Brigham and Women's Hospital
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# What's New in Rheumatology for the Generalist

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- Clinical focus: Vasculitis
- Research focus: Medical Education

# DISCLOSURES

**I have no relevant financial relationships with ineligible companies.**

# OBJECTIVES

- Review and apply recent advances in rheumatology to the evaluation and treatment of patients with:
  - Use of anti-rheumatic drugs
  - SLE
  - GCA
  - GLP1s

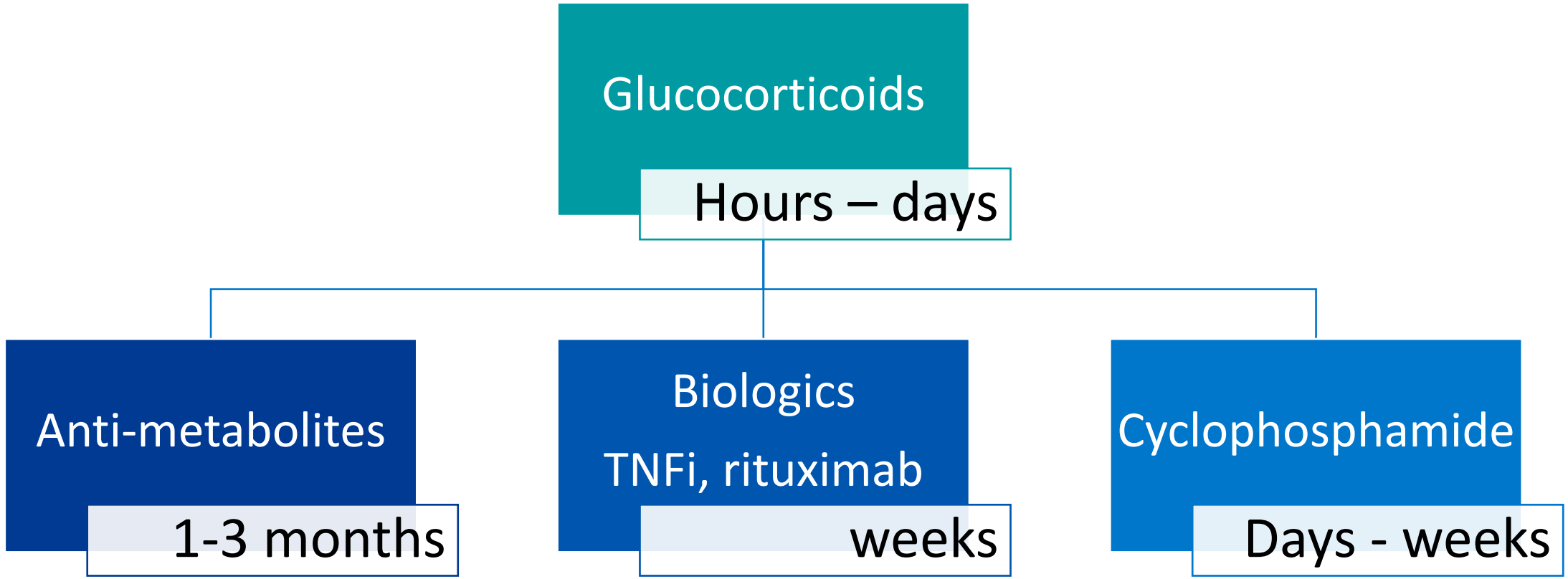
# Case 1

- 60 year old woman with a history of seropositive RA presents for routine visit
- Taking methotrexate and adalimumab for past year
- Symptoms are well controlled and there's no synovitis on exam
- ESR 40 (ULN 30), CRP 15 (ULN 10), RF and CCP positive

What lab monitoring is recommended

a. CBC, CMP every 1-2 months
b. CBC, CMP every 3 months
c. CBC, CMP every 6 months
d. CBC, CMP annually

