Brigham and Women's Hospital
Founding Member, Mass General Brigham

What's New in Rheumatology for the Generalist

Eli M. Miloslavsky, MD
Division of Rheumatology, Allergy and Immunology
Department of Medicine
Massachusetts General Hospital
Associate Professor of Medicine
Harvard Medical School

Eli Miloslavsky, MD

Icahn School of Medicine at Mount Sinai
Medicine Residency @ MGH
Rheumatology Fellowship @MGH
Associate Professor of Medicine@ HMS
Firm Chief, MGH Internal Medicine Program
Associate Program Director, MGH Rheumatology Fellowship

- Clinical focus: Vasculitis
- Research focus: Medical Education

DISCLOSURES

- None

OBJECTIVES

- Review and apply recent advances in rheumatology to the evaluation and treatment of patients with
  - Polymyalgia Rheumatica
  - SLE
  - Osteoarthritis
  - Obesity and consideration of GLP-1 use

Case 1

- 60 year old woman with a history of hypertension presents with rapid onset of bilateral shoulder pain x 2 weeks. 2 hrs of AM stiffness
- Exam with limitation of abduction to 70 degrees b/l active and passive
- Xrays with bilateral glenohumeral joint arthritis
- ESR 40 (ULN 30) and CRP 15 (ULN 10)

What is the most likely diagnosis?

a. Rotator cuff syndrome
b. Polymyalgia rheumatica
c. Osteoarthritis
d. Adhesive capsulitis

PMR classification criteria

Age at onset ≥ 50 years (required)
Bilateral shoulder aching (required)
Abnormal CRP and/or ESR (required)
Morning stiffness duration > 45 min (2 points)
Hip pain or limited range of motion (1 point)
Absence of RF or ACPA (2 points)
Absence of other joint involvement (1 point)
Required for classification: score of 4 or more

Dasgupta etalAnn Rheum Dis. 2012 Apr 1;71(4):484

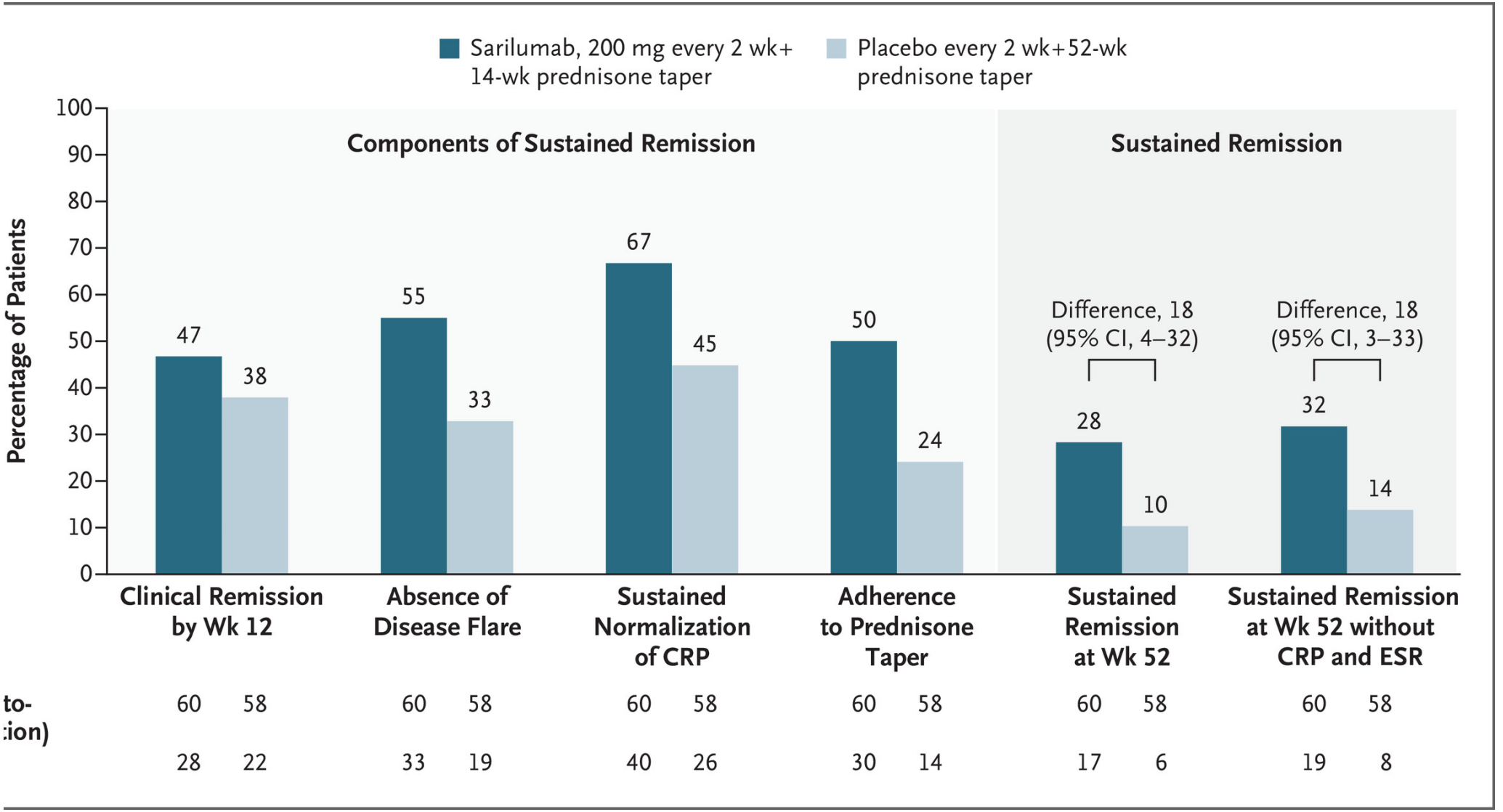
Case 1 (con't)

