Clinical Case Presentation

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Γενικο Νοσοκομειο Αθηνων
ΙΠΠΟΚΡΑΤΕΙΟ

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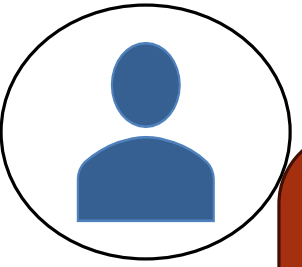
Case 2: Reason for Admission - PMHx



38-year-old man with:

Hospitalisation October 2022

- Fever
- Cough - Haemoptysis

- Arthralgia hands, feet, knees
- Purpuric rash on lower limbs
- Fatigue – Weight loss
- Severe anaemia
  (initially attributed to lower GI haemorrhage due to haemorrhoids)

} past 5 months

Past History

- Haemorrhoidopathy

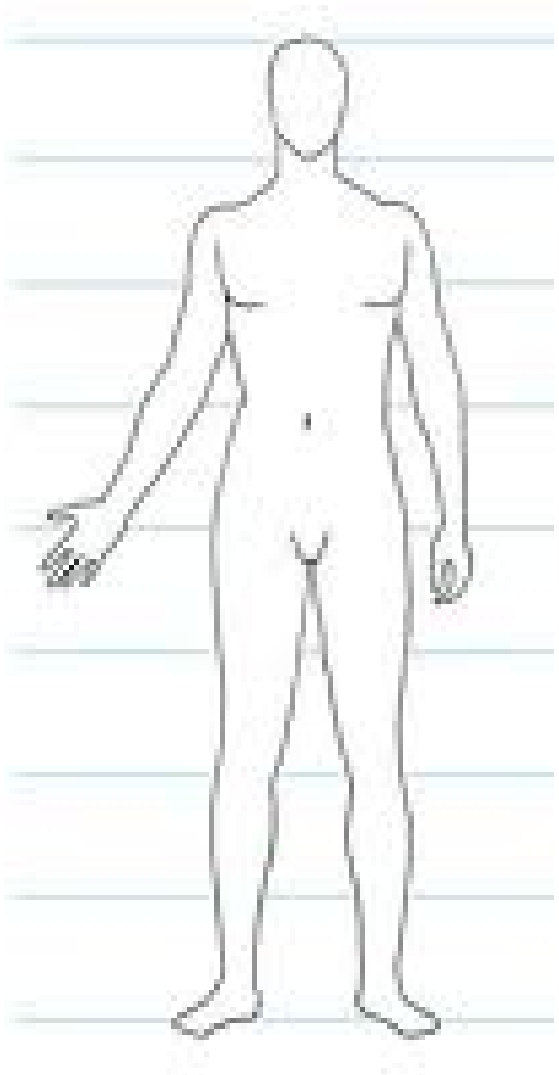
Medications

- None

Habits

- Current smoker
- Occasional marijuana user
- Former intranasal use of cocaine (last 4 years before presentation)

Case 2: Clinical examination



BP=120/70mmHg, HR=85/min,
T=36.9 °C, RR=**20/min**, $SatO_2$=97% (FiO2: 0.21)

General: **patient in mild distress**

Respiratory: **crackles in mid and lower lung fields bilaterally**

Cardiovascular: S1,S2, sinus rhythm, no murmurs or rubs
mild swelling lower limbs bilaterally

Abdomen: soft, non-tender, normal bowel sounds

MSK: **tenderness and swelling of right ankle**

Nervous: **mild sensory loss over the dorsum of left foot**

Head & LNs: normal

Vascular: no bruits

Case 2: Initial Labs and chest x-ray

Hb: 7g/dl **Ht:** 22%, MCV/MCH: 76/24

WBC: 11640 (N 70%) **PLTs**: 597000

CRP: 42 **(<5 mg/dl), TKE** 130 **mm/h**

BUN: 98 mg/dL, **Cr**:3.8 mg/dl,

eGFR:20 ml/min/1.73m^2, **Glu**: 112 mg/dl

AST/ALT: 17/31 U/L (<34/<55)

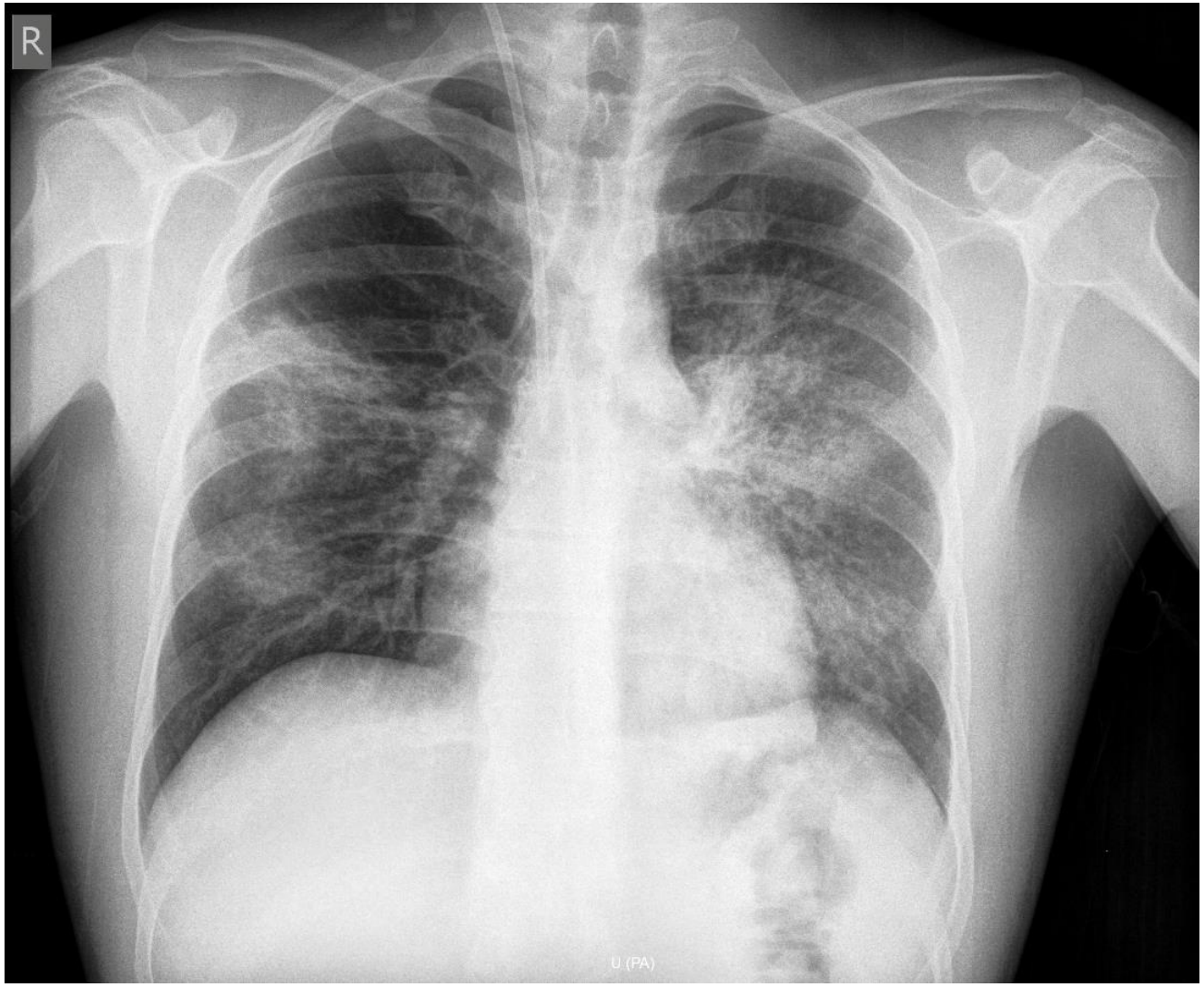
γ-GT 82 IU/l **LDH** 176 IU/l **CPK** 64 IU/l