# Approach to using immunomodulatory drugs

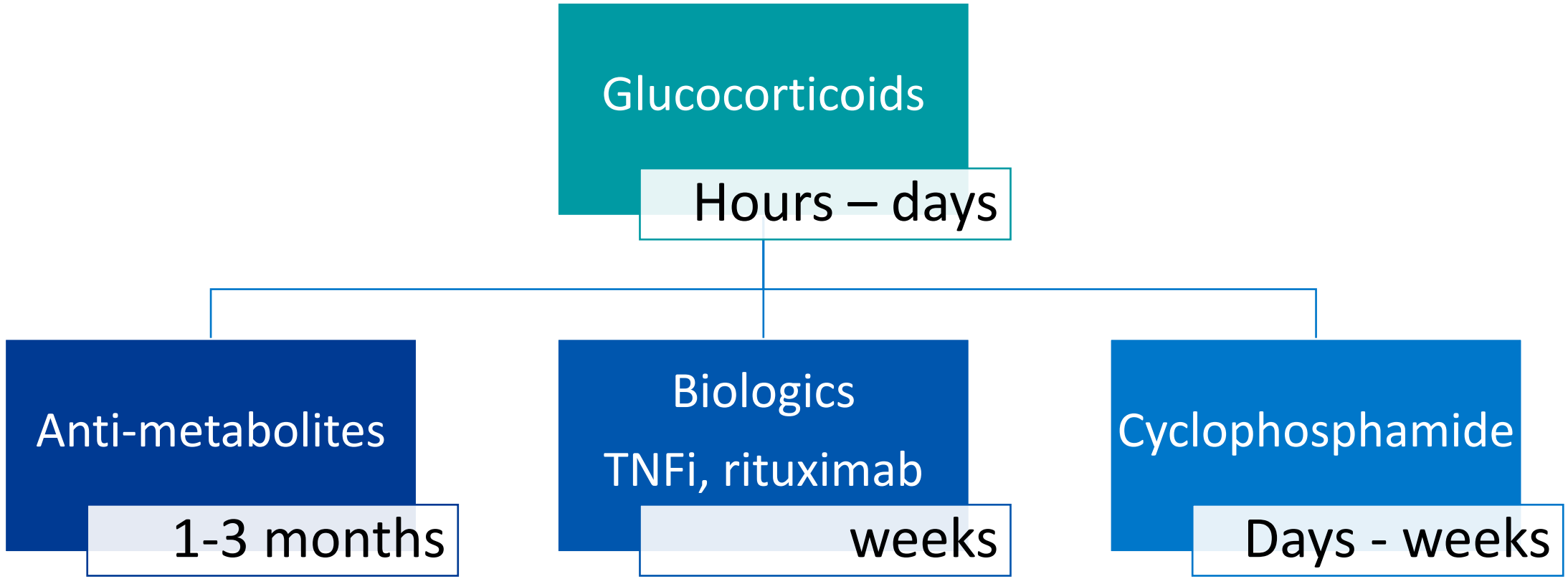



- TB/hepatitis +/- HIV, syphilis
- Lab monitoring
  - <3 mos – q4 weeks
  - 3-6 mos – 8-12 weeks
  - After – 3 months

- TB/hepatitis +/- HIV, syphilis
- Lab monitoring
  - Depending on drug but generally less frequent (JAKi more frequent)

- TB/hepatitis +/- HIV, syphilis
- IV vs PO
- Frequent lab monitoring

# Approach to using immunomodulatory drugs




- Toxicities generally reversible
- Lab abnormalities often respond to dose adjustments
- Risk of infection relatively low

- Toxicity more rare but potentially more serious
- Risk of infection higher

- Risk of infection high
- Malignancy / cytopenias

# Long-Term Routine Laboratory Toxicity Monitoring of Immunomodulatory Drugs in Rheumatoid Arthritis

| Laboratory Test | Threshold (Very Abnormal) | 2-Year Cumulative Incidence | 5-Year Cumulative Incidence |
|---|---|---|---|
| Leukocyte count | $2.0 \times 10^9$/L | 0.2% | 0.3% |
| Platelet count | $100 \times 10^9$/L | 0.5% | 0.8% |
| ALT | >300 U/L | 0.6% | 1.0% |
| Hemoglobin | 6 mmol/L | 2.3% | 3.8% |
| eGFR | 45 mL/min/1.73 $m^2$ | 6.6% | 11% |



Dasgupta et al Ann Rheum Dis. 2012 Apr 1;71(4):484

ORIGINAL RESEARCH

Annals of Internal Medicine

# Long-Term Routine Laboratory Toxicity Monitoring of Immunomodulatory Drugs in Rheumatoid Arthritis

| Clinical Context | Percentage |
|---|---|
| Already known or clinically suspected | 47.7% |
| Did not lead to any clinical action | 35.8% |
| Considered unrelated to DMARD use | 24.1% |
| Occurred after a dose increase | 6.5% |

