Review in Internal Medicine 2025

Common Rheumatologic Disease Consultation

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PMK
RHEUMATOLOGY

Scenario 1

- A 29-year-old SLE patient is planning to have a baby.
- She has been in clinical remission for 12 months.
- She takes mycophenolate mofetil (MMF) and hydroxychloroquine (HCQ).

What is your recommendation?

Scenario 2

- The SLE patient from SCENARIO 1 has delivered a baby.
- She has active lupus nephritis.
- Treatment was changed to MMF and 30 mg prednisolone (PRED).

What is your recommendation during feeding her baby?

Arthritis Care & Research
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American College of Rheumatology
Empowering Rheumatology Professionals

2020 American College of Rheumatology Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases

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Table 3. Maternal medication use: overview of medication use before and during pregnancy, and during breastfeeding

Medication	Pre-conception	During pregnancy	Breastfeeding
Conventional medications			
Hydroxychloroquine	++	++	++
Sulfasalazine	++	++	++
Colchicine	++	++	++
Azathioprine, 6-mercaptopurine	++	++	+ Low transfer
Prednisone	+ Taper to <20 mg/day by adding pregnancy-compatible immunosuppressants	+ Taper to <20 mg/day by adding pregnancy-compatible immunosuppressants	+ After a dose of >20 mg, delay breastfeeding for 4 hours
Cyclosporine, tacrolimus	+ Monitor blood pressure	+ Monitor blood pressure	+ Low transfer
Nonsteroidal antiinflammatory drugs (cyclooxygenase 2 inhibitors not preferred)	+ Discontinue if the woman is having difficulty conceiving	+ Continue in first and second trimesters; discontinue in third trimester	+ Ibuprofen preferred

Table 3. Maternal medication use: overview of medication use before and during pregnancy, and during breastfeeding

Medication	Pre-conception	During pregnancy	Breastfeeding
Not compatible with pregnancy			
Methotrexate	✕✕ Stop 1–3 months prior to conception	✕✕ Stop and give folic acid 5 mg/day	✕ Limited data suggest low transfer
Leflunomide	✕✕ Cholestyramine washout if detectable levels	✕✕ Stop and give cholestyramine washout	✕✕
Mycophenolate mofetil and mycophenolic acid	✕✕ Stop >6 weeks prior to conception to assess disease stability	✕✕	✕✕
Cyclophosphamide	✕✕ Stop 3 months prior to conception	+ Life-/organ-threatening disease in second and third trimesters	✕✕
Thalidomide	✕✕ Stop 1–3 months prior to conception	✕✕	✕✕
Tofacitinib, apremilast, baricitinib	Unable to determine due to lack of data; small molecular size suggests transfer across the placenta and into breast milk		

Scenario 3

- She is in active lupus nephritis.
- She takes MMF, HCQ, and PRED
- The SLE patient seeking contraception counseling.
- Lupus anticoagulant is positive (2 tests, 12-week time).

What is your recommendation for contraceptive method?

Safety and efficacy of various contraceptive methods in RMD

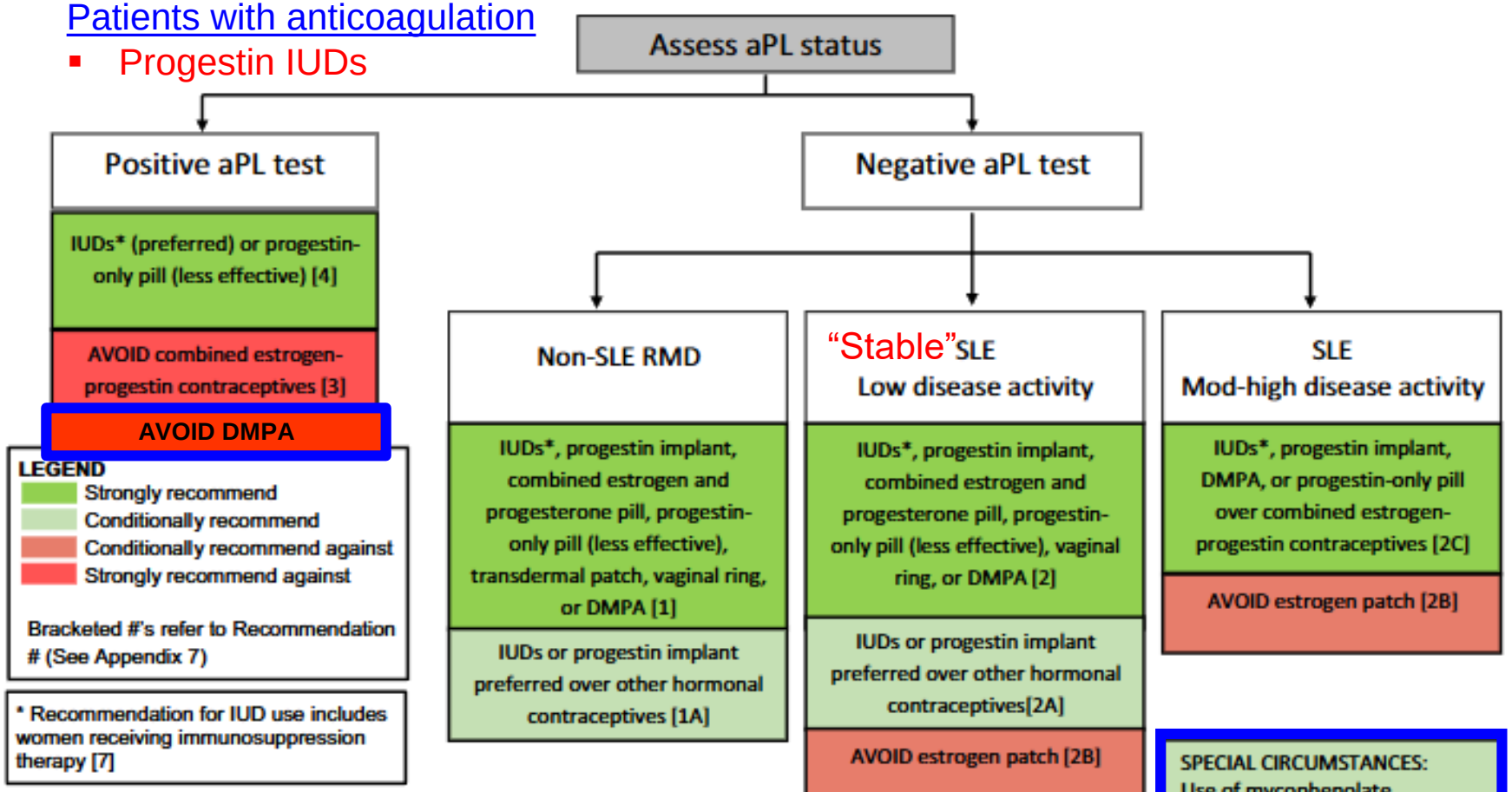
Method	Safety in women with RMD	1-year failure rate, %†
Highly effective (LARC)		
Copper IUD	Safe in all women with RMD; may increase menstrual bleeding	<1
Progestin IUD	Safe in all women with RMD; may decrease menstrual bleeding	<1
Progestin implant	Limited data, but likely safe in all women with RMD	<1
Effective		
Progestin-only pill (daily)	Safe in all women with RMD; higher rate of breakthrough bleeding than with combined contraceptives; must take same time every day for efficacy	5–8
DMPA (IM injection every 12 weeks)	Safe in most women with RMD; exceptions: positive aPL, at high risk for OP	3
Combined estrogen and progesterone pill (daily)	Safe in most women with RMD; exceptions: positive aPL, very active SLE	5–8
Transdermal patch (weekly)	Safe in most women with RMD; exceptions: positive aPL, SLE; serum estrogen levels higher than with pill or vaginal ring	5–8
Vaginal ring (monthly)	Safe in most women with RMD; exceptions: positive aPL, very active SLE	5–8
Less effective		
Diaphragm	Safe in all women with RMD	12
Condom	Safe in all women with RMD; only form to prevent STD	18
Fertility awareness–based methods‡	Safe in all women with RMD; limited efficacy, especially if menses are irregular	24
Spermicide	Safe in all women with RMD; use with condoms or diaphragm to improve efficacy	28

* RMD = rheumatic and musculoskeletal disease; LARC = long-acting reversible contraception; IUD = intrauterine device; DMPA = depot medroxyprogesterone acetate; IM = intramuscular; aPL = antiphospholipid antibody; OP = osteoporosis; SLE = systemic lupus erythematosus; STD = sexually transmitted disease.
† Percent of women who will become pregnant within the first year of typical use.
‡ Methods based on the timing of the menstrual cycle.

Discuss contraception and pregnancy planning at initial or early visit with women of reproductive age and counsel regarding efficacy and safety [GPS]. Recommend barrier methods if more effective methods are contraindicated [GPS]. Recommend emergency (post-coital) contraception when necessary [6].

Patients with anticoagulation

- Progestin IUDs



aPL test should be performed

- SLE or SLE-like disease
- Patients with suggestive histories or physical findings

"Positive aPL"

Persistent and mod-high titer

- 2 positive test results at least 12 weeks apart *plus*
- Moderate-high–titer aCL/anti-β2GPI (≥40 units)
- Positive LAC

DMPA = Depot Medroxyprogesterone Acetate
LNG = Levonorgestrel

Scenario 4

- The SLE patient is planning to visit Africa.
- She requires Yellow fever vaccination.
- She takes 2 gm/d MMF and HCQ.
- She is in disease remission for 1 year.

What is your recommendation?

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American College of Rheumatology
Empowering Rheumatology Professionals

2022 American College of Rheumatology Guideline for Vaccinations in Patients With Rheumatic and Musculoskeletal Diseases

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Medication management at the time of non–live attenuated vaccine administration

	Influenza vaccination	Other non–live attenuated vaccinations
Methotrexate	Hold methotrexate for 2 weeks *after* vaccination*	Continue methotrexate
Rituximab	Continue rituximab†	Time vaccination for when the next rituximab dose is due, and then hold rituximab for at least 2 weeks after vaccination
Immunosuppressive medications other than methotrexate and rituximab	Continue immunosuppressive medication	Continue immunosuppressive medication

□ = Conditional recommendation.
* Hold only if disease activity allows. Non-rheumatology providers, e.g., general pediatricians and internists, are encouraged to give the influenza vaccination and then consult with the patient's rheumatology provider about holding methotrexate to avoid a missed vaccination opportunity.
† Give influenza vaccination on schedule. Delay any subsequent rituximab dosing for at least 2 weeks after influenza vaccination if disease activity allows.

Influenza vaccination

For patients with RMD age ≥65 years and patients with RMD age>18 years and <65 years who are taking immunosuppressive medication

- Giving high-dose or adjuvanted influenza vaccination is conditionally recommended over giving regular-dose influenza vaccination.

Table 4. Whether to give or defer non–live attenuated vaccinations in patients taking glucocorticoids regardless of disease activity

	Influenza vaccination	Other non–live attenuated vaccinations
Prednisone ≤10 mg daily*	Give	Give
Prednisone >10 mg and <20 mg*	Give	Give
Prednisone ≥20 mg daily*	Give	Defer†

■ = Strong recommendation.
□ = Conditional recommendation.
* Or the equivalent dose of any other glucocorticoid formulation, or the equivalent pediatric dose.
† Defer vaccination until glucocorticoids are tapered to the equivalent of prednisone <20 mg daily.

Immunosuppressive agent management at the time of live attenuated virus vaccine administration

	Hold before live attenuated virus vaccine administration	Hold after live attenuated virus vaccine administration
Glucocorticoids†	4 weeks	4 weeks
Methotrexate, azathioprine‡	4 weeks	4 weeks
Leflunomide, mycophenolate mofetil, calcineurin inhibitors, oral cyclophosphamide	4 weeks	4 weeks
JAK inhibitors	1 week	4 weeks
TNF, IL-17, IL-12/23, IL-23, BAFF/BLyS inhibitors	1 dosing interval§	4 weeks
IL-6 pathway inhibitors	1 dosing interval¶	4 weeks
IL-1 inhibitors		
Anakinra	1 dosing interval¶	4 weeks
Rilonacept	1 dosing interval¶	4 weeks
Canakinumab	1 dosing interval¶	4 weeks
Abatacept	1 dosing interval§	4 weeks
Anifrolumab	1 dosing interval§	4 weeks
Cyclophosphamide, intravenous	1 dosing interval§	4 weeks
Rituximab	6 months	4 weeks
IVIG#		
300–400 mg/kg	8 months	4 weeks
1 gm/kg	10 months	4 weeks
2 gm/kg	11 months	4 weeks

Live attenuated virus vaccine

- Measles, mumps, rubella (MMR vaccine)
- Varicella zoster (chickenpox and shingles)
- Influenza (nasal spray)
- Oral polio, oral typhoid, and influenza
- Rotavirus
- Yellow fever

The AAP Red Book and the Infectious Diseases Society of America define low-level immunosuppression as

1. Methotrexate ≤0.4 mg/kg/week
2. Azathioprine ≤3 mg/kg/day
3. Prednisone <20 mg/day

Scenario 5

- After she came back from Africa, she had APS (LA+) due to DVT left leg 6 months ago.
- She is on warfarin 5 mg a day with INR level of 2.6, MMF and HCQ.
- She consulted for 10 weeks of pregnancy.
- Her lupus activity was remission for a year.
- Her actual body weight is 60 kgs.

What is the appropriate management of APS ?

HCQ 5 mg/kg/day (< 400 mg/day)

HCQ ≥ 400 mg/day in 1st trimester pregnancy and risk of birth defects (RR was 1.33; 95% CI, 1.08 – 1.65)

Am J Obstet Gynecol. 2021

"PATCH Study"

HCQ 400 mg/d reduced the recurrence of CHB by >50%.