Urine microscopy: WBC 0-1, **RBC: 20-30**

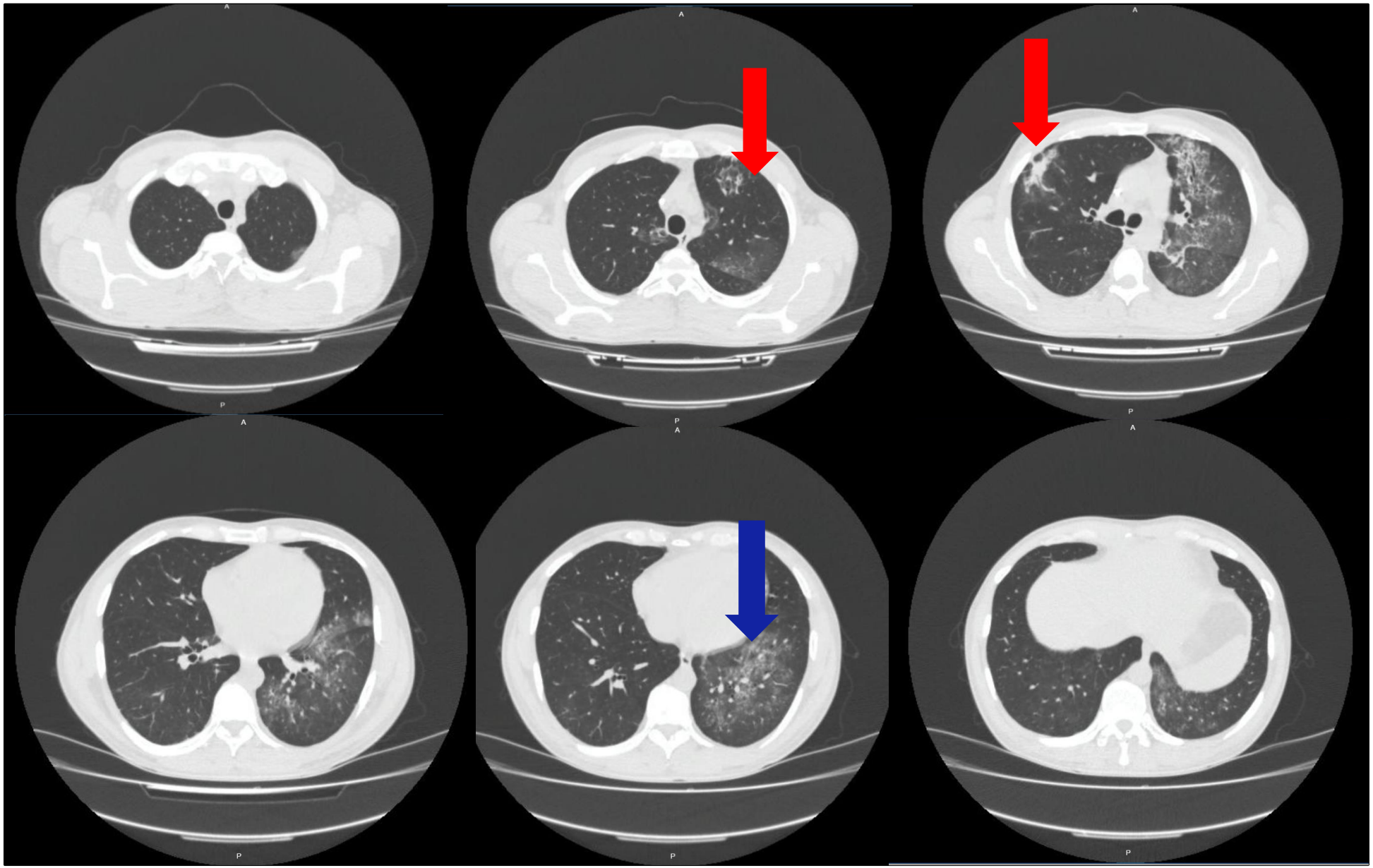
Hb (+++), **Pro: (++)**

Urinary sediment: 10% dysmorphic RBC

Proteinuria: 5g/24h



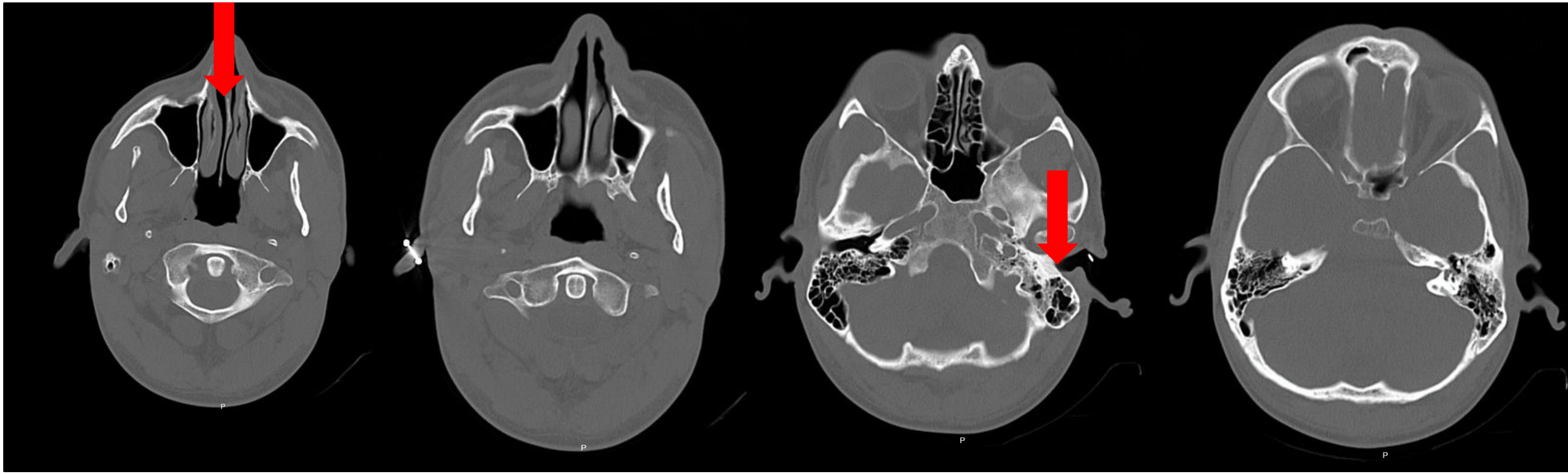
Case 2: CT Thorax



Areas with consolidation

Ground glass opacities in R upper and L lower lobe

Case 2: CT Head



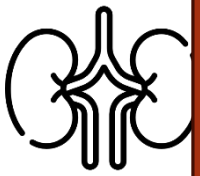
Thickening of nasal mucosa, partial occupation of mastoid cells on the left

Mucositis of parasinuses bilaterally

Case 2: Summary of presentation

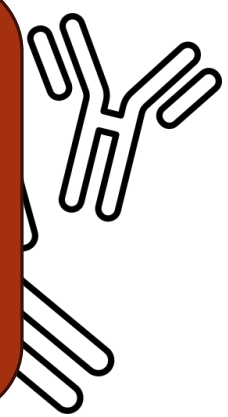
♂ 38 years old

✓ **Fever – Inflammatory syndrome – Severe anaemia**



Diagnosis

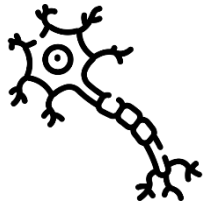
Granulomatosis with polyangiitis (GPA)



ANCA antibodies

✓ **Arthritis (Rt) ankle**

PR3 ANCA (+): 173IU/mL



✓ **Sensory loss Lt foot**

Case 2: Question-1

- Would you perform a renal biopsy on this patient and why?