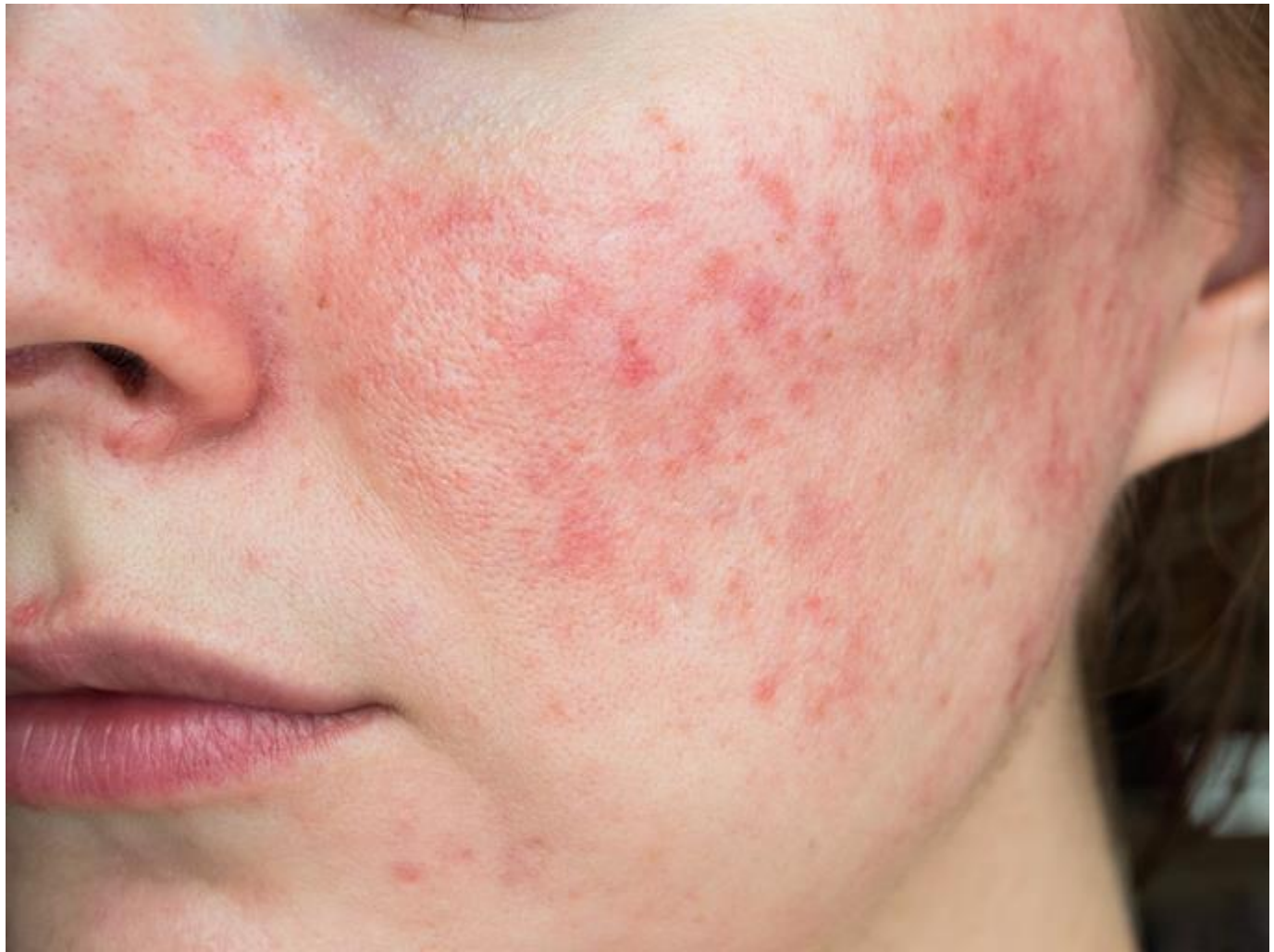


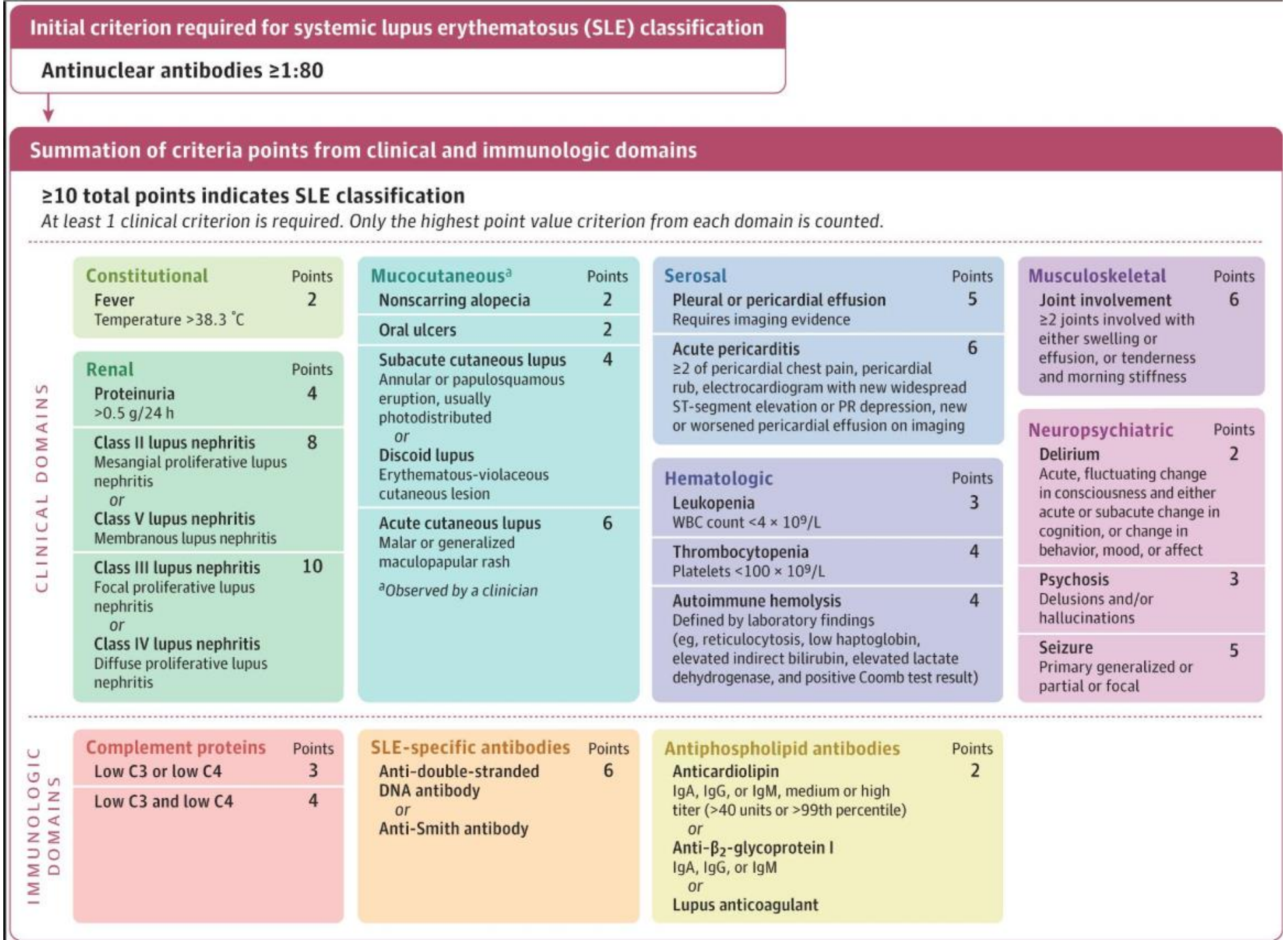
Dasgupta et al Ann Rheum Dis. 2012 Apr 1;71(4):484