J Am Coll Cardiol 2020

The ASPRE trial (RCT)

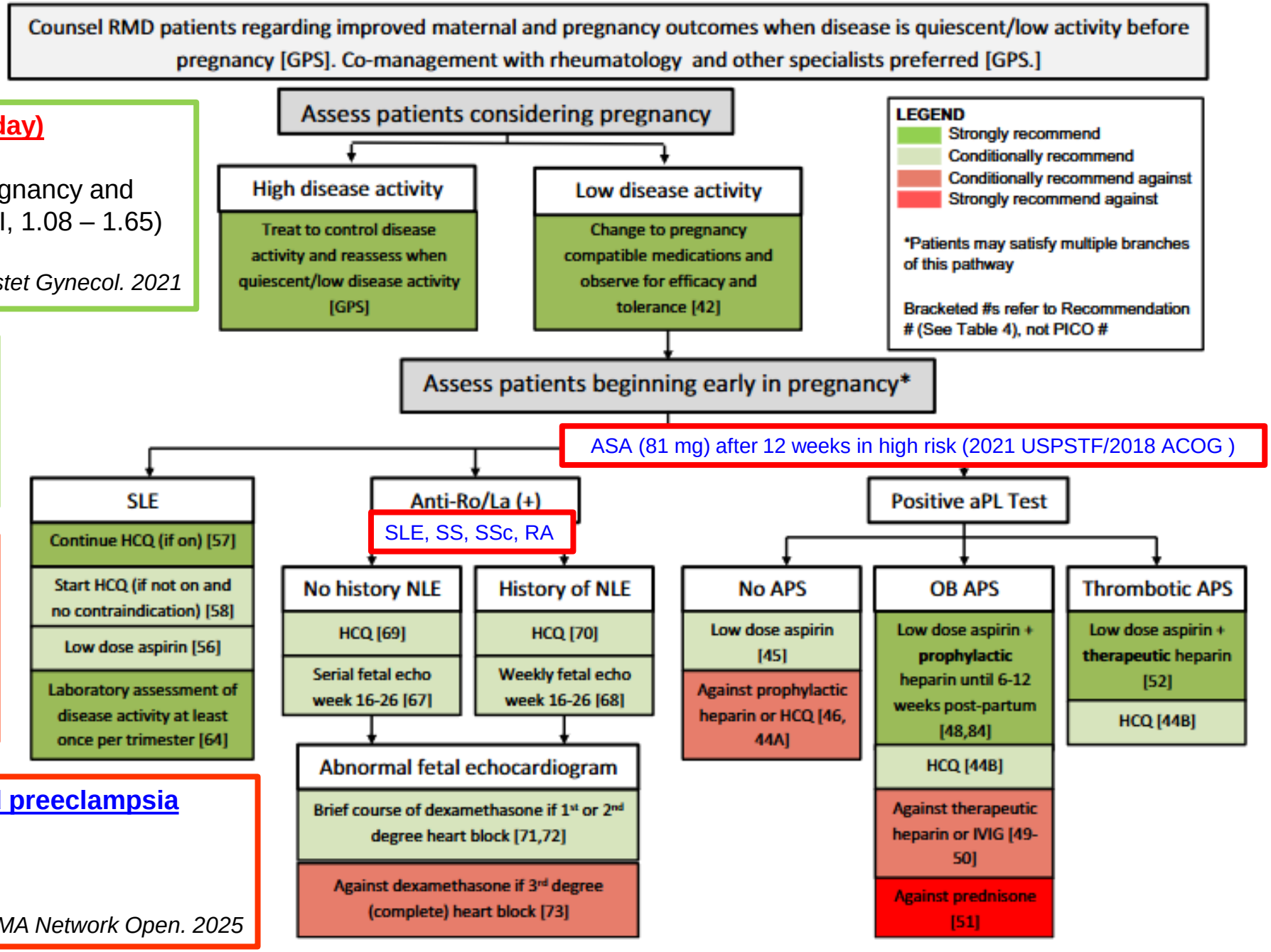
150 mg ASA vs PBO in women at high risk for preterm preeclampsia (OR, 0.38; p=0.004).

N Engl J Med 2017

ASA Cohort of 13,828 women developed preeclampsia

150 to 160 mg vs 75 mg ASA (aRR, 1.07; 95% CI, 0.93-1.24)

JAMA Network Open. 2025



2019 EULAR recommendations for the management of obstetric APS

Clinical circumstance	Recommendation
History of obstetric APS only • ≥ 3 recurrent spontaneous abortion < 10th week of gestation • Fetal loss ≥ 10th weeks of gestation	Low-dose ASA (75-100 mg/day) *and* heparin at prophylactic dosage during pregnancy and continue heparin for 6 weeks after delivery
History of obstetric APS only • One or more new born premature delivery < 34 weeks of gestation due to severe preeclampsia or recognized placental insufficiency	Low-dose ASA (75-100 mg/day) *or* Low-dose ASA (75-100 mg/day) and heparin at prophylactic dosage during pregnancy and continue heparin for 6 weeks after delivery Based on individual's risk profile
"Non-criteria" obstetric APS	Low-dose ASA (75-100 mg/day) *or* Low-dose ASA (75-100 mg/day) and heparin at prophylactic dosage during pregnancy Based on individual's risk profile
Pregnancy with history of thrombotic APS	Low-dose ASA (75-100 mg/day) and heparin at therapeutic dosage during pregnancy

Prophylactic LMWH: Enoxaparin 40 mg or 1 mg/kg once a day
Therapeutic LMWH: Enoxaparin 1 mg/kg twice daily or 1.5 mg/kg once a day
Prophylactic UFH: 5000 units SC twice daily
Therapeutic UFH: 250 units/kg SC twice daily

Scenario 6

A 55-year-old SLE with LN/APS patient is planning for THA due to ON.

She is in disease remission for 1 year.

She takes MMF, HCQ and Warfarin.

What is your recommendation for perioperative management in addition to warfarin bridging ?

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American College of Rheumatology
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2022 American College of Rheumatology/American Association of Hip and Knee Surgeons Guideline for the Perioperative Management of Antirheumatic Medication in Patients With Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthroplasty

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Management of Immunosuppressive Therapy (1)

แนะนำสามารถใช้ต่อได้ในช่วงผ่าตัด	Dosing interval	Recommended timing of surgery since last medication dose
Medications to continue through surgery		
DMARDs: continue these medications through surgery (all patients)		
Methotrexate	Weekly	Anytime
Sulfasalazine	Once or twice daily	Anytime
Hydroxychloroquine	Once or twice daily	Anytime
Leflunomide (Arava)	Daily	Anytime
Doxycycline	Daily	Anytime
Apremilast (Otezla)	Twice daily†	Anytime†
Severe SLE-specific medications: continue these medications in the perioperative period in consultation with the treating rheumatologist‡		
Mycophenolate mofetil	Twice daily	Anytime
Azathioprine	Daily or twice daily	Anytime
Cyclosporine	Twice daily	Anytime
Tacrolimus	Twice daily (IV and PO)	Anytime
Rituximab (Rituxan)	IV every 4–6 months†	Month 4–6†
Belimumab SC (Benlysta)	Weekly†	Anytime†
Belimumab IV (Benlysta)	Monthly†	Week 4†
Anifrolumab (Saphnelo)§	IV every 4 weeks†	Week 4†
Voclosporin (Lupkynis)§	Twice daily†	Continue†

2022 American College of Rheumatology/American Association of Hip and Knee Surgeons Guideline

Severe SLE

Currently treated (induction or maintenance) for

- **Severe organ manifestations:** lupus nephritis, CNS lupus, severe hemolytic anemia (hemoglobin <9.9 gm/dl), platelets <50,000, vasculitis (other than mild cutaneous vasculitis), myocarditis, lupus pneumonitis, severe myositis, lupus enteritis (vasculitis), lupus pancreatitis, cholecystitis, lupus hepatitis, protein-losing enteropathy, malabsorption, orbital inflammation/myositis, severe keratitis, posterior severe uveitis/retinal vasculitis, severe scleritis, optic neuritis, anterior ischemic optic neuropathy
- **A patient with severe SLE who has been stable for >6 months or who has a history of recurrent or severe infections might discontinue the medications in the perioperative period.**

Management of Immunosuppressive Therapy (2)

แนะนำให้หยุดช่วงผ่าตัด

	Dosing interval	Recommended timing of surgery since last medication dose
Medications to withhold prior to surgery¶		
Biologics: withhold these medications through surgery		
Infliximab (Remicade)	Every 4, 6, or 8 weeks	Week 5, 7, or 9
Adalimumab (Humira)	Every 2 weeks	Week 3
Etanercept (Enbrel)	Every week	Week 2
Golimumab (Simponi)**	Every 4 weeks (SQ) or every 8 weeks (IV)	Week 5 Week 9
Abatacept (Orencia)	Monthly (IV) or weekly (SC)	Week 5; week 2
Certolizumab (Cimzia)	Every 2 or 4 weeks	Week 3 or 5
Rituximab (Rituxan)	2 doses 2 weeks apart every 4–6 months	Month 7
Tocilizumab (Actemra)	Every week (SC) or every 4 weeks (IV)	Week 2; week 5
Anakinra (Kineret)	Daily	Day 2
IL-17 secukinumab (Cosentyx)	Every 4 weeks	Week 5
Ustekinumab (Stelara)	Every 12 weeks	Week 13
Ixekizumab (Taltz)§	Every 4 weeks†	Week 5†
IL-23 guselkumab (Tremfya)§	Every 8 weeks†	Week 9†
JAK inhibitors: withhold this medication 3 days prior to surgery#		
Tofacitinib (Xeljanz)	Daily or twice daily†	Day 4†
Baricitinib (Olumiant)§	Daily†	Day 4†
Upadacitinib (Rinvoq)§	Daily†	Day 4†
Not severe SLE: withhold these medications 1 week prior to surgery		
Mycophenolate mofetil	Twice daily	1 week after last dose†
Azathioprine	Daily or twice daily	1 week after last dose
Cyclosporine	Twice daily	1 week after last dose†
Tacrolimus	Twice daily (IV and PO)	1 week after last dose†
Rituximab (Rituxan)	Every 4–6 months	Month 7
Belimumab IV (Benlysta)	Monthly†	Week 5†
Belimumab SC (Benlysta)	Weekly†	Week 2†

Glucocorticoid Management

- The risk of short-term complications is increased by 8.4% for every 10-mg increase in GC dose in RA who underwent THA and TKA.
- Use of more than 10 mg of glucocorticoids per day (vs. no glucocorticoid use) resulted in a predicted risk for hospitalized infection of 13.25% and a predicted 1-year cumulative incidence of PJI of 3.83%.
- 2022 ACR/AAHKS conditionally recommended patients with rheumatic disease undergoing THA or TKA who are receiving GCs, continuing their current daily dose of GCs rather than administering supraphysiologic doses of GCs on the day of surgery.

Chukir T, et al. ACR Open Rheumatol 2021
George MD, et al. Ann Intern Med. 2019

Grade	General Characteristics	Characteristic Operations
1 (minor)	• Minimal to mild risk independent of anesthesia • Minimal to moderately invasive procedure • Potential blood loss of <500 mL	• Minor general surgical procedures (skin/ subcutaneous tissue procedures, inguinal hernia repair, breast biopsy) • Endoscopy (including cystoscopy, hysteroscopy, bronchoscopy, minor laparoscopy, arthroscopy) • Minor gynecologic procedures (tubal ligation, dilation, and curettage) • Minor otolaryngology procedures (myringotomy tubes, tonsillectomy/ rhinoplasty)
2 (moderate)	• Moderate risk independent of anesthesia • Moderately to significantly invasive procedures • Potential blood loss of 500-1500 mL	• Open or laparoscopic resection/reconstruction of the digestive tract; cholecystectomy • Thyroidectomy • Cystectomy, nephrectomy • Hysterectomy or myomectomy • Laminectomy • **Joint replacement**
3 (major)	• Major to critical risk independent of anesthesia • Highly invasive procedure Potential blood loss > 1500 mL • Usual postoperative intensive care unit stay with invasive monitoring	• Any major orthopedic-spinal, oropharyngeal, or genitourinary repair or reconstruction • Any intracranial, major vascular, or cardiothoracic procedure

Based on the modified Johns Hopkins surgical criteria, Donati A, et al. Br J Anaesth. 2004

Perioperative treatment regimens suggested for patient with glucocorticoid-induced AI

Degree of Surgical Stress	Glucocorticoid Regimen
Grade 1 (minor)	○ Continue daily dose of glucocorticoid ○ 25 mg of IV hydrocortisone at induction if not able to tolerate PO ○ Resume oral daily preoperative glucocorticoid regimen
Grade 2 (moderate)	○ Continue daily dose of glucocorticoid ○ 25-50 mg of hydrocortisone IV at induction ○ 15-25 mg hydrocortisone every 6 hours. until PO is tolerated and hemodynamically stable ○ Resume oral daily preoperative glucocorticoid regimen
Grade 3 (major)	○ Continue daily dose of glucocorticoid ○ 50 mg of hydrocortisone IV at induction ○ 25 mg of hydrocortisone IV every 6 hours on day 1 and until hemodynamically stable, then 15 mg IV every 6 hours until PO is tolerated ○ Resume oral daily preoperative glucocorticoid regimen
Adrenal crisis	○ 100 mg of hydrocortisone IV (IM if no IV access) ○ 50 mg every 6 hours until hemodynamically stable and ○ then taper
Patients who stopped or plan to stop glucocorticoids before surgery	○ Assess HPA axis in patients with intermediate to high risk ○ Treat based on the degree of surgical stress in those who have abnormal HPA axis

Journal of the Endocrine Society, 2023

Scenario 7

- A 38-year-old man with systemic sclerosis.
- He complained of frequent Raynaud with recurrent painful digital ulcers.
- He has reflux esophagitis.
- He is current smoker.
- Current medication is omeprazole.

What is the most appropriated management of Raynaud phenomenon in addition to smoking cessation?