Personal viewpoint :

Renal biopsy is possibly not mandatory in all cases of ANCA-vasculitis with signs of renal involvement. Nevertheless, it allows

- **CONFIRMATION** of renal vasculitis

- **EXCLUSION** of other diseases and overlap syndromes

- **PREDICTION** of renal (and patient) survival

- **EVALUATION** of vasculitis activity (addition of plasma exchange ? Early withdrawal of IS in elderly patients with severe renal dysfunction and no extrarenal involvement ?)

The risk linked to its procedure is low
(<3% haemorrhagic complications requiring transfusion or embolization)

Studies are needed to demonstrate that kidney pathology **may modify AAV treatment ?**

Case 2: Renal Biopsy

- 5 glomeruli
  4 (80%) cellular crescents
  1 (20%) fibrous crescent
  3 (60%) with fibrinoid necrosis

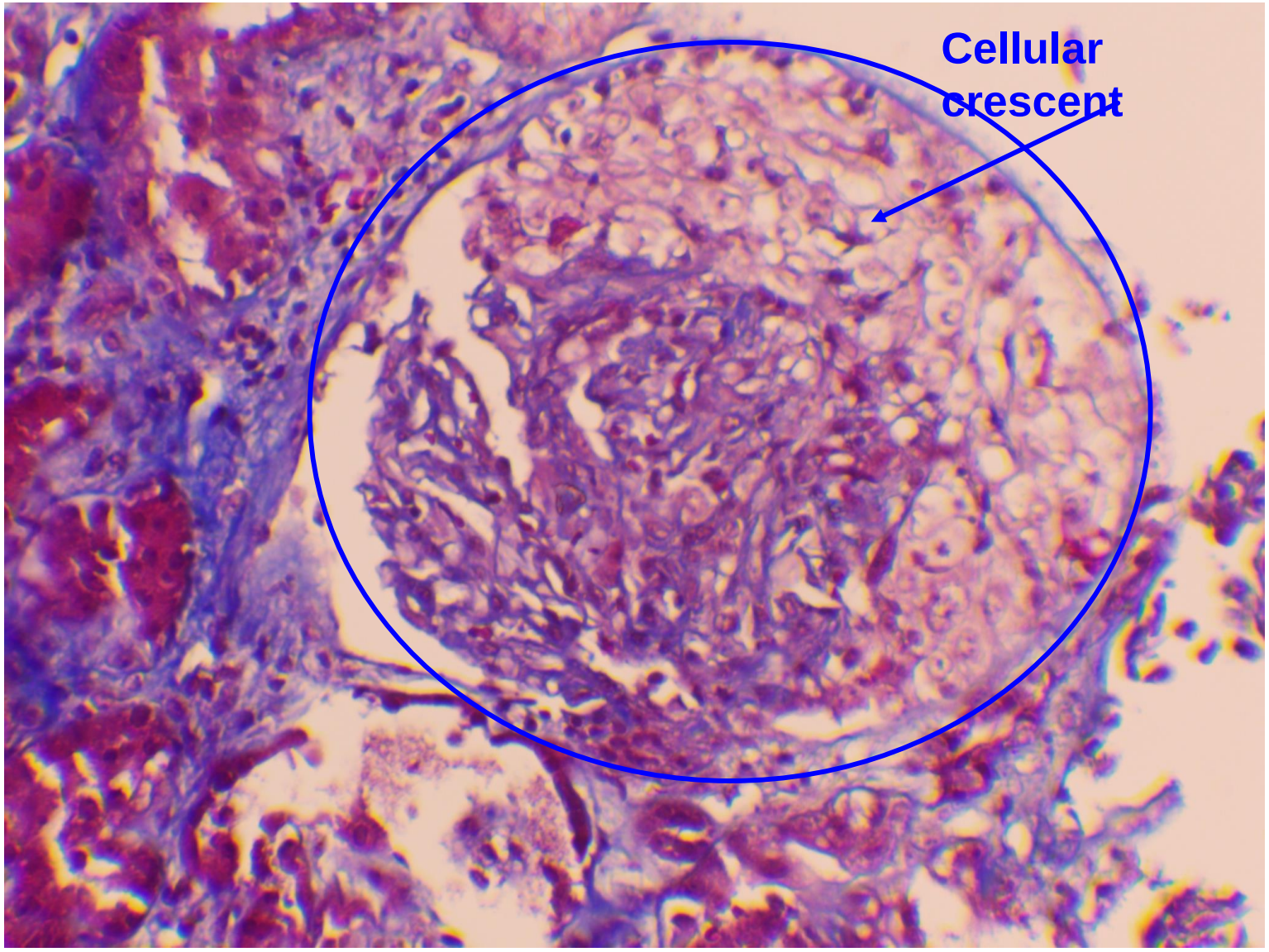
Berden class: crescentic
Brix score: high risk

- Moderate interstitial inflammation
- **35% Interstitial fibrosis**
- **Necrotizing arteritis**

- **Immunofluorescence: Negative**

- Final pathologic diagnosis**: Pauci-immune crescentic necrotizing glomerulonephritis**