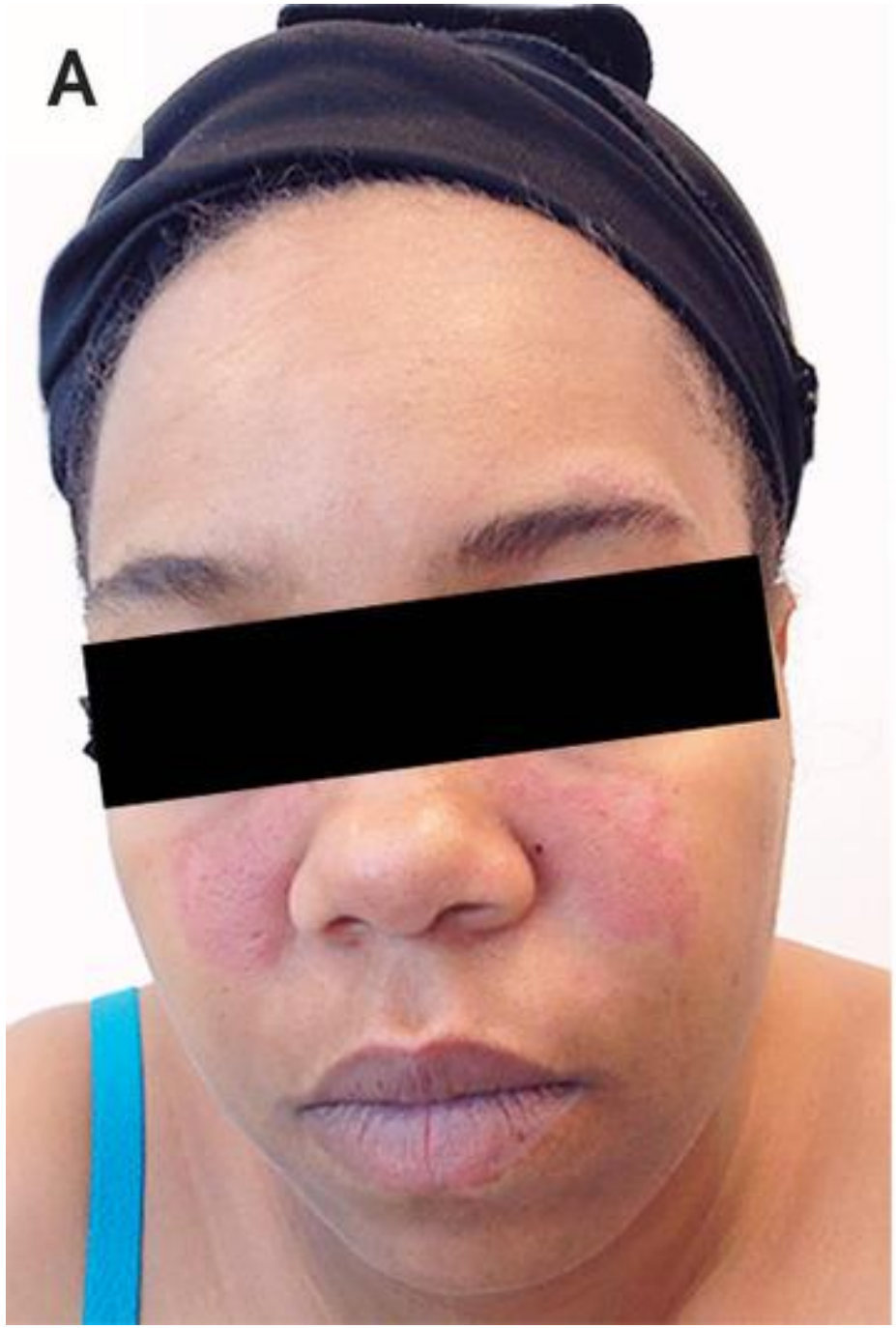
# Case 2

- 45 yo F presents with:
  - Raynaud's – started at age 16
  - Chronic fatigue
  - Facial rash
  - Normal CBC, CMP, TSH, ESR, CRP

