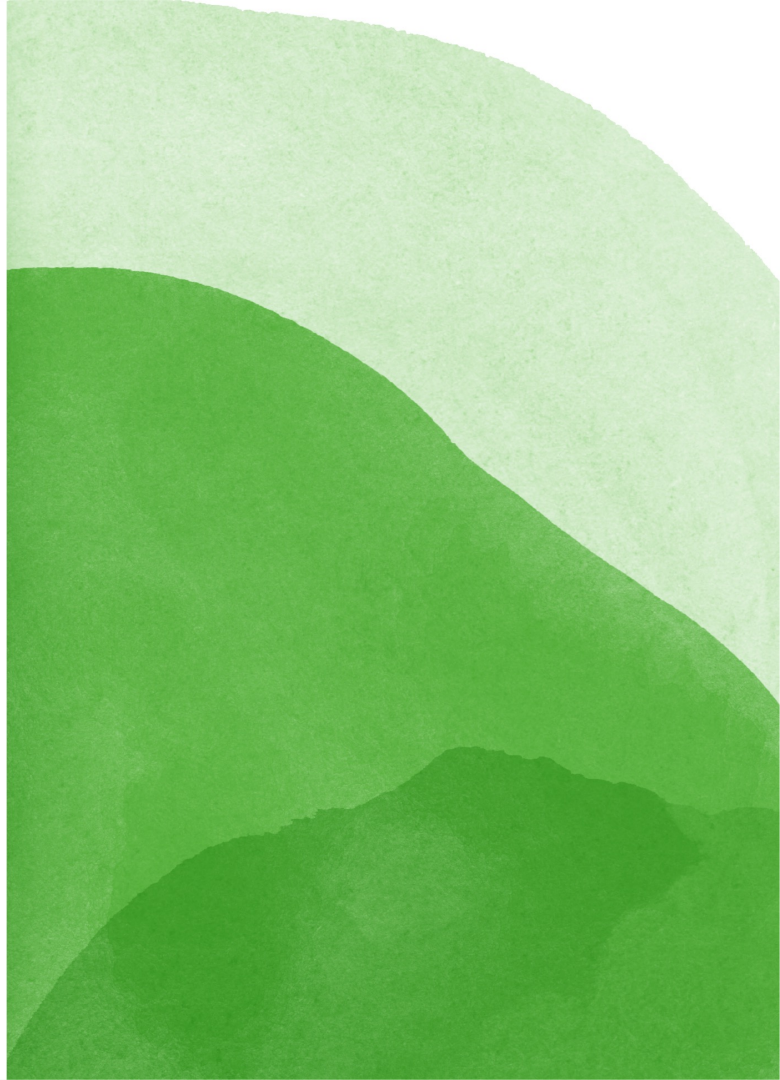
Rheumatology Updates 2023

Erin M. Bauer MD, RhMUS

2023



Virginia Mason Franciscan Health™

Disclosures

None

Topics Today

- Polymyalgia Rheumatica / Giant Cell Arteritis
  - Diagnostic Criteria
  - New Meds
  - GCA Guideline Updates
  - Glucocorticoid Induced Osteoporosis Guideline Updates
- Systemic Lupus Erythematosus
  - Updated Classification Criteria
  - New Meds / Treatment modalities
- VEXAS
- 2022 Perioperative guideline
- 2023 Vaccination Guidelines for immunosuppressed patients

Virginia Mason Franciscan Health™

Case 1

Ms. A is a 73 year old with well controlled diabetes, hyperlipidemia and hypertension presenting with 3 weeks of sudden onset neck, bilateral shoulder and low back pain.

Most prominent in morning, deep stiffness sensation, will improve with a 2 mile walk and Ibuprofen.

Low grade fevers x 1 week. No weight loss. No joint swelling. No rashes

Medications:
Metformin 1000 mg BID
Atorvastatin 40 mg daily
Lisinopril 40 mg daily
Amlodipine 5 mg daily

Exam:
BP: **126/76** **HR: 93** Wt: **87.3 kg**
Gen: uncomfortable, stiff appearing
Notable for 2+ temporal artery pulses
Normal respiratory effort
Heart rate regular, distal pulses 2+
No rashes
Myofascial tenderness over trapezius, deltoids, limited overhead reach due to pain. Tender over low back and gluteal area
No synovitis on exam
Strength 5/5 proximally and distally

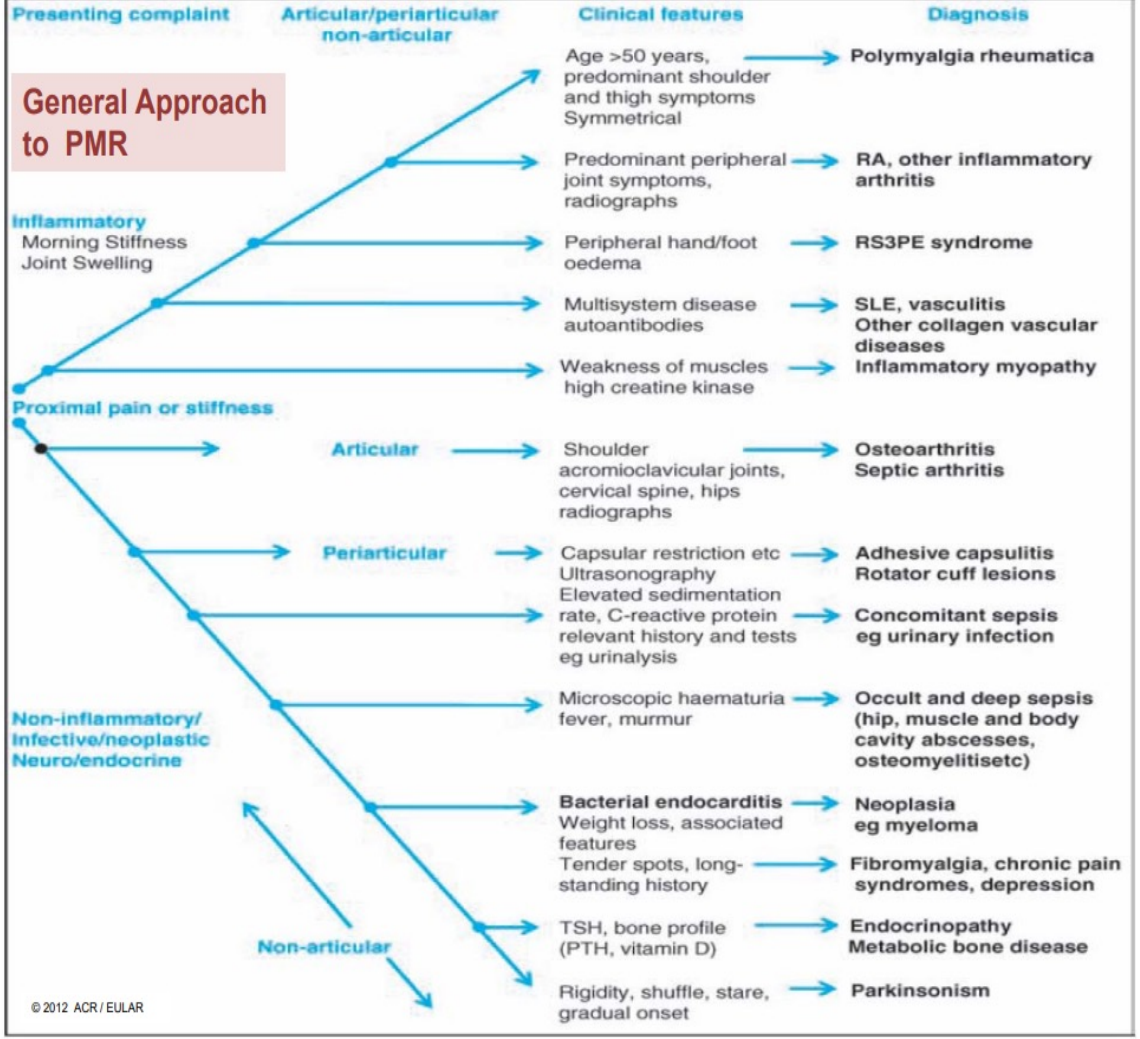
Differential:
Polymyalgia Rheumatica
Rheumatoid Arthritis
Multifocal local musculoskeletal disease
Autoimmune/inflammatory myositis
Bone disease
- Paget's, Multiple Myeloma
- Hyperparathyroidism, Osteomalacia

Drug induced myalgias or myositis
- Statins, Checkpoint inhibitors, Antiretroviral, Antipsychotic meds
- Antimalarial drugs, EtOH, Cocaine

Fibromyalgia
Infection (endocarditis, disseminated Lyme, osteomyelitis)
Spondyloarthropathy
(Parkinson's, hypothyroidism, malignancy, vasculitis)

Virginia Mason Franciscan Health

ARTHRITIS & RHEUMATISM
Vol. 64, No. 4, April 2012, pp 943–954
DOI 10.1002/art.34356



Virginia Mason Franciscan Heal

ARTHRITIS & RHEUMATOLOGY Vol. 67, No. 10, October 2015, https://www.rheumatology.org/Portals/0/Files/2015%20PMR%20guidelines.pdf

Audience Poll

Which lab test will be the most helpful in this case?

A. Creatine phosphokinase (CPK)
B. Antinuclear Antibody (ANA)
C. Erythrocyte Sedimentation Rate (ESR)
D. C Reactive Protein (CRP)
E. Complete Blood Count (CBC)

ARTHRITIS & RHEUMATISM
Vol. 64, No. 4, April 2012, pp 943-954
DOI 10.1002/art.34356

Arthritis & Rheumatism

An Official Journal of the American College of Rheumatology
www.arthritisrheum.org and wileyonlinelibrary.com

2012 Provisional Classification Criteria for Polymyalgia Rheumatica

A European League Against Rheumatism/American College of Rheumatology Collaborative Initiative

Bhaskar Dasgupta,[1] Marco A. Cimmino,[2] Hilal Maradit Kremers,[3] Wolfgang A. Schmidt,[4] Michael Schirmer,[5] Carlo Salvarani,[6] Artur Bachta,[7] Christian Dejaco,[8] Christina Duftner,[9] Hanne Slott Jensen,[10] Pierre Duhaut,[11] Gyula Poór,[12] Novák Pál Kaposi,[12] Peter Mandl,[12]

PMR is almost exclusively a disease of adults **over the age of 50**, with a prevalence that increases progressively with advancing age. The peak incidence of PMR occurs between ages 70 and 80.

PMR is relatively common. The lifetime risk of developing PMR has been estimated at 2.43 percent for women and 1.66 percent for men.

Women are affected two to three times more often than men.

Cases of familial aggregation are rare, but recognized.

The annual incidence varies geographically and is highest i
countries and in people of northern European decent.

Table 6. PMR classification criteria scoring algorithm—required criteria: age ≥50 years, bilateral shoulder aching, and abnormal CRP and/or ESR*

	Points without US (0–6)	Points with US (0–8)†
Morning stiffness duration >45 minutes	2	2
Hip pain or limited range of motion	1	1
Absence of RF or ACPA	2	2
Absence of other joint involvement	1	1
At least 1 shoulder with subdeltoid bursitis and/or biceps tenosynovitis and/or glenohumeral synovitis (either posterior or axillary) and at least 1 hip with synovitis and/or trochanteric bursitis	NA	1
Both shoulders with subdeltoid bursitis, biceps tenosynovitis, or glenohumeral synovitis	NA	1

CRP is nearly always elevated in PMR. An **elevated ESR** was noted in **92 to 94 percent of patients** at the time of diagnosis of PMR, while **99 percent** of such patients had an increased serum **CRP** level (greater than 5 mg/L).