- Started on prednisone 15mg with complete resolution of symptoms and normalization of inflammatory markers
- Return of shoulder pain at 10mg with rising ESR/CRP
- 5lb weight gain, insomnia, mood symptoms

What should you do next? (choose multiple)

a. Increase prednisone to 12.5mg
b. Start sarilumab
c. Start methotrexate
d. Start naproxen

Sarilumab for Relapse of Polymyalgia Rheumatica during Glucocorticoid Taper



Spiera et al NEJM 2024

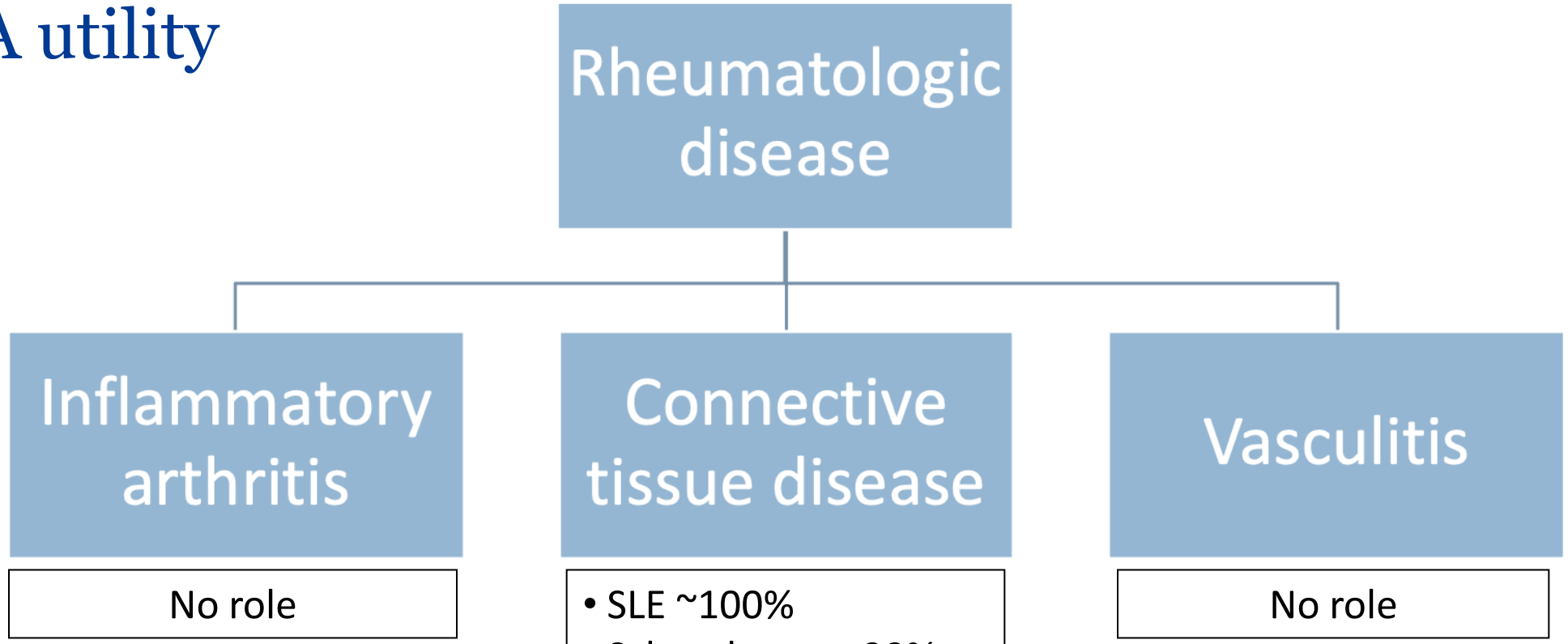
Case 2

- 25F with no PMH presents with
  - Joint pain in the wrists, MCPs, PIPs with 45 min of AM stiffness x 3 mos
  - Intermittent oral ulcers x 1 year
  - Exam with tenderness but no synovitis
  - Labs with ANA 1:320, nl CBC, inflammatory markers, +RF, -anti-CCP
  - C3/C4, DsDNA, Smith, Ro/La, RNP negative

What should you do next?

a. Diagnose SLE and start hydroxychloroquine
b. Diagnose RA and start methotrexate
c. Check urinalysis
d. Start naproxen and observe