- What is the pretest probability of SLE?
  a) Low
  b) Moderate
  c) High




Initial criterion required for systemic lupus erythematosus (SLE) classification
Antinuclear antibodies ≥1:80
Summation of criteria points from clinical and immunologic domains
≥10 total points indicates SLE classification
At least 1 clinical criterion is required. Only the highest point value criterion from each domain is counted.
CLINICAL DOMAINS
Constitutional
Points
Fever
Temperature >38.3 °C
2
Renal
Points
Proteinuria
>0.5 g/24 h
4
Class II lupus nephritis
Mesangial proliferative lupus nephritis
or
Class V lupus nephritis
Membranous lupus nephritis
8
Class III lupus nephritis
Focal proliferative lupus nephritis
or
Class IV lupus nephritis
Diffuse proliferative lupus nephritis
10
Mucocutaneous[a]
Points
Nonscarring alopecia
2
Oral ulcers
2
Subacute cutaneous lupus
Annular or papulosquamous eruption, usually photodistributed
or
Discoid lupus
Erythematous-violaceous cutaneous lesion
4
Acute cutaneous lupus
Malar or generalized maculopapular rash
6
[a]Observed by a clinician
Serosal
Points
Pleural or pericardial effusion
Requires imaging evidence
5
Acute pericarditis
≥2 of pericardial chest pain, pericardial rub, electrocardiogram with new widespread ST-segment elevation or PR depression, new or worsened pericardial effusion on imaging
6
Hematologic
Points
Leukopenia
WBC count <4 × 10⁹/L
3
Thrombocytopenia
Platelets <100 × 10⁹/L
4
Autoimmune hemolysis
Defined by laboratory findings (eg, reticulocytosis, low haptoglobin, elevated indirect bilirubin, elevated lactate dehydrogenase, and positive Coomb test result)
4
Musculoskeletal
Points
Joint involvement
≥2 joints involved with either swelling or effusion, or tenderness and morning stiffness
6
Neuropsychiatric
Points
Delirium
Acute, fluctuating change in consciousness and either acute or subacute change in cognition, or change in behavior, mood, or affect
2
Psychosis
Delusions and/or hallucinations
3
Seizure
Primary generalized or partial or focal
5
IMMUNOLOGIC DOMAINS
Complement proteins
Points
Low C3 or low C4
3
Low C3 and low C4
4
SLE-specific antibodies
Points
Anti-double-stranded DNA antibody
or
Anti-Smith antibody
6
Antiphospholipid antibodies
Points
Anticardiolipin
IgA, IgG, or IgM, medium or high titer (>40 units or >99th percentile)
or
Anti-β2-glycoprotein I
IgA, IgG, or IgM
or
Lupus anticoagulant
2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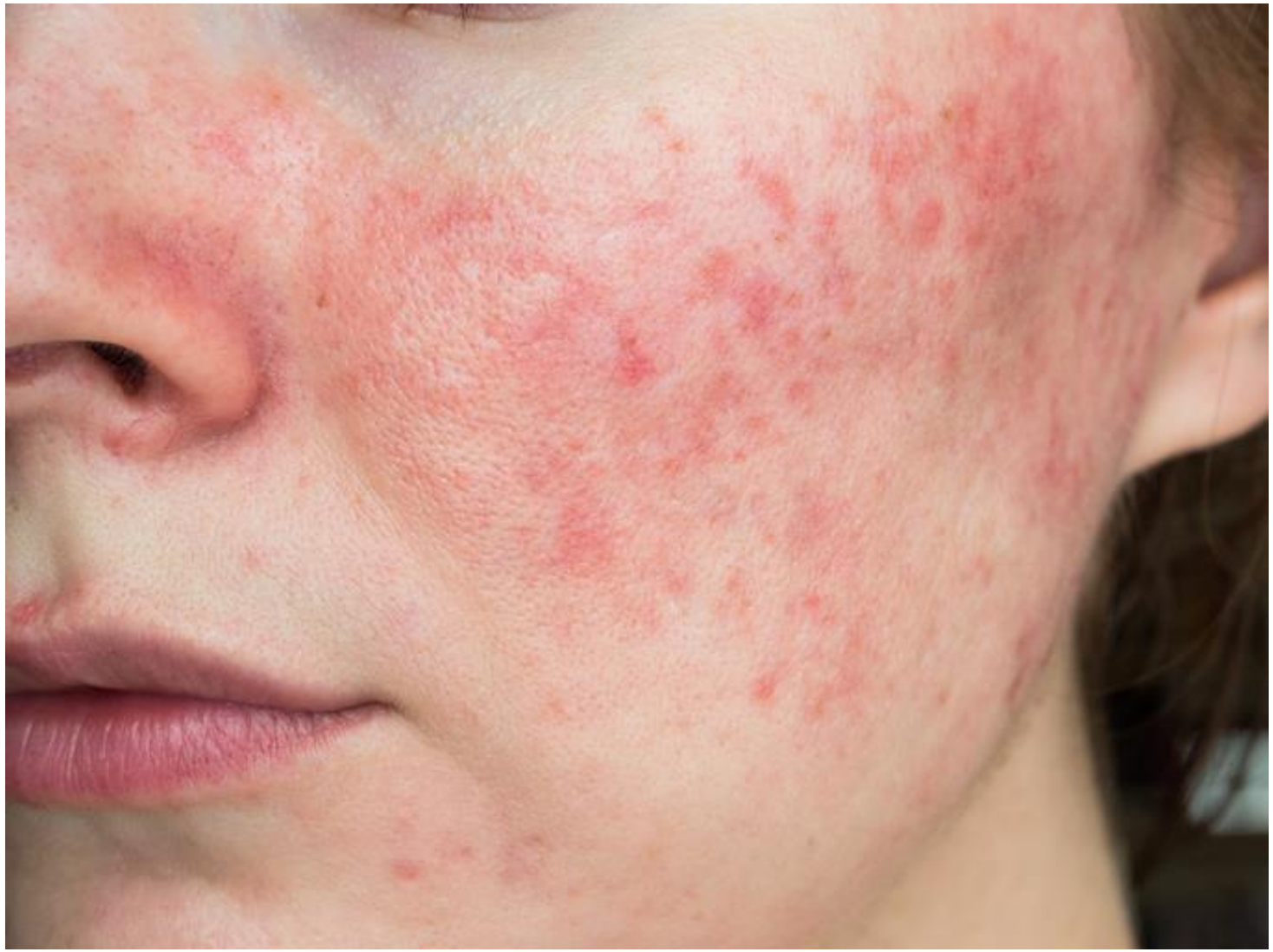


