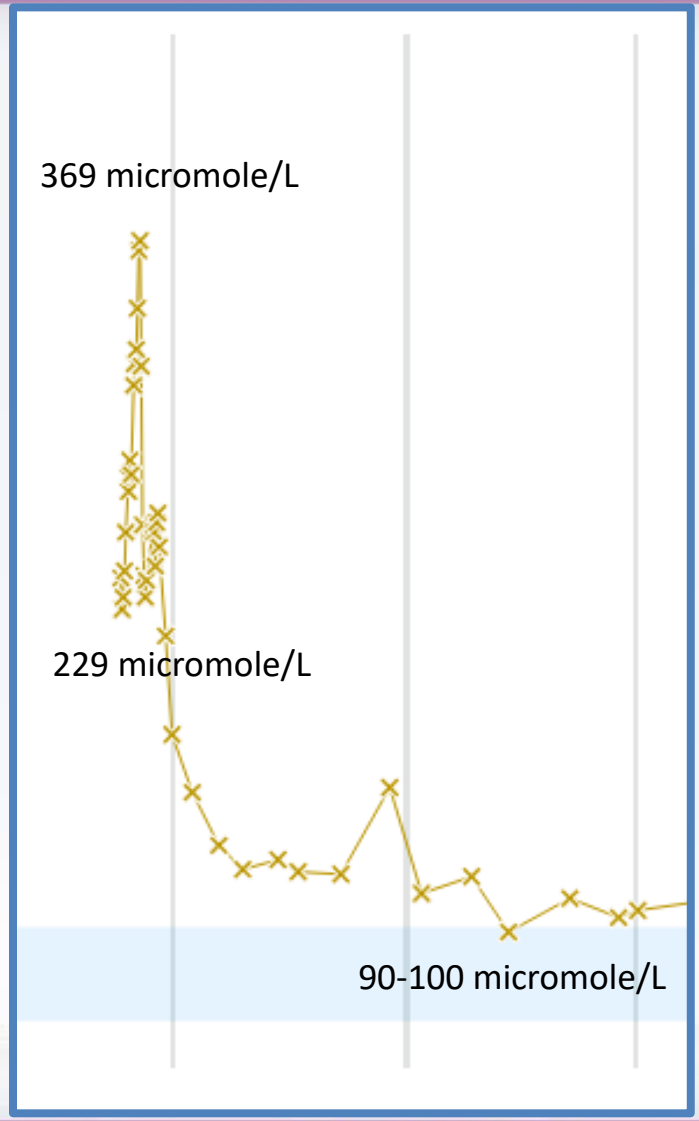
A. RIGHT KIDNEY, BIOPSY (10-SP-21-0007100 AND 1 BLOCK AND 11 SLIDES):
-Pauciimmune necrotizing and crescentic glomerulonephritis, acute, severe (p-ANCA associated/clinical).

**COMMENT**
Of the total 37 glomeruli sampled, 35 are involved with necrotizing crescents. The 2 remaining glomeruli are normocellular. Immunofluorescence and electron microscopy document the absence of significant immune complex deposition, supporting a pauciimmune process, correlating with the patient's positive ANCA serologies. The findings in this biopsy are consistent with a severely active ANCA vasculitis without significant chronicity.

