بسم الله الرحمن الرحيم

Eosinophilic granulomatosis with polyangiitis (EGPA) management

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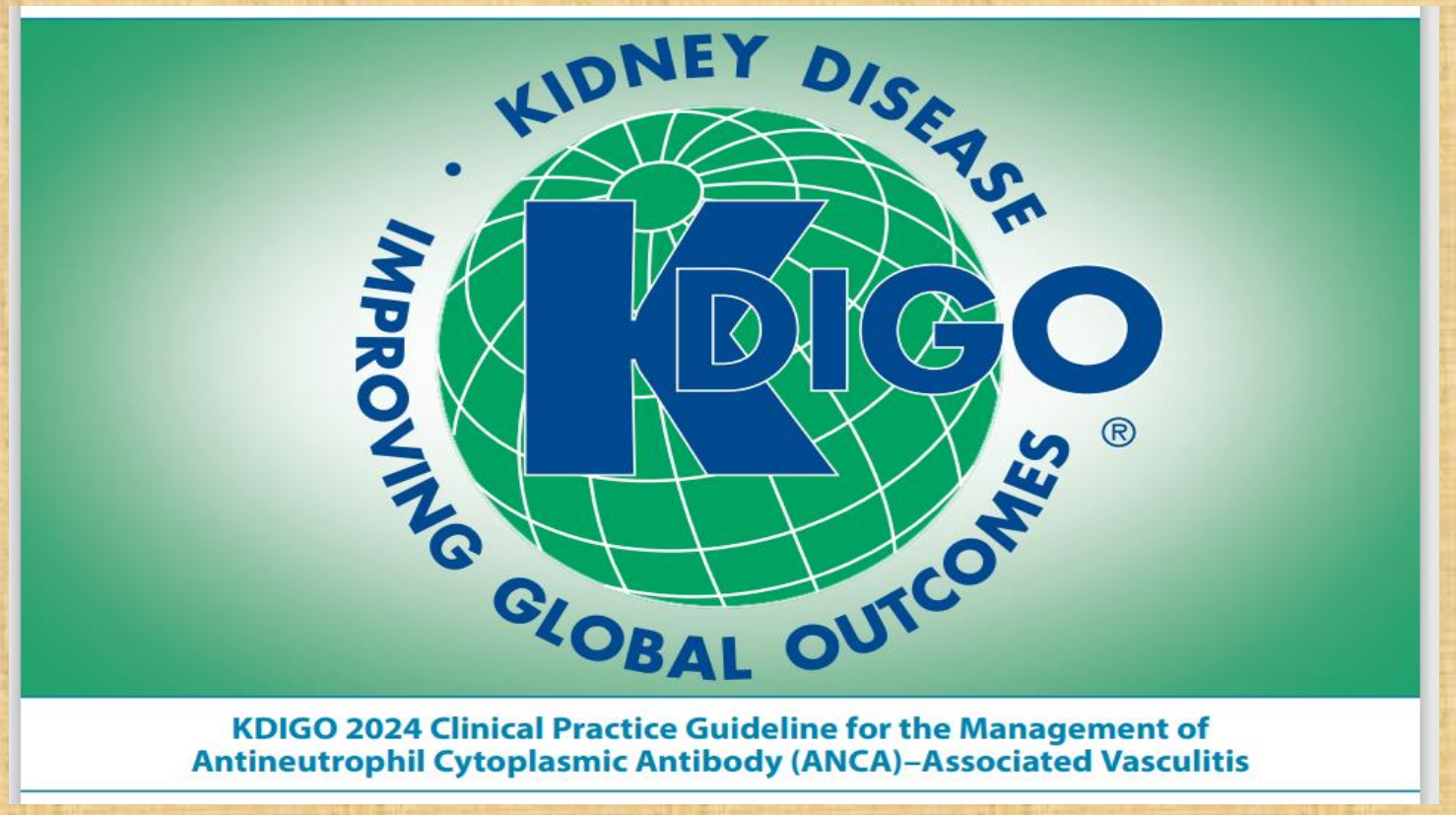


Recommendation

EULAR recommendations for the management of ANCA-associated vasculitis: 2022 update

2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Antineutrophil Cytoplasmic Antibody–Associated Vasculitis

INTRODUCTION

- **Multisystem manifestations**: asthma, chronic rhinosinusitis with or without polyposis, pulmonary involvement, eosinophilia .

- Vasculitis of the small and medium sized arteries.
- The most commonly involved organ : **lung**
  - vasculitis of extrapulmonary ⟹ the morbidity and mortality.
- Rapid onset of remission (organ-threatening manifestations), Maintain a long remission, Minimize complications of TX

ASSESSING VASCULITIS SEVERITY

- Active GN, pul hemorrhage, cerebral vasculitis, progressive peripheral or cranial neuropathy, GIB, pericarditis, myocarditis

- Five-factor score (FFS) :

  This scoring system has also been **correlated with prognosis**.