# Approach to connective tissue diseases

- SLE
- Sjogren's
- Scleroderma
- MCTD
- Myositis
- Undifferentiated CTD

CTD – non-differentiators

- Raynaud's
- Sicca
- Oral ulcers
- Inflammatory arthritis
- Serositis

# Approach to connective tissue diseases

- SLE

Is there sicca? → Sjogren's

Is there Raynaud's? → Scleroderma

Is there elevated CK or ILD? → Myositis

# Approach to laboratory workup of CTDs

- SLE → DsDNA, Smith; C3, C4, antiphospholipid antibodies
- Sjogren's → Ro, La
- Scleroderma → centromere *limited*; Scl70, RNApol3 *diffuse*
- MCTD → RNP
- Myositis → CK, aldolase, myositis panel, Jo-1

| Antibody | % |
|---|---|
| DsDNA | 60% |
| Smith | 30% |
| Ro | 40% |
| RNP | 50% |
| ↓C3/C4 | 50% |
| APLAs | 30% |

# Systemic Lupus Erythematosus

**HCQ** (unless contraindicated)

**Glucocorticoids: Only if necessary, at lowest effective dose for shortest possible duration***

**Taper to ≤5 mg/day by 6 months** (ideally to zero)

**Pulse glucocorticoid for organ- and life-threatening manifestations**

**Escalation of therapy (any organ system) when refractory to initial treatment**

**Early introduction of immunosuppressive agents to minimize glucocorticoid toxicity***

## Mucocutaneous

Sunscreen /Topicals

**ACLE, SCLE, CCLE**

Mild
- Add quinacrine
- Switch HCQ to CQ**

Moderate-Severe†
- Methotrexate
- MPAA
- Anifrolumab
- Belimumab

Refractory
- Lenalidomide

**Bullous LE**

Mild
- Dapsone

Severe
- Azathioprine
- Methotrexate
- MPAA
- Anti-CD20

**Chilblain LE**
- CCB
- PDE5i
- Pentoxifylline

**LCV**
- Colchicine
- Dapsone

## Musculoskeletal

**Arthritis**
- Azathioprine
- Methotrexate§
- MPAA∴

Low threshold to add/substitute for
- Anifrolumab
- Belimumab

## Serositis

**Pleuropericarditis**

Initial treatment, mild
- Colchicine
- NSAIDs
- and/or IVIG

Ongoing/recurrent
- Azathioprine
- MPAA∴
- Anifrolumab
- Belimumab
- IL-1 blockade

## Hematologic

**Leukopenia**

Asymptomatic
- **No** IS treatment unless other SLE activity present

**Thrombocytopenia**

Asymptomatic <30,000 platelets/ mcL
- Azathioprine
- CNI
- MPAA∴
- Belimumab
- Anti-CD20 and/or IVIG

Symptomatic
- Anti-CD20 and/or IVIG

**Hemolytic anemia**

Symptomatic
- Anti-CD20 and/or IVIG

## Neuropsychiatric

**Psychosis/seizures**

Anti-psychotic / anti-seizure therapy
- MPAA
- Anti-CD20
- IV CYC

**Optic neuritis, acute confusional state, mononeuritis multiplex**
- IV CYC‖
- MPAA
- Anti-CD20

**Myelitis**
- IV CYC

**Cognitive Dysfunction**

Cognitive therapy
- **No** IS treatment

## Cardiac

**Myocarditis**
- IV CYC
- MPAA
- Anti-CD20 and/or IVIG

**Libman-Sacks Endocarditis**
- Anticoagulation
- IS therapy

## Vasculitis
- Azathioprine
- IV CYC
- MPAA
- Anti-CD20
- Anifrolumab
- Belimumab

Severe
- IV CYC
- Anti-CD20

Life-threatening
Addition of:
- PLEX and/or IVIG

Strong recommendation for

Conditional recommendation for

Conditional recommendation against

*Good practice statements

# Case 3

- 68 yo F presents to her PCP c/o 4 weeks of headache and jaw pain (worse with chewing, better with rest)
- ROS
  - - scalp tenderness, visual changes, PMR symptoms, fevers/chills/night sweats
- Exam – no TA abnormalities, nl vascular exam
- ESR – 42 (< 20mm/hr), CRP – 29 (<8mg/L)
- Started on steroids with improvement but not resolution of sxs
- Temporal artery ultrasound and biopsy are negative
- What is the next best step
  - Treat as GCA
  - Rapid steroid taper
  - CTA chest/abdomen/pelvis

# A probability score to aid the diagnosis of suspected giant cell arteritis

Low prob < 9
Intermediate 9-12
High >12

| Weightage | -3 | 0 | +1 | +2 | +3 |
|---|---|---|---|---|---|
| Demographics | | | | | |
| Age (years) | | ≤49 | 50-60 | 61-65 | ≥66 |
| Sex | | | M | F | |
| Duration | | | | | |
| Onset of symptoms | | >24 weeks | 12-24 weeks | 6-12 weeks | <6 weeks |
| Laboratory | | | | | |
| CRP | | 0-5 mg/L | 6-10 mg/L | 11-25 mg/L | ≥25 mg/L |
| Symptoms | | | | | |
| Headache | | N | Y | | |
| Polymyalgic | | N | | Y | |
| Constitutional | | N | Single | | Combination |
| Ischaemic | | N | | | Y |
| Signs | | | | | |
| Visual (AION, CRAO, Field loss, RAPD) | | N | | | Y |
| TA abnormality | | N | Tenderness | Thickening | Pulse loss |
| Extra-cranial artery abnormality | | N | Thickening | Bruit | Pulse loss |
| Cranial nerve paisy | | N | | | Y |
| Alternative | | | | | |
| Infection | Y | | | | |
| Cancer | Y | | | | |
| Systemic Rheumatic diseases | Y | | | | |
| Head and neck pathology | Y | | | | |
| Other | Y | | | | |
| Total score | | | | | |