Systemic sclerosis

	Limited	Diffused
Skin sclerosis	Distal to elbows/knee joints/face	Proximal limb or trunk (rapid involvement)
Time between RP and onset sclerosis	Long (a few years)	Short (less than a year)
Complication	Late complications (>5-7 years)	Early complications (<3 years)
[1]Severe lung fibrosis	Less common	More common
[2]Renal crisis	Rare	Less Common
Cardiac involvement	Less common	Common
Pulmonary hypertension	More common (PAH)	Common (ILD-related)
Severe gut disease	Common (+PBC)	More common
Autoantibodies	Centromere, PM/Scl, Th/To	RNAP-III, Scl-70

Risk factor of

[1]SSc-ILD: male, smoking, early course of disease, extensive diffused skin (MRSS>20), anti-SCL70

[2]SRC: early course of disease, tendon friction rub, anti-RNAPIII, prednisolone > 15 mg/d, cyclosporin

Global management of systemic sclerosis – treatment considerations

British Society for Rheumatology

2024

Neurological

Neurological complications of SSc require multi-speciality management with careful exclusion of other relevant causes 1C
Peripheral Sensory neuropathy of the feet is common 2C

ILD

MMF is recommended as first line treatment with rituximab or cyclophosphamide i.v. as alternative 1B
Consider adding rituximab or tocilizumab to MMF for progressive disease 2C
Nintedanib recommended for progressive pulmonary fibrosis 1B

PAH

PAH diagnosis by right heart catheter and treatment 1A initiated by a designated Pulmonary Hypertension Centres 1B
Anticoagulation is not recommended in PAH-SSc 1B

Renal

ACEi should be used in all cases of diagnosed SRC 1A
Glucocorticoid treatment avoided in adult SSc due increased SRC risk 1A
Renal biopsy should be considered when diagnosis uncertain 1C
Referral for renal transplantation in cases without significant renal recovery 1B

Skin

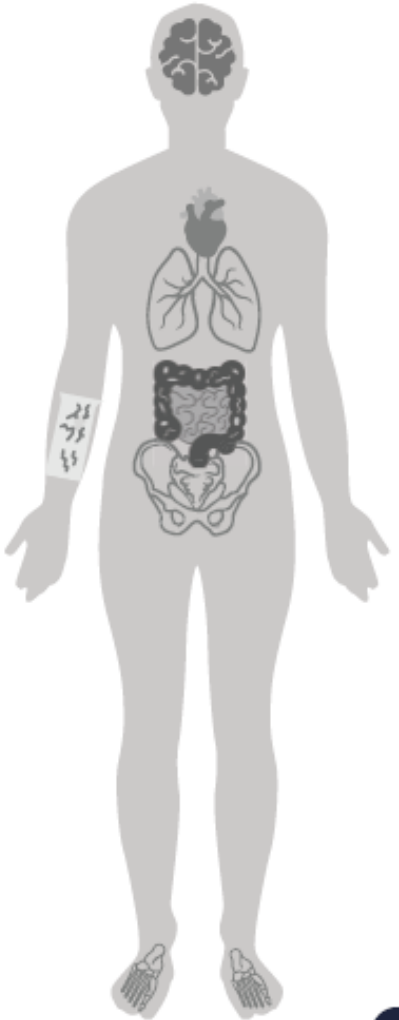
MMF is first line treatment for skin fibrosis in dcSSc 1C
Antihistamines are often used for itch 2C
Options for telangiectasia include skin camouflage, pulsed dye laser or intense pulsed light therapy 2C

Musculoskeletal

Musculoskeletal manifestations of SSc may benefit from immunomodulatory treatments given for other complications 1C

Digital ulcers

Severe digital vasculopathy with new tissue necrosis or critical ischaemia requires urgent clinical assessment 1C
Sildenafil (or tadalafil) as 1st line agent in DU healing and secondary prevention and bosentan as second line treatment 1C
Expert opinion supports use of IV prostanoids in promoting DU healing 1C



Fatigue and Health related Quality of Life

Physical and occupational therapy may improve quality of life, pain, and fatigue 2C

Cardiac

Immunosuppression with MMF for SSc- pHI when investigation suggests myocardial inflammation 2C
Glucocorticoids and other bDMARDs may be added if appropriate and/or cyclophosphamide 2C

Gastrointestinal

PPI and/or H2 receptor antagonists for reflux 1C
Parenteral nutrition for severe malnutrition 1B
Intermittent or rotational antibiotics SIBO 2B
Anti-diarrhoeal agents or laxatives 2B
Surgical intervention should be avoided 1C

Reproductive health

Sexual dysfunction needs engagement of gynaecology, urology, and sexual health clinical services 1C
For planned pregnancy in SSc identify significant organ dysfunction and discontinue harmful medication 1C
Pregnancy management requires integrated multi-disciplinary care 2C

Raynaud's phenomenon

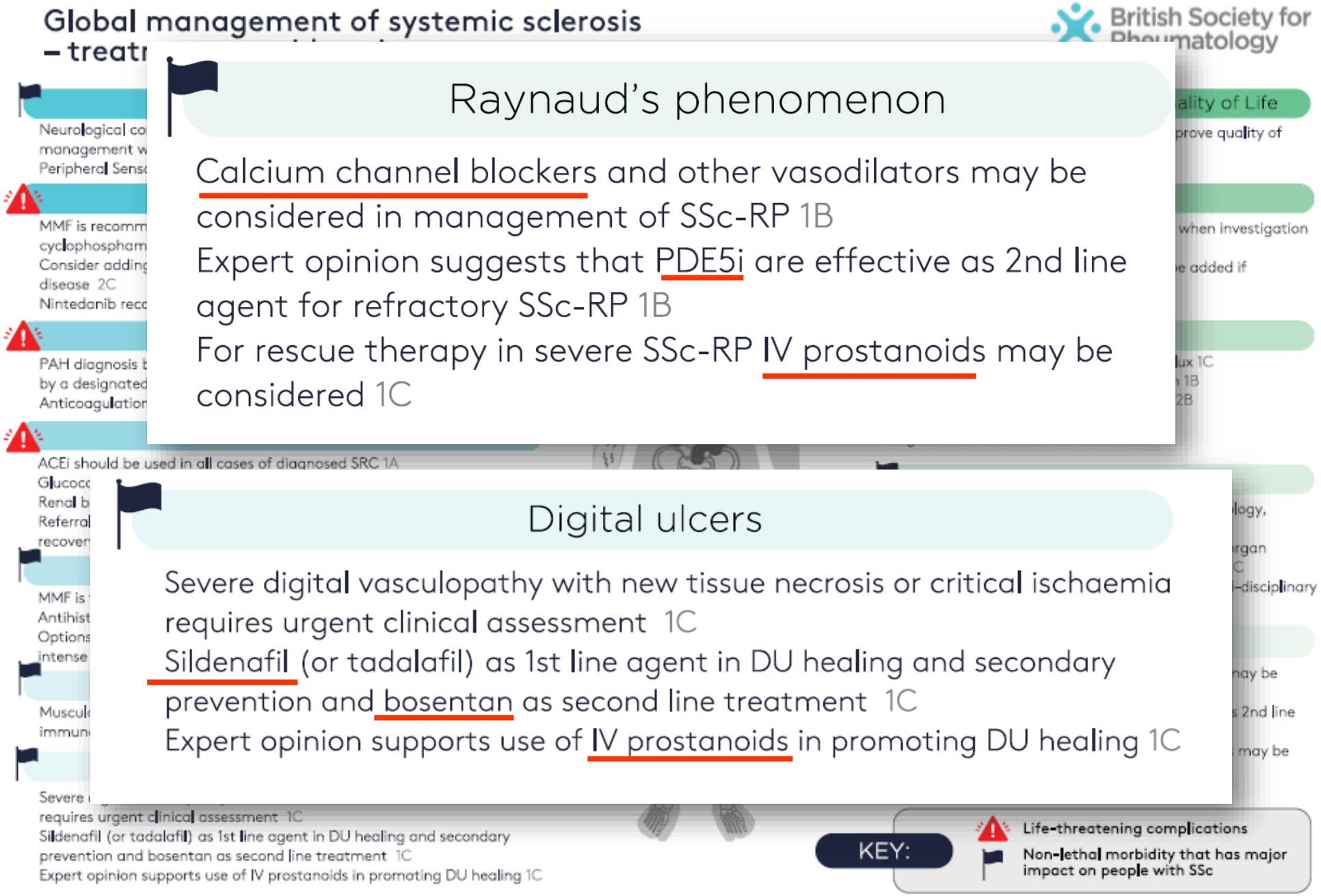
Calcium channel blockers and other vasodilators may be considered in management of SSc-RP 1B
Expert opinion suggests that PDE5i are effective as 2nd line agent for refractory SSc-RP 1B
For rescue therapy in severe SSc-RP IV prostanoids may be considered 1C

KEY:

Life-threatening complications

Non-lethal morbidity that has major impact on people with SSc

2024


Global management of systemic sclerosis
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Expert opinion supports use of IV prostanoids in promoting DU healing 1C
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EULAR recommendations for the treatment of systemic sclerosis: 2023 Updated

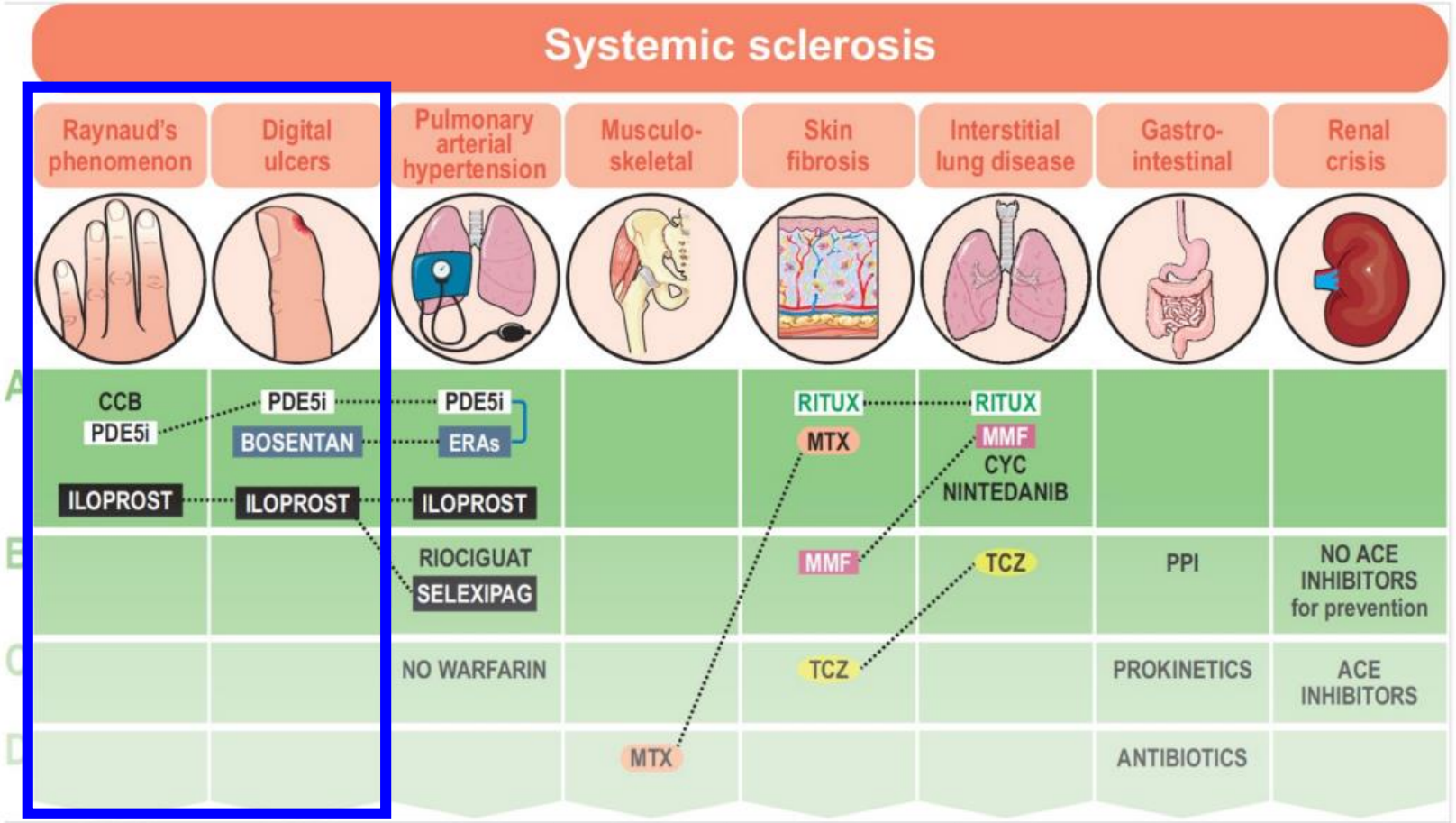


Figure 1 Schematic representation of the eight clinical domains covered by the 2023 recommendations. Note that severe prognosis is not represented. The different shades of green boxes labelled A–D represent the Strength of the Recommendation (SoR) as shown in the relative column of table 1. Dotted lines connect same drug or drug class across distinct clinical domains. CCB, calcium channel blocker; CYC, cyclophosphamide; ERAs, endothelin receptor antagonists; MMF, mycophenolate mofetil; MTX, methotrexate; PDE5i, phosphodiesterase five inhibitors; PPI, proton pump inhibitors; RITUX, rituximab; TCZ, tocilizumab.

IS (LoE)	RP	Digital ulcer
CCB (Nifedipine)	1A	
PDE5i (sildenafil/ tadalafil)	1A	1A (treatment/ prevention)
ERAs (Bosentan)		1A (prevention)
iv.Prostacyclin (Iloprost)	1A	1A (treatment)

Del Galdo F, et al. Ann Rheum Dis 2024;0:1–12.

Scenario 8

- A 42-year-old female presented with progressive diffused skin sclerosis 2 years ago.
- She denied any cardiopulmonary symptom.
- Chest x-ray showed small reticulations without loss of lung volume.
- HRCT revealed 10% reticulations and GGO.
- PFT; FVC 86% predicted value.
- Anti-Scl70 (topoisomerase 1) positive.
- CRP 25 mg/L.

What is the proper management of this patient in term of ILD ?

Global management of systemic sclerosis – treatment considerations

British Society for Rheumatology

2024

Neurological

Neurological complications of SSc require multi-speciality management with careful exclusion of other relevant causes 1C
Peripheral Sensory neuropathy of the feet is common 2C

ILD

MMF is recommended as first line treatment with rituximab or

Fatigue and Health related Quality of Life

Physical and occupational therapy may improve quality of life, pain, and fatigue 2C

Cardiac

Immunosuppression with MMF for SSc- pHI when investigation

ILD

MMF is recommended as first line treatment with rituximab or cyclophosphamide i.v. as alternative 1B
Consider adding rituximab or tocilizumab to MMF for progressive disease 2C
Nintedanib recommended for progressive pulmonary fibrosis 1B

Musculoskeletal

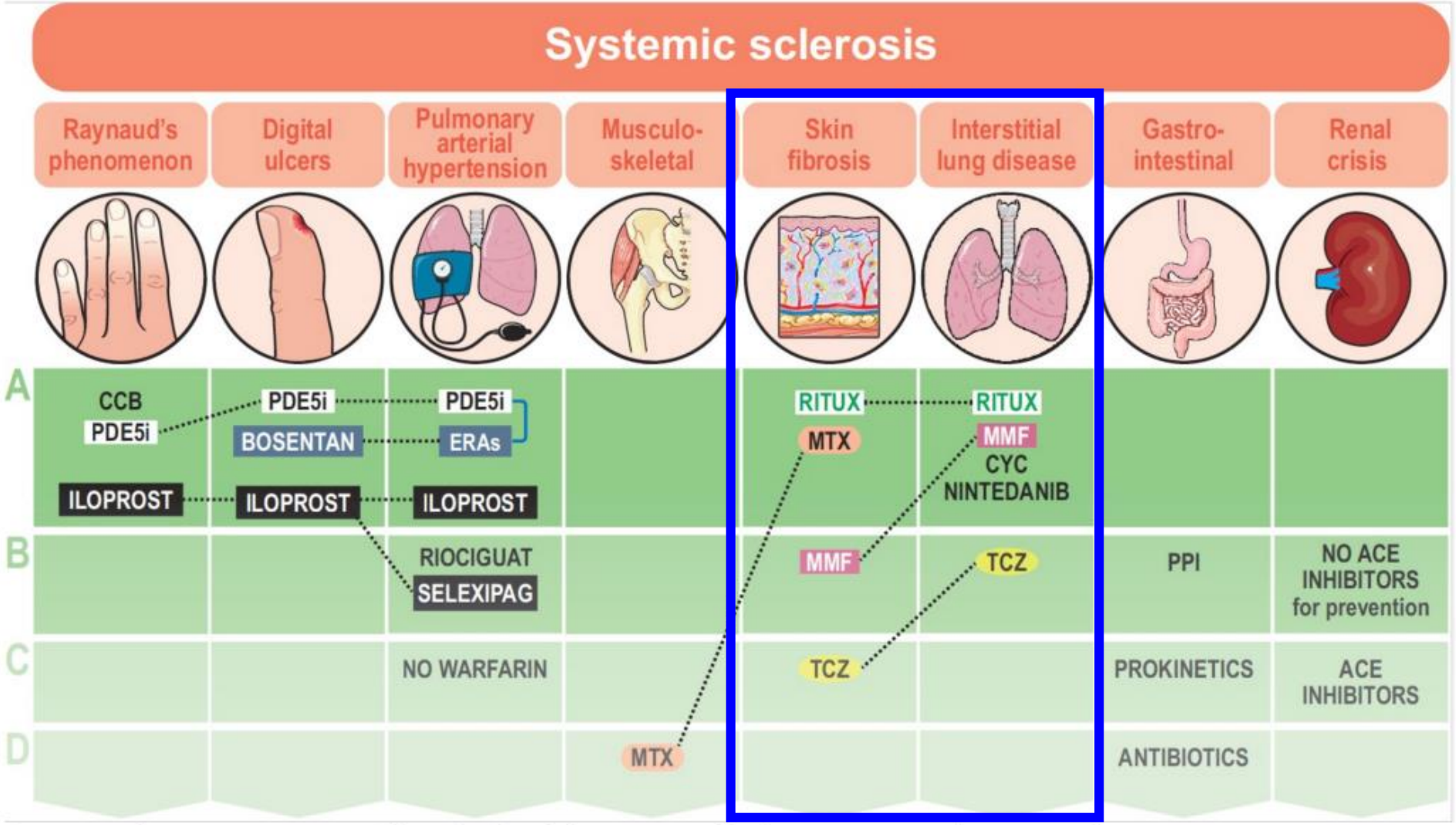
Musculoskeletal manifestations of SSc may benefit from immunomodulatory treatments given for other complications 1C