ANA utility



ANA titer

1:40 – negative
1:80 – 1:160 – low
1:320-1:640 – moderate
1:280 and above - high

Inflammatory arthritis test characteristics

A. RF – 50-60% sensitive, 70% specific
B. CCP – 50-60% sensitive, 95% specific
C. ESR/CRP – normal in ~1/3 of patients

2019 SLE classification criteria

Clinical domains and criteria	Weight	Immunology domains and criteria	Weight
Constitutional		***Antiphospholipid antibodies***	
Fever	2	Anti-cardiolipin antibodies OR	
Hematologic		Anti-β2GP1 antibodies OR	
Leukopenia	3	Lupus anticoagulant	2
Thrombocytopenia	4	***Complement proteins***	
Autoimmune hemolysis	4	Low C3 OR low C4	3
Neuropsychiatric		Low C3 AND low C4	4
Delirium	2	***SLE-specific antibodies***	
Psychosis	3	Anti-dsDNA antibody* OR	
Seizure	5	Anti-Smith antibody	6
Mucocutaneous			
Non-scarring alopecia	2		
Oral ulcers	2		
Subacute cutaneous OR discoid lupus	4		
Acute cutaneous lupus	6		
Serosal			
Pleural or pericardial effusion	5		
Acute pericarditis	6		
Musculoskeletal			
Joint involvement	6		
Renal			
Proteinuria >0.5g/24h	4		
Renal biopsy Class II or V lupus nephritis	8		
Renal biopsy Class III or IV lupus nephritis	10		

Total score:

↓

Classify as Systemic Lupus Erythematosus with a score of 10 or more if entry criterion fulfilled.

Aringer et al Arthritis Rheumatol. 2019 Aug 6;71(9):1400

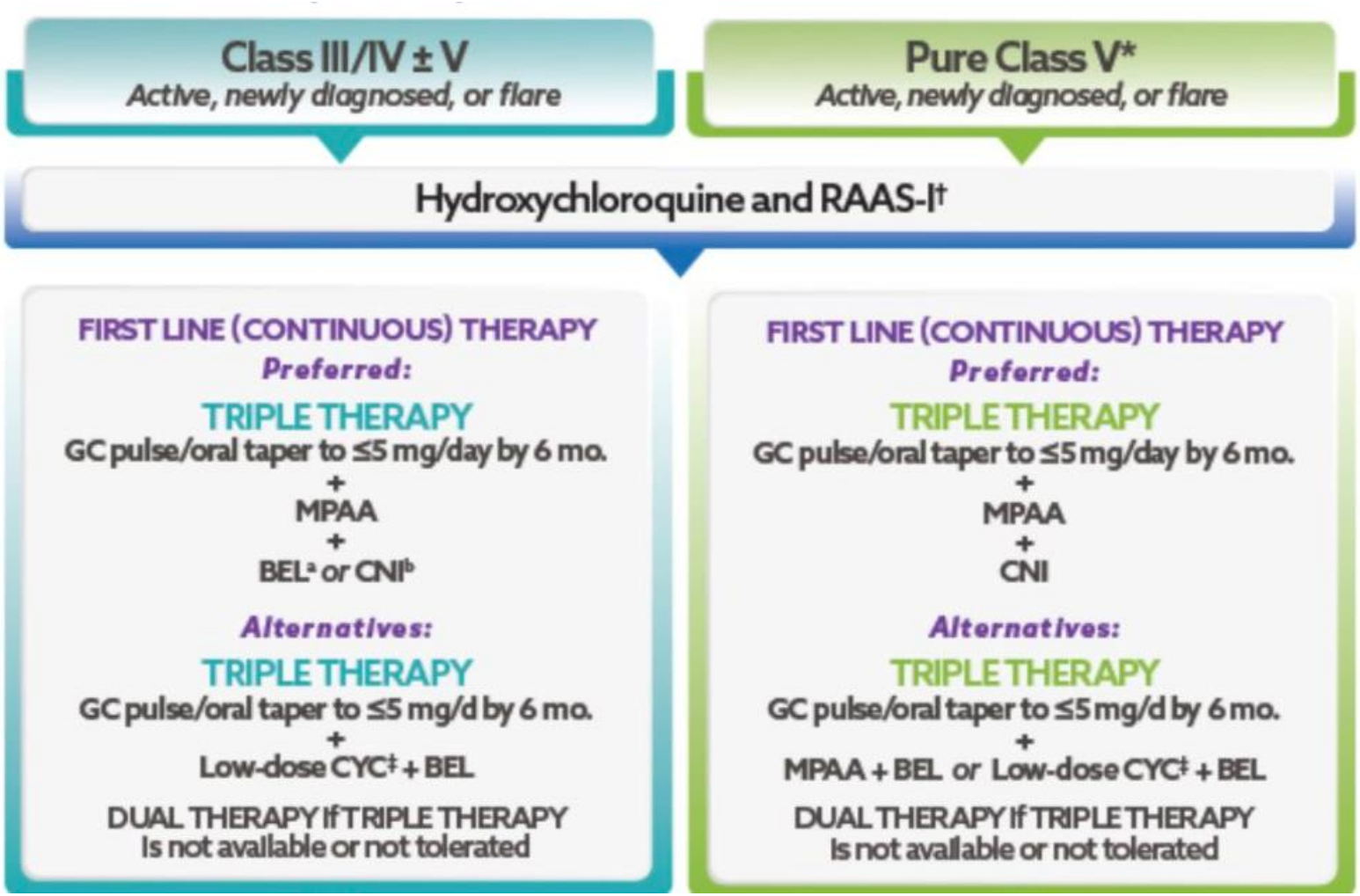
Case 2 (con't)

- Urinalysis reveals 4g proteinuria, 50-100 RBCs and RBC casts
- Biopsy reveals class IV lupus nephritis

What is the most appropriate treatment?

