RhAPP

RHEUMATOLOGY ADVANCED PRACTICE PROVIDERS

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Beyond Steroids: Reviewing and Exploring New Treatments in Polymyalgia Rheumatica (PMR)

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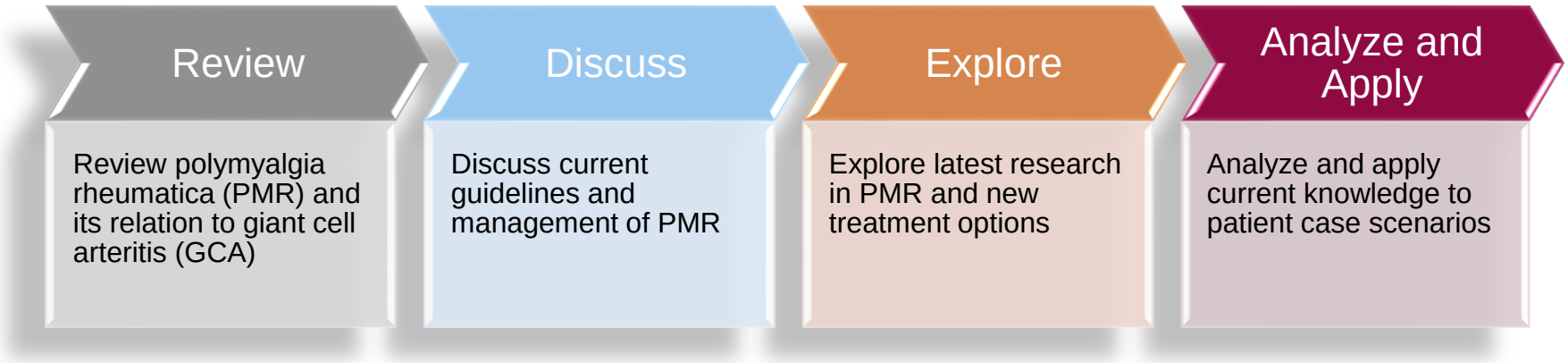
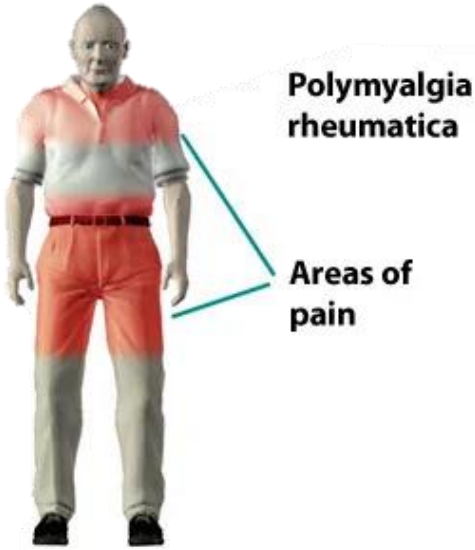
- Danielle Gatti-Palumbo, PharmD:
  - Advisory Board: Boehringer Ingelheim

Objectives


Review
Review polymyalgia rheumatica (PMR) and its relation to giant cell arteritis (GCA)
Discuss
Discuss current guidelines and management of PMR
Explore
Explore latest research in PMR and new treatment options
Analyze and Apply
Analyze and apply current knowledge to patient case scenarios

Polymyalgia Rheumatica (PMR)

- Inflammatory rheumatic disorder associated with muscle pain and stiffness in the neck, shoulder, and hip
- Exclusively a disease of adults > 50
  - Increases age: peak 70 – 80yrs
- Women 2-3x> Men
- Highest incidence in Scandinavian and Northern Europe
  - Less common in African, Asian, and Latino



Lundberg IE, et al., J Intern Med. 2022 Nov;292(5):717-732.; Doran MF, et al. J Rheumatol. 2002 Aug;29(8):1694-7; Clinical manifestations and diagnosis of polymyalgia rheumatica: UPTODATE:. Mar

Relation to GCA

- PMR 2-3x more common than GCA
- Both associated with HLA- DR4 allele
- PMR can precede, accompany or follow GCA
- 50% of GCA pts have PMR symptoms
  - Minnesota pop. study, 15 % of PMR had temporal arteritis (TA) verified by biopsy
  - In PMR pts, with no symptoms of GCA, 21% had biopsy and 32% had US TA features
- Concomitant diagnosis of GCA in PMR should be suspected if new-onset head-symptoms or severe ache, jaw claudication, new or unexplained visual constitutional symptoms (fever, weight loss, fatigue)