Cantini F, Salvarani C, Olivieri I, Macchioni L, Ranzi A, Niccoli L, Padula A, Boiardi L. Erythrocyte sedimentation rate and C-reactive protein in the evaluation of disease activity and severity in polymyalgia rheumatica: a prospective follow-up study. Semin Arthritis Rheum. 2000 Aug;30(1):17-24. doi: 10.1053/sarh.2000.8366. PMID: 10966209. https://pubmed.ncbi.nlm.nih.gov/10966209/

Virginia Mason Franciscan Health™

Case 1

Ms. A is a 73 year old with well controlled diabetes, hyperlipidemia and hypertension presenting with 3 weeks of sudden onset neck, bilateral shoulder and low back pain.

Most prominent in morning, deep stiffness sensation, will improve with a 2 mile walk and Ibuprofen.

Low grade fevers x 1 week. No weight loss. No joint swelling. No rashes

Laboratory Testing:
ESR: 67 mm/hr
CRP: 50 mg/L
CBC: normal WBCs, mild normocytic anemia, thrombocytosis
CMP: normal renal function, liver enzymes and calcium
CPK: 150 mg/dL
RF/CCP: negative

(TSH, SPEP, PTH, blood cultures, UA)

Virginia Mason Franciscan Health

Scoring Algorithm with Ultrasound – *3 required criteria: age ≥50 years, bilateral shoulder aching, abnormal ESR/CRP*

Optional classification criteria	OR (95% CI)	Points
Morning stiffness >45 minutes	5.0 (2.8, 9.1)	2
Hip pain, limited range of motion	1.4 (0.8, 2.6)	1
Normal RF or ACPA	5.2 (2.1, 12.6)	2
Absence of other joint pain	2.2 (1.3, 4.0)	1
ULTRASOUND CRITERIA		
At least 1 shoulder with subdeltoid bursitis and/or biceps tenosynovitis and/or glenohumeral synovitis AND at least 1 hip with synovitis and/or trochanteric bursitis	2.6 (1.3, 5.3)	1
Both shoulders with subdeltoid bursitis, biceps tenosynovitis or glenohumeral synovitis	2.1 (1.2, 3.7)	1

Optimal cut-off point = 5

- A score 5 had 71% sensitivity and 70% specificity for discriminating all comparison subjects from PMR.
- The specificity was higher (86%) for discriminating shoulder conditions from PMR and lower (65%) for discriminating RA from PMR.
- The c-statistic for the scoring algorithm was 78%.
- A total of 32 (29%) PMR cases and 47 (30%) of comparison subjects were incorrectly classified.

American College of Rheumatology
Education • Treatment • Research

eular

Imaging in PMR

We now understand PMR to be a distinct chronic inflammatory disease of musculotendinous structure, with differentiating features from other rheumatic diseases most notably its **extra-capsular nature** with associated **peritendon** and **myofascial** inflammation.

- Ultrasound (US)
- Magnetic resonance imaging (MRI)
- Positron emission tomography and computed tomography (PET-CT)

Virginia Mason Franciscan Health™

Case 1

Ms. A is started on 15 mg daily of prednisone.

She feels 99% better after 2 days and calls your office to express her gratitude.

She is tolerating prednisone well

You see her back in clinic 6 weeks later.

Laboratory Testing:
ESR: 18 mm/hr
CRP: <3 mg/L

Next steps?

Initial tapering: Taper dose to an oral dose of 10 mg/day prednisone equivalent within **4–8 weeks.**

Tapering once remission is achieved: **Taper daily oral prednisone by 1 mg every 4** weeks (or by 2.5 mg increments using schedules such as 10/7.5 mg on alternate days, etc.) until discontinuation as long as remission is maintained.

Recommend using a single rather than divided daily doses of oral GCs

Virginia Mason Franciscan Health

ARTHRITIS & RHEUMATOLOGY Vol. 67, No. 10, October 2015, pp 2569–2580 DOI 10.1002/art.39333 VC 2015, American College of Rheumatology

https://www.rheumatology.org/Portals/0/Files/2015%20PMR%20guidelines.pdf

Case 1

Ms. A returns to clinic **6 months** after her initial PMR diagnosis. She had been doing well until about 2 weeks ago when she decrease **prednisone to 7 mg daily**. Now with increased achy shoulder pain and fatigue. No headaches, vision changes, scalp tenderness. Some newer hand stiffness.

Laboratory Testing:
ESR: 57 mm/hr
CRP: 22 mg/L

Next steps?

Relapse therapy: Increase oral prednisone to the pre-relapse dose and decrease it gradually (within 4–8 weeks) to the dose at which the relapse occurred.

50% of patients will relapse, most commonly on <10 mg daily

? Methotrexate, IL-6 inhibition

Virginia Mason Franciscan Health

Future PMR Treatments

IL-6 inhibitors

- Sarilumab

  SAPHYR study: 2 weeks of treatment with SAR 200 mg q 2 weeks + 14 week GC tapered regimen vs placebo Q2W + 52 wk GC tapered regimen. The primary endpoint: proportion of patients achieving sustained remission at wk 52(disease remission by wk 12, absence of disease flare, CRP normalization from wks 12 to 52 and adherence to the per protocol GC taper from wks 12 to 52)

- Tocilizumab

  SEMAPHORE study: Patients randomly assigned to intravenous tocilizumab (8 mg/Kg) (n=51) or placebo (n=50) every 4 weeks for 24 weeks, combined with predefined standardized oral prednisone tapering. The primary efficacy endpoint was CRP PMR-AS< 10 (Min=0-Max 100 with higher values indicating greater activity, no MCID defined) combined with either prednisone ≤5 mg/day or a ≥10-mg prednisone decrease at week 24.

JAK inhibitors

- Efficacy and Safety of Tofacitinib in Patients with Polymyalgia Rheumatica (EAST PMR) Study: Patients with newly diagnosed PMR were randomized to tofacitinib (5mg bid) group and Glucocorticoids (Pred 15mg/day, gradually tapered) group. All PMR patients underwent clinical and laboratory examinations at 0, 4, 8, 12, 16, 20, and 24 weeks, and PMR activity disease scores (PMR-AS) were also calculated. The primary endpoint was the proportion of patients with PMR-AS≤10 at weeks 12 and 24.

NEWS RELEASE

PRESS RELEASES | MEDIA STATEMENTS

REGENERON®

February 28, 2023 at 8:00 PM EST

« Back

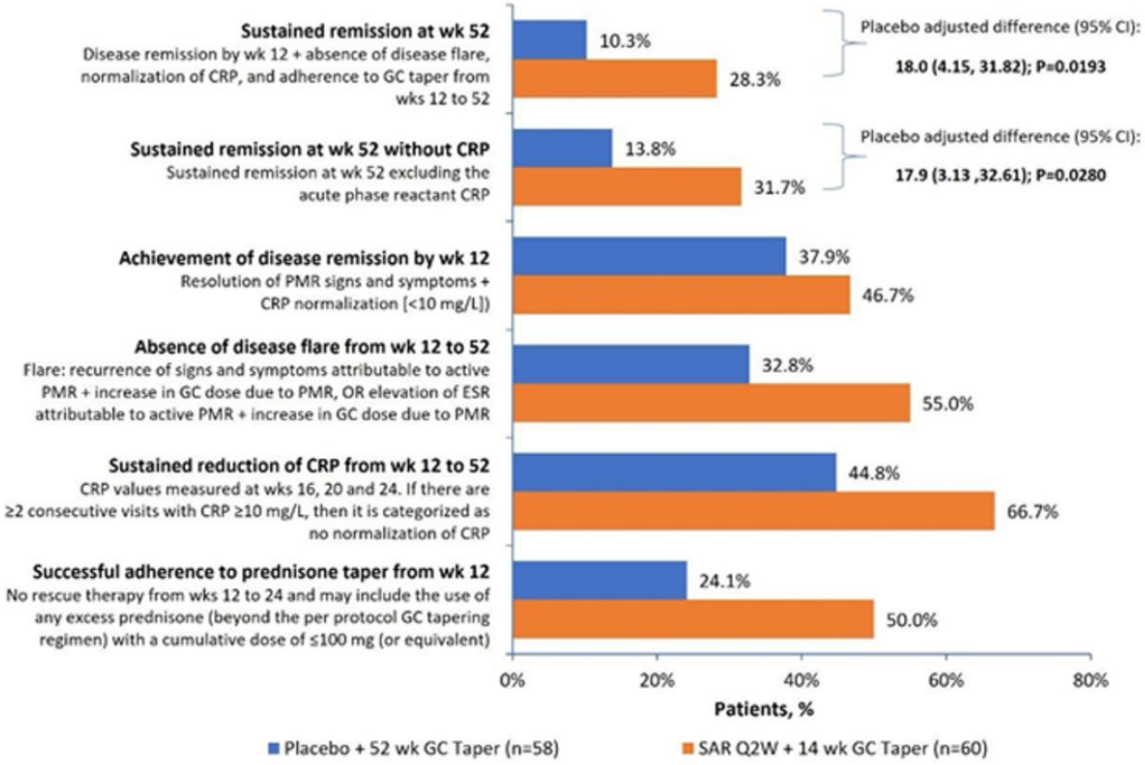
KEVZARA® (SARILUMAB) APPROVED BY FDA AS FIRST AND ONLY BIOLOGIC INDICATED FOR PATIENTS WITH POLYMYALGIA RHEUMATICA

Three times more patients treated with Kevzara achieved sustained remission compared to placebo in Phase 3 trial

Kevzara now approved to treat two chronic inflammatory disorders

TARRYTOWN, N.Y. and CAMBRIDGE, Mass., Feb. 28, 2023 (GLOBE NEWSWIRE) -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) and Sanofi today announced that the U.S. Food and Drug Administration (FDA) has approved Kevzara® (sarilumab) for the treatment of polymyalgia rheumatica (PMR), an inflammatory rheumatic disease, in adult patients who have had an inadequate response to corticosteroids or who cannot tolerate corticosteroid taper.

Figure. Summary of disease remission, disease flare, CRP reduction, and adherence to prednisone taper



CI, confidence interval; EQ-5D, EuroQol 5-dimension questionnaire; FACIT-Fatigue, functional assessment of chronic illness therapy fatigue scale; HAQ-DI, Health Assessment Questionnaire Disability Index; MD-VAS, physician global assessment of disease activity-Visual Analog Scale; SD, standard deviation; SF-36, short form 36-item questionnaire.

SAR + 14 week GC taper demonstrated significant efficacy vs the comparator arm in steroid refractory PMR patients, including clinically meaningful improvement in quality of life.

Safety was consistent with the known safety profile of SAR.