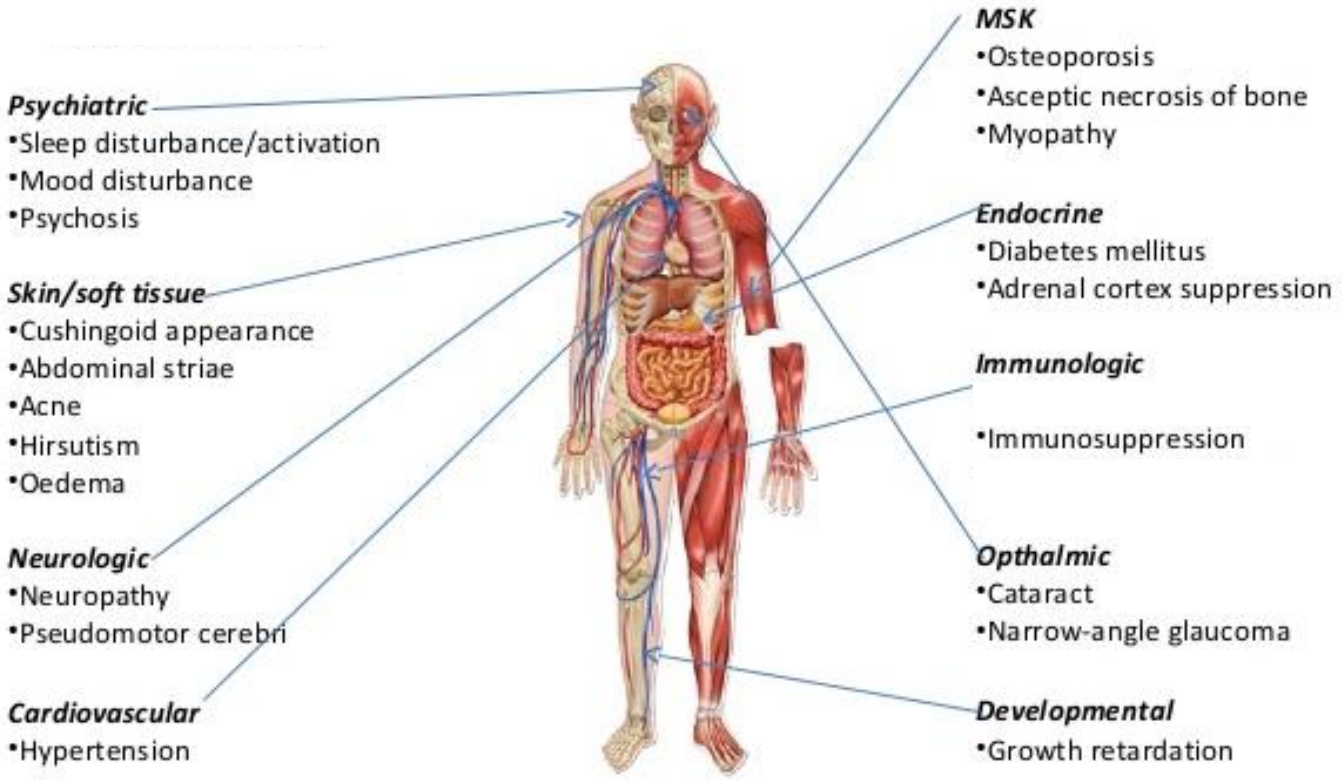
a. Prednisone
b. Prednisone and mycophenolate
c. Prednisone and mycophenolate and belimumab
d. Prednisone and mycophenolate and voclosporin

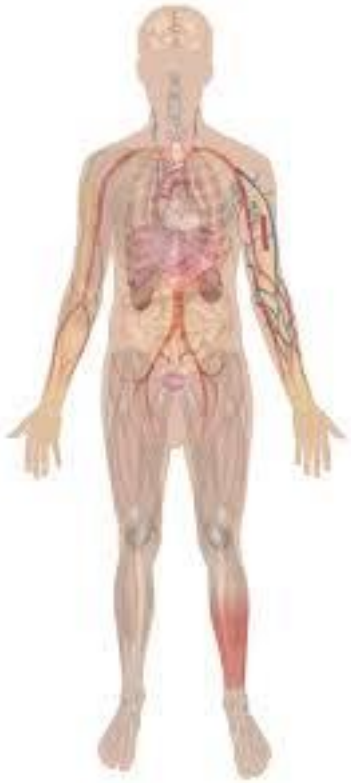
2024 ACR Lupus Nephritis Treatment Guideline



Sammaritona et al. Arthritis Care Res (Hoboken). 2025 Mar 24.