Digital ulcers

Severe digital vasculopathy with new tissue necrosis or critical ischaemia requires urgent clinical assessment 1C
Sildenafil (or tadalafil) as 1st line agent in DU healing and secondary prevention and bosentan as second line treatment 1C
Expert opinion supports use of IV prostanoids in promoting DU healing 1C

Calcium channel blockers and other vasodilators may be considered in management of SSc-RP 1B
Expert opinion suggests that PDE5i are effective as 2nd line agent for refractory SSc-RP 1B
For rescue therapy in severe SSc-RP IV prostanoids may be considered 1C

KEY:
Life-threatening complications
Non-lethal morbidity that has major impact on people with SSc



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IS (LoE)	Skin	ILD
RTX	1A	1A
MMF	1B	1A
CYC	1B	1A
*TCZ	1B	1B
MTX	1B	
**Nintedanib		1A

***TCZ** = early inflammatory (mild or subclinical) ILD

****Nintedanib** = Progressive Pulmonary Fibrosis (PF-ILD)

“Expert opinion” on treatment of SSc-ILD

Thai recommendation of SSc-ILD 2564

1. การพิจารณาเริ่มรักษาด้วยยากดภูมิคุ้มกัน (immunosuppressive drugs)

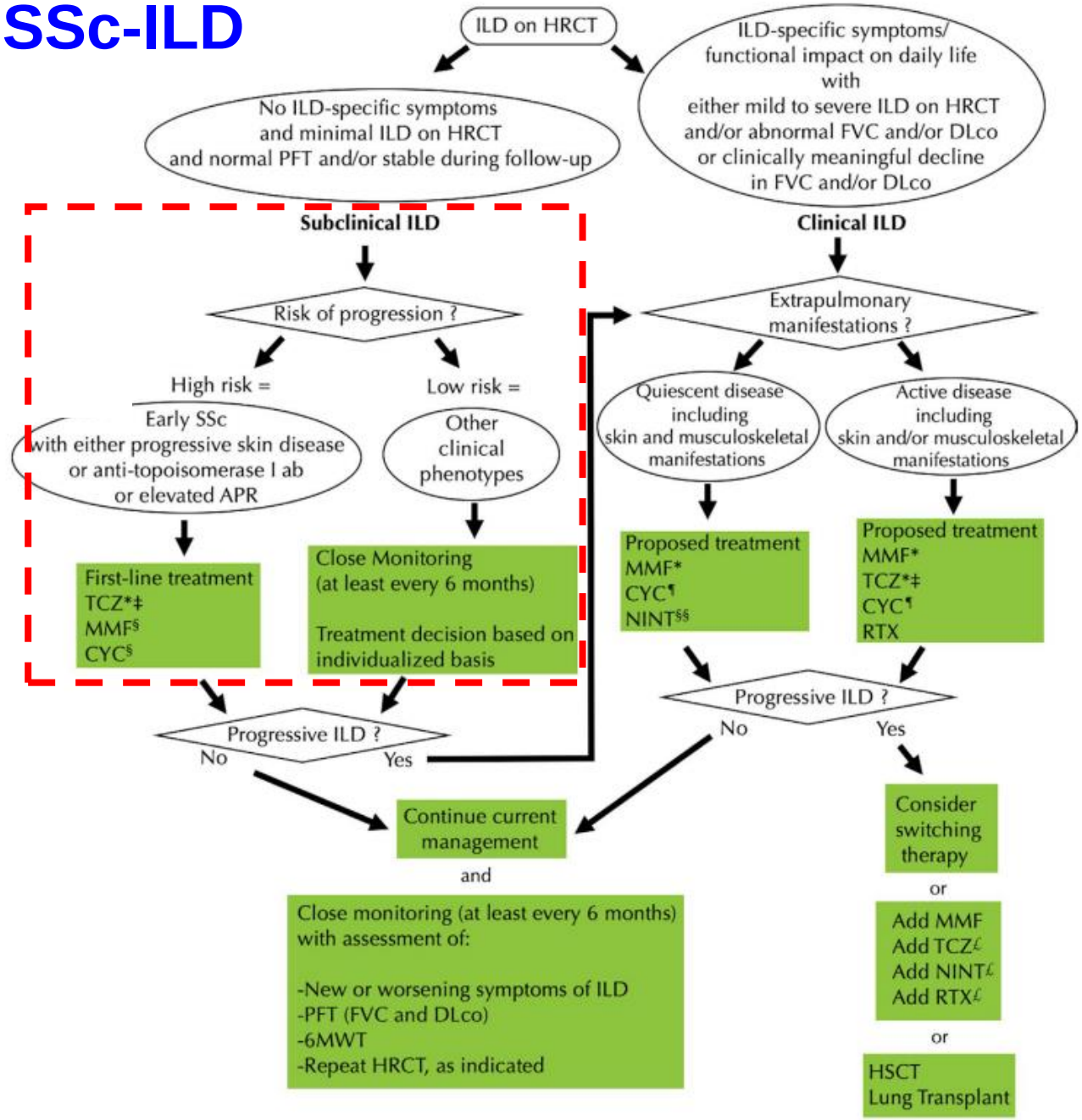
ปัจจัยพิจารณาเริ่มการรักษาด้วยยา immunosuppressive drugs มีดังต่อไปนี้

1.1 ประเมินความรุนแรงของโรค โดยพิจารณาจากค่า FVC และปริมาณความผิดปกติจาก HRCT โดยใช้เกณฑ์ข้อใดข้อหนึ่งต่อไปนี้ (3, 5, 13)

- FVC < 70% predicted
- ปริมาณความผิดปกติจาก HRCT > 20%

1.2 กรณีไม่เข้าเกณฑ์ข้อ 1.1 หรือไม่สามารถตรวจ pulmonary function tests ได้ ให้พิจารณาเริ่มการรักษาจากลักษณะต่อไปนี้

- ลักษณะทางคลินิกแย่ลงโดยไม่มีสาเหตุมาจากโรคหรือภาวะอื่น เช่น
- ผู้ป่วยที่มีปัจจัยเสี่ยงในการเกิดการลุกลามของโรค ดังแสดงในตารางที่ 1
- HRCT มีลักษณะที่เข้าได้กับ organizing pneumonia ร่วมด้วย (ตารางที่ 3) โดยไม่พบสาเหตุอื่นที่ทำให้มี HRCT เป็นแบบนั้น เช่น infection เป็นต้น
- มีข้อบ่งชี้ในการรักษาตามความผิดปกติในระบบอวัยวะอื่น



Khanna D, Lescoat A, Roofeh D, et al. Arthritis Rheumatol. (2022)
Rahaghi et al. Respiratory Research (2023)

Scenario 9

- A 60-year-old man presented one week of painful proximal muscle weakness.
- He has gout and hypercholesterolemia.
- His current medications are colchicine, allopurinol, and statin.
- He had pneumonia and was on 5 days-clarithromycin a weeks ago.
- Physical exam revealed grade IV muscle weakness and DTR 1+.
- CK 1500 ng/ml. ANA was negative.

What is the cause of myopathy in this patient?

Drug induced myopathy

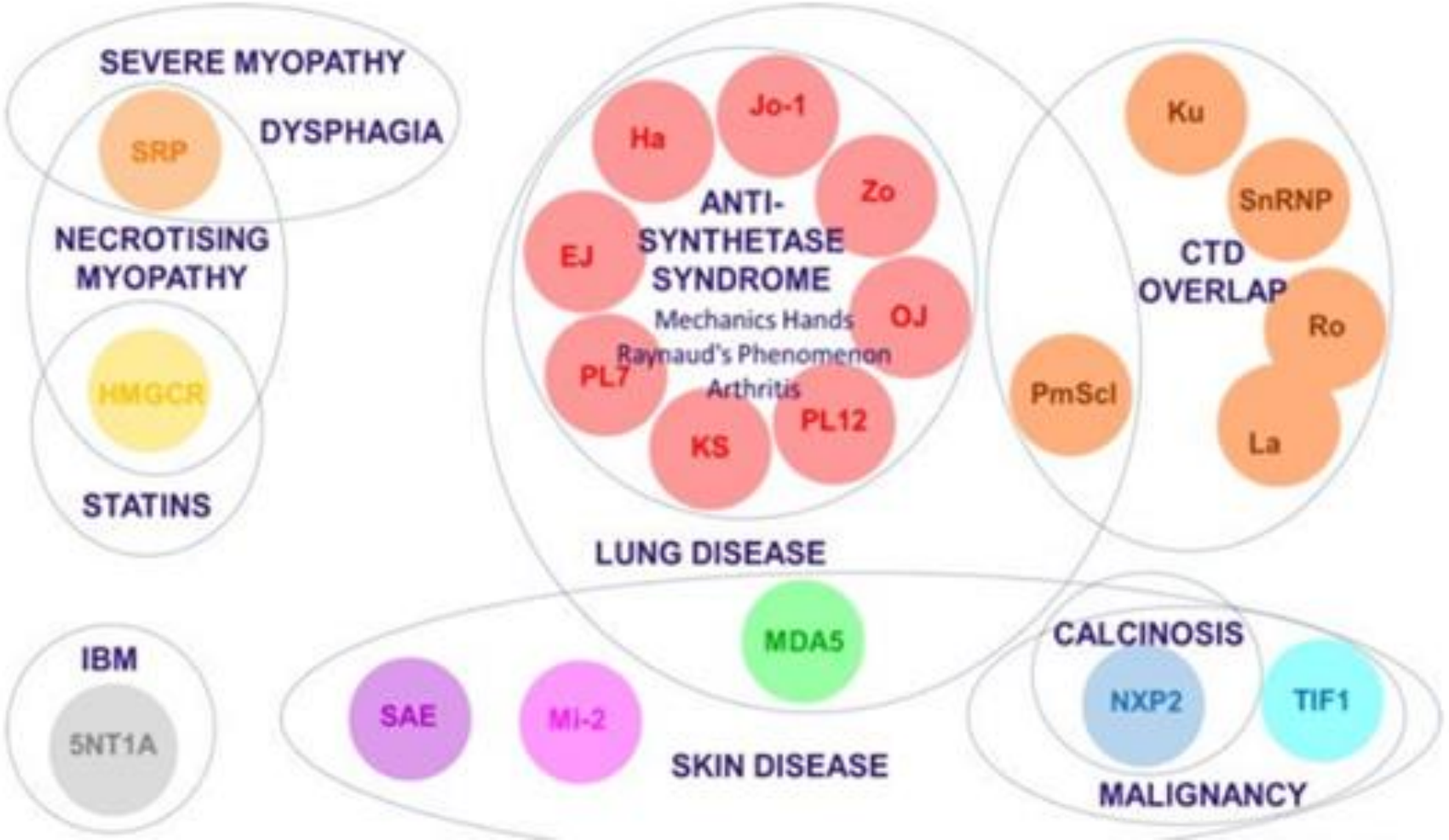
	Steroid	Anti-malarials	Colchicine	Statin
Onset	Subacute-chronic	Chronic	Acute-subacute	
Risk	▪ Prednisolone > 20 mg/day at least 2 WK ▪ Cushingoid	▪ Duration > 5 Y ▪ Cardiomyopathy ▪ Arrythmia ▪ Retinopathy	▪ CKD ▪ Drug interaction with CYP3A4/P-glycoprotein inhibitors (*cyclosporine, clarithromycin, ketoconazole, itraconazole, ritonavir, diltiazem, verapamil, erythromycin, fluconazole)* ▪ Concomitant drug (*statin , fibrate, or digoxin)*	▪ CKD ▪ Drug interaction ▪ Hypothyroid ▪ Anti-HMGCR (ANA)
Myopathy	▪ Myopathic	Myopathic and neuropathic pattern		Myopathic
CK	Normal	Abnormal		
Biopsy	▪ Muscle fiber type 2 atrophy ▪ No inflammation	▪ Muscle fiber hypertrophy ▪ Vacuoles ▪ Rarely inflammation ▪ Curvilinear bodies (anti-malarials)		▪ Necrotizing myositis ▪ Myocyte necrosis ▪ Rarely inflammation (macrophage)
Rx	▪ Steroid discontinuation or tapering with steroid-sparing agents	▪ Anti-malarial/colchicine discontinuation		▪ Statin discontinuation ▪ Short course of steroid (Anti-HMGCR) ▪ ±Re-challenging

Scenario 10

- A 40-year-old woman presented with dyspnea for 2 weeks.
- She had rashes over upper eye lids and ulcerative lesions at knuckles.
- On admission, SpO2 was 90% on room air. ABG revealed a PaO2 of 65 mmHg.
- Musculoskeletal exam showed grade V.
- HRCT showed bilateral GGO and consolidation.
- Sputum examination and septic work up showed no organism.
- CK 200 ng/ml. Anti-MDA-5 positive.