Virginia Mason Franciscan Health™

Dasgupta B, Unizony S, Warrington KJ, *et al*
LB0006 SARILUMAB IN PATIENTS WITH RELAPSING POLYMYALGIA RHEUMATICA: A PHASE 3, MULTICENTER, RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED TRIAL (**SAPHYR**)
Annals of the Rheumatic Diseases 2022;**81:**210-211.
https://ard.bmj.com/content/81/Suppl_1/210.1

COMMON ADVERSE REACTIONS IN PRE-RESCUE, PLACEBO-CONTROLLED TRIALS[1*]

Preferred Term	Placebo + DMARD(s) N=579	KEVZARA 150 mg +DMARD(s) N=579	KEVZARA 200 mg +DMARD(s) N=582
Neutropenia	0.2%	7%	10%
ALT increased	2%	5%	5%
Injection site erythema	0.9%	5%	4%
Injection site pruritus	0.2%	2%	2%
Upper respiratory tract infection	2%	4%	3%
Urinary tract infection	2%	3%	3%
Hypertriglyceridemia	0.5%	3%	1%
Leukopenia	0%	0.9%	2%

*Adverse reactions occurring in ≥2% of patients administered KEVZARA 200 mg or KEVZARA 150 mg + DMARD(s) and greater than observed in patients on placebo + DMARD(s).

- Medically relevant AE occurring at an incidence of less than 2% in patients with RA treated with KEVZARA in controlled studies was oral herpes[1]
- Decrease in ANC was not associated with higher incidence of infections, including serious infections[1]
- In the long-term safety population, the overall rates of serious infections, GI perforations, neutrophil counts, platelet counts, and lipid parameters were consistent with what was observed in the placebo-controlled trials[1]

Virginia Mason Franciscan Health™

Dasgupta B, Unizony S, Warrington KJ, *et al*
LB0006 SARILUMAB IN PATIENTS WITH RELAPSING POLYMYALGIA RHEUMATICA: A PHASE 3, MULTICENTER, RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED TRIAL (**SAPHYR**)
Annals of the Rheumatic Diseases 2022;**81:**210-211.

Case 2

Ms. B is a 77 year old with well controlled diabetes, hyperlipidemia and hypertension who was diagnosed with PMR about 1 month ago by her primary care physician. She started on prednisone 10 mg daily with initial improvement in her symptoms.

She ran out of prednisone 2 weeks ago and is now in clinic with return of hip and shoulder girdle symptoms. Newer severe headaches primarily over the right temple with some tingling over the whole scalp.

Laboratory Testing:
ESR: 78 mm/hr
CRP: 55 mg/L
CBC: normal WBCs, mild normocytic anemia, thrombocytosis
CMP: normal renal function, liver enzymes and calcium
Glucose of 290 mg/dL
CPK: 150 mg/dL
RF/CCP: negative

Audience Poll

What percentage of patients with PMR will develop GCA?

A. 1-2%
B. 10-20 %
C. 30-40%
D. >50%

Giant Cell Arteritis

About **10-20 percent of PMR patients** will experience GCA at some point. PMR can precede, accompany, or follow GCA

PMR occurs in approximately **50 percent** of patients with GCA

Only **4 percent** of patients with GCA have both the ESR and CRP in the normal range

Virginia Mason Franciscan Health™

Pujades-Rodriguez M, Duyx B, Thomas SL, *et al*
Associations between polymyalgia rheumatica and giant cell arteritis *Heart* 2016;**102:**383-389.
https://heart.bmj.com/content/102/5/383

2022 American College of Rheumatology/EULAR classification criteria for giant cell arteritis

Cristina Ponte ,[1,2] Peter C Grayson ,[3] Joanna C Robson,[4,5] Ravi Suppiah,[6] Katherine Bates Gribbons,[3] Andrew Judge ,[7,8,9] Anthea Craven ,[7] Sara Khalid,[7] Andrew Hutchings ,[10] Richard A Watts ,[7,11] Peter A Merkel ,[12] Raashid A Luqmani ,[7] For the DCVAS Study Group

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/ard-2022-223480).

For numbered affiliations see end of article.

Correspondence to
Professor Peter A Merkel, Rheumatology, University of Pennsylvania, Philadelphia, PA 19104, USA;
pmerkel@upenn.edu

This article is published simultaneously in *Arthritis & Rheumatology*.

Received 13 October 2022
Accepted 13 October 2022
Published Online First
9 November 2022

ABSTRACT

Objective To develop and validate updated classification criteria for giant cell arteritis (GCA).

Methods Patients with vasculitis or comparator diseases were recruited into an international cohort. The study proceeded in six phases: (1) identification of candidate items, (2) prospective collection of candidate items present at the time of diagnosis, (3) expert panel review of cases, (4) data-driven reduction of candidate items, (5) derivation of a points-based risk classification score in a development data set and (6) validation in an independent data set.

Results The development data set consisted of 518 cases of GCA and 536 comparators. The validation data set consisted of 238 cases of GCA and 213 comparators. Age ≥50 years at diagnosis was an absolute requirement for classification. The final criteria items and weights were as follows: positive temporal artery biopsy or temporal artery halo sign on ultrasound (+5); erythrocyte sedimentation rate ≥50 mm/hour or C reactive protein ≥10 mg/L (+3); sudden visual loss (+3); morning stiffness

widespread use of non-invasive and advanced vascular imaging modalities, which have become increasingly incorporated in the clinical assessment of GCA. Vascular ultrasound can be used to diagnose GCA, and depending on the clinical setting, a non-compressible 'halo' sign of a temporal±axillary artery may replace the need for temporal artery biopsy (TAB).[5–8] Moreover, vascular imaging has demonstrated that arterial involvement in GCA is not exclusively confined to the cranial arteries[9 10] and can commonly affect the aorta and primary branches in a pattern similar to Takayasu arteritis (TAK).[11 12]

The limitations of the ACR 1990 criteria for GCA have become more apparent in the conduct of recent clinical trials and other research studies, in which investigators typically modify the 1990 ACR criteria to reflect modern practice.[6 13 14] Notably, the 1990 ACR criteria focus mostly on cranial features of GCA and do not perform well in classifying patients with disease predominantly affecting

Virginia Mason Franciscan Health

https://www.rheumatology.org/Portals/0/Files/Guideline-Management-Giant-Cell-Arteritis-Takayasu-Arteritis-2021.pdf

2022 AMERICAN COLLEGE OF RHEUMATOLOGY / EULAR

CLASSIFICATION CRITERIA FOR **GIANT CELL ARTERITIS**

CONSIDERATIONS WHEN APPLYING THESE CRITERIA

- These classification criteria should be applied to classify the patient as having giant cell arteritis when a diagnosis of medium-vessel or large-vessel vasculitis has been made
- Alternate diagnoses mimicking vasculitis should be excluded prior to applying the criteria

ABSOLUTE REQUIREMENT

Age ≥ 50 years at time of diagnosis	

ADDITIONAL CLINICAL CRITERIA

Morning stiffness in shoulders/neck	+2
Sudden visual loss	+3
Jaw or tongue claudication	+2
New temporal headache	+2
Scalp tenderness	+2
Abnormal examination of the temporal artery[1]	+2

LABORATORY, IMAGING, AND BIOPSY CRITERIA

Maximum ESR ≥ 50 mm/hour or maximum CRP ≥ 10 mg/liter[2]	+3
Positive temporal artery biopsy or halo sign on temporal artery ultrasound[3]	+5
Bilateral axillary involvement[4]	+2
FDG-PET activity throughout aorta[5]	+2

Sum the scores for 10 items, if present. A score of ≥ 6 points is needed for the classification of GIANT CELL ARTERITIS.

Virginia Mason Franciscan Health™

Ponte C, Grayson PC, Robson JC For the DCVAS Study Group, *et al* 2022 American College of Rheumatology/EULAR classification criteria for giant cell arteritis *Annals of the Rheumatic Diseases* 2022;**81:**1647-1653.https://ard.bmj.com/content/81/12/1647

Temporal Artery Biopsy

Within two weeks of starting treatment

Initial unilateral biopsy of at least 1 cm

Sensitivity of the temporal artery biopsy ranges from **50 to 95%**
In a large meta-analysis including 3092 patients, the diagnostic sensitivity of the temporal artery biopsy was found to be **77%**

The increased yield of contralateral biopsy for the diagnosis ~5%

Rarely, temporal artery biopsy will disclose pathology other than GCA, such as systemic necrotizing vasculitis, antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, polyarteritis nodosa, amyloidosis, or lymphoma

Rubenstein E, Maldini C, Gonzalez-Chiappe S, Chevret S, Mahr A. Sensitivity of temporal artery biopsy in the diagnosis of giant cell arteritis: a systematic literature review and meta-analysis. Rheumatology (Oxford). 2020 May 1;59(5):1011-1020. doi: 10.1093/rheumatology/kez385.
https://pubmed.ncbi.nlm.nih.gov/31529073/

Virginia Mason Franciscan Health

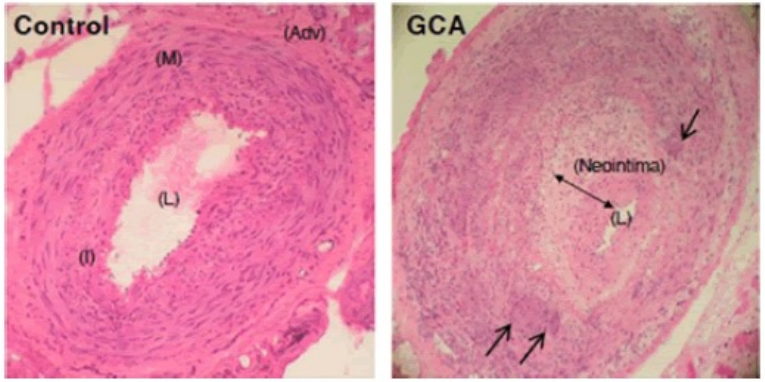
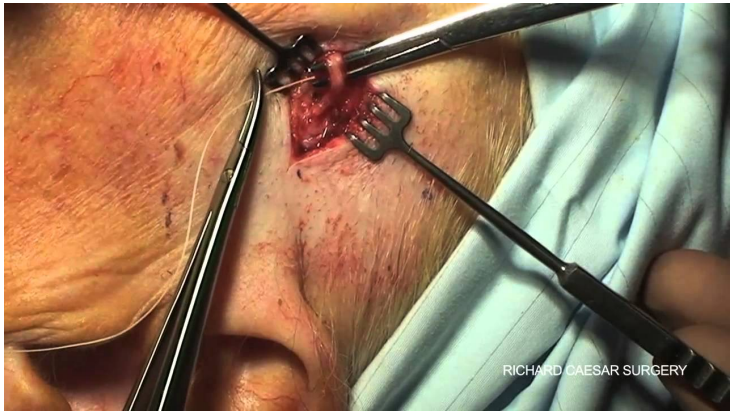


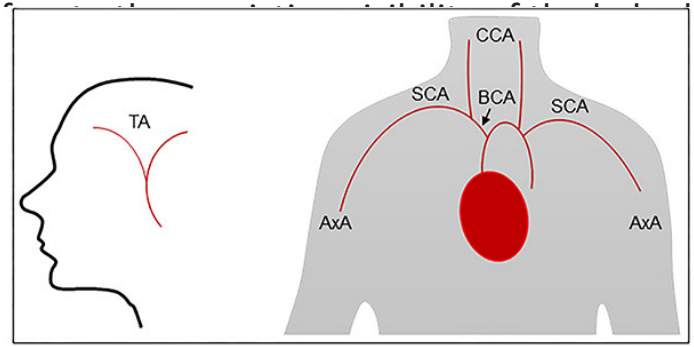
Figure 1: Normal temporal artery biopsy (left) as opposed to a temporal artery biopsy from a patient with giant-cell arteritis (right) disclosing typical transmural mononuclear cell infiltration, internal elastic lamina breakdown and intimal hyperplasia. Double head arrow remarks the thickened intima and single head arrows indicate the presence of giant-cells. Haematoxylin-eosin staining. L: lumen; I: intima; M: media; Adv: adventitia.