  The presence of each factor is given one point.

NOTE:

1996 five-factor score[1]	Revised 2011 five-factor score[2]
Cardiac involvement	Age >65 years
Gastrointestinal disease (bleeding, perforation, infarction, or pancreatitis)	Cardiac insufficiency
Renal insufficiency (plasma creatinine concentration >1.6 mg/dL [141 mmol/L])	Renal insufficiency (stabilized peak creatinine 1.7 mg/dL [150 micromol/L])
Proteinuria (>1 g/day)	Gastrointestinal involvement
Central nervous system involvement	Absence of ENT manifestations (presence is associated with a better prognosis)

REMISSION INDUCTION

- Prednisone 0.5 to 1 mg/kg (up to 80 mg) /day .
- Higher dose: more severe vasculitis (respiratory failure, cardiac involvement, GN, neuropathy).
- Acute multiorgan disease: MP 500 to 1000 mg/d 3-5 d, followed by oral glucocorticoid
- Most EGPA, who do not have poor prognostic factors, achieve a remission with glucocorticoid alone, although relapses..?!!!
- Pts with involvement of the heart, kidney, GI tract, CNS usually require additional immunosuppressive tx.

Severe EGPA :

For patients with severe EGPA and organ or life-threatening disease manifestations as defined by the American College of Rheumatology/Vasculitis Foundation (ACR/VF) guidelines :

Cyclophosphamide or Rituximab in the remission induction regimen rather than glucocorticoids alone, in agreement with the ACR/VF guidelines .

Choice of agent

- Preference for **cyclophosphamide** :
- active cardiac involvement .
- (ANCA)-negative and severe neurologic or GI manifestations.

- Preference for **rituximab** :

positive ANCA, active GN, prior CYC tx, risk for gonadal toxicity .

Cyclophosphamide

- (FFS) of 2 or greater
- Orally (1.5 to 2 mg/kg /day for 3-6 months) or IV (15 mg/kg every 2 weeks for 3 doses and then every 3 weeks for at least 3 doses.

- Outcomes with daily and monthly regimens are similar.

six pulses of cyclophosphamide

Rituximab

- 375 mg/mm IV weekly for 4 doses or 1000 mg IV on days 1&15.

- Majority of the EGPA patients treated with rituximab achieved **remission** (80 percent partial and complete remission rate) !!

Non severe EGPA:

- Rhinosinusitis, asthma, eosinophilic pneumonia or transient eosinophilic pulmonary infiltrates, and mild systemic disease (uncomplicated cutaneous) manifestations
- **adding mepolizumab or benralizumab to systemic glucocorticoids**

- Anti-IL-5 or anti-IL-5R agents:
- Mepolizumab : 300 mg every four weeks
- Benralizumab : 30 mg subcutaneously every four weeks

Alternative induction regimens:

- (FFS of 1, but mild non organ-threatening disease) :
- initial tx with glucocorticoids plus AZT, MTX, MMF .
- These agents are preferred over cyclophosphamide or rituximab.

- MTX :15 mg/wk orally/sc, incr 2-8 wks of 5 mg/wk up to 25 mg/wk
- AZT: initiated at a dose of 50 mg/day….
- MMF : 750 -1500 mg orally twice daily (1.5 to 3 g daily).

REMISSION MAINTENANCE:(12 to 18 months)

- Glucocorticoid dosing and taper :(≤10 mg/d!!!)

gradually tapered over variable time ranging from 3 to 18 months

For patients who received mepolizumab or benralizumab…continuing those agents.

For patients who achieved MTX,AZT, MMF…continuation of that agent

severe EGPA:

- If CYC for induction…**transition to an alternative** maintenance agent. (2-4 weeks after the last dose of cyclophosphamide).

- If rituximab…. to **continue rituximab** …. 500 to 1000 mg IV every 4-6 months…redosing based on a schedule rather than based on ANCA levels.

Ig levels should be checked **prior to each course**.

LESS COMMON THERAPIES:

- Leflunomide: remission maintenance…10-30 mg/d(glucocorticoid-sparing agent)
- Anti-IgE therapy: omalizumab

- Hydroxyurea :glucocorticoid-sparing agent!!!!

- IVIG: in patients with refractory disease
- Plasma exchange: RPGN or DAH
- Interferon-alpha: if unresponsive to glucocorticoids and CYC

MONITORING:

- following symptoms,EOS count, PFT, **any previously abnormal** lab parameters.
- Radiographic manifestations **may** remain stable or may rapidly regress with glucocorticoid treatment.
- Kidney : urinalysis and creatinine….at **3 month intervals**, sooner if they experience any change in clinical status.
- Persistence of (ANCA) positivity in EGPA : **cannot be used** by itself to determine changes in therapy.