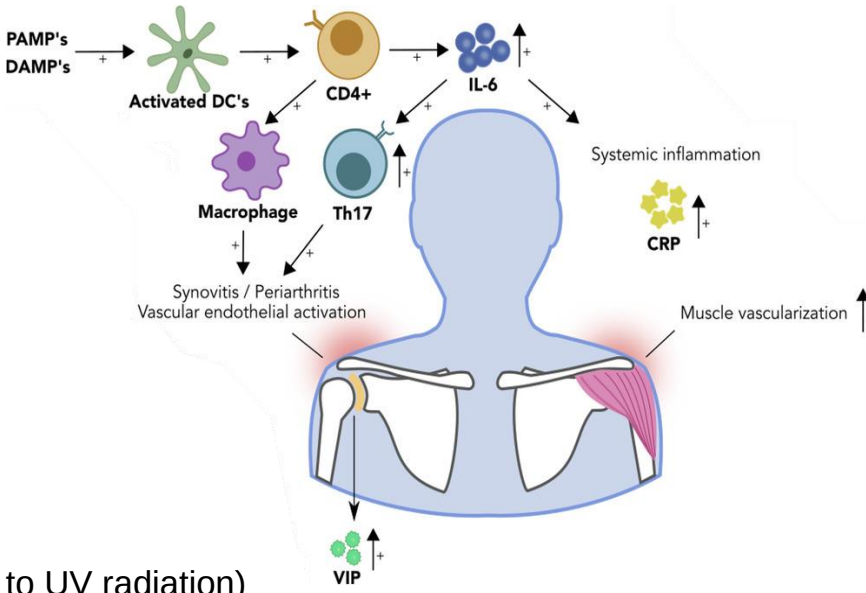
Lundberg IE, et al., J Intern Med. 2022 Nov;292(5):717-732.; Doran MF, et al. J Rheumatol. 2002 Aug;29(8):1694-7; Clinical manifestations and diagnosis of polymyalgia rheumatica: UPTODATE:. Mar 23, 2023; DR.Hitakshi Hirpara Polymyalgia Rheumatica. January 22, 2023

Etiology

- Similar distribution of circulating CD4+ T-cell subsets
  - Subclinical arterial inflammation, including activated dendritic cells, IL-1, and IL-6 found in temporal arteries of PMR pts without GCA
  - GCA but not PMR, have high levels of interferon gamma

- Proinflammatory cytokine IL 6
- T helper 17 (Th17)

- Regulatory T (Treg)



- Environmental Infectious Triggers
  - Cyclical pattern in incidence and seasonal variation
  - Virus (SARS-CoV-2)
  - Vaccine (influenza, COVID-19 vaccination)
  - Sun (Damage to Superficial arteries by high exposure to UV radiation)

Lundberg IE, et al., J Intern Med. 2022 Nov;292(5):717-732.

Clinical Presentation

Acute onset proximal muscle pain and stiffness in neck, hips. shoulders, upper arms, thighs

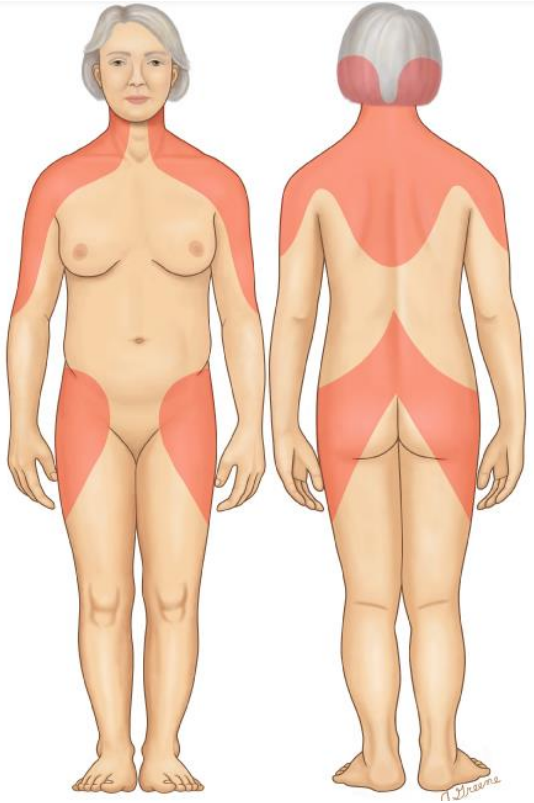
- Bilateral shoulder pain-70-95%
- Neck and girdle- 50-70%
- Can be initially unilateral, but soon become symmetrical