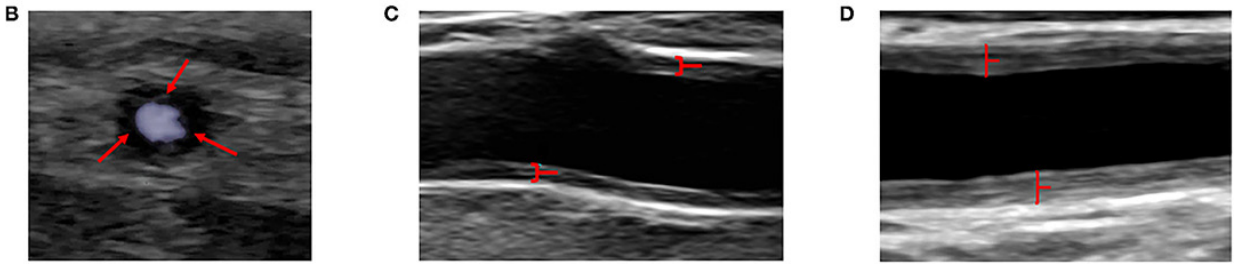
Ultrasound in GCA

Must be done within <u>one week</u>

“Halo sign”- 0.3 to 2.0 mm hypoechogenic, is highly specific for GCA. The **"compression sign"** also has high specificity for the

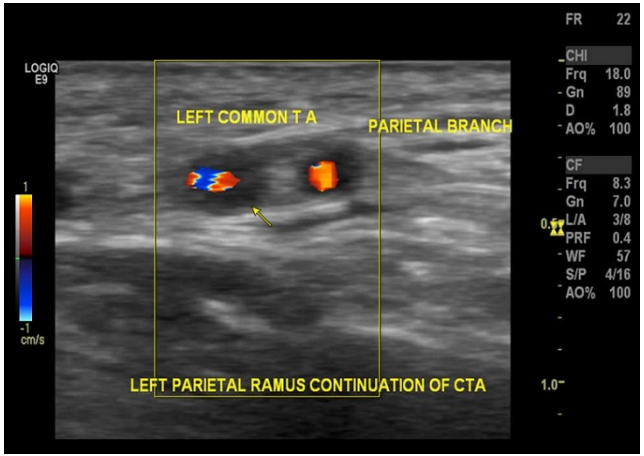


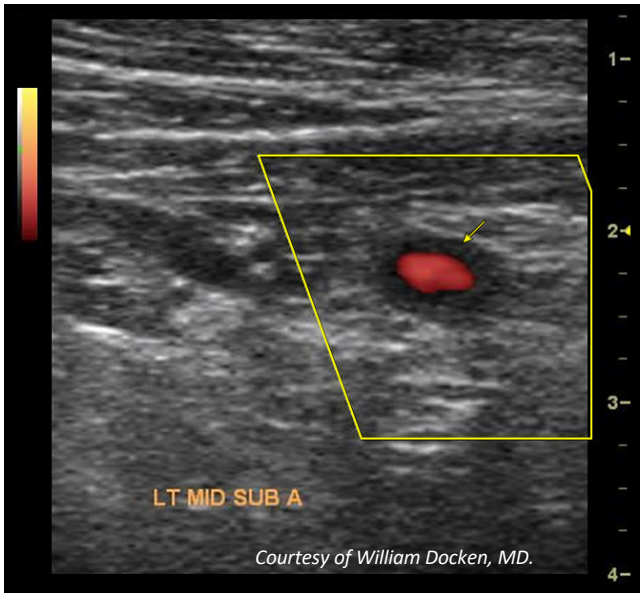
Skoog J, Svensson C, Eriksson P, Sjöwall C and Zachrisson H (2022) The Diagnostic Performance of an Extended Ultrasound Protocol in Patients With Clinically Suspected Giant Cell Arteritis. Front. Med. 8:807996



Virginia Mason Franciscan Health

Arida A, Kyprianou M, Kanakis M, Sfikakis PP. The diagnostic value of ultrasonography-derived edema of the temporal artery wall in giant cell arteritis: a second meta-analysis. BMC Musculoskelet Disord. 2010 Mar 8;11:44. doi: 10.1186/1471-2474-11-44. PMID: 20210989; PMCID: PMC2837862
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2837862/





US for *screening* of GCA in PMR patients

ABSTRACT NUMBER: 0478

Sonographic Prevalence of Subclinical GCA in Newly Diagnosed PMR

Colm Kirby[1], Rachael Flood[1], Ronan Mullan[1], Grainne Murphy[2] and David Kane[1], [1]Tallaght University Hospital, Dublin, Ireland, [2]Cork University Hospital, Cork, Ireland

Meeting: ACR Convergence 2022

Keywords: giant cell arteritis, Imaging, Polymyalgia Rheumatica (PMR), Ultrasound

SESSION INFORMATION

Date: Saturday, November 12, 2022

Session Type: Poster Session A

Session Title: Vasculitis – Non-ANCA-Associated and Related Disorders

Session Time: 1:00PM-3:00PM

Poster I: Giant Cell Arteritis

Background/Purpose: It has been reported that 20-50% of patients with PMR have subclinical GCA. The natural history of US-defined subclinical GCA in PMR is not known.

Virginia Mason Franciscan Health

Twenty five newly-diagnosed PMR patients who met a clinical diagnosis for PMR, verified by 2 rheumatologists, were examined by US. US of all 6 branches of the superficial temporal arteries and both axillary arteries

Five patients (20%) were identified as having subclinical GCA on US (5/5 met 2012 ACR/EULAR PMR classification criteria, 0/5 met ACR GCA classification criteria).
Temporal artery involvement was identified in 5/5, with axillary involvement in 1/5.

Arthritis Care & Research
Vol. 73, No. 8, August 2021, pp 1071–1087
DOI 10.1002/acr.24632

American College of Rheumatology
Empowering Rheumatology Professionals

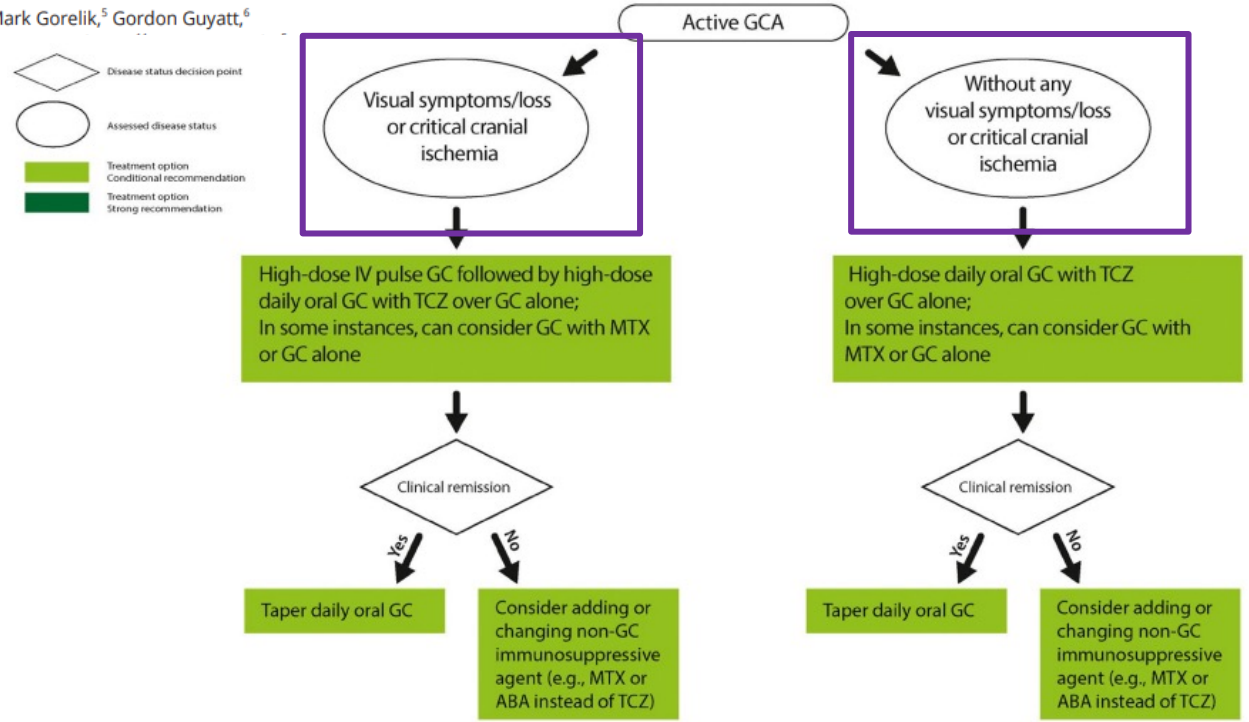
2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Giant Cell Arteritis and Takayasu Arteritis

Mehrdad Maz,[1] Sharon A. Chung,[2] Andy Abril,[3] Carol A. Langford,[4] Mark Gorelik,[5] Gordon Guyatt,[6]

IV pulse GCs: IV methylprednisolone 500–1,000 mg/day equivalent for 3–5 days

High-dose oral GCs: Prednisone 1 mg/kg/day up to 80 mg or equivalent

Overview of treatment of giant cell arteritis (GCA)



ABA = abatacept, AZA = azathioprine, GC = glucocorticoids, IV = intravenous, MTX = methotrexate, TCZ = tocilizumab

Virginia Mason Franciscan Health

Table 3. Recommendations/statements for treatment (medical management and surgical intervention) and clinical/laboratory monitoring in GCA*

Recommendation/statement	GCA PICO question informing recommendation and discussion	Level of evidence
Medical management		
Recommendation: For patients with newly diagnosed GCA without manifestations of cranial ischemia, we conditionally recommend initiating treatment with high-dose oral GCs over IV pulse GCs.	11	Very low to low
Recommendation: For patients with newly diagnosed GCA with threatened vision loss, we conditionally recommend initiating treatment with IV pulse GCs over high-dose oral GCs.	12	Very low
Recommendation: For patients with newly diagnosed GCA, we conditionally recommend dosing oral GCs daily over an alternate-day schedule.	18	Low
Recommendation: For patients with newly diagnosed GCA, we conditionally recommend initiating treatment with high-dose oral GCs over moderate-dose oral GCs.	14	Very low to low
Recommendation: For patients with newly diagnosed GCA, we conditionally recommend the use of oral GCs with tocilizumab over oral GCs alone.	15, 16, 17	Low to high
Recommendation: For patients with GCA with active extracranial large vessel involvement, we conditionally recommend treatment with oral GCs combined with a non-GC immunosuppressive agent over oral GCs alone.	21	Very low to low
Ungraded position statement: The optimal duration of therapy with GCs for GCA is not well established and should be guided by the patient's values and preferences.	20	Low to moderate
Recommendation: In patients with newly diagnosed GCA, we conditionally recommend *against* the use of an HMG-CoA reductase inhibitor ("statin") specifically for the treatment of GCA.	19	Very low
Recommendation: For patients with GCA who have critical or flow-limiting involvement of the vertebral or carotid arteries, we conditionally recommend adding aspirin.	13	Very low to moderate
Recommendation: For patients with GCA who experience disease relapse while receiving moderate-to-high–dose GCs, we conditionally recommend adding a non-GC immunosuppressive drug.	Relapse 2	†
Recommendation: For patients with GCA who experience disease relapse with symptoms of cranial ischemia, we conditionally recommend adding a non-GC immunosuppressive agent and increasing the dose of GCs over increasing the dose of GCs alone.	Relapse 1, 3	†
Recommendation: For patients with GCA who experience disease relapse with symptoms of cranial ischemia while receiving GCs, we conditionally recommend adding tocilizumab and increasing the dose of GCs over adding methotrexate and increasing the dose of GCs.	Relapse 4	†
Surgical intervention		

FDA NEWS RELEASE

FDA approves first drug to specifically treat giant cell arteritis

More Press Announcements

For Immediate Release: May 22, 2017

Español

The U.S. Food and Drug Administration today expanded the approved use of subcutaneous Actemra (tocilizumab) to treat adults with giant cell arteritis. This new indication provides the first FDA-approved therapy, specific to this type of vasculitis.