Laskou, Clin Exp Rheumatology 20224

# Approach to GCA

New headache

Elevated inflammatory markers

- Jaw claudication
- Ocular ischemia
- PMR

## Low risk

- TA U/S

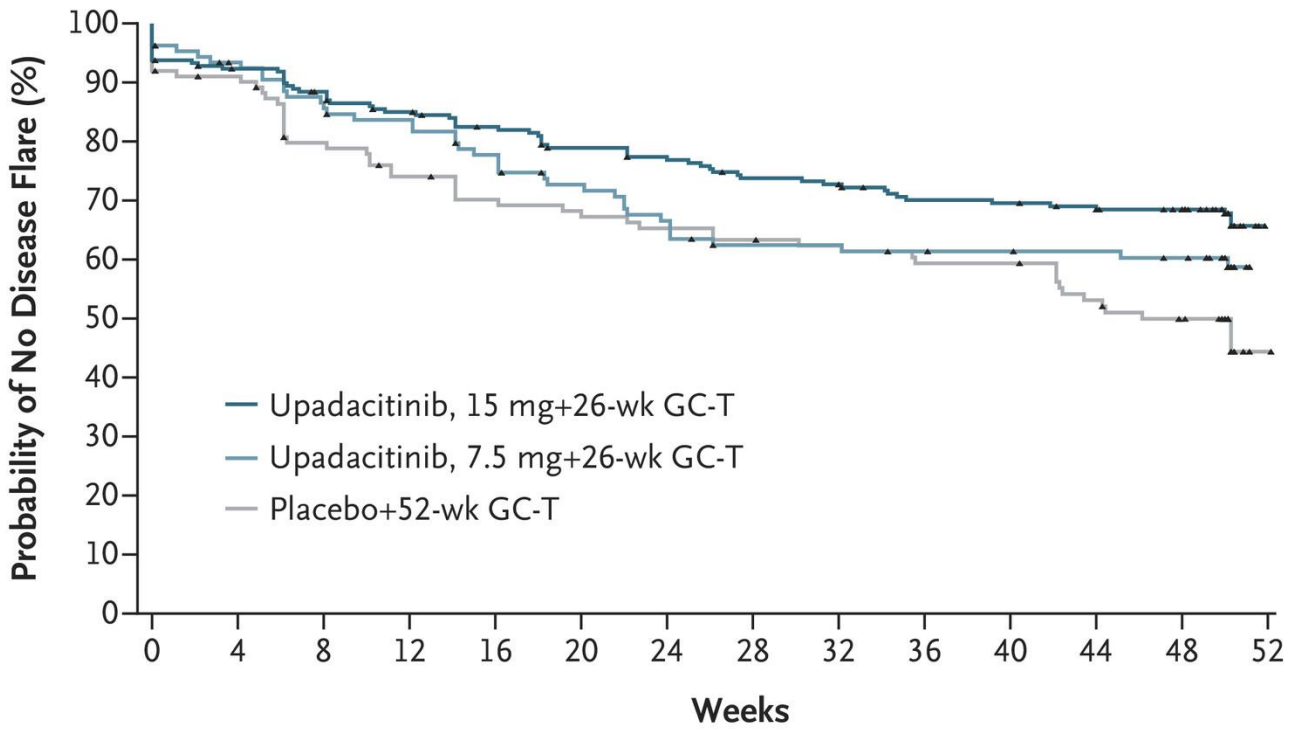
## Medium risk

- Start prednisone
- TA U/S -> TAB -> CTA
- Stop prednisone if negative

## High risk

- Start prednisone
- Full workup
- Likely treat as GCA

# A Phase 3 Trial of Upadacitinib for Giant-Cell Arteritis

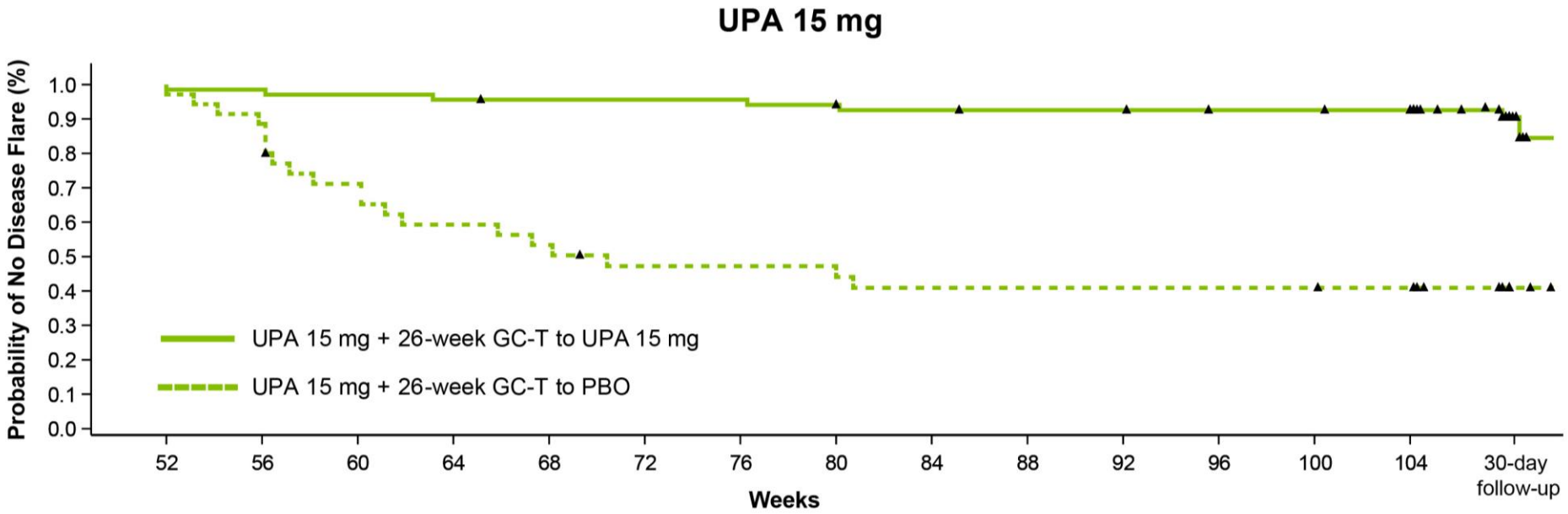



**No. at Risk**

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Upadacitinib, 15 mg +26-wk GC-T | 209 | 190 | 180 | 171 | 163 | 154 | 150 | 142 | 140 | 132 | 131 | 128 | 123 |
| Upadacitinib, 7.5 mg +26-wk GC-T | 107 | 96 | 89 | 85 | 78 | 71 | 65 | 59 | 59 | 58 | 57 | 56 | 54 |
| Placebo+52-wk GC-T | 112 | 98 | 84 | 77 | 72 | 70 | 67 | 65 | 63 | 59 | 59 | 51 | 45 |

ORIGINAL ARTICLE

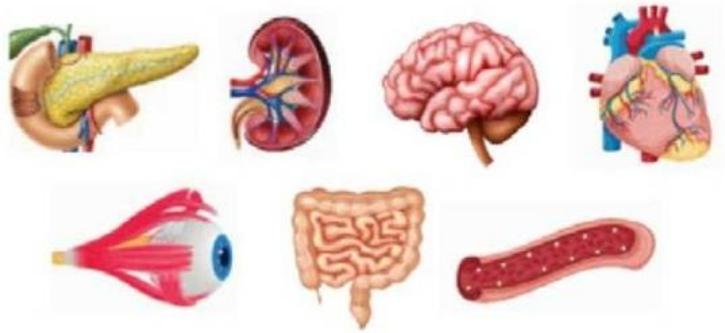
# A Phase 3 Trial of Upadacitinib for Giant-Cell Arteritis




| No. at Risk | | | | | | | | | | | | | | | Median Disease Flare |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| UPA 15 mg + 26 week GC-T to UPA 15 mg | 68 | 67 | 66 | 65 | 64 | 64 | 64 | 63 | 61 | 60 | 60 | 58 | 58 | 57 | NE (N |
| UPA 15 mg + 26-week GC-T to PBO | 35 | 31 | 24 | 20 | 18 | 15 | 15 | 15 | 13 | 13 | 13 | 13 | 13 | 12 | 70.4 (6 |

Schmidt et al. ACR Convergence (abstract)

## Glucagon Like Peptide-1 Receptor Expression



**Immune system**

Lymphocytes T and B

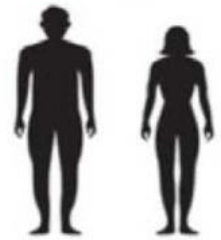
Macrophages

iNTK cells

Eosinophils

Neutrophils