Pronounced morning stiffness (>45min), difficulty turning in or getting out bed in AM

- Spontaneous relief later in the day, but prolonged stiffness can recur
- Absence excludes diagnosis

Nonspecific symptoms: Fatigue, depression, arthralgia, loss of appetite, weight loss, or fever

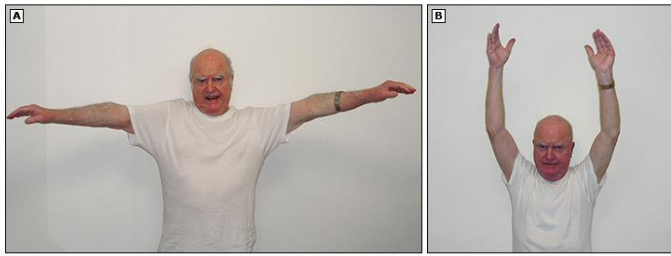
- High spike fever seen in GCA, not PMR



Lundberg IE, et al., J Intern Med. 2022 Nov;292(5):717-732.
Clinical manifestations and diagnosis of polymyalgia rheumatica: UPTODATE:. Mar 23, 2023

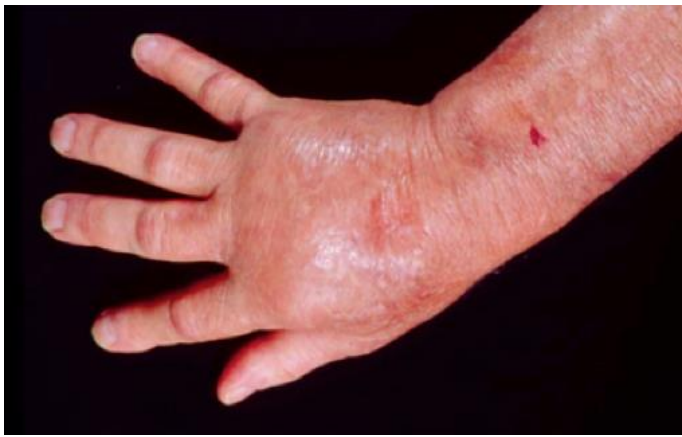
Clinical Presentation

- Joint examination and range of motion
  - Distal symptoms 50%
    - Clinical synovitis of wrists, MCP joints, knees
    - Carpal tunnel syndrome
    - Non-erosive
    - PMR-related peripheral arthritis is nonerosive, seronegative, and highly responsive to low doses of glucocorticoids
    - Overlap of PMR and seronegative RA in older adults with peripheral synovitis
      - 30 % initially with PMR, reclassified as "late-onset" or "elderly onset" RA
  - Restricted shoulder motion
    - Classic inability to abduct shoulders past 90 degrees
    - Puffy edematous hand syndrome, or remitting seronegative symmetrical synovitis with pitting edema (RS3PE) syndrome



(A) Inability to abduct actively the arms above 90 degrees in a patient presenting with two weeks of proximal achiness and protracted morning stiffness.

(B) Painless active abduction of the shoulders after one week on prednisone 10 mg/day.



Lundberg IE, et al., J Intern Med. 2022 Nov;292(5):717-732.; Clinical manifestations and diagnosis of polymyalgia rheumatica: UPTODATE:. Mar 23, 2023

Laboratory Findings

Erythrocyte sedimentation rate (ESR)

- May or may not be elevated
- ~5-20% are normal

C-reactive protein (CRP)

- Almost always elevated in PMR

Rule out other diseases: RA, Malignancy, Myositis, Pain syndrome, hypothyroidism, infection

- Negative RF, anti-CCP
- CBC, Platelet count, glucose, SCr, LFTs, calcium, TSH, creatine kinase (CK), vitamin D
- Thrombocytosis, normochromic normocytic anemia, leukocytosis seen in active inflammation

Lundberg IE, et al., J Intern Med. 2022 Nov;292(5):717-732.
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Imaging

- Not required for diagnosis
- Periarticular structures (bursitis and tenosynovitis) found on US, MRI, PET
- Acute onset, age >50 and evidence of bilateral subacromial/subdeltoid bursitis and tenosynovitis of the long head of the biceps, especially if bilateral support PMR diagnosis
- Useful for atypical presentations, non-responders to initial therapy, and differentiating classic mimickers of PMR, (rotator cuff tendinitis, RA)