Case 2: Renal Biopsy

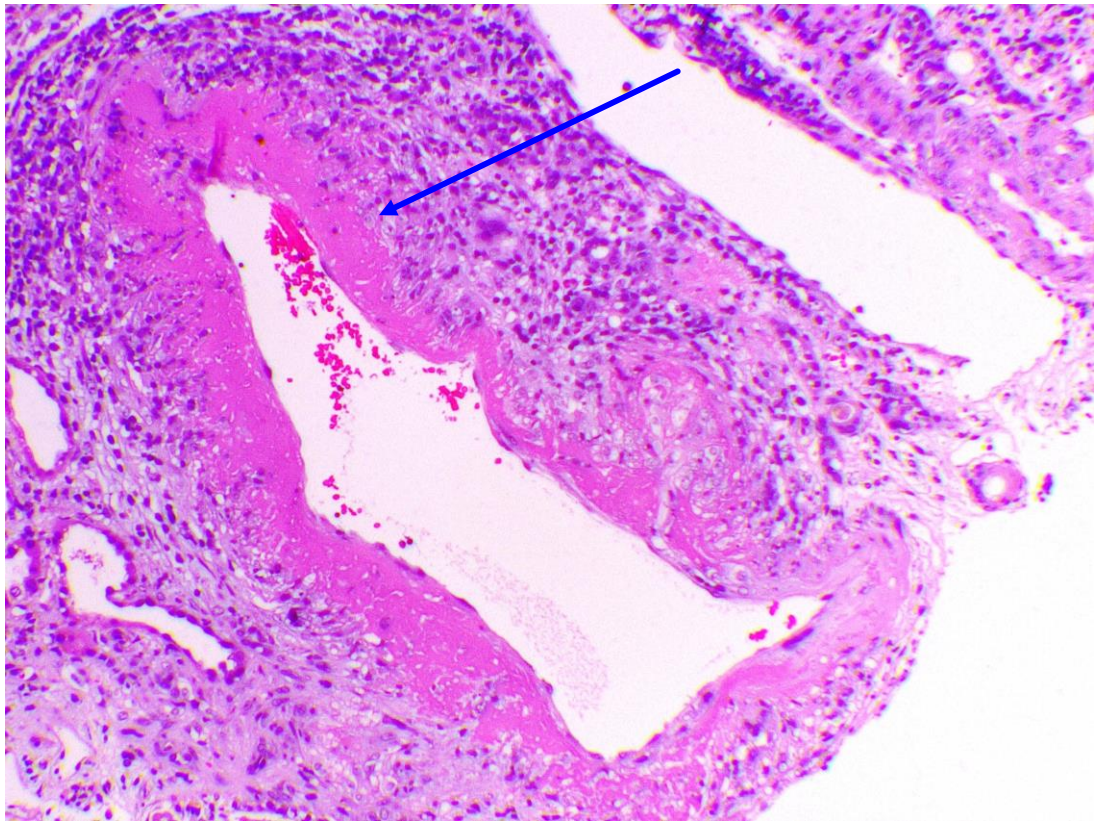


Masson x 200

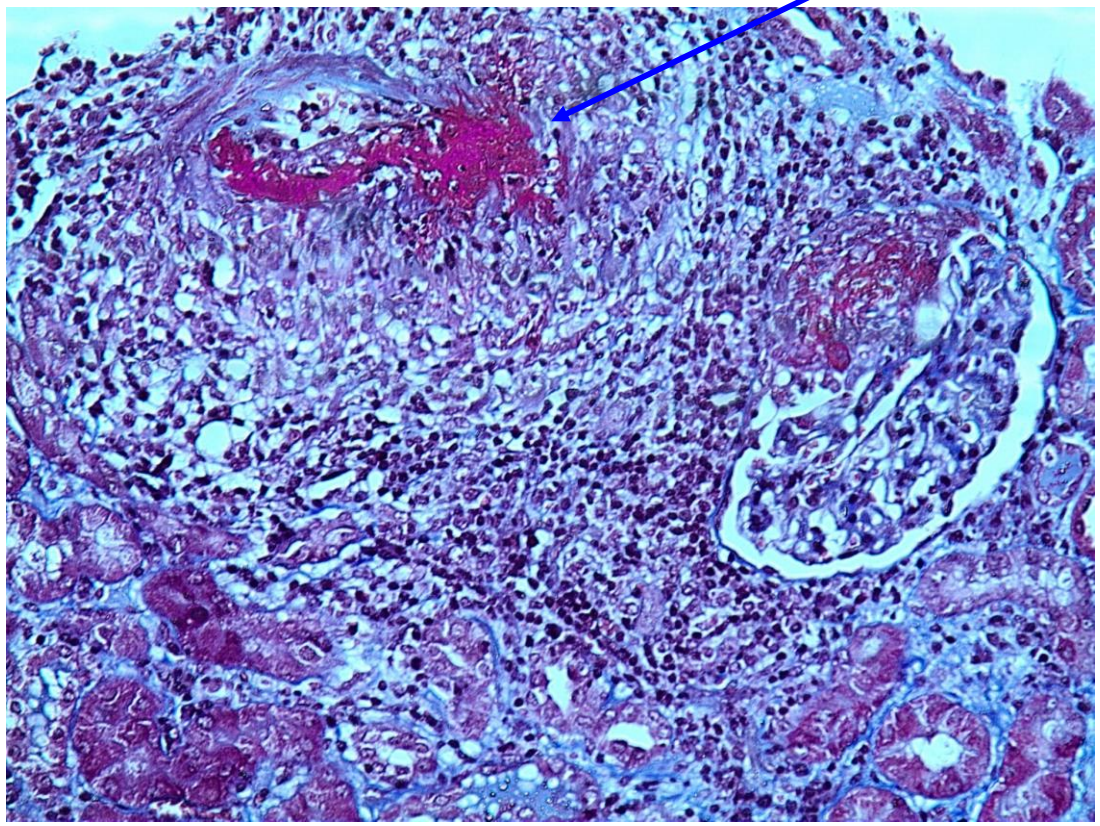
Courtesy of Harikleia Gakiopoulou MD, Aglaia Chalkia MD

Case 2: Renal Biopsy

Necrotizing arteritis



Necrotizing arteritis



Courtesy of Harikleia Gakiopoulou MD, Aglaia Chalkia MD

Case 2: Question-2

- What induction regimen would you use for this patient?
- What about PLEX?