"We expedited the development and review of this application because this drug fulfills a critical need for patients with this serious disease who had limited treatment options," said Badrul Chowdhury, M.D., Ph.D., director of the Division of Pulmonary, Allergy, and Rheumatology Products in the FDA's Center for Drug Evaluation and Research.

Content current as of:
03/28/2018

Follow FDA
Follow @US_FDA
Follow FDA
Follow @FDAmedia

AMERICAN COLLEGE of RHEUMATOLOGY
Empowering Rheumatology Professionals

Empowering rheumatology professionals to excel in their specialty

2200 Lake Boulevard NE, Atlanta, GA 30319
Phone: (404) 633-3777 • Fax (404) 633-1870 • www.rheumatology.org

2022 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis

Recommend risk stratifying patients via FRAX score

For all adults initiating or continuing **GC therapy ≥ 2.5mg/day for > 3 months**, who have never had fracture risk assessment or been treated with OP therapy, initial clinical fracture risk assessment is strongly recommended

Clinical fracture risk factor assessment includes the dose, duration, and pattern of GC use, alcohol use, smoking history, hypogonadism, history of prior fractures, low body weight, significant weight loss, parental history of hip fracture, fall history, thyroid disease, hyperparathyroidism, rheumatoid arthritis, malabsorption, chronic liver disease, inflammatory bowel disease, and height loss.

If available**, BMD testing is recommended within 6 months of starting GC therapy for adults and every 1-2 years thereafter while continuing GC therapy.**

Virginia Mason Franciscan Health

Table 2. Recommendations for initial treatment for prevention of GIOP in adults beginn GC therapy

Recommendations for patients taking prednisone ≥ 2.5mg/day for > 3months	Certainty of evidence	PICO evidence report basis
For adults and children beginning or continuing chronic GC treatment at low, moderate, or high risk of fracture, optimizing dietary and supplemental calcium and vitamin D in addition to lifestyle modifications (CAL/VIT D/LM) is **conditionally** recommended. All additional recommendations are in addition to CAL/VIT D/LM).	Low or Very Low	1.1a,b,c-1.3a,b,c, 2.1-2.3, 7.16-7.26
In adults ≥ 40 years		
With ***LOW*** fracture risk, adding any OP medications to CAL/VIT D /LM based on known harms with no evidence of benefit is **strongly** recommended ***against***.	Very Low	1.4a-1.28a
With ***MODERATE*** fracture risk, oral or IV BP, PTH/PTHrP, or DEN over no OP therapy is **conditionally** recommended.	Moderate to Very Low	1.4b-1.28b
With ***MODERATE*** fracture risk, using ROM or SERM is **conditionally** recommended *against* except for in patients intolerant of other agents, due to risk of life-threatening harms.	Very Low	1.12b, 1.16b,1.17b,1.21 b-1.25b, 1.28b
With ***HIGH*** fracture risk, oral BP over not giving OP therapy is **strongly** recommended[#]. IV BP, PTH/PTHrP, or DEN over no OP therapy is **conditionally** recommended[$].	Low or Very Low	1.5c-1.28c
With ***HIGH*** fracture risk, using ROM or SERM is **conditionally** recommended ***against*** except for patients intolerant of other agents due to risk of life- threatening harms	Very Low	1.16c, 1.21c, 1.28c

https://www.rheumatology.org/Portals/0/Files/Prevention-Treatment-GIOP-Guideline-Summary.pdf

Lupus Updates

Criteria

2019 European League Against Rheumatism/ American College of Rheumatology classification criteria for systemic lupus erythematosus

Martin Aringer,[1] Karen Costenbader,[2] David Daikh,[3] Ralph Brinks,[4] Marta Mosca,[5] Rosalind Ramsey-Goldman,[6] Josef S Smolen,[7] David Wofsy,[8] Dimitrios T Boumpas,[9,10] Diane L Kamen,[11] David Jayne,[12] Ricard Cervera,[13] Nathalie Costedoat-Chalumeau,[14] Betty Diamond,[15] Dafna D Gladman,[16] Bevra Hahn,[17] Falk Hiepe,[18] Søren Jacobsen,[19] Dinesh Khanna,[20] Kirsten Lerstrøm,[21] Elena Massarotti,[22,23] Joseph McCune,[20] Guillermo Ruiz-Irastorza,[24] Jorge Sanchez-Guerrero,[25,26] Matthias Schneider,[27] Murray Urowitz,[28] George Bertsias,[29] Bimba F Hoyer,[18,30] Nicolai Leuchten,[1] Chiara Tani,[31] Sara K Tedeschi,[23,32] Zahi Touma,[33] Gabriela Schmajuk,[3] Branimir Anic,[34] Florence Assan,[35] Tak Mao Chan,[36] Ann Elaine Clarke,[37] Mary K Crow,[38] László Czirják,[39] Andrea Doria,[40] Winfried Graninger,[41] Bernadett Halda-Kiss,[39] Sarfaraz Hasni,[42] Peter M Izmirly,[43] Michelle Jung,[37] Gábor Kumánovics,[39] Xavier Mariette,[44,45] Ivan Padjen,[34] José M Pego-Reigosa,[46] Juanita Romero-Diaz,[47] Íñigo Rúa-Figueroa Fernández,[48] Raphaèle Seror,[35] Georg H Stummvoll,[49] Yoshiya Tanaka,[50] Maria G Tektonidou,[51] Carlos Vasconcelos,[52] Edward M Vital,[53,54] Daniel J Wallace,[55] Sule Yavuz,[56] Pier Luigi Meroni,[57] Marvin J Fritzler,[58] Ray Naden,[59] Thomas Dörner,[18] Sindhu R Johnson[60,61]

Handling editor David S Pisetsky

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136annrheumdis-2018-214819).

For numbered affiliations see end of article.

ABSTRACT

serosal, musculoskeletal, renal) and three immunological

Entry criterion
Antinuclear antibodies (ANA) at a titer of ≥1:80 on HEp-2 cells or an equivalent positive test (ever)

↓

If absent, do not classify as SLE
If present, apply additive criteria

↓

Additive criteria
Do not count a criterion if there is a more likely explanation than SLE.
Occurrence of a criterion on at least one occasion is sufficient.
SLE classification requires at least one clinical criterion and ≥10 points.
Criteria need not occur simultaneously.
Within each domain, only the highest weighted criterion is counted toward the total score§.

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.

Figure 2 Classification criteria for systemic lupus erythematosus. §Additional criteria items within the same domain will not be counted. *Note: In an assay with at least 90% specificity against relevant disease controls.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6827566/

Virginia Mason Franciscan He

When to Order an ANA

- Do you think this patient has an ANA associated Rheumatologic condition?
    1. SLE / drug induced lupus
    2. Scleroderma
    3. Autoimmune Myositis (polymyositis, dermatomyositis)
    4. Sjogrens

- Is this a young person with Raynaud's or older person with new Raynaud's

- New JIA diagnosis

Virginia Mason Franciscan Health™

Updates: Lupus management

Medication	Mechanism of action	Indication	Considerations for use	Side Effects/Monitoring
Belimumab (Benlysta) Approved 2020 for LN	B-lymphocyte stimulator (**BLyS**) inhibitor IV monthly or SQ weekly	SLE Lupus Nephritis	Rash and joint predominant SLE Nephritis that has failed MMF	Infection Diarrhea **Depression?** ($2,288.78/ month)
Anifrolumab-fnia (Saphnelo) Approved 2021	Interferon Receptor Antagonist IV Monthly	SLE	?	Infection Hypersensitivity ($2,760.33/month)
Voclosporin (Lupkynis) Approved 2021	Calcineurin Inhibitor PO BID	Lupus Nephritis	?	Hypertension Diarrhea Prolonged QT interval ($5,000/month)

Hematopoietic stem cell transplantation in SLE

The basic principle of HSCT is to achieve a broad immune depletion, providing an initial ‘‘debulking’’ of the immunologic memory repertoire

- Memory T and B lymphocytes
- Plasma cells

To date, more than 300 patients have received autologous HSCT specifically for SLE

Pooled data from the largest 15 single-center experiences and multicenter trials with 339 patients included indicate a **disease free survival of 50% to 66% at 5 years** despite discontinuation of immunosuppressive and other targeted disease-modifying treatment

Matteo Doglio et al. New insights in systemic lupus erythematosus: From regulatory T cells to CAR-T-cell strategies, *Journal of Allergy and Clinical Immunology* Volume 150, Issue 6, 2022, Pages 1289-1301. https://doi.org/10.1016/j.jaci.2022.08.003.https://www.sciencedirect.com/science/article/pii/S0091674922010569

Virginia Mason Franciscan Health™

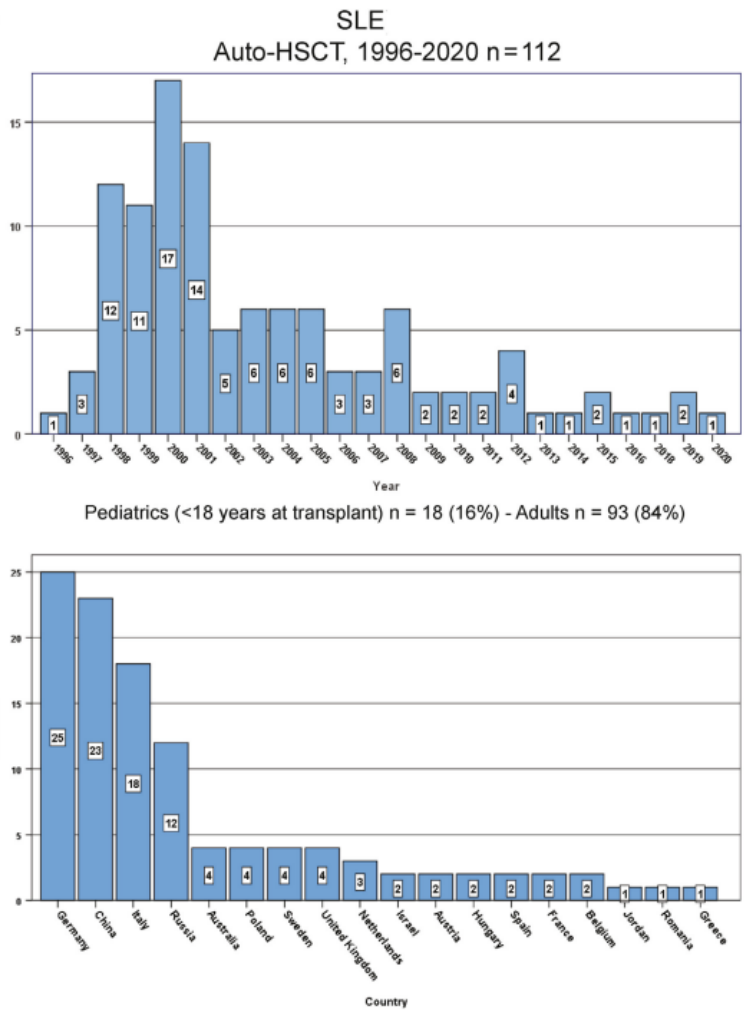


FIG 2. Number of HSCTs for SLE. **A,** The frequency of autologous HSCTs for SLE from 1996 to 2020 included in the EBMT registry. The overall number of pediatric and adult patients is reported. **B,** The number of HSCTs for SLE by country from 1996 to 2020. *Auto-HSCT,* Autologous HSCT.