TABLE 2: DIFFERENTIATING PMR FROM RA

IMAGING MODALITY	KEY FINDINGS	ADVANTAGES	LIMITATIONS
Ultrasound[5]	— shoulder: subacromial, subdeltoid bursitis, biceps tenosynovitis, glenohumeral synovitis — hip: bilateral trochanteric bursitis	— can differentiate PMR from musculoskeletal cause when bilateral hip or shoulder or one hip/one shoulder structures are involved — readily available	— cannot differentiate from RA — limited to a site (shoulders, hips or peripheral joints) — operator dependent — cost +
MRI[4-7]	— findings are the same as with ultrasound with better sensitivity and specificity — extracapsular changes including peritendinitis, myofascial inflammation, and peripheral joint images are additionally recognized — pelvis will be preferred site	— MRI helps confirm peritendineum as the inflammation target of PMR — can help differentiate PMR from RA. PMR patients have more extracapsular inflammation while RA patients have intracapsular inflammation. — MRA can be done at the same time if concerned for large vessel GCA	— cost ++ — availability
PET/CT[9-11]	— similar to ultrasound and MRI but with sensitivity of 93.9% and specificity of 91.7–97% by combining the sites of characteristic extracapsular pathology	— can help document the PMR in the whole-body distribution — can help rule out concomitant large vessel vasculitis, malignancy, or infection	— cost +++ — availability

Lundberg IE, et al., J Intern Med. 2022 Nov;292(5):717-732.
Clinical manifestations and diagnosis of polymyalgia rheumatica: UPTODATE:. Mar 23, 2023
Desh Nepal et al. The Rheumatologist. February 13, 2023

Diagnosis

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

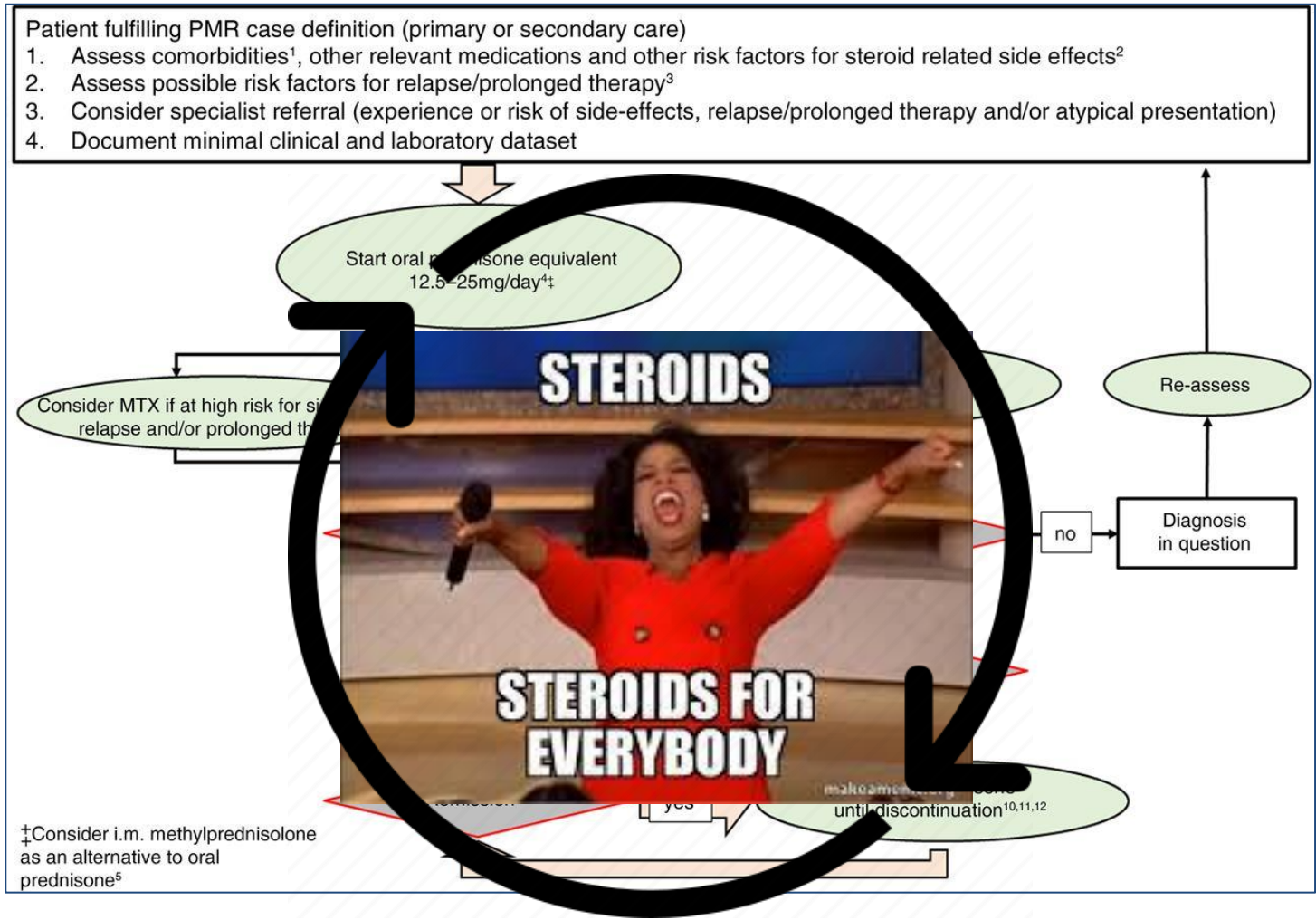
	Points without US (0–6)	Points with US† (0–8)
Morning stiffness duration >45 min	2	2
Hip pain or limited range of motion	1	1
Absence of RF or ACPA	2	2
Absence of other joint involvement	1	1
At least one shoulder with subdeltoid bursitis and/or biceps tenosynovitis and/or glenohumeral synovitis (either posterior or axillary) and at least one hip with synovitis and/or trochanteric bursitis	Not applicable	1
Both shoulders with subdeltoid bursitis, biceps tenosynovitis or glenohumeral synovitis	Not applicable	1