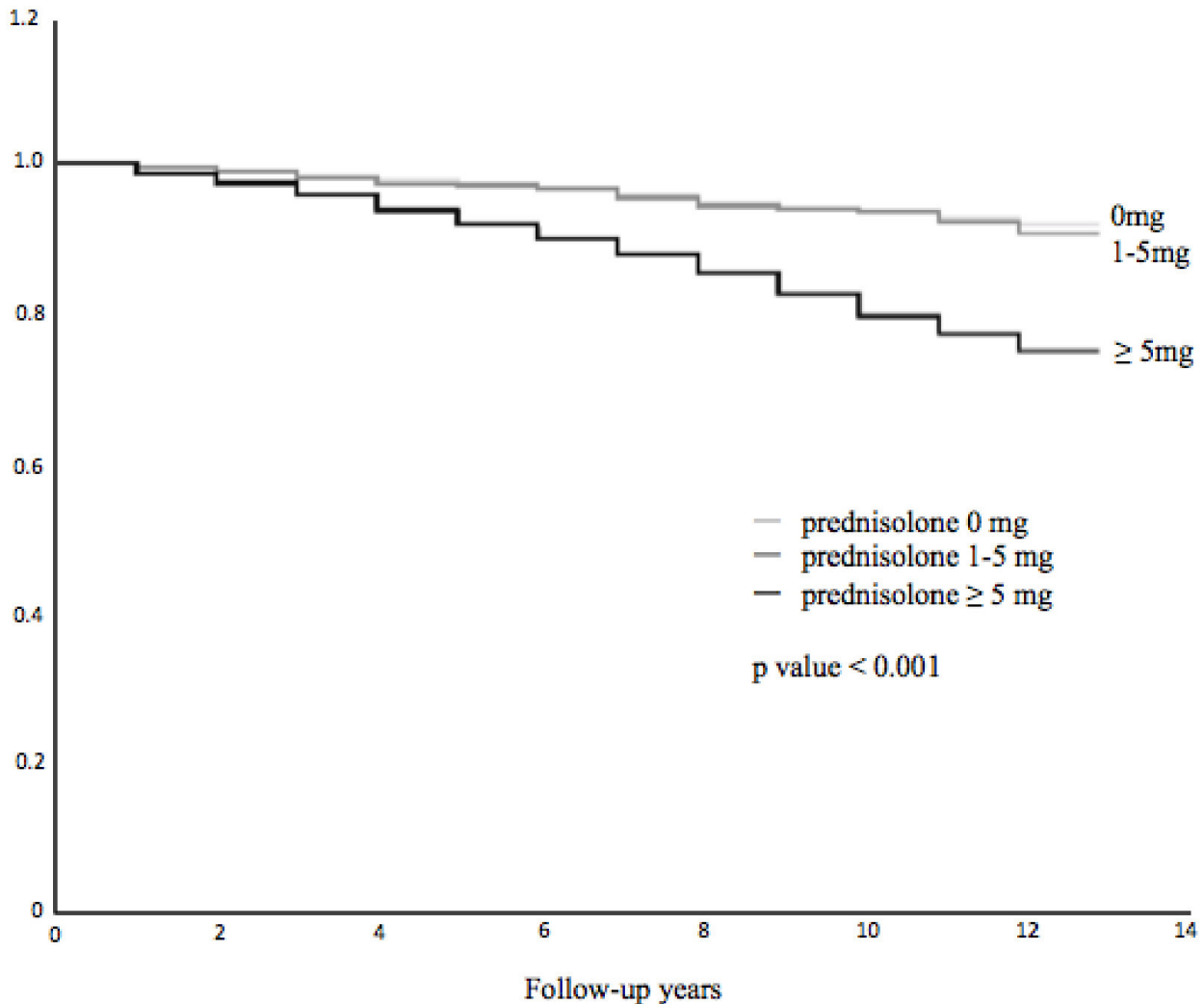
A tale of two patients





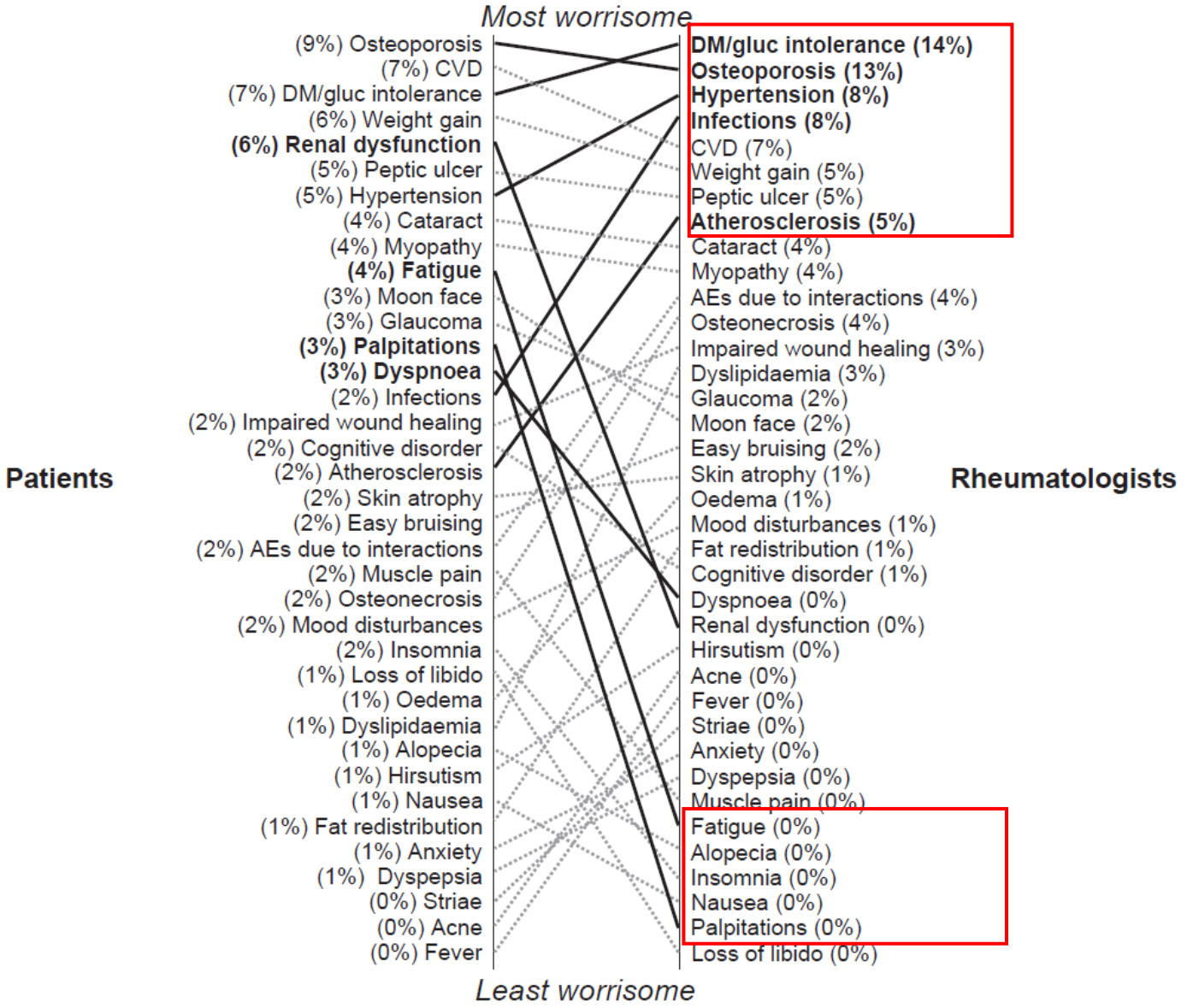
No steroid toxicity

Time and dose-dependent effect of systemic glucocorticoids on major adverse cardiovascular event in patients with rheumatoid arthritis: a population-based study



So H, et al. Ann Rheum Dis 2023;82:1387–1393.

Patient vs physician perspectives