Treatment-related mortality gradually declined from 12% in the first EBMT registry survey in 2004 to less than 5% in most recent reports between 2017 and 2019

Potential candidates for HSCT would reasonably include those with sustained or relapsed steroid dependence after at least 6 months of the best standard therapy, using mycophenolate mofetil or CYC with or without mAbs, with documented evidence of visceral involvement or refractory SLE

TREG Cell based therapies in SLE

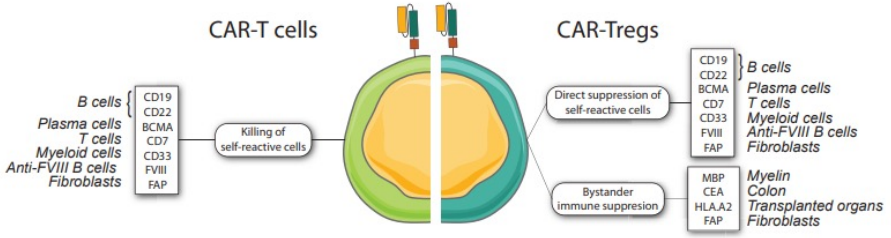


FIG 3. CAR-T-cell strategies comparison. A comparison between conventional CAR-T cells and CAR-Treg cells is reported with a list of the most-studied targets. For each molecule, the associated cellular target is also reported. In addition, for each target, the therapeutic strategy is provided. CAR-T cells can be used to selectively deplete target components relevant for the autoreactive process. CAR-Treg cells can control the autoimmune process by exerting an immune-regulatory activity. Two different strategies can be adopted with CAR-Treg cells: a direct suppression of target cells through a cell-to-cell contact or a broader locoregional immune suppression, especially localized in target organs. *BCMA*, B-cell maturation antigen; *CEA*, carcino-embryonic antigen; *FAP*, fibroblast activation protein; *MBP*, myelin basic protein.

TABLE II. Summary of active clinical trials with CAR-Treg cells

Disease	Target	Starting date	Identifier	Study design	End points
Renal transplantation	HLA-A2	March 2021	NCT04817774	Phase I/IIa multicenter open-label trial	Safety and tolerability Prevention of rejection
Liver transplantation	HLA-A2	January 2022	NCT05234190	Phase I/IIa multicenter open-label trial	Safety and tolerability Prevention of rejection Immunosuppressive withdrawal
R/R $CD19^{+}$ B-ALL	CD19	November 2022	NCT05114837	Phase I/IIa single-center open-label trial	Safety and tolerability Antitumor efficacy

Deep B cell depletion using a single infusion with autologous CD19 chimeric antigen receptor (CAR) T cells induced drug-free clinical remission in severe SLE.

As of January 2023, seven SLE patients (6 female, 1 male, aged range 19-39) had been treated with CD19 CAR-T cells with a median follow up of 13 months

- Median number of 7 failed treatments
- All patients had active kidney disease..
- All patients experienced drug free remission

Virginia Mason Franciscan Health™

Scientific Abstracts
Oral Presentations The future perspectives in the treatment of SLE & Sjören's

PDF

OP0141 LONG TERM SAFETY AND EFFICACY OF CAR-T CELL TREATMENT IN REFRACTORY SYSTEMIC LUPUS ERYTHEMATOSUS - DATA FROM THE FIRST SEVEN PATIENTS FREE

J. Taubmann [1,2], F. Müller [2,3], S. Boeltz [1,2], S. Völkl [2,3], M. Aigner [2,3], A. Kleyer [1,2], I. Minnopoulou [1,2], F. Locatelli [4], M. A. D'agostino [5], R. Gary [2,3], S. Krestchmann [2,3], S. Kharboutli [2,3], D. Mougiakakos [2,3,6], G. Krönke [1,2], M. Andreas [2,3], G. Schett [1,2]

Abstract

Background Despite better treatment modalities some patients with systemic lupus erythematosus (SLE) suffer from severe and treatment-resistant disease. This situation puts patients at high risk for organ failure or even death. Furthermore, many patients with SLE have to take long-term, sometimes even life-long immune suppressive medication to control the disease without being able to enjoy drug-free remission. Recently, we reported that deep B cell depletion using a single infusion with autologous CD19 chimeric antigen receptor (CAR) T cells induced drug-free clinical remission in severe SLE patients with refractory disease [1,2]. This abstract presents the long-term clinical efficacy and safety data of the first seven SLE patients receiving autologous CD19-directed CAR-T cell therapy.

Objectives To test whether administration of autologous CD19 chimeric antigen receptor (CAR) T cells is tolerable and effective in patients with severe refractory SLE.

CD19 CAR T-cell therapy can abrogate disease and delete autoimmunity in patients with severe SLE. After CD19 CAR T-cell therapy SLE patients remain in drug free-remission of SLE even if B cells recur. This remission can be long-lasting as the longest disease -free observation period is now 22 months

	Pat #1	Pat #2	Pat #3	Pat #4	Pat #5	Pat#6	Pat#7
Age (ys)	22	23	22	24	18	33	33
Sex (F/M)	F	M	F	F	F	F	F
Disease Duration (ys)	4	1	6	9	3	18	1
N organs involved	4	3	5	6	4	6	3
N failed treatments	7	5	4	7	5	15	7
Baseline SLEDAI (score)	16	16	10	8	9	16	10
Baseline C3 (mg/dl)	49	43	56	88	68	33	49
Baseline anti-dsDNA (IE/ml)	5600	2060	479	4	52	1335	680
Baseline Proteinuria (mg/g crea)	2015	3080	6539	8096	88	2025	5044
Conditioning Dose (%)	100	100	100	100	100	100	50
Peak CAR T (cells/µl)	167	461	33	697	146	24	117
Peak CAR T (% of T cells)	27	41	11	59	26	13	12
Duration of B cell Aplasia (days)	148	196	120	93	63	205	58
Follow-up (months)	22	16	14	13	11	8	4
Seroconversion	+	+	+	+	+	+	+
SLEDAI (lastfollow-up)	0	0	0	0	0	0	0
LLDAS (lastfollow-up)	+	+	+	+	+	+	+
DORIS Remission (lastfollow-up)	+	+	+	+	+	+	+
CRS (grade 0-4)	0	1	0	1	0	1	1
ICANS (grade 0-4)	0	0	0	0	0	0	0

Table 1 contains baseline demographic data from seven SLE patients treated with CD19 CAR T-cell therapy. Patient number one to seven, age in years (ys), sex in female (F) and male (M). Disease duration in years (ys). Number (N) of organs involved and number (N) of failed treatments, disease activity at baseline presented with SLE disease activity index (SLEDAI). Conditioning dose referred to 1x cyclophosphamide 1g/m2 and 3x fludarabine 25mg/m2. Maximum of CAR-T cell expansion after administration of 1 million CAR-T cells /kg body weight given as peak of CAR-T cells absolute and percent CAR+ of CD3+ T-cells. Efficacy criteria listed as seroconversion, disappearance of SLE specific antibodies (antidsDNA), Lupus Low Disease Activity State (LLDAS), definitions of remission in systemic lupus erythematosus (DORIS) remission. Adverse events listed at Cytokine-release syndrome (CRS) and Immune-related effector Cell Neurotoxicity Syndrome (ICANS) in grade 0-4.

Virginia Mason Franciscan Health

NIH RESEARCH MATTERS

February 14, 2023

VEXAS syndrome more common than realized

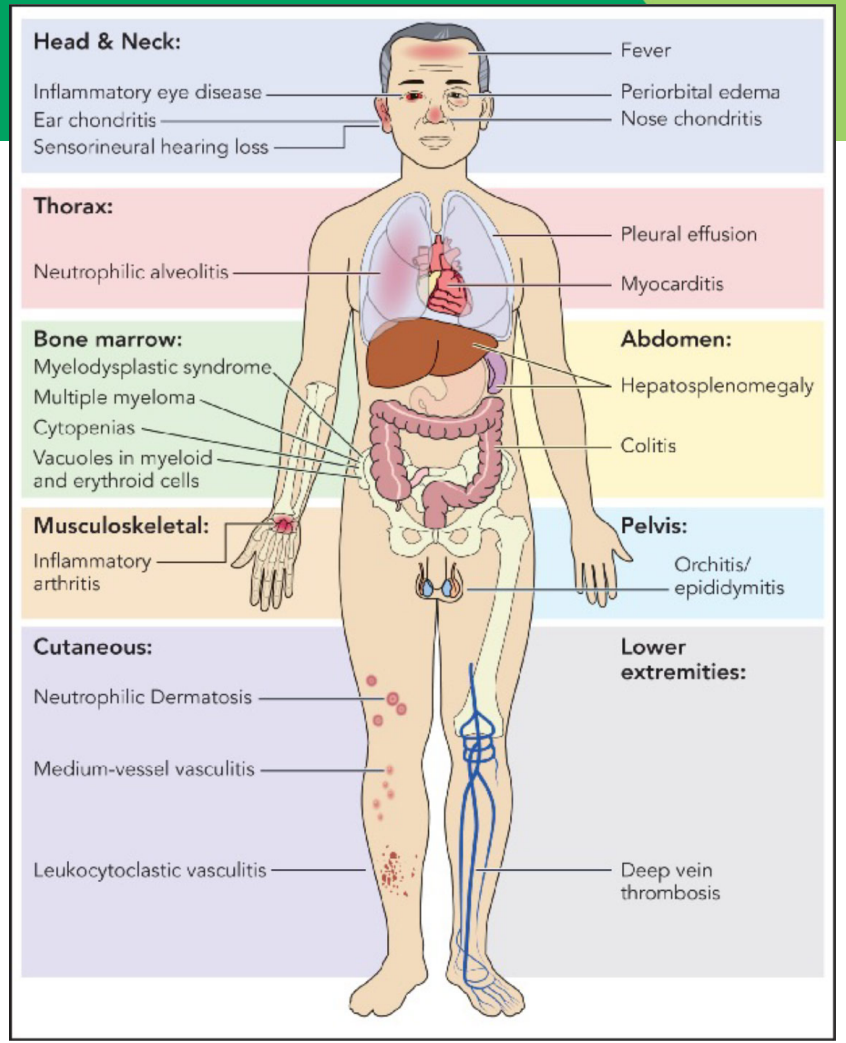
At a Glance

- A severe inflammatory disease called VEXAS is more prevalent and has a broader range of symptoms than expected.
- Additional studies of racially diverse populations are needed to better understand the scope and symptoms of this hard-to-recognize disease.