*A score of 4 or more is categorised as PMR in the algorithm without US and a score of 5 or more is categorised as PMR in the algorithm with US.
†Optional ultrasound criteria.
ACPA, anticitrullinated protein antibody; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PMR, polymyalgia rheumatica; RF, rheumatoid factor; US, ultrasound.

- ❑ >4 w/o US
- ❑ >5 with US

Dasgupta B, et al. Annals of the Rheumatic Diseases 2012;71:484-492.

Treatment


Patient fulfilling PMR case definition (primary or secondary care)
1. Assess comorbidities[1], other relevant medications and other risk factors for steroid related side effects[2]
2. Assess possible risk factors for relapse/prolonged therapy[3]
3. Consider specialist referral (experience or risk of side-effects, relapse/prolonged therapy and/or atypical presentation)
4. Document minimal clinical and laboratory dataset
Start oral prednisone equivalent 12.5–25mg/day[4‡]
Consider MTX if at high risk for si
relapse and/or prolonged th
Re-assess
no
Diagnosis in question
STEROIDS
STEROIDS FOR EVERYBODY
until discontinuation[10,11,12]
‡Consider i.m. methylprednisolone as an alternative to oral prednisone[5]

The Perfect Scenario

- AB is an 81 year old man who presents for acute onset of b/l shoulder and hip achy pain with use, AM stiffness, mild difficulty/struggling getting off low seats, hands/wrists R>L feeling more swollen and painful over same time course, Pain is affecting his sleep
- Initially saw Ortho for neck pain, started on Meloxicam 15mg daily which resolved neck pain and improved shoulder/hand pain by 25%
- Reports being very active, daily exercises including light weight arm exercises but recently struggling
- Labs: Negative ANA, RF, HLA B27, ESR. CRP elevated
- 11/14/2019- ESR 100 mm/hr (0-20), CRP 5.14 mg/dL (0-0.40)- Started on Prednisone 10mg/day

Date	ESR mm/hr (0-20)	CRP mg/dL (0-0.40)	
10/29/19	17	>10.0	Started Prednisone 10mg/day
11/14/19	100	5.14	Marked improvement
12/17/19	41	0.45	No joint complaints, back to his exercises Prednisone taper 9mg x1 month, then 8mg
2/25/20	16	0.15	On 7mg/day x 1 week. - Tolerating Taper by 1mg q2weeks as tolerated, taper monthly if any recurrence of symptoms
06/01/20	13	0.73	Off steroids, no further symptoms