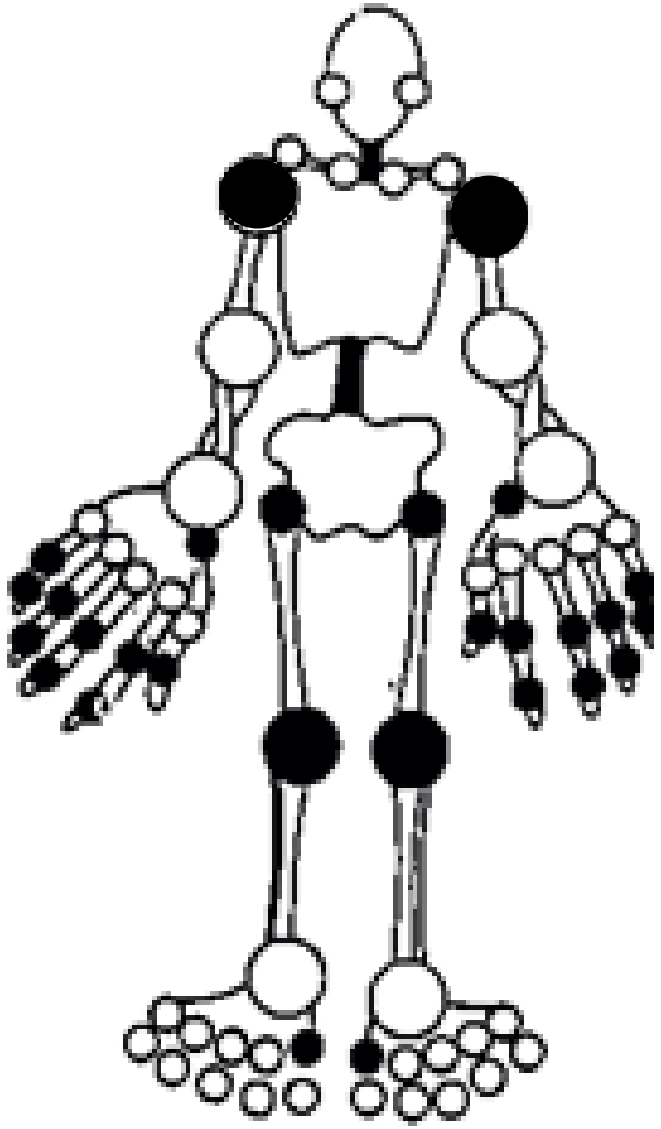
Case 3

- 42 year old woman with hypothyroidism and obesity presents with pain and stiffness in the PIPs and DIPs b/l x 6 mos
- Exam with pain and mild swelling of multiple PIPs and DIPs
- Inflammatory markers are normal
- Xrays unremarkable

What is the most likely diagnosis?

a. Osteoarthritis
b. Rheumatoid arthritis
c. Psoriatic arthritis
d. Reactive arthritis