# Case 1 cont'd

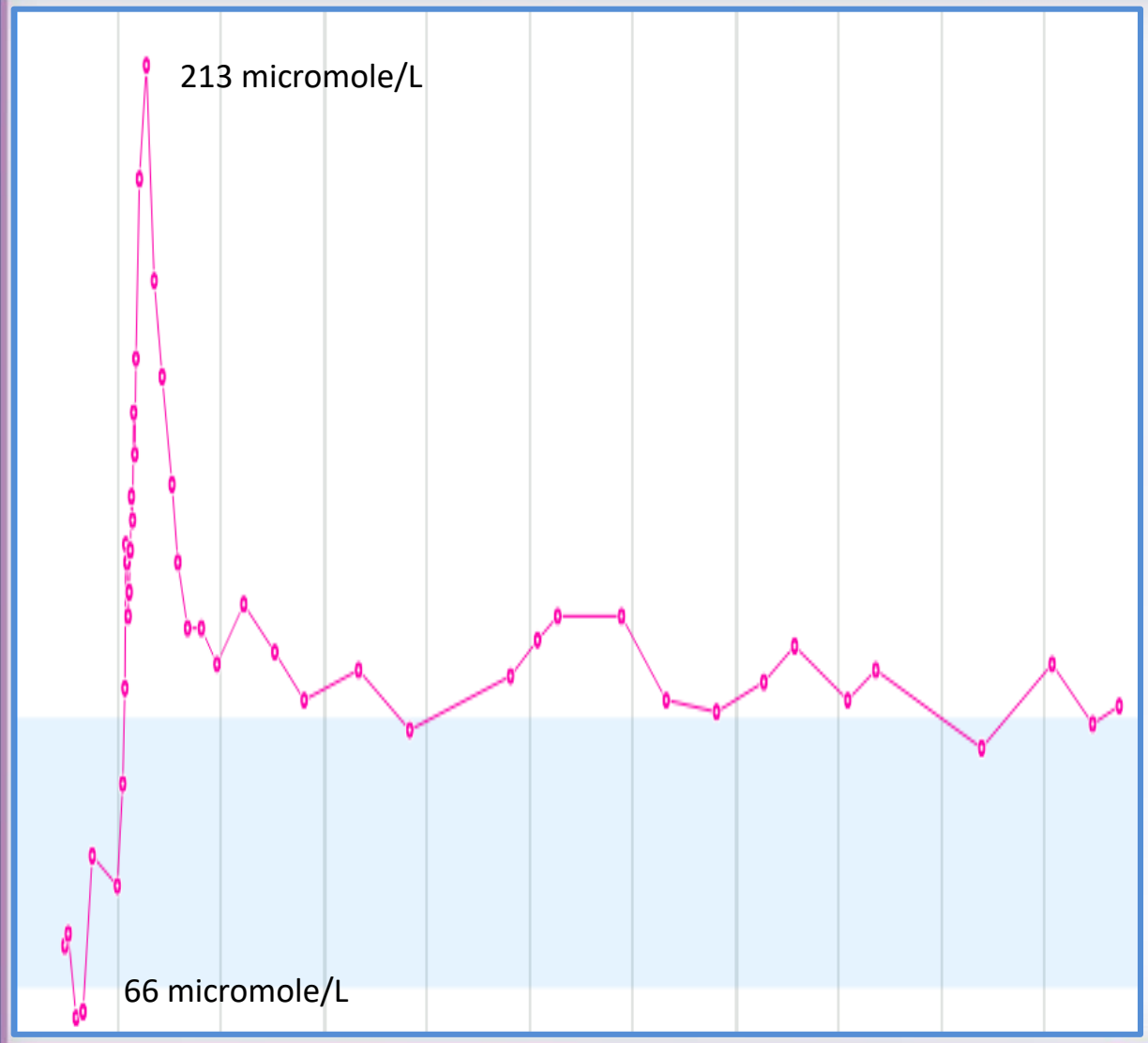
❑ **Management:**

- Pulse steroids: 500 mg methylprednisolone daily for 3 days
- Rituximab 1 g x 2, 2 weeks apart
- IV cyclophosphamide 500 mg x 2 doses
- UPCR down to 20 mg/mmole after ~ two years. UA: 1 + protein, 1-3 RBCs/hpf



# Case 2

- 39 year old male
- Initially presented with sudden onset otalgia and right facial palsy. CT showed right osteomastoiditis and TM perforation. Treated with IV antibiotics and steroids. He also underwent tympanoplasty with mastoidectomy and right and facial nerve decompression.
- This was then followed with left ear pain and hearing impairment**,** weight loss, myalgia, arthralgia, feverishness, with high ESR and RA factor**. CT chest: Moderate-sized soft tissue mass of the anterior segment of the right upper lobe with an aggressive appearance** extending along the margin of the pleura with pleural retraction and parasitization of the adjacent vasculature. There are multiple other metastatic lesions involving the anterior segment of the right middle lobe, and a small nodules of the right lateral segment of the upper lobe, and medial right lower lobe. **PET CT was suspicious for lung malignancy.**
- **Bronchoscopy was suggestive of hemorrhagic features. Lung biopsy was suspicious for necrotizing capillaritis**
- He was started on IV pulse steroids