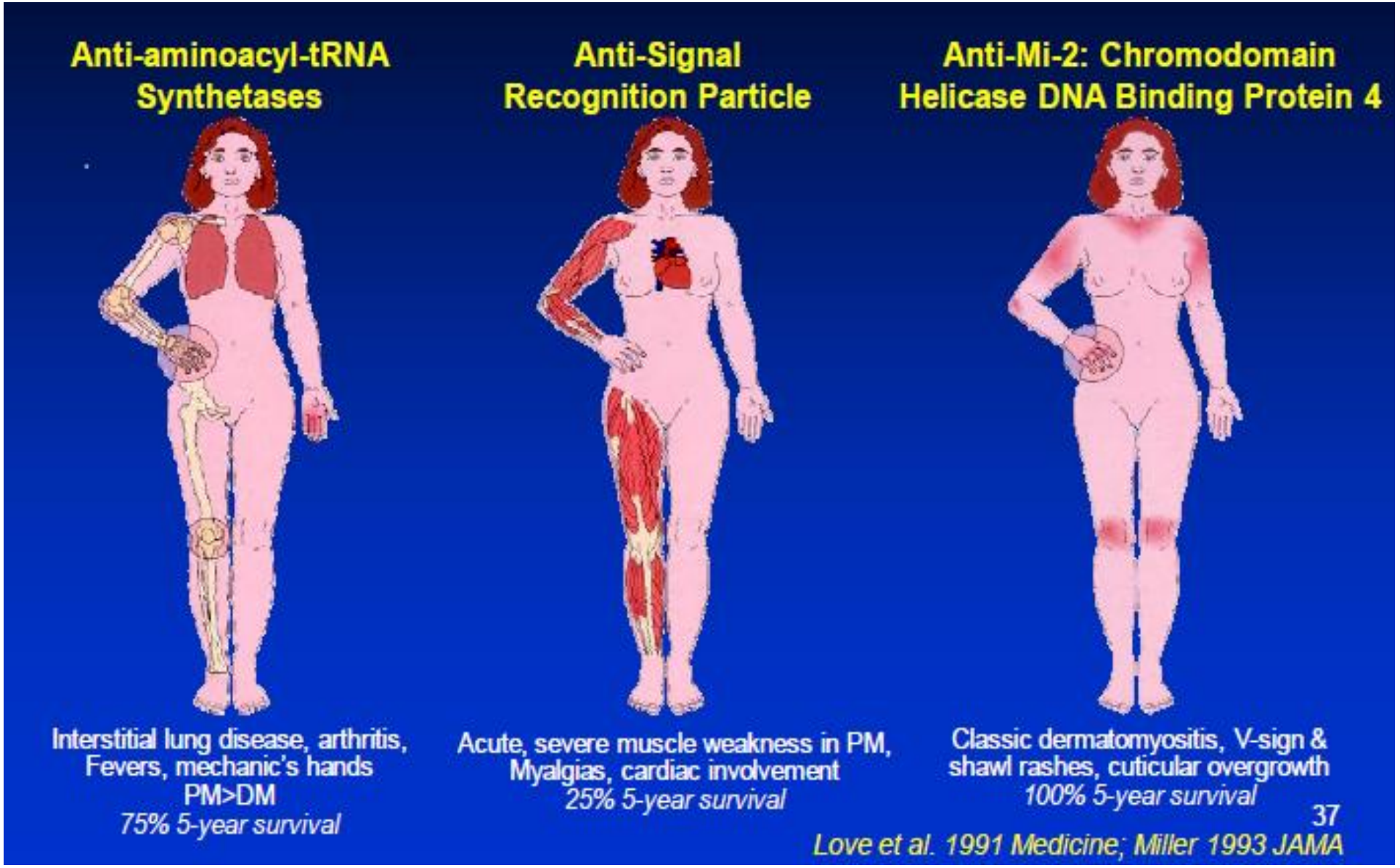
Which one is the most appropriated treatment for this patient in addition to high dose systemic steroid ?

Myositis antibodies & Clinical associations



J Intern Med. 2016 Jul;280(1):8-23

Autoantibody Phenotypes in IIM



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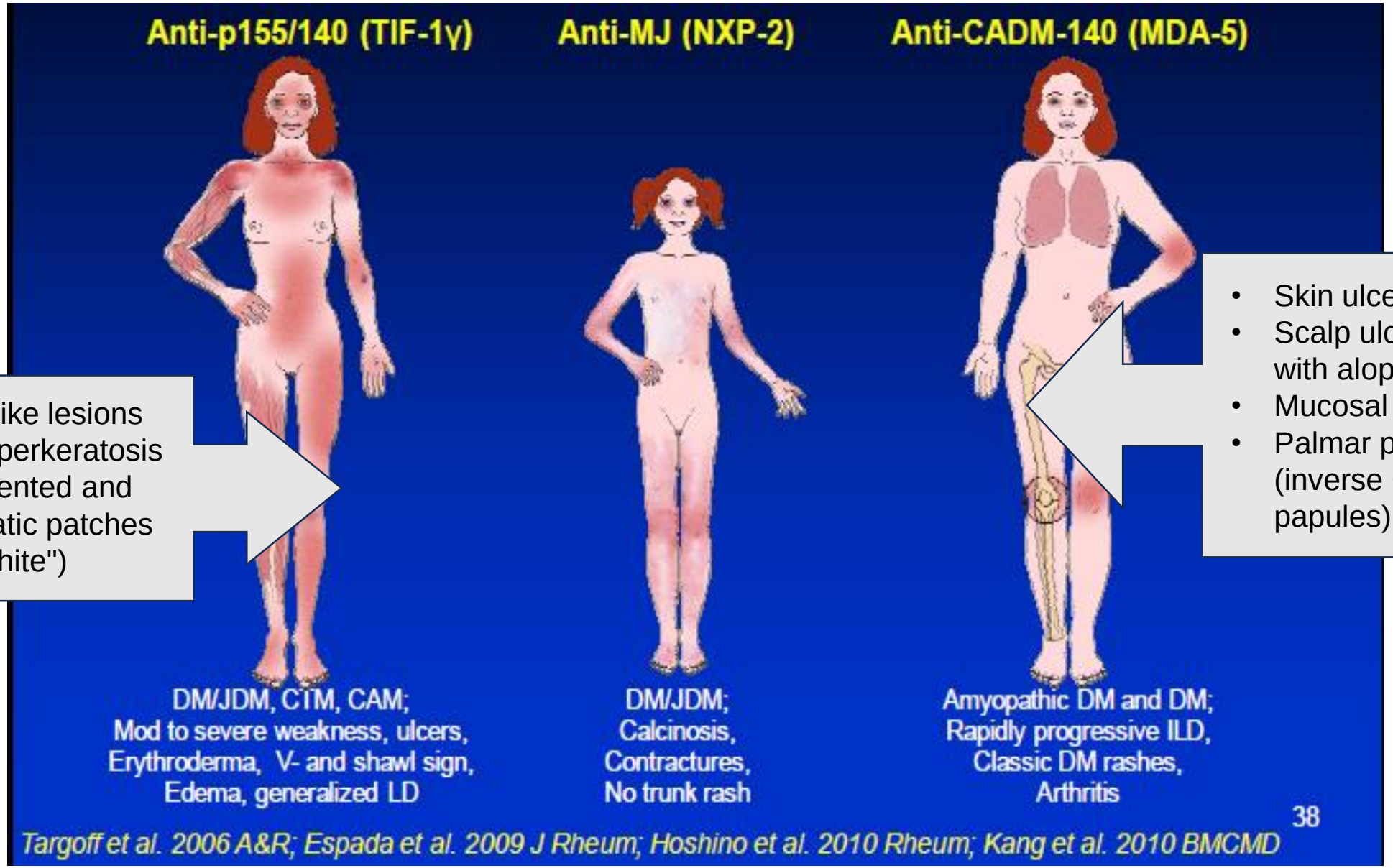
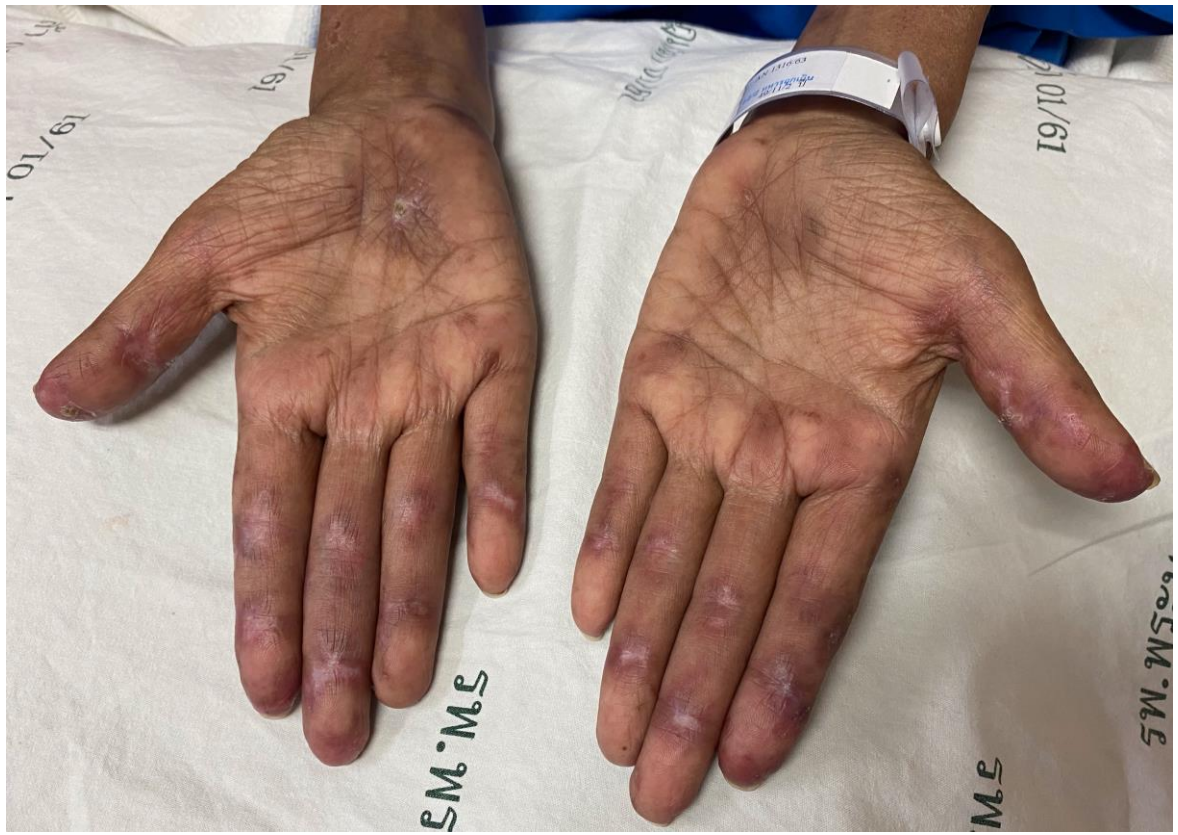


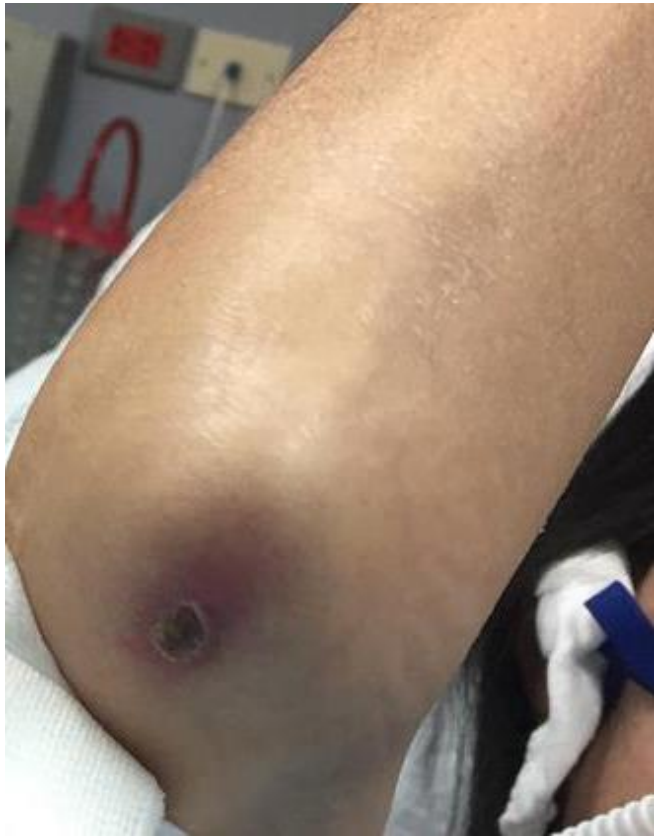
- Psoriasis-like lesions
- Palmar hyperkeratosis
- Hypopigmented and telangiectatic patches ("red on white")

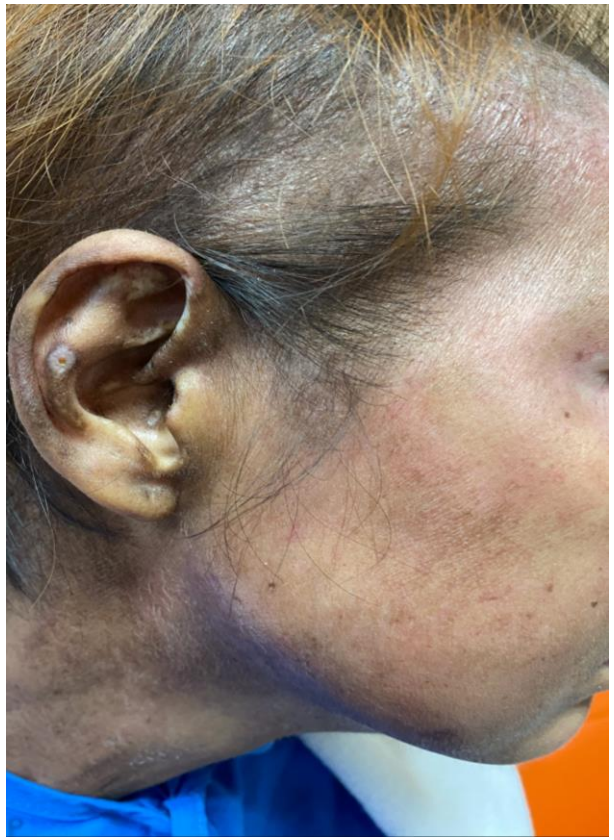
- Skin ulceration
- Scalp ulceration with alopecia
- Mucosal ulcer
- Palmar papules (inverse Gottron' papules)

Skin Manifestations of Anti-MDA-5 CADM



Palmar papules
(inverse Gottron' sign)