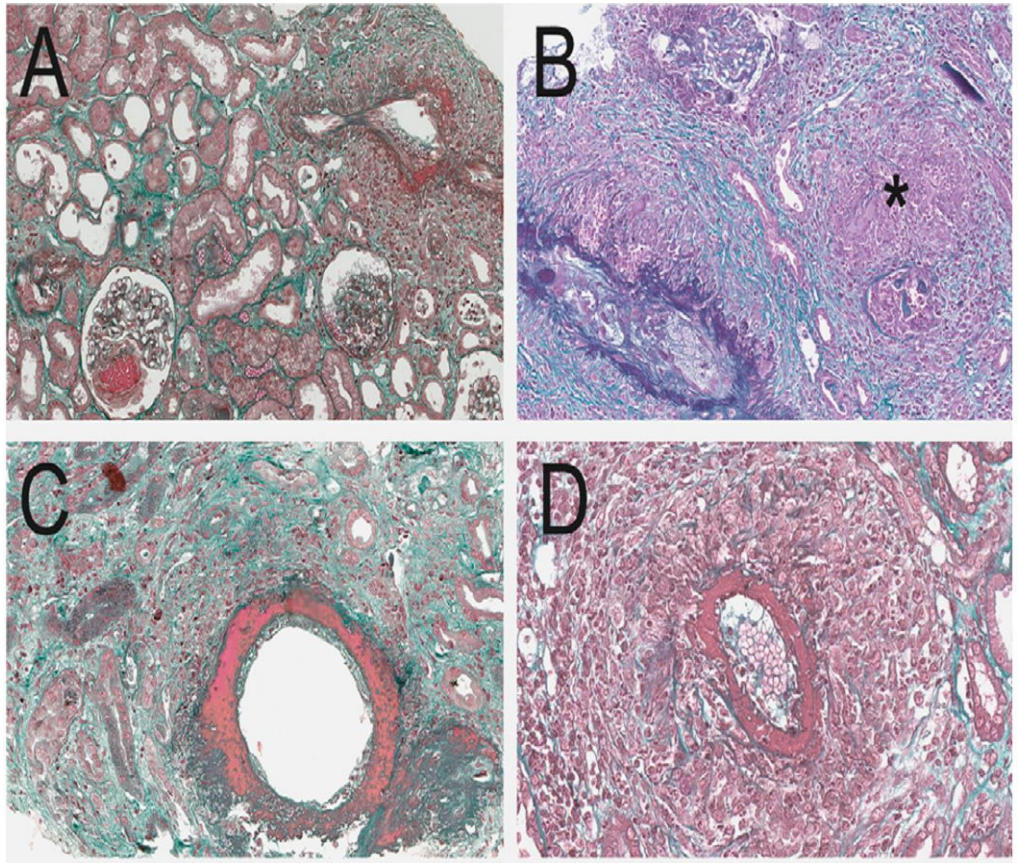
INDUCTION THERAPY : proposal

Severe AKI with sCreat >350 =>

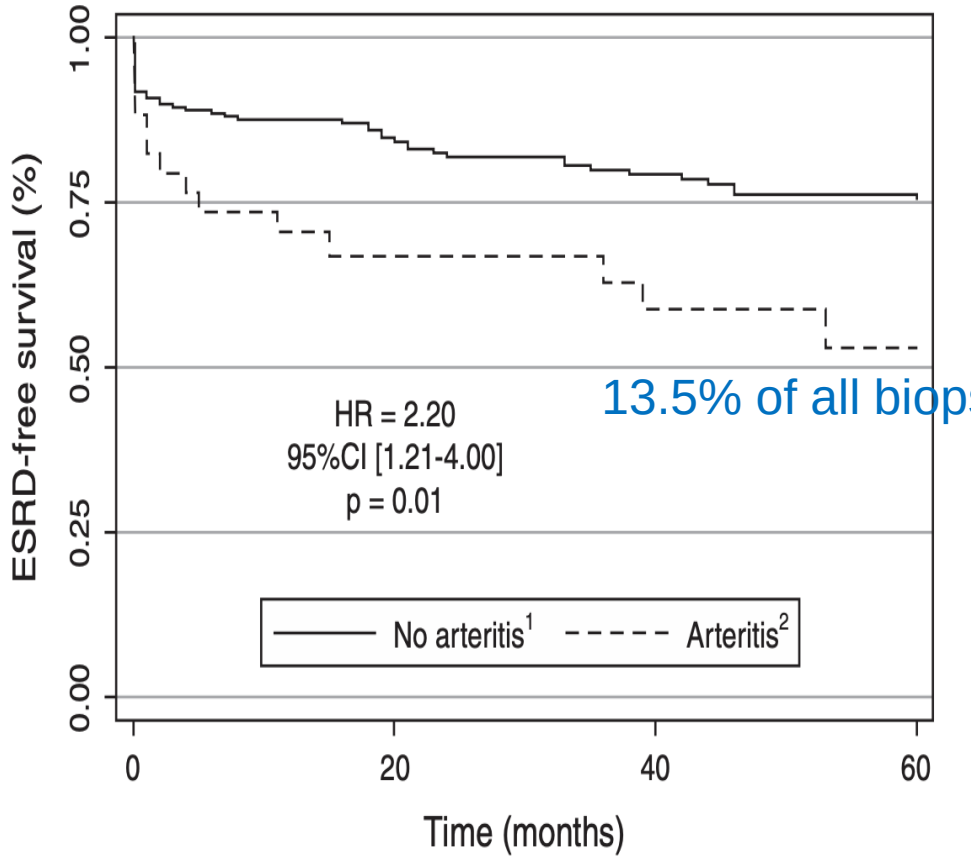
CYC or Combination CYC-RTX

Plasma exchange, based on
sCreat kinetics. (rapidly progressing AKI)
young age of the patient
kidney biopsy findings (non major fibrosis and arteritis)

Reappraisal of Renal Arteritis in ANCA-associated Vasculitis: Clinical Characteristics, Pathology, and Outcome



Arteritis involving the small kidney arteries (interlobular and/or arcuate arteries)



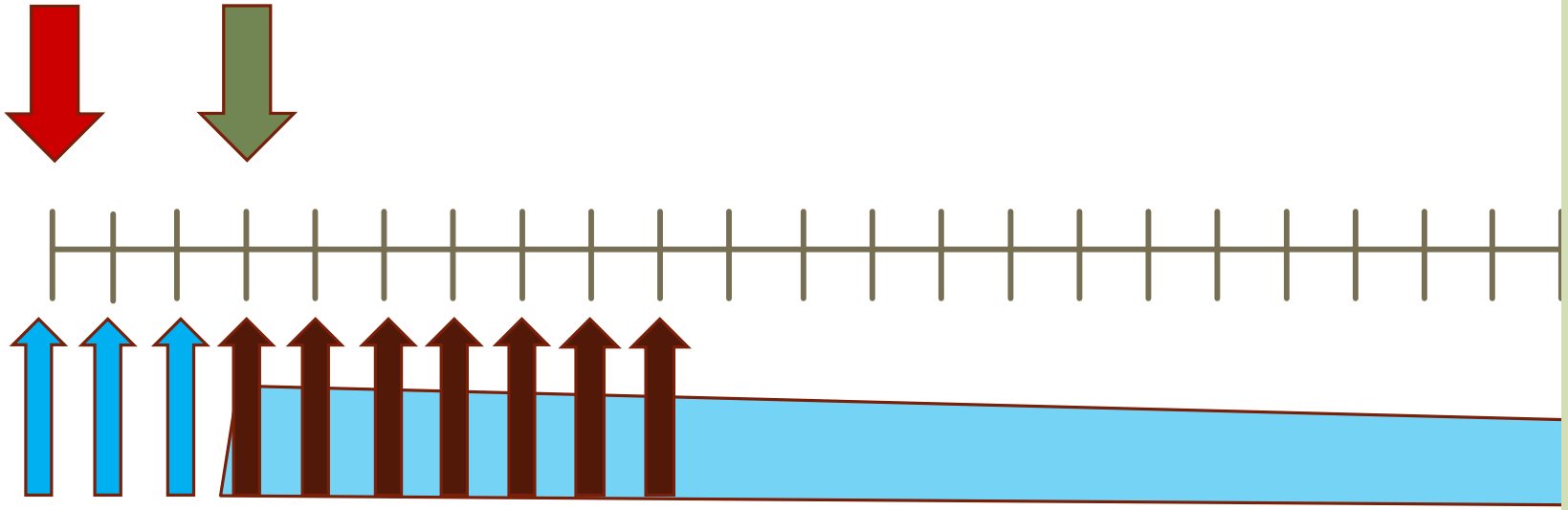
13.5% of all biopsies

Number at risk

Arteritis = 0	217	151	114	90
Arteritis = 1	34	18	15	8

Boudhabhay, Karras JASN 2021

Case 2: Initial management



- **Steroids**
  - IV methylprednisolone 1 gm/day x 3 days
  - Per Os Methylprednisolone (as per PEXIVAS reduced regimen)
- **Combination RTX+CYC**
  - **Rituximab** 1g x2 (14d apart)
  - **CYC** 15mg/kg x 2 (14d apart)
- **PLEX**

  -7 sessions

RTX 1gm

CYC 15mg/kg (1gm)

MethylPred

PLEX

Case 2: further follow up

Notification from the lab
Anti-GBM (+)