Urinalysis: 2-3 + protein, > 25 RBCs/hpf, no WBCs. UPCR 84 mg/mmole

- ANA negative, ENA panel unremarkable, complement levels normal
- FLC assay normal, SPEP and serum IFE: no M spike
- Anti GBM negative. Anti PR3 ANCA positive at >8, anti- MPO ANCA negative. P-ANCA negative, C-ANCA positive at 1:40

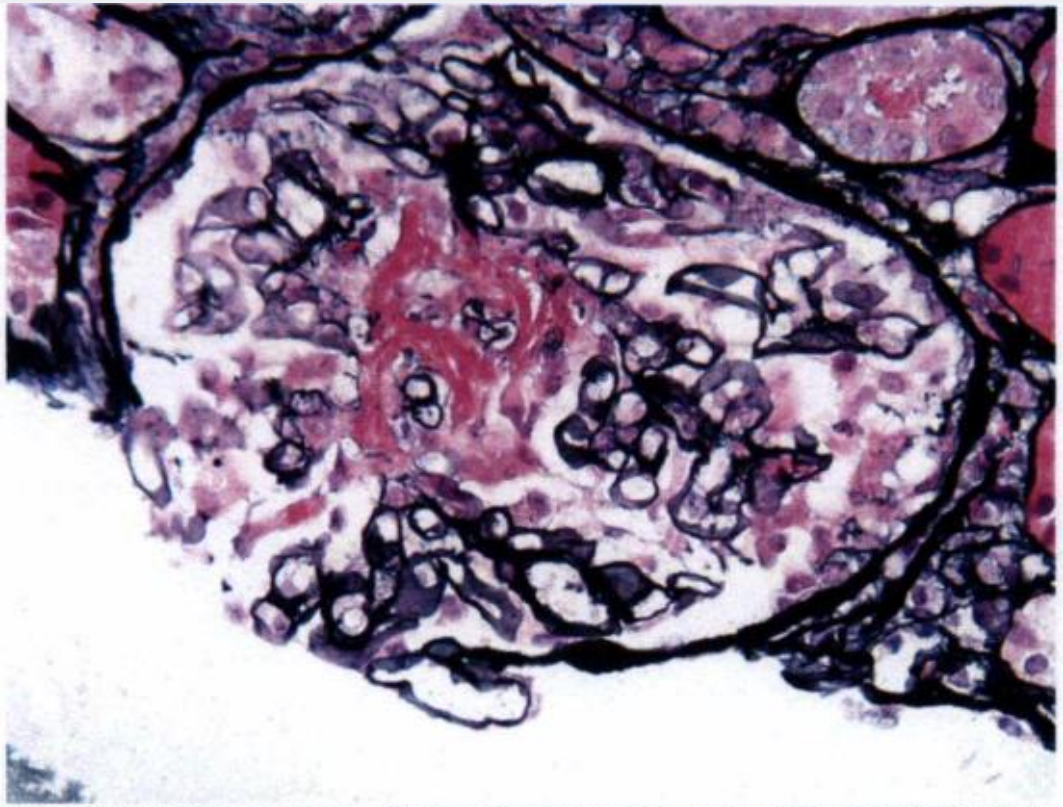


Image 1: GBM rupture, fibrinoid necrosis, early crescent formation

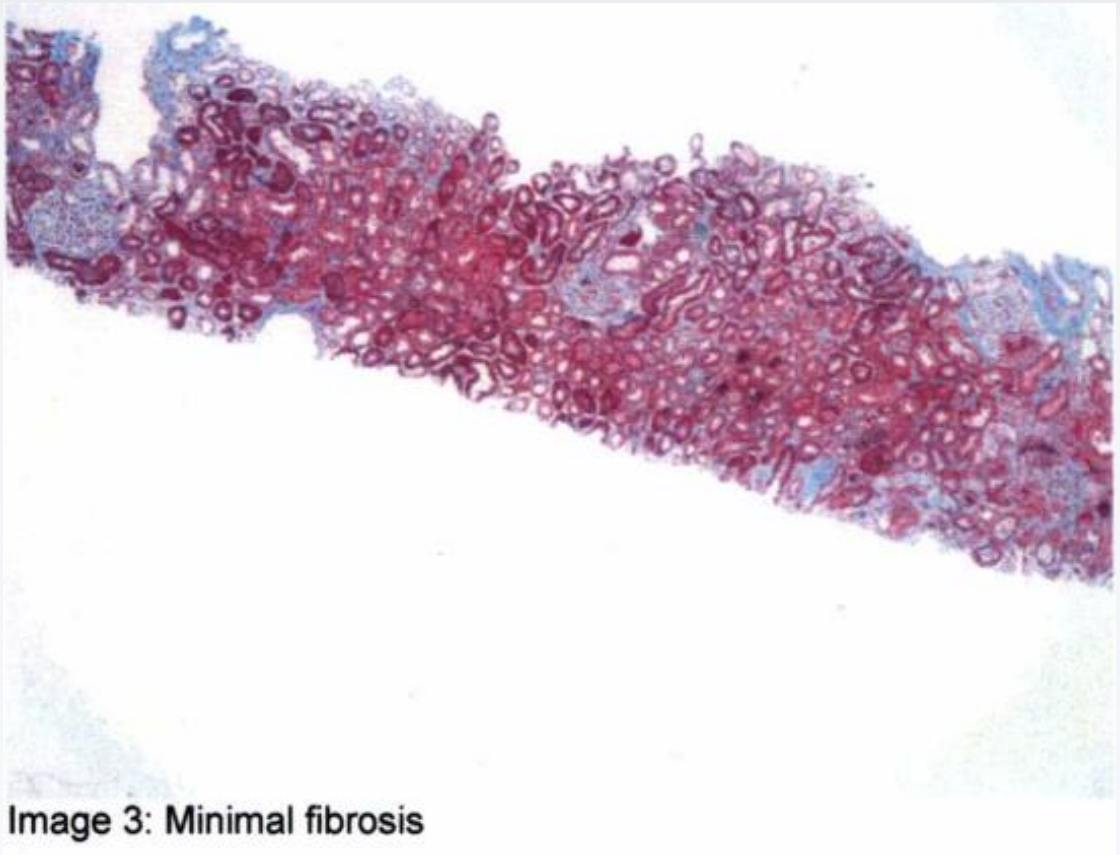


Image 3: Minimal fibrosis

**FINAL DIAGNOSIS**

A. Native right kidney biopsy:

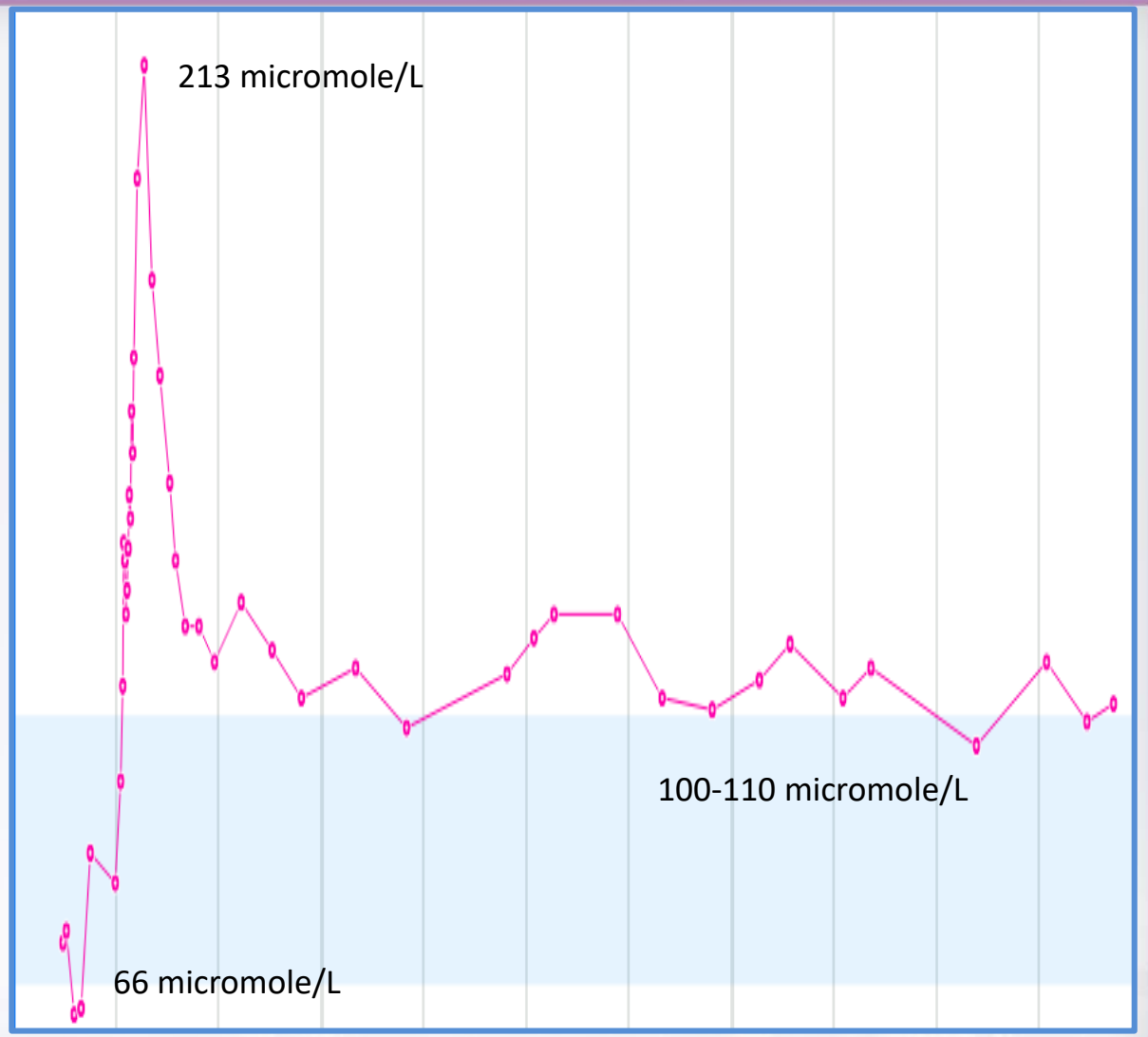
– Pauciimmune necrotizing crescentic glomerulonephritis consistent with ANCA vasculitis (41 glomeruli, 14 with necrotizing crescents, nonsclerotic).

- The patient was treated with pulse steroids followed by oral prednisone 60 mg daily tapered slowly and stopped after ~ 5-6 months
- 4 weekly doses of IV rituximab 375 mg/m2 followed by maintenance rituxumab initially 1 g every 4 months then decreased to 1 g every 6 months.