Osteoarthritis joint distribution



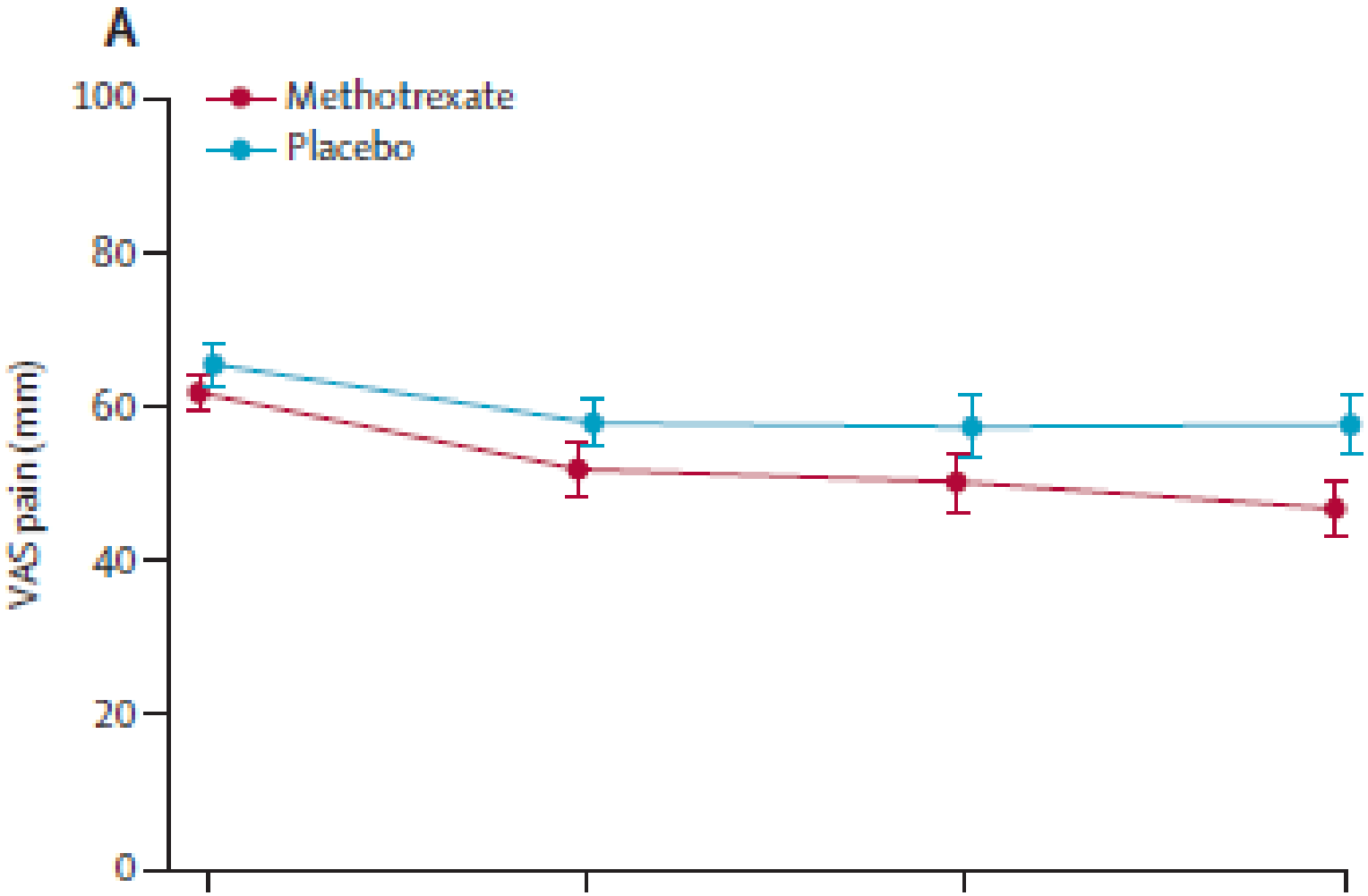
Case 3 (con't)

- PT, Topical NSAIDs, Tylenol and systemic NSAIDs without improvement
- Onset of bilateral knee pain x 1 year
- Plain films with moderate b/l knee osteoarthritis

What is the next best step?

a. Refer for initiation of methotrexate
b. Start GLP-1 agonist
c. Start duloxetine
d. Start tramadol

Methotrexate for inflammatory hand OA



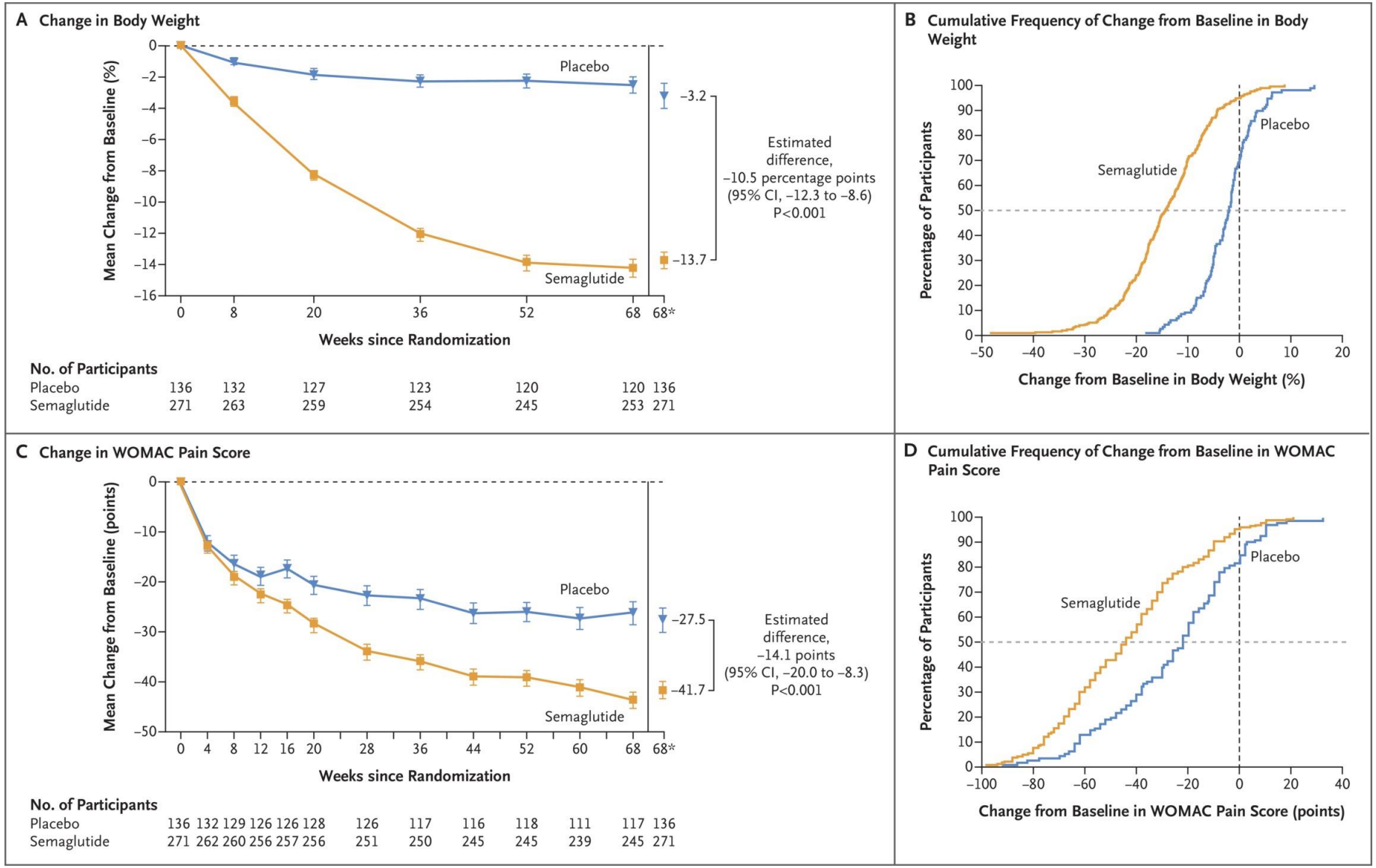
Wang et al. Lancet. 2023 Nov 11;402(10414):1764