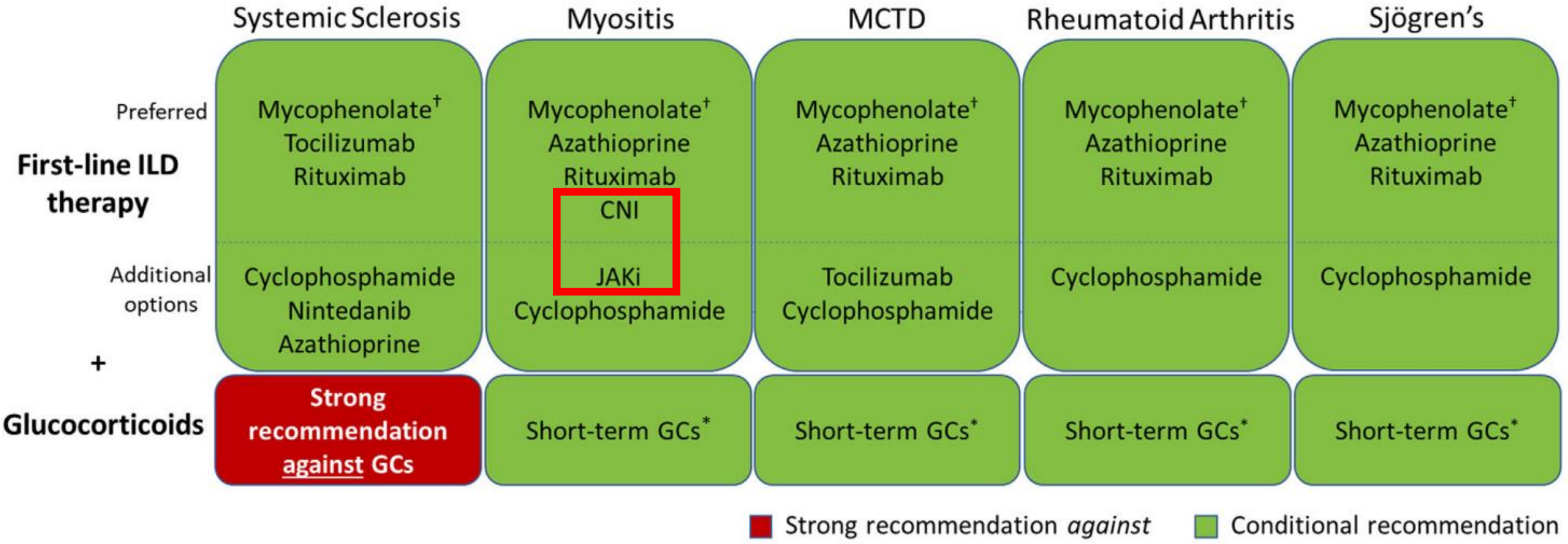




Cutaneous ulcerations

2023 ACR/CHEST Guideline

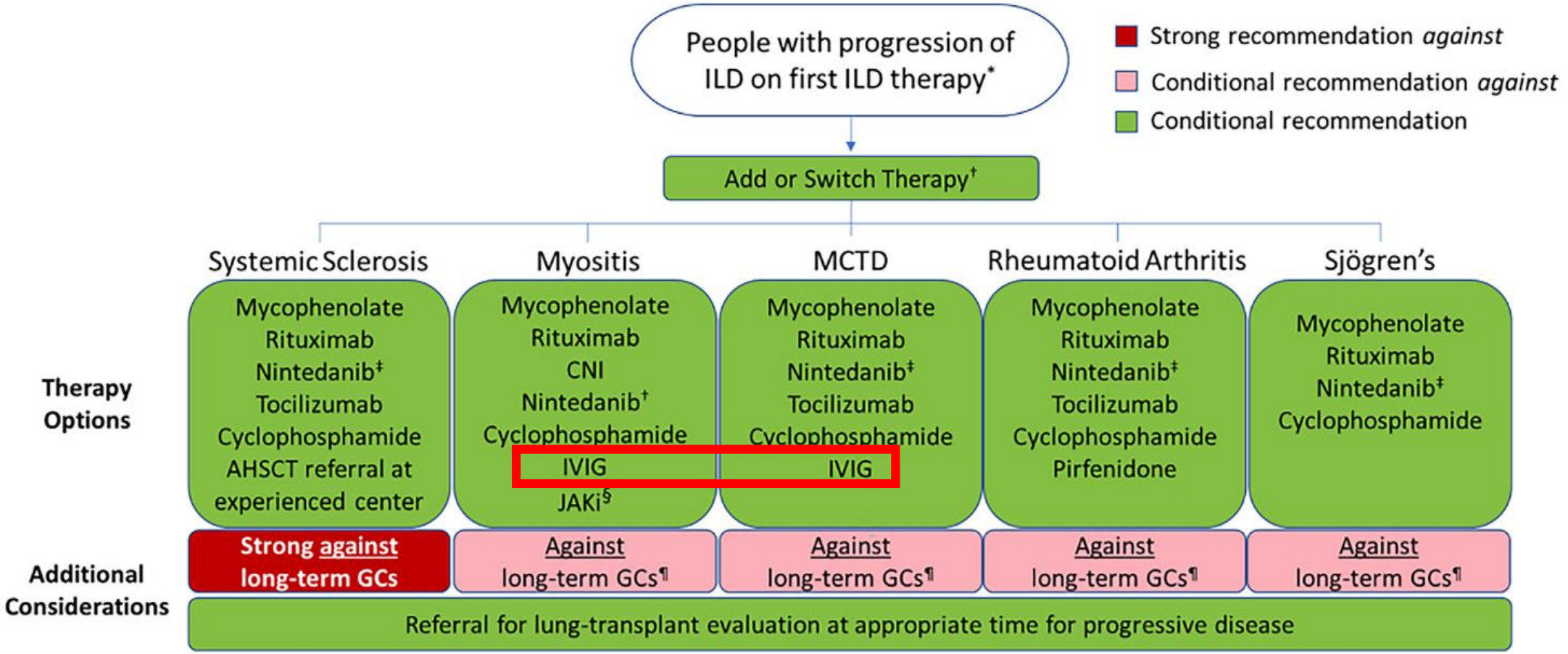
Initial treatment options for the treatment of SARD-ILD



Calcineurin inhibitors (CNI) = Cyclosporin A, tacrolimus (most evidences from IIM-ASS)
Janus kinase inhibitor (JAKi) = Tofacitinib (indirect evidence from anti-MDA-5 not RP-ILD)

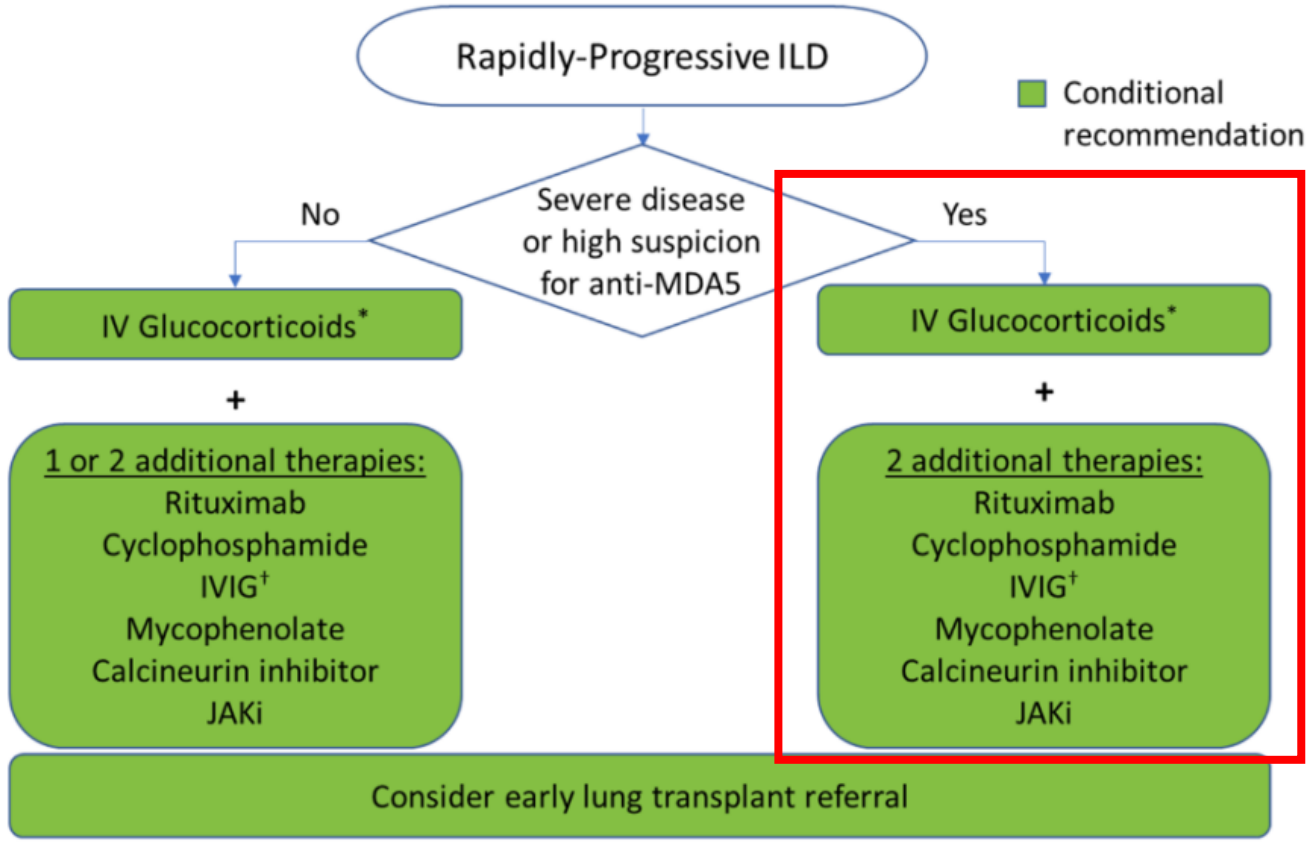
2023 ACR/CHEST Guideline

Management of SARD-ILD with progression of ILD despite first ILD therapy.



1. IVIG is effective for myositis and dysphagia IIM (myositis predominant–MCTD).
2. IVIG may be useful when rapid onset of action is desired, eg, presence of severe respiratory muscle weakness.
3. IVIG may be used in the acute setting if infection is a concern, BUT limited ILD efficacy data.

Guideline for the Treatment of RP-ILD



* In rare patients with systemic sclerosis with rapidly progressive ILD, there was no consensus on whether or not to use glucocorticoids – if used, patients should be monitored closely for evidence of renal crisis.

† Rituximab and cyclophosphamide recommended over IVIG, but IVIG may be preferred if there is high concern for infection.

ILD = interstitial lung disease; IV = intravenous; IVIG = intravenous immune globulin; JAKi = janus kinase inhibitor

Thai Guideline Treatment of IIM-ILD 2022

ลำดับ	คำแนะนำ	คุณภาพของหลักฐาน	ระดับของคำแนะนำ	การเห็นพ้องต้องกัน (ร้อยละ)
1	แนะนำให้เริ่มการรักษาด้วยคอร์ติโคสเตียรอยด์เป็นยาหลักในผู้ป่วย IIM-ILD	3	D	94.8
2	ในผู้ป่วย IIM-ILD ที่มีลักษณะทางคลินิกแบบกึ่งเฉียบพลัน แนะนำให้ใช้การรักษาแบบผสม ได้แก่ คอร์ติโคสเตียรอยด์ร่วมกับยากดภูมิคุ้มกันพื้นฐานอย่างน้อย 1 ชนิดต่อไปนี้	2-	D	96.9
	2.1 Azathioprine	2-	D	93.8
	2.2 Calcineurin inhibitors	2-	D	93.8
	2.3 Cyclophosphamide	3	D	94.8
	2.4 Mycophenolate mofetil	2-	D	97.9
3	ในผู้ป่วย IIM-ILD ที่มีลักษณะทางคลินิกลุกลามเฉียบพลัน (RP-ILD) และตรวจพบ anti-MDA5 antibodies อาจพิจารณาให้การรักษาด้วยคอร์ติโคสเตียรอยด์ร่วมกับยากดภูมิคุ้มกันพื้นฐานแบบผสมอย่างน้อย 2 ชนิดตั้งแต่เริ่มต้นมากกว่าการรักษาด้วยการเพิ่มยาทีละชนิดแบบขั้นตอน	2-	D	95.8
4	ไม่แนะนำให้ใช้ methotrexate ในการรักษา IIM-ILD เนื่องจากไม่มีหลักฐานเชิงประจักษ์ที่แสดงถึงประสิทธิผลในผู้ป่วย IIM-ILD	4	D	96.9

ลำดับ	คำแนะนำ	คุณภาพของหลักฐาน	ระดับของคำแนะนำ	การเห็นพ้องต้องกัน (ร้อยละ)
5	ในผู้ป่วย IIM-ILD ที่ไม่ตอบสนองต่อการรักษาด้วยคอร์ติโคสเตียรอยด์และยากดภูมิคุ้มกันพื้นฐาน อาจพิจารณาให้การรักษาอื่นร่วมด้วย ได้แก่	2-	D	97.9
	5.1 Intravenous immunoglobulin	2-	D	96.9
	5.2 Plasma exchange	2-	D	96.9
	5.3 Rituximab	2-	D	97.9
	5.4 Tocilizumab	3	D	91.7
	5.5 Tofacitinib	2-	D	91.7
6	ในผู้ป่วย IIM-ILD ที่มีการลุกลามของพังผืดในปอด (progressive pulmonary fibrosis) และไม่ตอบสนองต่อการรักษาด้วยคอร์ติโคสเตียรอยด์และยากดภูมิคุ้มกัน โดยลักษณะทางคลินิกที่แย่ลงไม่ได้มีสาเหตุมาจากภาวะหรือโรคอื่น แนะนำให้การรักษาด้วยยาต้านพังผืด	1+	D	94.8

Scenario 11

- A 65-year-old woman presented with acute painless visual loss left eye 3 days ago.
- She had left temporal headache with morning stiffness of shoulders 1 month ago.
- Physical examination showed tenderness at left temporal area and carotid bruit.
- Eye ground examination revealed pale and swollen left optic disc.
- Temporal artery ultrasound showed halo sign.
- ESR 60 mm/h.

What is the most appropriated management in this patient in addition to high dose corticosteroid ?