*Qasim A, Al Qassimi S, **Ghosn M** and Namas R. Granulomatosis with Polyangiitis Masquerading as Lung Cancer. Oman Medical Journal. 2024 Jan 9. doi 10.5001/omj.2026.16*

# Case 2 cont'd

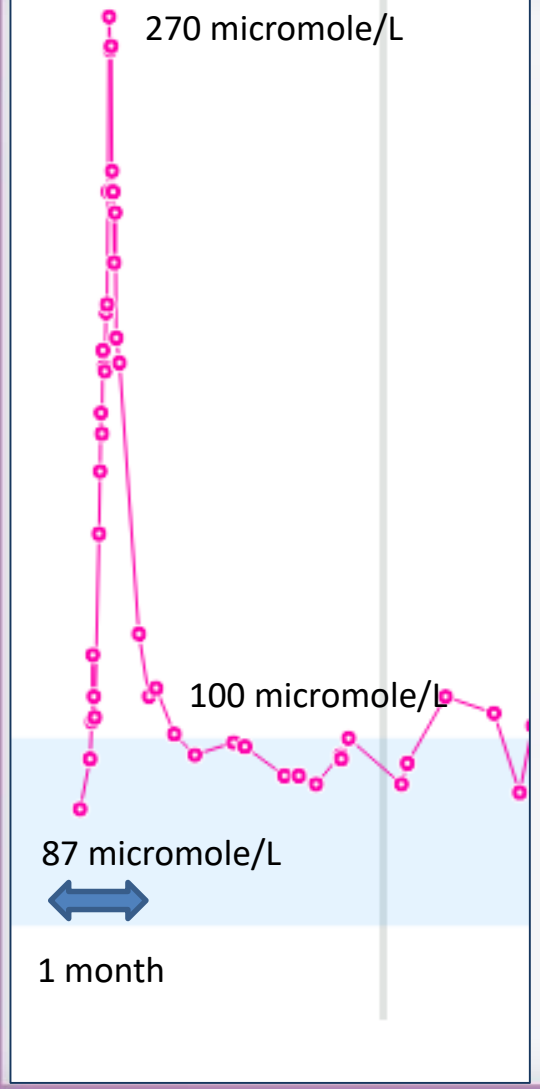
- ❑4 weekly doses of IV rituximab 375 mg/m2 followed by maintenance rituxumab initially 1 g every 4 months then decreased to 1 g every 6 months. Completed 2.5 years of maintenance therapy.
- ❑Facial palsy improved, still with hearing impairment. Lung nodules resolved.
- ❑ Scr 100-110 micromole/L. No proteinuria.
- ❑Serial PR3- ANCA and C-ANCA negative. IgG levels normal.