Clinical trials in osteoarthritis

- Hydroxychloroquine
- Colchicine
- TNF inhibitors
- Nerve growth factor inhibitors
- Bisphosphonates
- Matrix metalloproteinases
- Senolytic agents

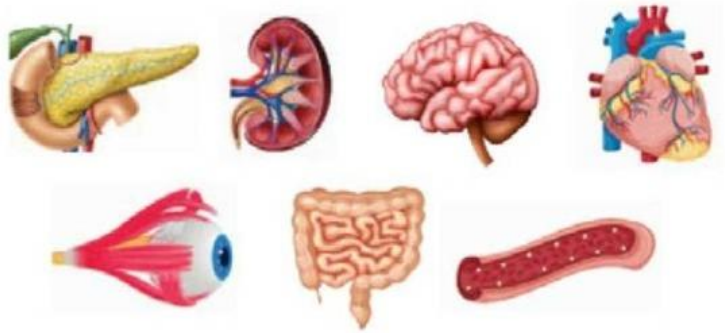
- Sprifermin
- Gene therapy
- Mesenchymal stem cells
- IL-1 inhibitors
- IL-17 inhibitors

Once-Weekly Semaglutide in Persons with Obesity and Knee Osteoarthritis



Bliddal et al. N Engl J Med. 2024 Oct 31;391(17):1573

Glucagon Like Peptide-1 Receptor Expression



Immune system

Lymphocytes T and B

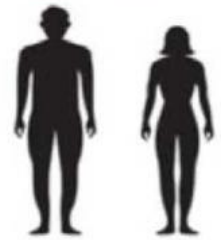
Macrophages

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 treatment in SLE

Outcomes	Events, n		Follow-up Time, years		Incidence Rate (per 1000 person years)		Hazard Ratio (95% CI)
	DPP4i	GLP-1RA	DPP4i	GLP-1RA	DPP4i	GLP-1RA	
Per-Protocol							
Cardiovascular outcomes							
MACE	23	18	1.0	1.2	193.0	122.2	0.64 (0.41-0.98)
Myocardial infarction	5	2	1.2	1.4	32.7	11.0	0.34 (0.10-1.09)
Stroke	4	2	1.2	1.4	25.3	14.7	0.58 (0.18-1.85)
Heart Failure	16	15	1.1	1.2	124.9	98.5	0.78 (0.48-1.28)
VTE	5	4	1.2	1.3	38.3	24.9	0.62 (0.25-1.56)
Kidney outcome							
eGFR decline by ≥30% or new ESKD	35	28	0.9	1.1	325.2	213.3	0.70 (0.49-1.00)
All-cause death	5	3	1.2	1.4	36.5	16.2	0.46 (0.16-1.37)
Control outcome							
Genital Infection	8	9	1.1	1.3	62.9	56.6	0.90 (0.48-1.68)

MACE, major adverse cardiac events; VTE, venous thromboembolism; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease. MACE outcome includes combined myocardial infarction, ischemic stroke, or heart failure hospitalization. Heart failure outcome includes heart failure hospitalization.

Jorge et al. ACR Convergence abstract 2024

KEY TAKE HOME POINTS

- Steroid sparing options in PMR are increasing
- SLE treatment is evolving towards lower use of GCs and increasing use of combination non-glucocorticoid immunosuppression
- Osteoarthritis treatment options remain limited with traditional options including weight loss and physical therapy remaining the cornerstone of management
- GLP1 agonists may have a significant role in the management of rheumatic diseases and their complications

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