In 2020, a team of NIH researchers reported the discovery of a rare and often-deadly inflammatory disorder, which they named VEXAS. Affected people have varying symptoms that can include anemia, recurrent fevers, painful rashes, blood clots, and shortness of breath. Because these symptoms overlap with other autoimmune and inflammatory diseases, VEXAS can be hard to recognize. But having an accurate diagnosis is important for effective treatment.

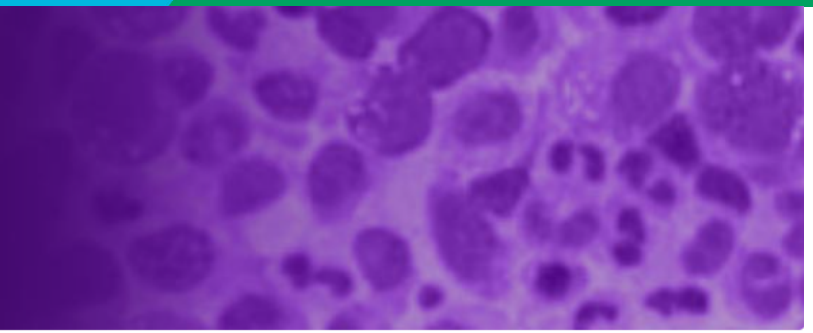
The study suggests that VEXAS disease, which was only recently discovered, may be more common than previously thought. *Lucky Business / Shutterstock*

VEXAS was discovered by searching for genetic variants that were shared among more than 2,500 patients with body-wide inflammation or other unusual and undiagnosed conditions. The identified gene, *UBA1*, is on the X chromosome, and all 25 people initially diagnosed with VEXAS were male. Since men have only one X chromosome, they only have one copy of the gene. Women typically have two X chromosomes and therefore two copies of *UBA1*. In women, a mutation in only one copy is likely to cause less severe or no disease. The genetic mutations that cause this disease occur after birth and so aren't transmitted from parents to children.



VEXAS

VEXAS syndrome is a disease that causes inflammatory and hematologic (blood) manifestations. The syndrome is caused by mutations in the *UBA1* gene of blood cells and acquired later in life. Patients do not pass the disease to their children.



What does VEXAS mean?

VEXAS is an acronym defined as follows:

- **V** - **v**acuoles are often seen in cells identified in bone marrow biopsies from patients with VEXAS syndrome.
- **E** - **E1** ubiquitin activating enzyme, encoded by the *UBA1* gene which is mutated in patients.
- **X** - the *UBA1* gene is located on the **X** chromosome.
- **A** - patients have **a**utoinflammation.
- **S** - the mutations are **s**omatic, meaning they are acquired at some point in life and not inherited.

VEXAS

Patients with VEXAS can have a wide range of inflammatory symptoms affecting multiple organs including:

- skin (rashes that can be painful).
- cartilaginous structures (pain and swelling of the ear and nose).
- lungs (cough and shortness of breath).
- joints (swelling and pain).
- vasculature (inflammation of vessels).

Patients often have fever and extreme fatigue. The hematologic features can include anemia, low platelets, and blood clots.

On many occasions patients with VEXAS have associated clinical diagnoses, including relapsing polychondritis, polyarteritis nodosa, sweet syndrome and myelodysplastic syndrome.

There is no standardized treatment for VEXAS currently, however the inflammatory features can be treated with steroids and other immunosuppressants. Some patients may be candidates for bone marrow transplantation.

Virginia Mason Franciscan Health™

VEXAS syndrome: An inflammatory and hematologic disease.
Patel BA, Ferrada MA, Grayson PC, Beck DB *Semin Hematol.* **2021 Oct;** 58(4).

American College of Rheumatology
Empowering Rheumatology Professionals

AAHKS
American Association of Hip and Knee Surgeons

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

Guideline Summary

Updated March 17, 2022

This updated guideline includes changes in the recommendations regarding rituximab and belimumab for patients with severe SLE, and now includes anifrolumab and voclosporin. For patients with spondyloarthritis, recommendations have been added on management of ixekizumab and guselkumab. The recommendations have changed for management of JAK inhibitors and suggest withholding for 3 days before surgery; tofacitinib, upadicitinib, and baricitinib are now included.

This updated guideline addresses the perioperative management of disease modifying medications for adults with rheumatic diseases, specifically inflammatory arthritis (IA) and systemic lupus erythematosus (SLE) undergoing elective total hip arthroplasty (THA) and total knee arthroplasty (TKA). A panel of rheumatologists, orthopaedic surgeons, and infectious disease specialists updated the systematic literature review and included currently available medications for the clinically relevant population, intervention, comparator, and outcomes (PICO) questions, updating the 2017 recommendations*. As patients with IA and SLE are at increased risk of infection after THA and TKA, these recommendations aim to balance the risk of perioperative infection and the risk of disease flares, recognizing that all flares have an impact on quality of life but a flare in a patient with severe SLE at risk for organ damage warrants unique considerations. This updated guideline includes recently introduced immunosuppressive medications to help decision-making by clinicians and patients regarding perioperative disease modifying medication management for patients with IA and SLE at the time of elective THA or TKA.

Virginia Mason Franciscan Health

https://pubmed.ncbi.nlm.nih.gov/35718887/

MEDICATIONS TO CONTINUE THROUGH SURGERY		
DMARDs: CONTINUE these medications through surgery. (All patients)	**Dosing Interval**	**Recommended timing of surgery since last medication dose**
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.	**Dosing Interval**	**Recommended timing of surgery since last medication dose**
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 (Benlysta)	***Weekly SQ***	***Anytime***
Belimumab (Benlysta)	***Monthly IV***	***Week 4***
Anifrolumab (Saphnelo)†	***IV Every 4 weeks***	***Week 4***
Voclosporin (Lupkynis)†	***Twice daily***	***Continue***

MEDICATIONS TO WITHHOLD PRIOR TO SURGERY***		
BIOLOGICS: WITHHOLD these medications through surgery		**Recommended timing of surgery since last medication dose**
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
Abatacept (Orencia)	Monthly (IV) or weekly (SQ)	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 (SQ) 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	**Dosing Interval**	**1 week after last dose**
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 SQ (Benlysta)	***Weekly***	***Week 2***

Virginia Mason Franciscan Heal

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 71 / No. 7
February 18, 2022

Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older — United States, 2022

Neil Murthy, MD[1]; A. Patricia Wodi, MD[1]; Henry Bernstein, DO[2]; Veronica McNally, JD[3]; Sybil Cineas, MD[4]; Kevin Ault, MD[5]

Virginia Mason Franciscan Health™

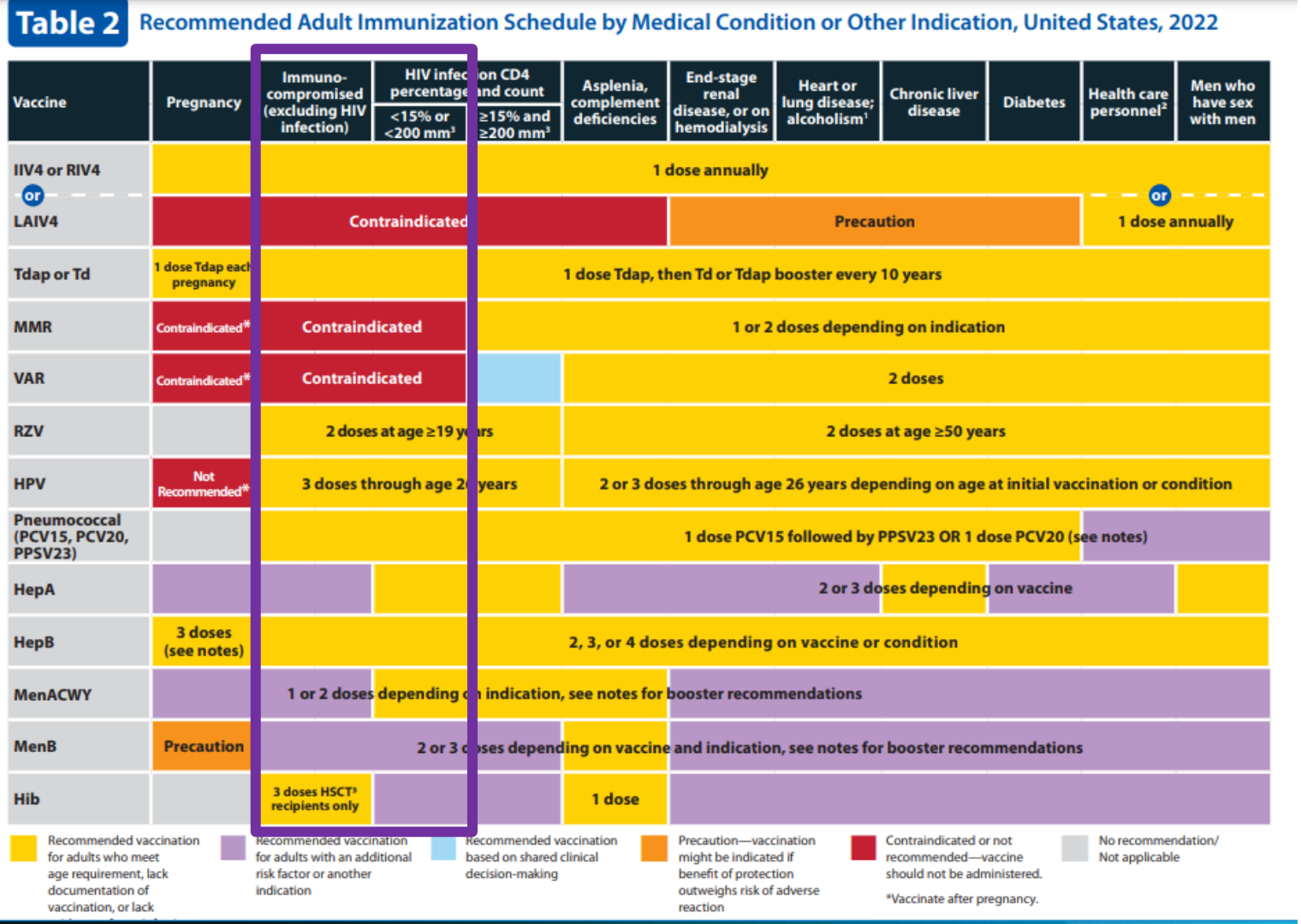


Table 2 Recommended Adult Immunization Schedule by Medical Condition or Other Indication, United States, 2022

Vaccine	Pregnancy	Immuno-compromised (excluding HIV infection)	HIV infection CD4 percentage and count: <15% or <200 mm³	HIV infection CD4 percentage and count: ≥15% and ≥200 mm³	Asplenia, complement deficiencies	End-stage renal disease, or on hemodialysis	Heart or lung disease; alcoholism[1]	Chronic liver disease	Diabetes	Health care personnel[2]	Men who have sex with men
IIV4 or RIV4	1 dose annually										
or										or	
LAIV4	Contraindicated					Precaution				1 dose annually	
Tdap or Td	1 dose Tdap each pregnancy	1 dose Tdap, then Td or Tdap booster every 10 years									
MMR	Contraindicated*	Contraindicated	1 or 2 doses depending on indication								
VAR	Contraindicated*	Contraindicated			2 doses						
RZV	2 doses at age ≥19 years				2 doses at age ≥50 years						
HPV	Not Recommended*	3 doses through age 26 years			2 or 3 doses through age 26 years depending on age at initial vaccination or condition						
Pneumococcal (PCV15, PCV20, PPSV23)	1 dose PCV15 followed by PPSV23 OR 1 dose PCV20 (see notes)										
HepA	2 or 3 doses depending on vaccine										
HepB	3 doses (see notes)	2, 3, or 4 doses depending on vaccine or condition									
MenACWY	1 or 2 doses depending on indication, see notes for booster recommendations										
MenB	Precaution	2 or 3 doses depending on vaccine and indication, see notes for booster recommendations									
Hib	3 doses HSCT[3] recipients only			1 dose							

- Recommended vaccination for adults who meet age requirement, lack documentation of vaccination, or lack
- Recommended vaccination for adults with an additional risk factor or another indication
- Recommended vaccination based on shared clinical decision-making
- Precaution—vaccination might be indicated if benefit of protection outweighs risk of adverse reaction
- Contraindicated or not recommended—vaccine should not be administered.
- No recommendation/ Not applicable

*Vaccinate after pregnancy.