*Qasim A, Al Qassimi S, **Ghosn M** and Namas R. Granulomatosis with Polyangiitis Masquerading as Lung Cancer. Oman Medical Journal. 2024 Jan 9. doi 10.5001/omj.2026.16*

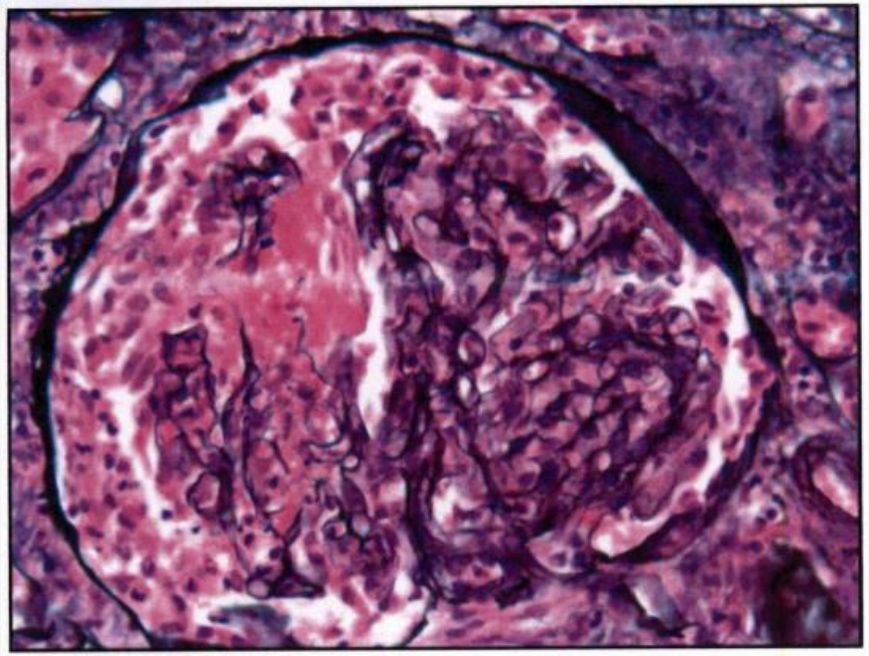
# Case 3

- 17 year old male patient
- 6 weeks history of right ear pain and discharge not responding to antibiotics
- 4 weeks history of generalized fatigue, intermittent fevers, rhinorrhea, dyspnea on exertion, pleuritic chest pain, diffuse arthralgias and purpuric rash over lower extremities
- CT chest: Multiple nodular foci of presumed airspace disease in both lungs (greater than 10 in number) with the largest being in the left lower lobe measuring 22 mm x 21 mm.