Pregnancy:

- Rare during the child-bearing years.
- fetal death rate may be slightly increased.
- adverse fetal effects of immunosuppressive medications.
- cyclophosphamide -AZT are teratogenic and MTX is an abortifacient.
- Systemic glucocorticoids are relatively safer, but may not control active vasculitis

PROGNOSIS:

- Improved significantly since the use of systemic agents.
- Much improved survival rate (70 to 90 percent at five years).
- Most deaths result from :

  CHF or MI

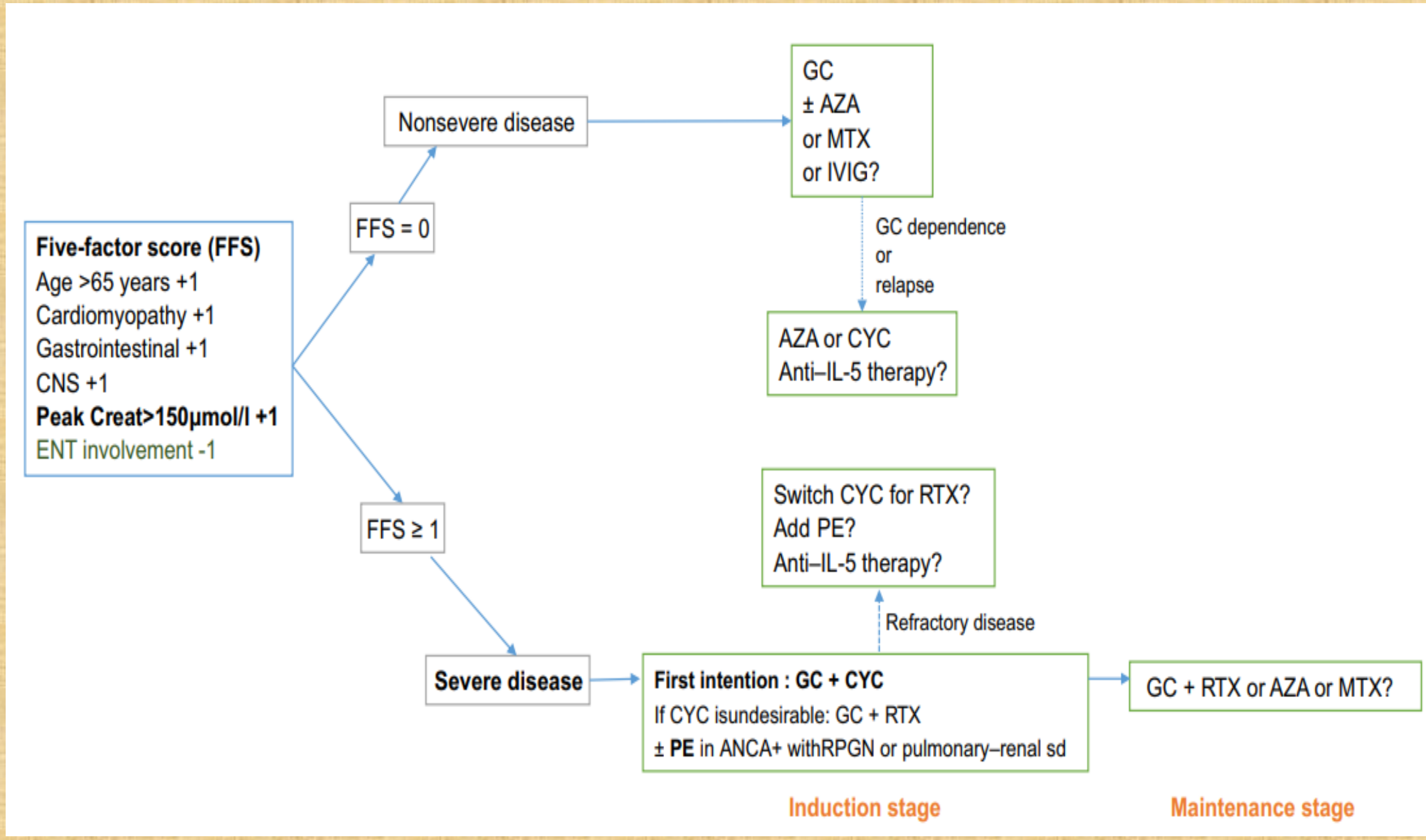
  Cerebral hemorrhage

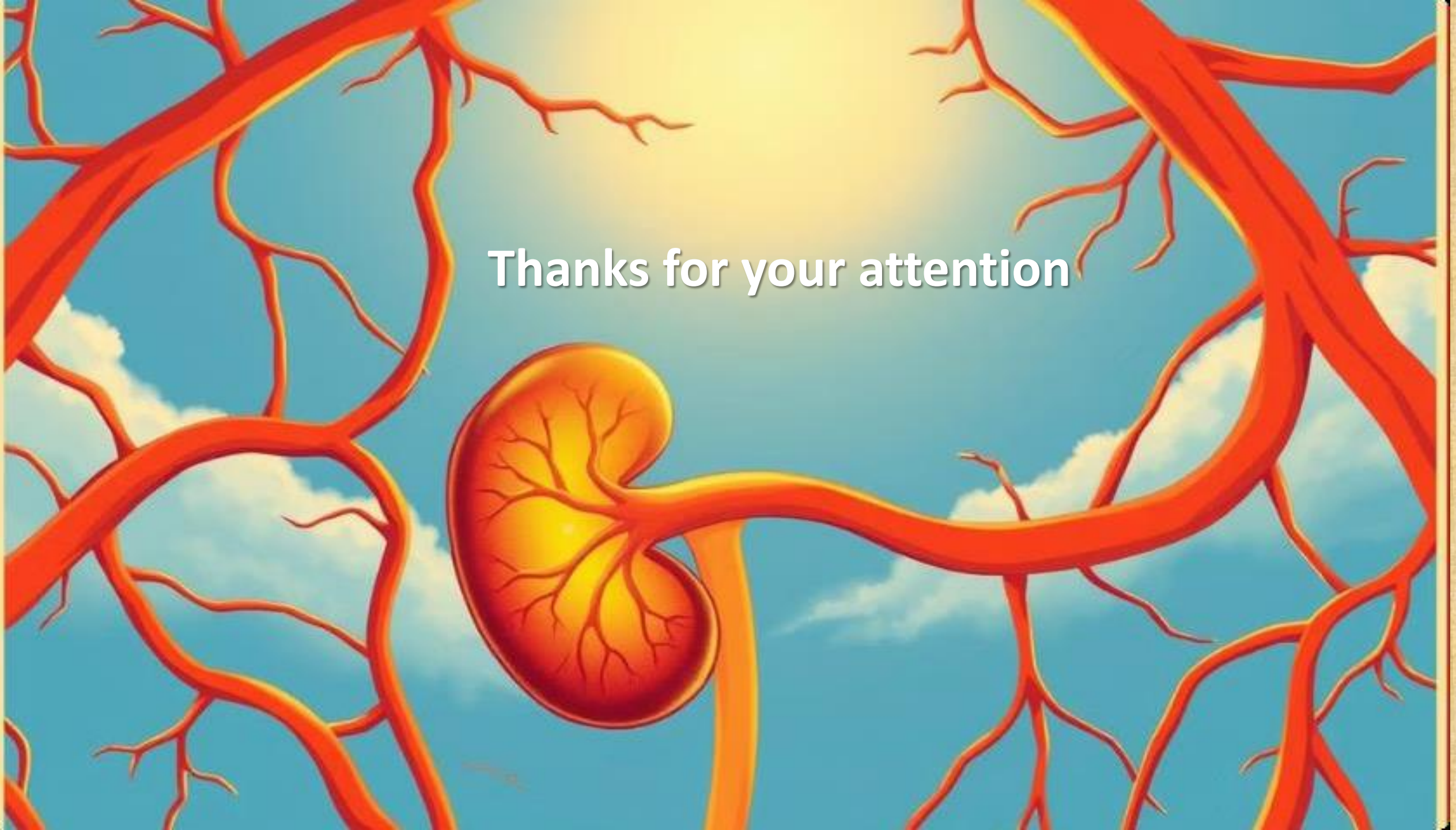
  Renal failure

  GIB

  Status asthmaticus

cardiac involvement, GI disease, age ≥65 :the strongest indicators of poor prognosis


Five-factor score (FFS)
Age >65 years +1
Cardiomyopathy +1
Gastrointestinal +1
CNS +1
Peak Creat>150µmol/l +1
ENT involvement -1
FFS = 0
Nonsevere disease
GC
± AZA
or MTX
or IVIG?
GC dependence
or
relapse
AZA or CYC
Anti–IL-5 therapy?
FFS ≥ 1
Severe disease
Switch CYC for RTX?
Add PE?
Anti–IL-5 therapy?
Refractory disease
First intention : GC + CYC
If CYC isundesirable: GC + RTX
± PE in ANCA+ withRPGN or pulmonary–renal sd
GC + RTX or AZA or MTX?
Induction stage
Maintenance stage


Thanks for your attention