Human papillomavirus vaccination

Routine vaccination

- **HPV vaccination recommended for all persons through age 26 years:** 2- or 3-dose series depending on age at initial vaccination or condition:

Special situations

- **Age ranges recommended above for routine and catch-up vaccination or shared clinical decision-making also apply in special situations**
  - **Immunocompromising conditions, including HIV infection**: 3-dose series, even for those who initiate vaccination at age 9 through 14 years.
  - **Pregnancy**: Pregnancy testing is not needed before vaccination; HPV vaccination is not recommended until after pregnancy; no intervention needed if inadvertently vaccinated while pregnant

Pneumococcal vaccination

Routine vaccination

- **Age 65 years or older** who have not previously received a pneumococcal conjugate vaccine or whose previous vaccination history is unknown: 1 dose PCV15 or 1 dose PCV20. If PCV15 is used, this should be followed by a dose of PPSV23 given at least 1 year after the PCV15 dose. A minimum interval of 8 weeks between PCV15 and PPSV23 can be considered for adults with an immunocompromising condition,* cochlear implant, or cerebrospinal fluid leak to minimize the risk of invasive pneumococcal disease caused by serotypes unique to PPSV23 in these vulnerable groups.
- For guidance for patients who have already received a previous dose of PCV13 and/or PPSV23, see www.cdc.gov/mmwr/volumes/71/wr/mm7104a1.htm.

Special situations

- **Age 19–64 years** with certain underlying medical conditions or other risk factors** who have not previously received a pneumococcal conjugate vaccine or whose previous vaccination history is unknown: 1 dose PCV15 or 1 dose PCV20. If PCV15 is used, this should be followed by a dose of PPSV23 given at least 1 year after the PCV15 dose. A minimum interval of 8 weeks between PCV15 and PPSV23 can be considered for adults with an immunocompromising condition,* cochlear implant, or cerebrospinal fluid leak to minimize the risk of invasive pneumococcal disease caused by serotypes unique to PPSV23 in these vulnerable groups.
- For guidance for patients who have already received a previous dose of PCV13 and/or PPSV23, see www.cdc.gov/mmwr/volumes/71/wr/mm7104a1.htm.

Zoster vaccination

Routine vaccination

- **Age 50 years or older:** 2-dose series RZV (Shingrix) 2–6 months apart (minimum interval: 4 weeks; repeat dose if administered too soon), regardless of previous herpes zoster or history of zoster vaccine live (ZVL, Zostavax) vaccination (administer RZV at least 2 months after ZVL)

Special situations

- **Pregnancy:** There is currently no ACIP recommendation for RZV use in pregnancy. Consider delaying RZV until after pregnancy.
- **Immunocompromising conditions (including HIV):** RZV recommended for use in persons age 19 years or older who are or will be immunodeficient or immunosuppressed because of disease or therapy. For detailed information, see www.cdc.gov/mmwr/volumes/71/wr/mm7103a2.htm.

Audience Poll

It is November and a 22 year old female patient with Rheumatoid Arthritis on Methotrexate who recently started Adalimumab is in your office for an annual exam. She's not had any vaccinations since childhood. Which of the following vaccination recommendations are correct (per the ACR)?

A. Annual flu shot
B. Annual flu shot- hold MTX for 2 weeks
C. Annual flu shot- hold Humira for 2 weeks
D. High dose annual flu shot, pneumococcal vaccination, recombinant VZV, HPV and Tdap- hold MTX for 2 weeks after
D. None

Virginia Mason Franciscan Health™

Arthritis & Rheumatology
Vol. 75, No. 3, March 2023, pp 333–348
DOI 10.1002/art.42386

American College of Rheumatology
Empowering Rheumatology Professionals

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

Anne R. Bass,[1] Eliza Chakravarty,[2] Elie A. Akl,[3] Clifton O. Bingham,[4] Leonard Calabrese,[5] Laura C. Cappelli,[4] Sindhu R. Johnson,[6] Lisa F. Imundo,[7] Kevin L. Winthrop,[8] Reuben J. Arasaratnam,[9] Lindsey R. Baden,[10] Roberta Berard,[11] S. Louis Bridges Jr.,[1] Jonathan T. L. Cheah,[12] Jeffrey R. Curtis,[13] Polly J. Ferguson,[14] Ida Hakkarinen,[15] Karen B. Onel,[1] Grayson Schultz,[16] Vidya Sivaraman,[17] Benjamin J. Smith,[18] Jeffrey A. Sparks,[10] Tiphanie P. Vogel,[19] Eleanor Anderson Williams,[20] Cassandra Calabrese,[5] Joanne S. Cunha,[21] Joann Fontanarosa,[22] Miriah C. Gillispie-Taylor,[19] Elena Gkrouzman,[12] Priyanka Iyer,[23] Kimberly S. Lakin,[1] Alexandra Legge,[24] Mindy S. Lo,[25] Megan M. Lockwood,[26] Rebecca E. Sadun,[27] Namrata Singh,[28] Nancy Sullivan,[22] Herman Tam,[29] Marat Turgunbaev,[30] Amy S. Turner,[30] and James Reston[22]

Virginia Mason Franciscan Health

https://pubmed.ncbi.nlm.nih.gov/36597810/

Table 3. Medication management at the time of non–live attenuated vaccine administration. Color table can be viewed in the online issue,which is available at http://onlinelibrary.wiley.com/doi/10.1002/art.42386/abstract.

	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.

Recommendations	Level of evidence†	PICO	numbers
Expanded indications for specific vaccines in patients with RMDs receiving immunosuppression			
Influenza vaccination			
For patients with RMD age ≥65 years and patients with RMD age >18 and <65 years who are taking immunosuppressive medication, giving high-dose or adjuvanted influenza vaccination is **conditionally** recommended over giving regular-dose influenza vaccination.	PICO 9. Very low (indirect evidence only)‡	PICO 9. In patients with RMD age ≥65 years, is high-dose influenza vaccine more effective than seasonal regular-dose influenza vaccine?	728
	PICO 10. Very low (indirect evidence only)‡	PICO 10. In patients with RMD age ≥65 years, is adjuvanted influenza vaccine more effective than seasonal regular-dose influenza vaccine?	728

Franciscan Health

https://onlinelibrary.wiley.com/doi/epdf/10.1002/art.42386

Table 5. Immunosuppressive medication 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

Pneumococcal vaccination

For patients with RMD age <65 years who are taking immunosuppressive medication, pneumococcal vaccination is **strongly** recommended.

Recombinant VZV vaccination

For patients with RMD age >18 years who are taking immunosuppressive medication, administering the recombinant VZV vaccine is **strongly** recommended.

HPV vaccination

For patients with RMD age >26 and <45 years who are taking immunosuppressive medication and are not previously vaccinated, vaccination against HPV is **conditionally** recommended.

Whether to hold immunosuppressive medication at the time of non–live attenuated vaccination to maximize vaccine immunogenicity, although holding medications could be associated with disease flare

For patients with RMD, *holding* methotrexate for 2 weeks after influenza vaccination is **conditionally** recommended, assuming disease activity allows.

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Search | Vaccines site

Vaccine Information Statements (VISs)

VIS Home > Current VISs

- VIS Home
- Current VISs
  - Respiratory Syncytial Virus Infection (RSV) VIS
- What's New with VISs
- About VISs
- Dates of Current and Past VISs
- VIS Barcodes

Related Link

- Vaccines & Immunizations
- Immunization Schedules

Respiratory Syncytial Virus (RSV) VIS

RSV Vaccine: What You Need to Know

Print

Current Edition Date: 7/24/2023

- Print VIS [2 pages]
- RTF file [3 pages]
  (For use in electronic systems)
- More information about RSV

On This Page

Why get vaccinated?

RSV vaccine can prevent lower respiratory tract disease caused by **respiratory syncytial virus (RSV)**. RSV is a common respiratory virus that usually causes mild, cold-like symptoms.

RSV is usually spread through direct contact with the virus, such as droplets from another person's cough or sneeze contacting your eyes, nose, or mouth. It can also be spread by touching a surface that has the virus on it, like a doorknob, and then touching your face before washing your hands.

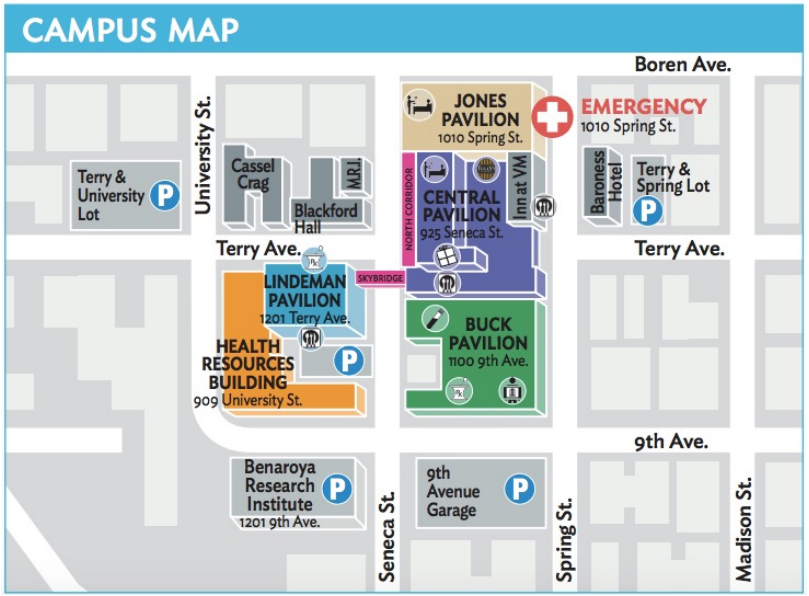
Virginia Mason Franciscan Health™

CDC recommends **adults 60 years and older** may receive a single dose of RSV vaccine "based on discussions between the patient and health care provider. **"**

Questions?

Virginia Mason
Hospital & Seattle Medical Center

VirginiaMason.org



Erin.Bauer@virginamason.org
Phone: (206) 223-6824
Fax: (206) 625-7288
Pager: (206) 540-3499

Virginia Mason Franciscan Health