Features	Giant cell arteritis	Takayasu's arteritis
F:M; Age	2:1; >50 years (Caucasian)	8:1; <40 years (Asian)
Fever	Common	Uncommon
PMR	Common	Rare
Headache	Common (temporal arteritis)	Rare
AION/stroke (carotid and vertebrobasilar hypoperfusion)	Common	Uncommon
Claudication	Jaw	Extremities
Aorta and major branches	Uncommon (LV-GCA)	Common
Bruit, unequal BP, renovascular hypertension	Rare	Common
Investigation	• Gold standard: >1- cm-unilateral temporal artery biopsy (C-GCA) (within 2 weeks after treatment) • Colour duplex temporal artery ultrasound (optional) • MRA/CTA/PET (LV-GCA) (within 72 hours after therapy)	MRA/CTA/PET > Conventional angiography

2021 ACR/Vasculitis Foundation Guideline for GCA

IV pulse GCs

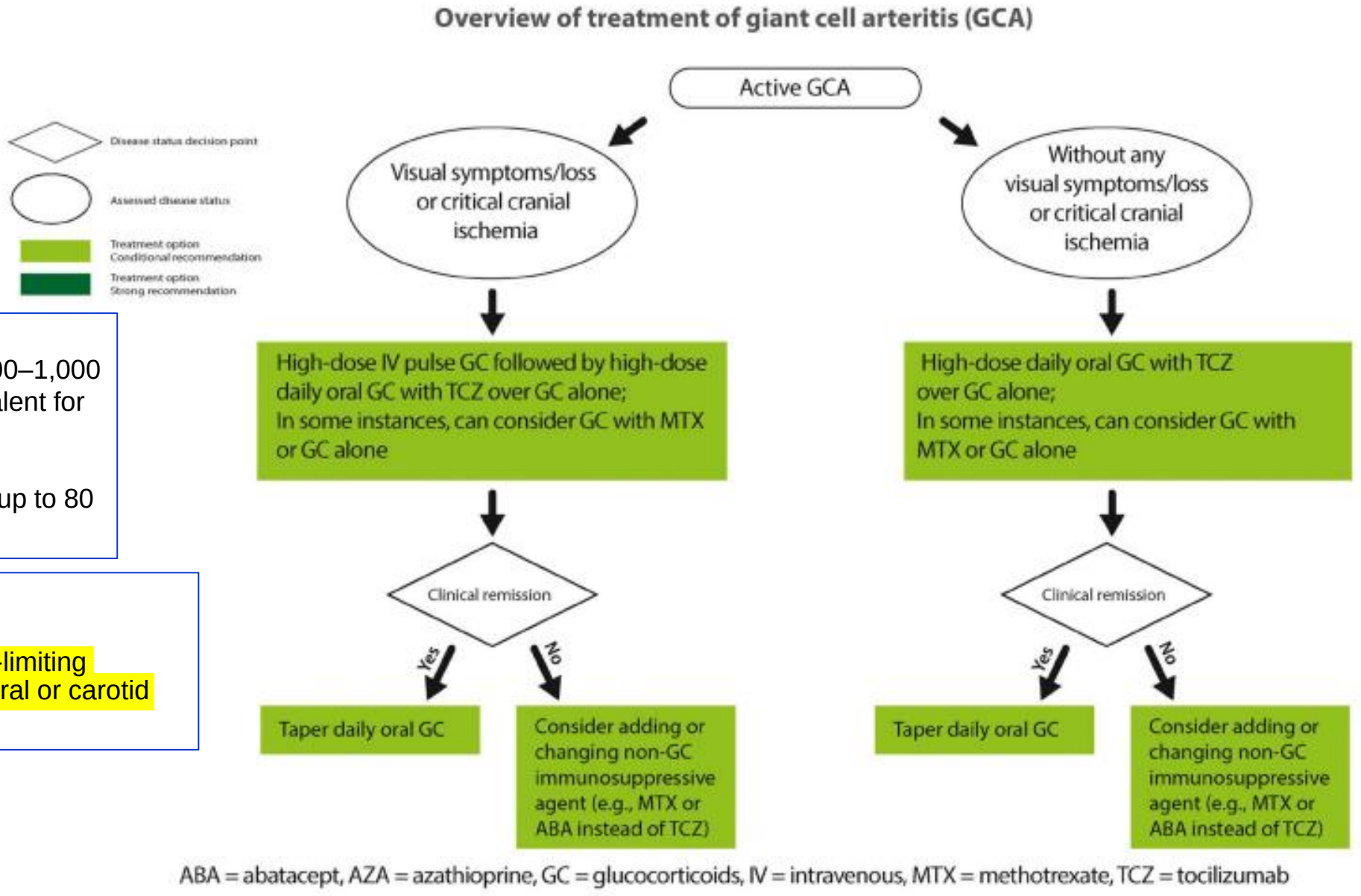
- IV methylprednisolone 500–1,000 mg/day (adults) or equivalent for 3–5 days

High-dose oral GCs

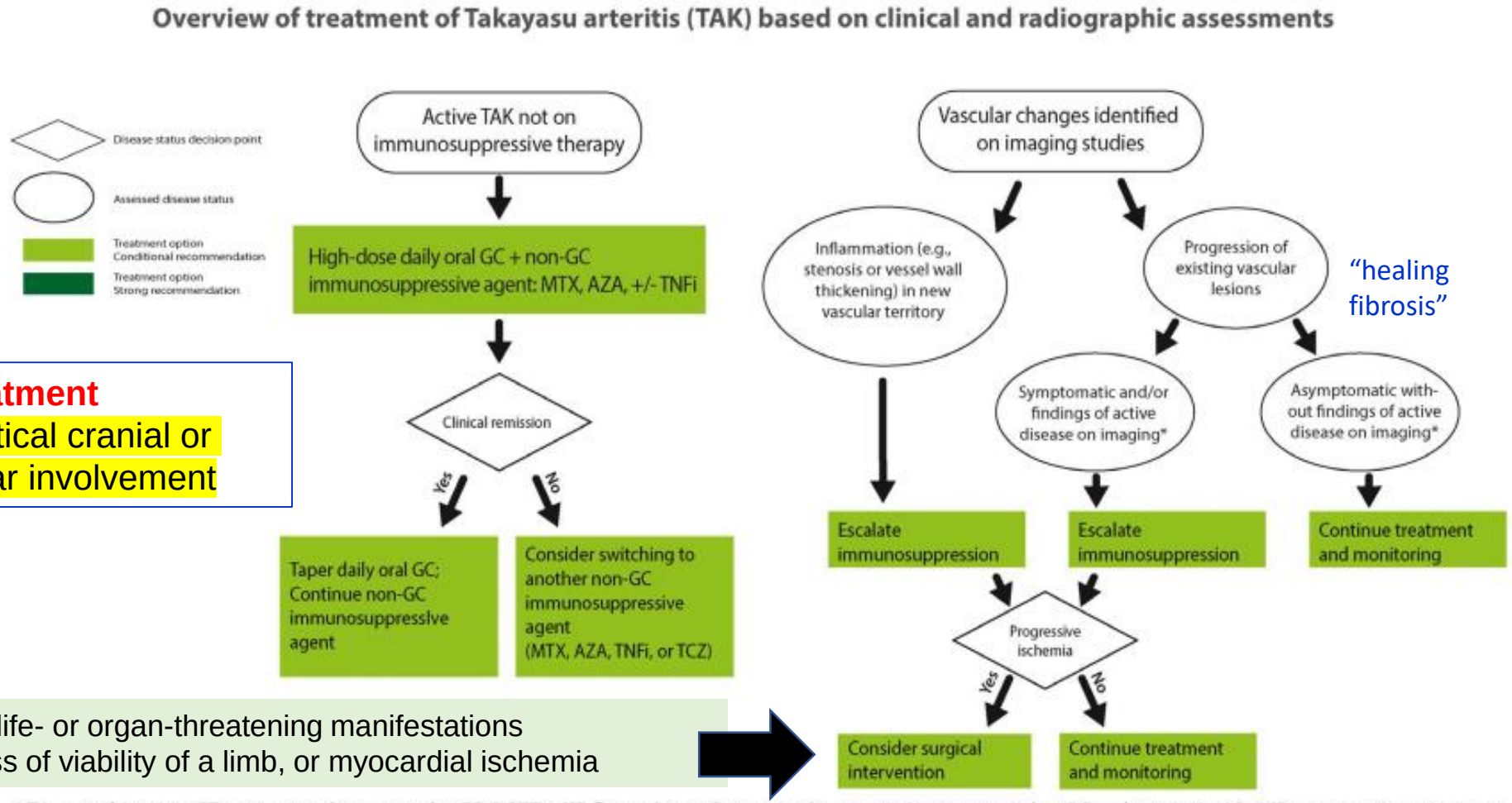
- Prednisone 1 mg/kg/day up to 80 mg or equivalent

Adjunctive treatment

- Statin in high CVD risk
- LD-ASA in critical or flow-limiting involvement of the vertebral or carotid arteries



2021 ACR/Vasculitis Foundation Guideline for TKA



Adjunctive treatment

- LD-ASA in critical cranial or vertebrobasilar involvement

*If the patient has life- or organ-threatening manifestations such as stroke, loss of viability of a limb, or myocardial ischemia

AZA = azathioprine; CT = computed tomography; FDG-PET = ^{18}F-fluorodeoxyglucose positron emission tomography; GC = glucocorticoids; MR = magnetic resonance; MTX = methotrexate; TCZ = tocilizumab; TNFi = tumor necrosis factor inhibitor

* Can be suggested by vascular edema, contrast enhancement, and/or increased wall thickness on MR or CT angiography, or supra-physiologic FDG uptake in the arterial wall on PET imaging

Scenario 12

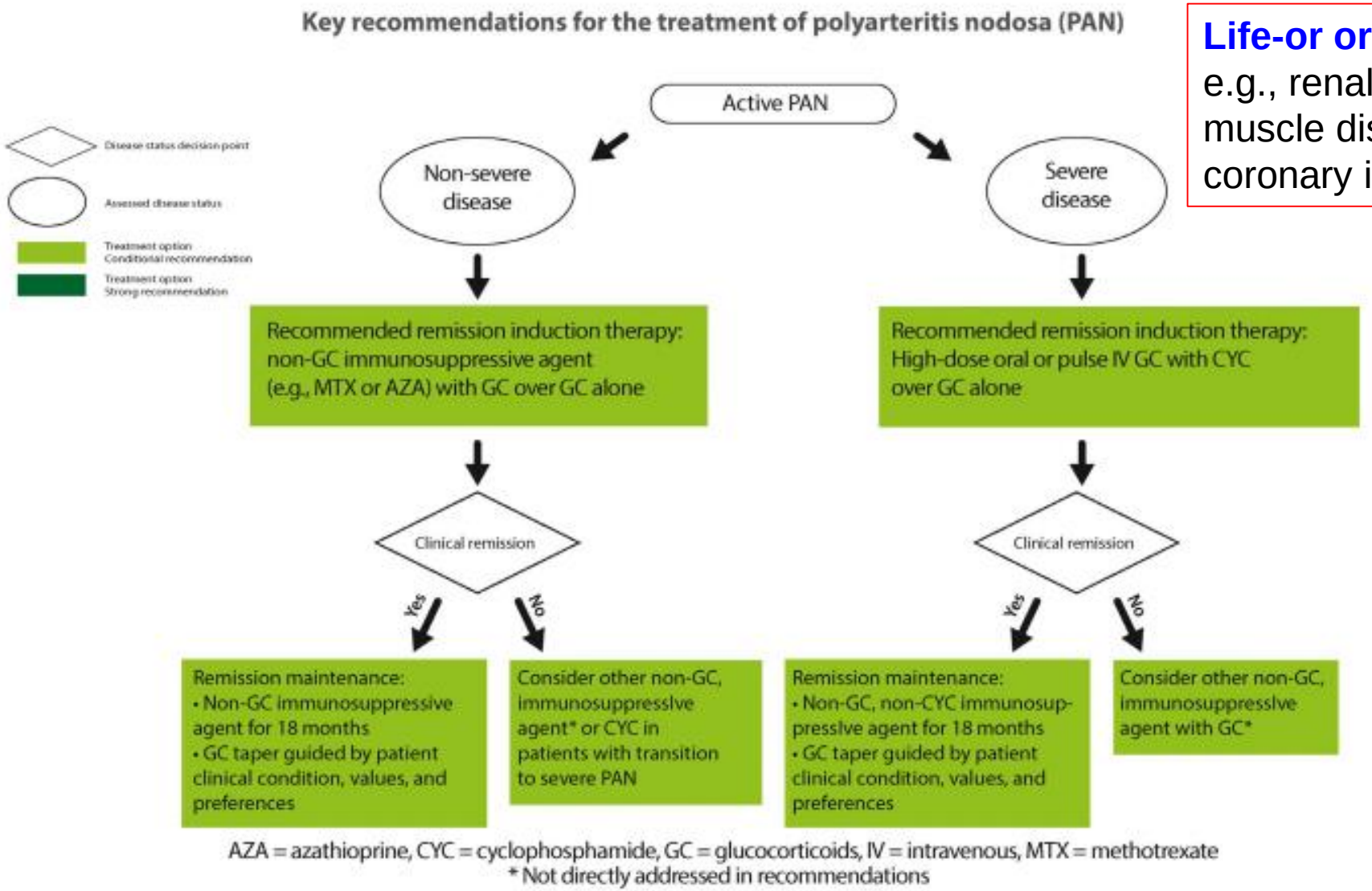
- A 45 years old female presented with right foot drop for 1 month.
- She had prolonged fever with significantly weight loss.
- Physical examination reveals BP 160/100 mmHg, no bruit.
- Painful subcutaneous nodules of skin at both thighs.
- Urine examination shows RBC 20-30/HPF, no dysmorphic change/cast.
- Serum creatinine is 2.8 mg/dl.
- ANA-negative, normal level of complement.

What is the most helpful investigation on the diagnosis?