Case 2 – Question 3

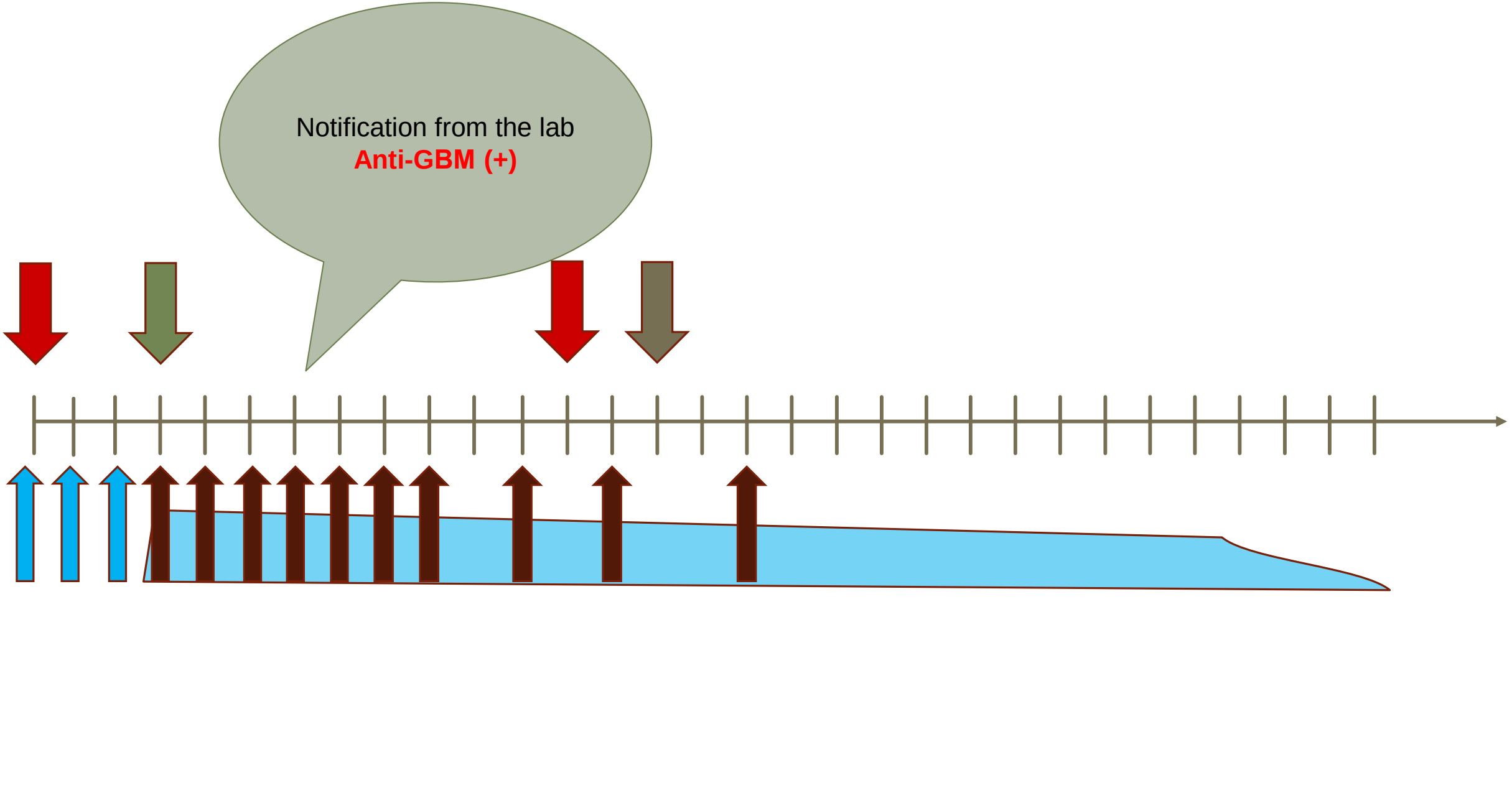
- What would this change to your management?

Case 2: Final diagnosis

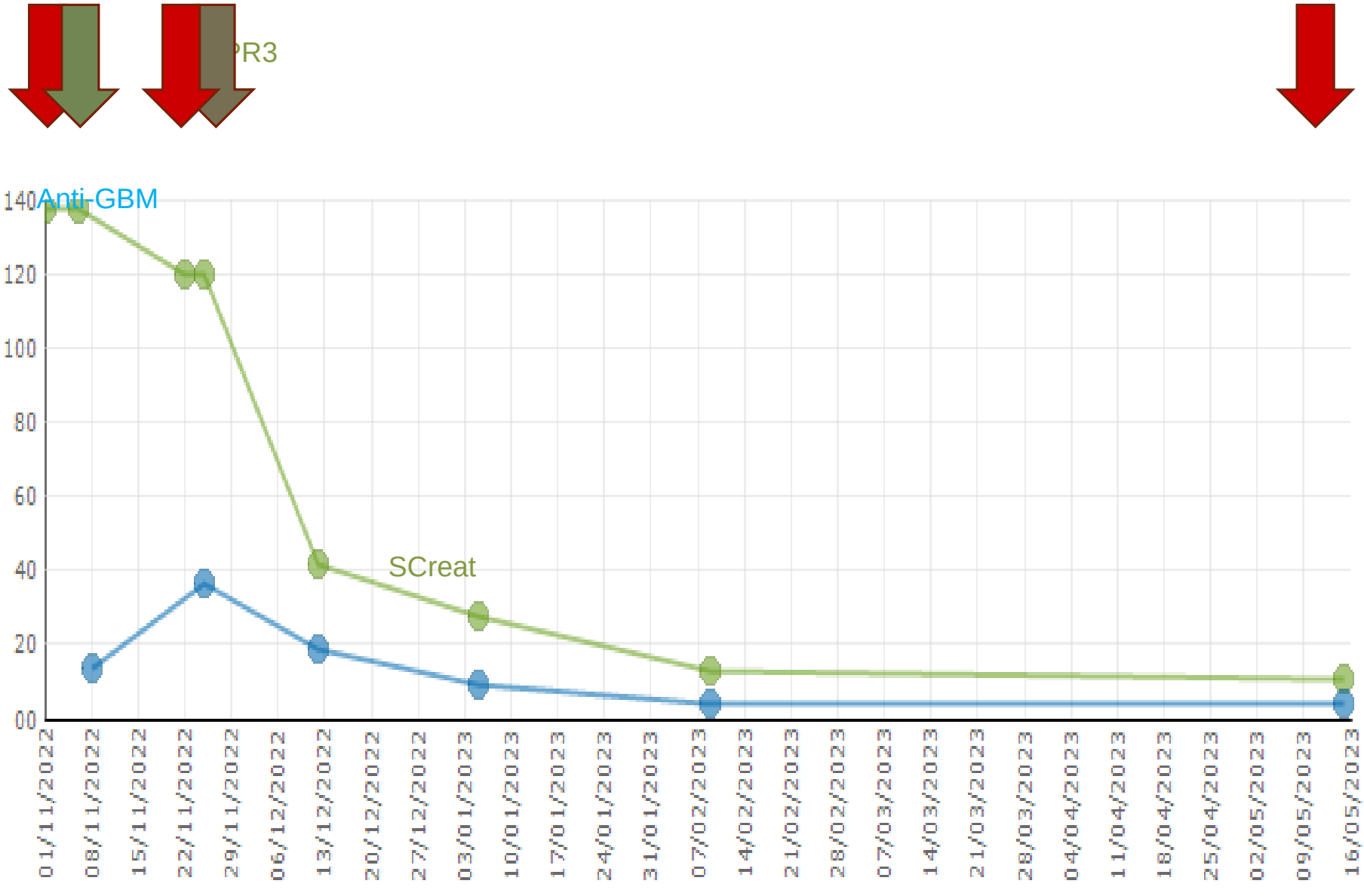
Severe GPA
(Dual positive for PR3-ANCA and anti-GBM) with:

kidney, lung, ENT, musculoskeletal, skin and peripheral nerve involvement

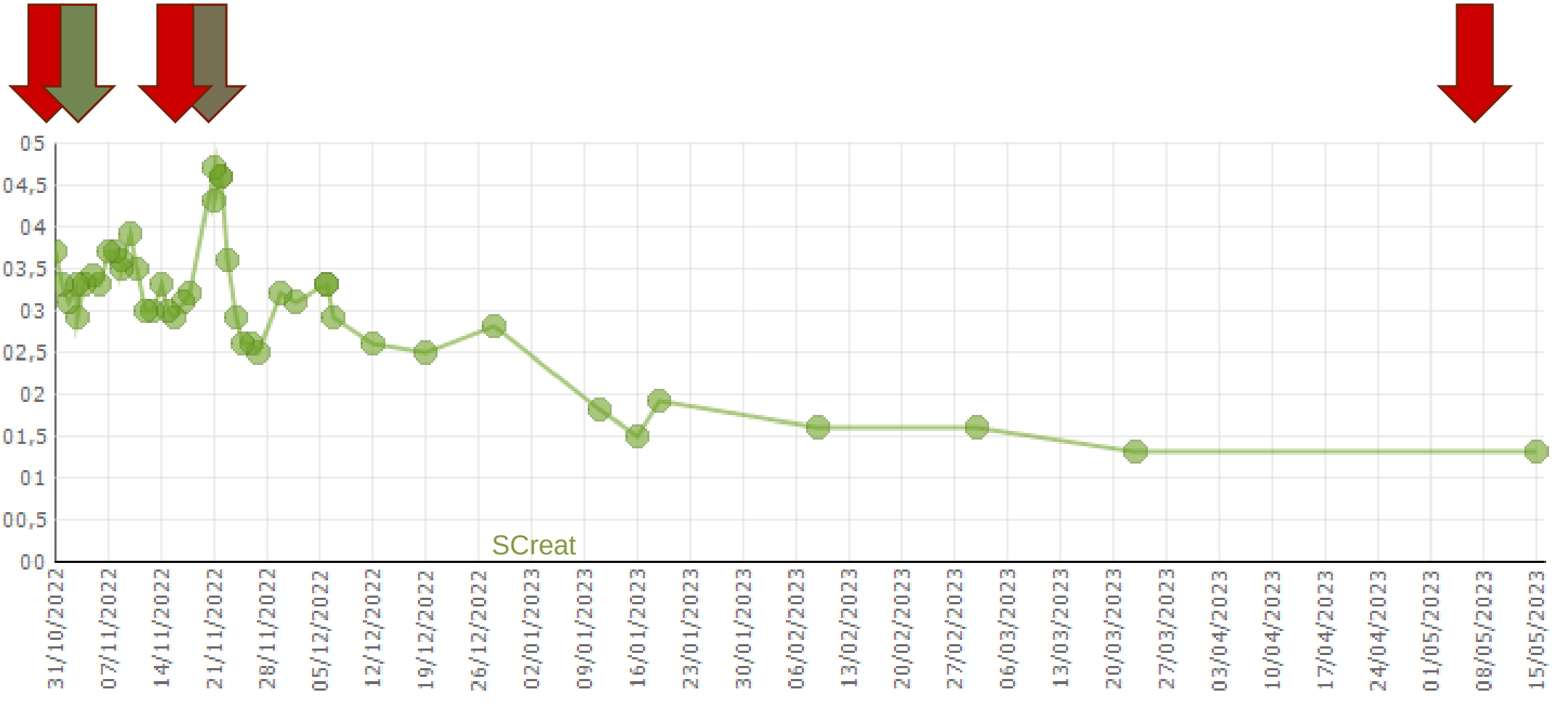
BVAS=28


Notification from the lab
Anti-GBM (+)
RTX 1gm
CYC 15mg/kg (1gm)
MethylPred
PLEX

Case 2: further follow up



Case 2: further follow up



Case 2: Question-3

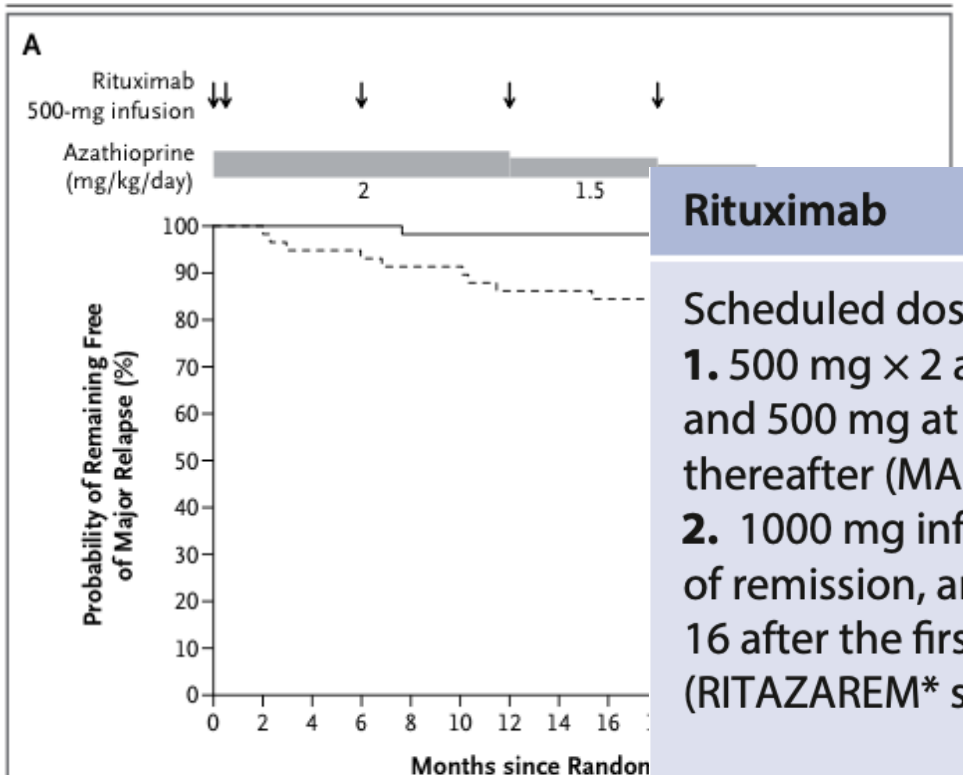
- What maintenance regimen would you use for this patient and for how long?

KDIGO 2024 Clinical Practice Guideline for the Management of Antineutrophil Cytoplasmic Antibody (ANCA)–Associated Vasculitis

Kidney International 2024

Recommendation 9.3.2.1: We recommend maintenance therapy with either rituximab, or azathioprine and low-dose glucocorticoids after induction of remission *(1C)*.