## Glucagon Like Peptide-1 Receptor Agonists Actions

| In vitro | Murine models | Clinical trials |
|---|---|---|
|  |  |  |

↓ Citokines production

↓ Pro-inflammatory T-cells

↓ Macrophage infiltration

↑ Regulatory T-cells

**Conclusion**: Glucagon Like Peptide-1 Receptor Agonists demonstrated to exert anti-inflammatory and immunological proprieties in different experimental models

Bendotti et al Pharmacologic Research 2022

# GLP1 agonists in the rheumatic diseases

- Osteoarthritis – good evidence, RCT 407 pts with moderate OA (NEJM 2024)

- SLE – preliminary evidence
  - Target trial emulation – 910 GLP1 vs 1,004 DPP4i, lower risk of MACE, renal progression, all cause mortality (Arthritis and Rheumatology 2026)
  - Retrospective study – 9,386 pts, 0.59RR of lupus nephritis (American Journal of Medicine 2026)

- RA – preliminary evidence
  - Retrospective study of 215 patients improved disease activity (ACR Open 2025)

- Psoriatic arthritis
  - RCT 31 patients demonstrated reduced PASI scores (Biomolecules 2025)

# KEY TAKE HOME POINTS

- Lab monitoring of DMARDs is important but optimal frequency remains uncertain
- SLE classification criteria continues to evolve and treatment options are expanding enabling less glucocorticoid use with improved disease control
- Steroid sparing treatment options in GCA are expanding while duration of treatment remains uncertain
- GLP1 agonists may have a significant role in the management of rheumatic diseases and their complications

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