Polyarteritis nodosa

ACR Classification of Polyarteritis Nodosa (3 of 10 are required)	Other features
Weight loss ≥4 kg (90%)	Fever (current and previous)
Livedo reticularis (60%)	Purpura, nodules, ulcers, bullous or vesicular eruptions, and segmental skin edema
Testicular pain or tenderness (20%)	
Myalgias, weakness, or leg tenderness	Arthritis, arthralgia; when muscle is involved, it provides a useful site for biopsy.
Mononeuropathy or polyneuropathy (75%)	
Diastolic blood pressure >90 mm Hg Elevated blood urea nitrogen or creatinine (50%)	• Renal ischemia or infarcts causing activation of the renin-angiotensin system • Vasculitis involving the intra-renal arteries or rupture of renal arterial aneurysms • Glomerular ischemia may result in rising creatinine, mild proteinuria or hematuria, but red cell casts are absent.
Hepatitis B virus (HCV, HIV, Idiopathic)	• Mesenteric artery involvement (40%) • Bowel, liver, or splenic infarction • Bowel perforation or bleeding from a ruptured arterial aneurysm
Abdominal vascular imaging	• Renal artery stenosis, or renal, hepatic and mesenteric arterial aneurysms (1-5 mm)
Deep-skin biopsy/sural nerve and muscle biopsy	• Necrotizing vasculitis, containing polymorphonuclear neutrophils
Suggesting alternative diagnosis	• Ear, nose, throat and respiratory involvement • Glomerulonephritis • ANCA, cryoglobulin positive or hypocomplementemia • Granulomatous vasculitis

2021 ACR/Vasculitis Foundation Guideline for PAN



Life-or organ-threatening manifestations
e.g., renal disease, mononeuritis multiplex, muscle disease, mesenteric ischemia, coronary involvement, limb/digit ischemia

Polyarteritis nodosa: treatment

Type	Treatment
Idiopathic PAN	• FFS=0 (cutaneous PAN, Mild arthritis): prednisolone 1 MKD + MTX, AZA
	• FFS≥1: IV pulse GCs -> prednisolone 1 MKD + IVCY monthly 3-6 infusions then AZA/MTX 18 months • Catastrophic cases: ± plasmapheresis
HBV-associated PAN	• FFS = 0: Anti-viral TX
	• FFS ≥ 1: Anti-viral TX, prednisolone 1 MKD + plasmapheresis
Five factor scores (1996) 1. Cr> 1.58 mg/dl 2. Proteinuria > 1 g/d 3. GI involvement 4. Cardiomyopathy 5. Neurological involvement	**Revised Five factor scores (2001)** 1. Cr> 1.7 mg/dl 2. GI involvement 3. Cardiomyopathy 4. Age > 65 y FFS = 0; 5-year mortality 12% FFS > 0; 5-year mortality 26-46%

Scenario 13

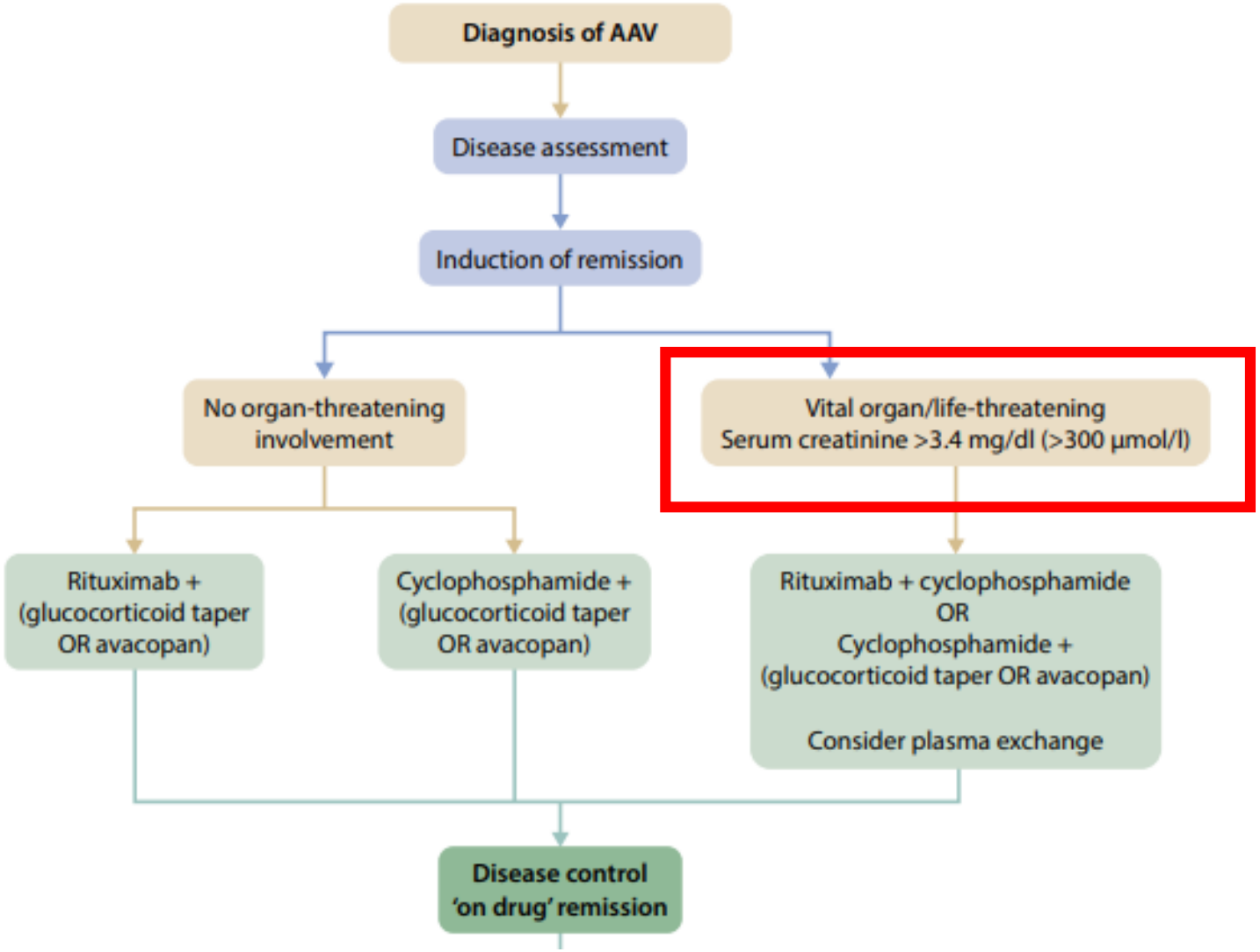
- A 68-year-old patient with limited GPA presented with DAH.
- Her current medications were prednisolone 5 mg and 20 mg- MTX weekly.
- BP was 160/90 mmHg.
- Creatinine 4.8 mg/dl (GFR 14 cc/min). Urine test showed red blood cell casts.
- Kidney biopsy showed cellular crescents.
- Arterial blood gas was PaO2 88.
- PR3-ANCA 3+.
- ANA and anti-GBM negative.

What is the appropriate management including pulse steroid and PLEX?

ANCA-associated vasculitis

	GPA	MPA	E-GPA
Upper respiratory tract	▪ Nasal involvement, sinusitis ▪ Saddle-nose deformity ▪ Subglottic stenosis ▪ Hearing loss	Absent	▪ Allergic rhinitis ▪ Nasal polyps ▪ EO > 10% (>1000/uL)
Lung	Nodule, cavity, DAH	Fibrosis, ILD, DAH	Severe, late-onset asthma Migratory pulmonary infiltration
Kidney	Necrotizing crescentic GN, RPGN (pauci-immune)	Necrotizing crescentic GN, RPGN (pauci-immune)	Uncommon
Others	Scleritis, proptosis (GPA), pachymeningitis (GPA) Fever, arthritis, myositis, palpable purpura, skin ulcer (E-GPA) Myocarditis (E-GPA), mononeuritis multiplex (E-GPA), enteritis (E-GPA)		
Pathology (Pauci-immune)	▪ Granulomatous necrotizing vasculitis	▪ Necroizing vasculitis ▪ No granulomatous	▪ Granulomatous necrotizing vasculitis ▪ Abundant extravascular eosinophils
ANCA	C-ANCA/PR3 Generalized (80-95%) Localized (40-75%)	P-ANCA/MPO (60-85%)	P-ANCA/MPO (30-60%)
Biopsy (diagnostic yield)	▪ 91% Renal biopsy (+renal involvement) ▪ 68% ENT (non-specific inflammation, granuloma) ▪ 12% transbronchial biopsies for GPA and 66.7% for EGPA, open lung biopsy (higher yield)		

2024 KDIGO Treatment for AAV with Kidney



Rituximab preferred

- Children and adolescents
- Concerned about their fertility
- Frail older adults
- Glucocorticoid-sparing especially important
- Relapsing disease
- PR3–ANCA disease
- Azathioprine allergy

Consider plasma exchange for patients

1. SCr >3.4 mg/dl (>300 mmol/l), requiring dialysis or with RPGN
2. DAH with hypoxemia
3. An overlap syndrome with anti-GBM

Data from RCTs of Rituximab induction in GPA/MPA

	Population	Intervention	Comparator	Outcomes
RAVE (N=197)	GPA or MPA (ANCA+) - newly diagnosed (48%) - relapsing (78% CYC) - sCr <4 mg/dl	RTX 375 mg/m2 weekly x 4	CYC 2 MKD (3-6 months)/AZA	Remission without PRED at 6 months - RTX (64%) non-inferior CYC (53%) (p< 0.001) - Better for relapsing disease (67% vs 42%, p = 0.01) (esp. PR-3) - Similar AE
RITUXVAS (N=44)	GPA or MPA (ANCA+) - newly renal - eGFR 18 ml/min/m2	RTX 375 mg/m2 weekly x 4 + IVCY 15 mg/kg x at week1,3	IVCY 15 mg/kg q 2-3 weeks (13-24week)/AZA	Remission at 12 months - Similar RTX+IVCY vs IVCY (76% vs 82%) - Similar AE

Stone J. H. et al. NEJM 2010

Jones RB et al. NEJM 2010

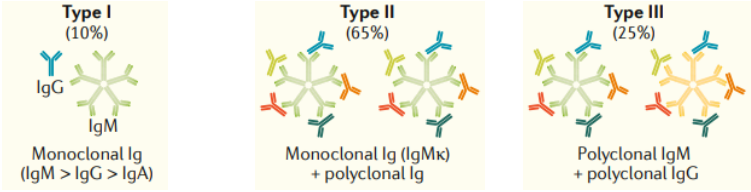
Scenario 14

- A 58-year-old woman presented with severe dry eyes and a 4-week of rising creatinine.
- Her hands and feet turned bluish and some gangrene.
- BP 160/90 mmHg. Palpable purpura was presented.
- Serum creatinine 4.3 mg/dl.
- UA showed protein 2+ with dysmorphic red blood cells.
- ANA 1:160 cytoplasmic pattern.
- Anti-SSA was strong positive. Anti-dsDNA was negative.
- Low level of complement 4. Rheumatoid factor was 110 IU.

What is the appropriate management in addition to high dose of steroid?

Cryoglobulins

Type	RF, low C4	Monoclonality	Associated disease	Presentation
Type 1 (10-15%)	-	Yes (IgG *OR* IgM)	MM, Waldenstrome's macroglobulinemia, non-Hodgkin's lymphoma, MGUS	• Cold provokes Raynaud's phenomenon, acrocyanosis or gangrene or livedo reticularis • Hyper-viscosity (dizzy, confusion, stroke)
Type 2* (50-60%)	++	Yes (polyclonal IgG, monoclonal IgM)	HCV (30-100%)** HIV, HBV SLE, Sjogren, RA 10% essential	Meltzer triad • purpura, weakness, arthralgia Necrotizing vasculitis • mononeuritis, MPGN, diffused alveolar hemorrhage
Type 3* (30-40%)	++	No (polyclonal IgG, IgM)		



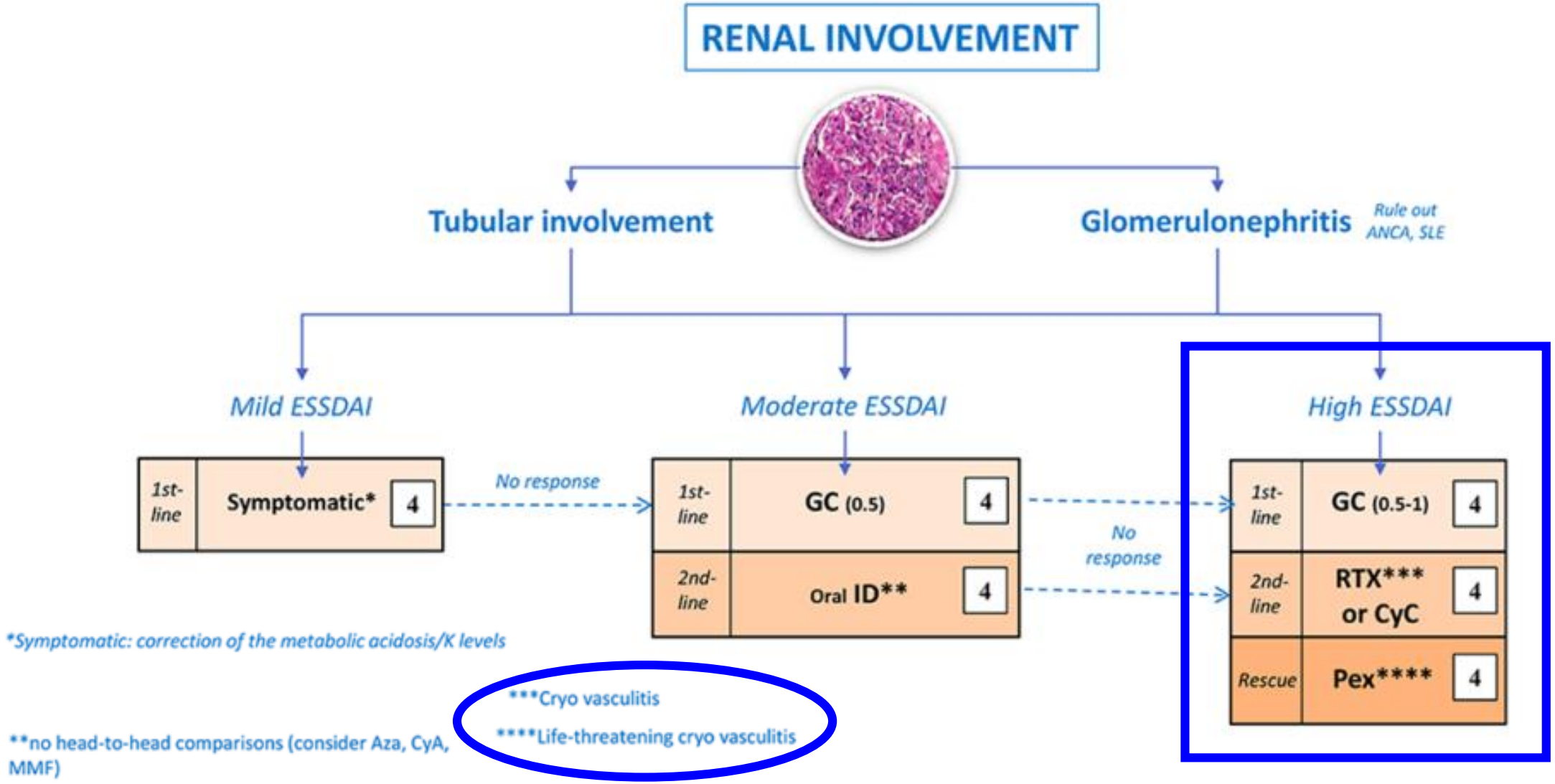
Investigation	Cryoglobulin level, C4, RF, Anti-HCV, ANA, skin biopsy (LCV, lymphocytes), kidney biopsy (MPGN, PAS plugs (cryoplugs))

*mixed cryoglobulin, ** associated disease: *non-essential mixed cryoglobulin*

Cryoglobulins

	Treatment
Type I cryoglobulinemia	• Treatment of underlying disease
HCV	• Interferon free regimens, the oral direct acting anti viral agents (DAAs) and the newer protease inhibitors • Interferon + ribavirin
Minor • **purpura, arthritis, myalgia**	• 0.1-0.3 MKD Prednisolone
Life threatening condition • **Severe renal involvement** • **Extensive skin ulcer or limb necrosis** • **Pulmonary hemorrhage** • **Intestinal vasculitis** • **CNS** • **Hyper-viscosity syndrome**	• 0.5-1.5 MKD Prednisolone and • Rituximab (treatment of choice) • Cyclophosphamide • Plasma exchange

Primary SjS presenting with RENAL involvements (EULAR Recommendation 2020)



Good luck