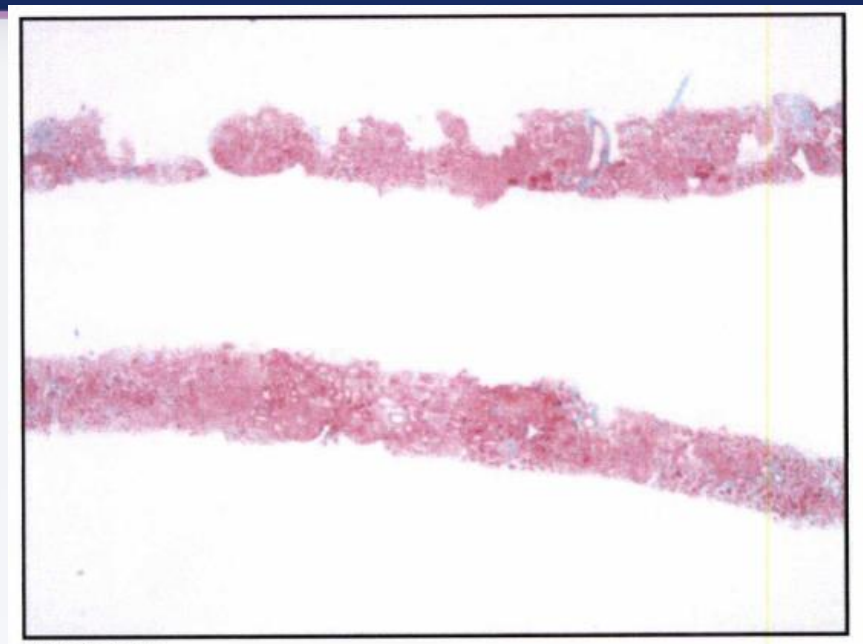



Urinalysis: 2 + protein, > 25 RBCs/hpf, no WBCs. UPCR 81 mg/mmole

| AUTOIMMUNE | | | | | | |
|---|---|---|---|---|---|---|
| Anticentromere B antibodies | | | | | | <0.2 |
| Chromatin antibodies | | | | | | 0.2 |
| DNA antibodies, double stranded | | | | | | <1 |
| Glomerular basement membrane a... | | | | | | <0.2 |
| Jo-1 antibodies | | | | | | <0.2 |
| Myeloperoxidase antibodies | | | | | | <0.2 |
| Proteinase 3 antibodies | | | | | | >8.0 |
| Scleroderma (Scl) 70 antibodies | | | | | | <0.2 |
| Neutrophil cytoplasmic Abs (cAN... | | | 1:160 | | | |
| Neutrophil cytoplasmic Abs (pAN... | | | <1:20 | | | |
| Rheumatoid Factor | | | | | | 513 |
| Ribosomal Protein (Quant) | | | | | | <0.2 |
| RNP antibodies | | | | | | 0.3 |
| Sm / RNP antibodies | | | | | | <0.2 |
| Smith antibodies | | | | | | <0.2 |
| Cardiolipin antibodies, IgG | | | | | | <1.6 |
| Cardiolipin antibodies, IgA | | | | | | 0.5 |
| Antinuclear antibodies (ANA), other | | | | | | Refer bel... |
| Antinuclear antibodies (ANA), inte... | | | | | | . |
| Antinuclear antibodies (ANA), IFA | | | | | | Negative |
| SS-A antibodies (Ro) | | | | | | <0.2 |
| SS-B antibodies (La) | | | | | | <0.2 |
| Complement C3 | | | | | | 177 |
| Complement C4 | | | | | | 33 |



Necrotizing crescent



Mild fibrosis

## FINAL DIAGNOSIS

Native kidney biopsy:
- Pauciimmune necrotizing crescentic glomerulonephritis, acute, severe (PR3-ANCA associated/clinical).
- Tubular atrophy and interstitial fibrosis, minimal.

LH/srj 03/28/2019

**COMMENT**
The immunofluorescence findings confirm the presence of a pauciimmune glomerulonephritis. Approximately 50% of the glomeruli sampled in this biopsy are involved by active necrotizing crescents while chronic scarring and glomerulosclerosis are minimal. These findings correlate are consistent with ANCA vasculitis.

# Case 3 cont'd

❑**Management:**

- Pulse steroids: 500 mg methylprednisolone daily for 3 days
- Rituximab 375 mg/m2 weekly for 4 doses
- 5 sessions of PLEX added after one week
- UPCR normalized after ~ one year. UA: 0-1 + protein, 3-5 RBCs/hpf