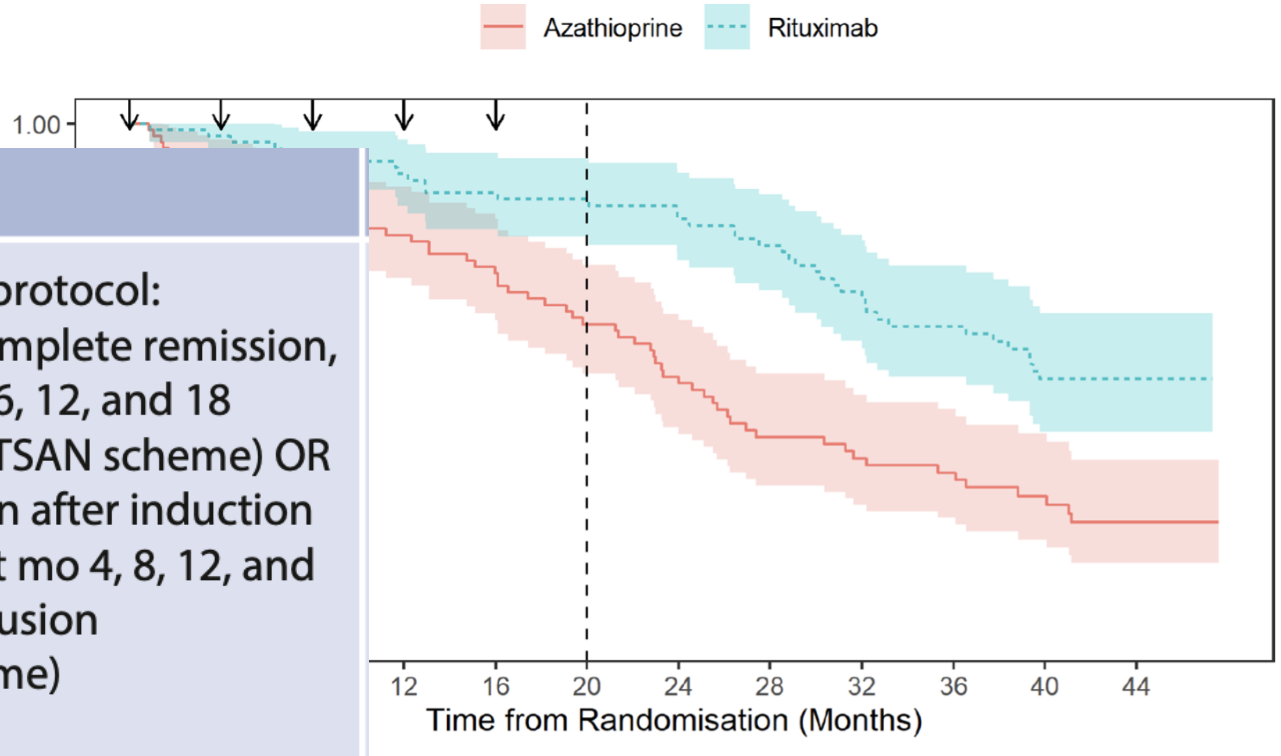
MAINRITSAN Trial Guillevin, NEJM 2014



Rituximab

Scheduled dosing protocol:
1. 500 mg × 2 at complete remission, and 500 mg at mo 6, 12, and 18 thereafter (MAINRITSAN scheme) OR
2. 1000 mg infusion after induction of remission, and at mo 4, 8, 12, and 16 after the first infusion (RITAZAREM* scheme)

RITAZAREM Trial Smith, Ann Rheum Dis 2023



KDIGO 2024 Clinical Practice Guideline for the Management of Antineutrophil Cytoplasmic Antibody (ANCA)–Associated Vasculitis

Kidney International 2024

Recommendation 9.3.2.1: We recommend maintenance therapy with either rituximab, or azathioprine and low-dose glucocorticoids after induction of remission *(1C)*.

Practice Point 9.3.2.2: The optimal duration of remission therapy is between 18 months and 4 years after induction of remission.

Practice Point 9.3.2.3: When considering withdrawal of maintenance therapy, the risk of relapse should be considered, and patients should be informed of the need for prompt attention if symptoms recur (Figure 12).

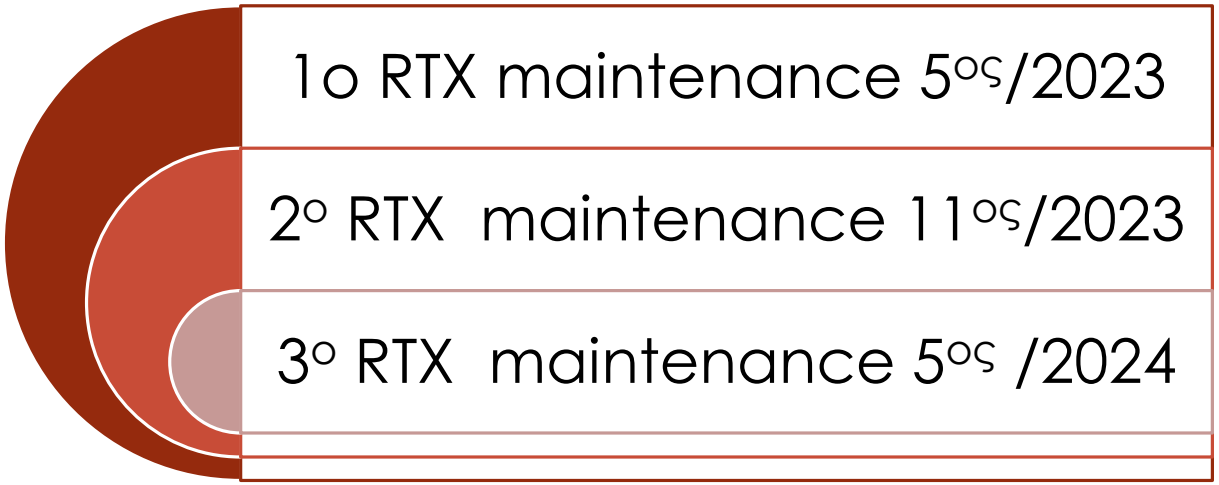
Baseline factors	Factors after diagnosis	Treatment factors
• Diagnosis of granulomatosis with polyangiitis • PR3–ANCA subgroup • Higher serum creatinine • More extensive disease • Ear, nose, and throat disease	• History of relapse • ANCA positive at the end of induction • Rise in ANCA	• Lower cyclophosphamide exposure • Immunosuppressive withdrawal • Glucocorticoid withdrawal

Figure 12 | Factors that increase relapse risk for AAV. AAV, ANCA-associated vasculitis; ANCA, antineutrophil cytoplasmic antibody; PR3, proteinase 3.

Maintenance treatment

RITUXIMAB
1gr/6mo

+ RASi



- Stable/normal renal function (eGFR:79 mL/min/1.73m2)
- Haematuria (-)
- PR3-ANCA (-)
- Anti-GBM (-)

Acknowledgements

Rheumatologists:
Dimitrios Vassilopoulos, Christos Koutsianas, Christina Tsalapaki

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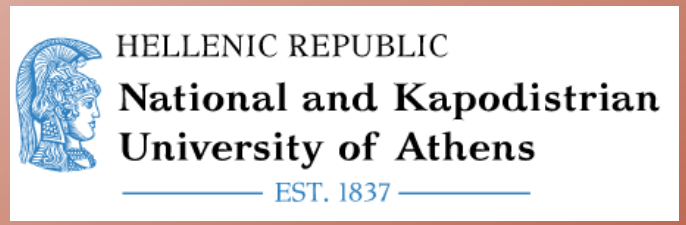
Pathologist:
Harikleia Gakiopoulou



Final points