Further follow-up, off steroids, no further symptoms

2015 EULAR/ACR PMR

Glucocorticosteroid (GC) over NSAIDs	• Exception of short term NSAIDs or analgesics
Minimum effective dose of GC (12.5-25mg prednisone initial)	• Higher range dose if high risk of relapse and low risk of adverse events • Lower range doses if comorbidities (DM, osteoporosis glaucoma, HTN, CVD, infection etc) • Discourages initial GC dose ≤7 mg/day or >30mg/day • Single daily dose > divided daily dose, except if prominent night pain while tapering GC below the low dose range (<5mg daily)
Clinical improvement should be noted after 2 weeks, almost complete response after 4 weeks	• If lack of initial response (2 weeks), increase GC to 25mg • If on im Methylprednisonolone, consider switch to oral GC

Dejaco C, Singh YP, Perel P, et al. Ann Rheum Dis 2015;74:1799–1807

2015 EULAR/ACR PMR

Initial Taper

- Taper to 10mg/day prednisone equivalent within 4-8 weeks

Relapse Taper

- Increase oral prednisone to the pre-relapse dose and decrease gradually (within 4-8 weeks) to the dose when relapse occurred

Tapering once remission is achieved

- Following initial and relapse therapies
- Taper oral prednisone by 1mg/4 weeks (or by 1.25mg decrements using alternating days, 7.5/10mg) until d/c with remission

Dejaco C, Singh YP, Perel P, et al. Ann Rheum Dis 2015;74:1799–1807

2015 EULAR/ACR PMR

IM Methylprednisolone as alternative to oral GC (ie. 120mg every 3 weeks until week 9)

- Taper: 100mg IM at week 12, then monthly reduction of dose by 20mg every 12 weeks until week 48, then reduced by 20mg every 16 weeks until d/c

Early introduction of Methotrexate (MTX) in addition to GC

- High risk of relapse and/or prolonged therapy, high risk of GC side effects (comorbidities and/or concomitant medications)
  - Relapse Risk Factors
    - Female
    - ESR >40mm/hr
    - Peripheral inflammatory arthritis
- Relapse without significant response to GC or experiencing GC side effects
- Doses 7.5mg- 10mg/week
- Pts on GCs plus MTX and GCs have been withdrawn already, D/C of MTX may be considered

Exercise to maintain muscle mass and function, reduce risk of falls

Against use of TNFα

Against use of Chinses herbal preparations Yanghe and Biqi caps

Dejaco C, Singh YP, Perel P, et al. Ann Rheum Dis 2015;74:1799–1807.

The Overlapper

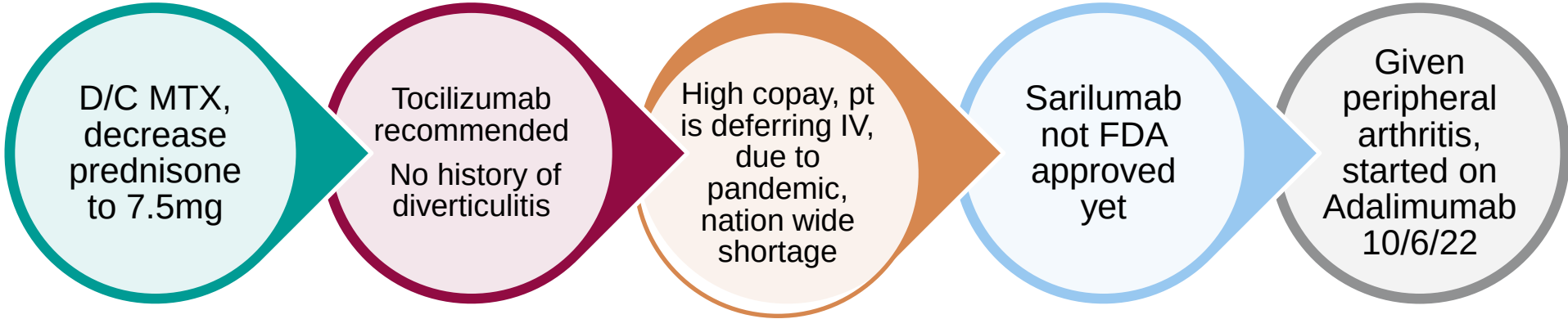
- OG is an 83F with DMII, HTN, with Shoulder and hip girdle stiffness for the past 2-3 months, interfering with sleep, also with mild lateral hip pain
- 8/8/20- ESR 115 CRP 16- PMR
- Started Meloxicam for knee pain and Prednisone 15mg with significant improvement in her pain, able to lift her arms and walk without pain
- Plan: Prednisone 15mg to complete 2 weeks, then taper to 12.5mg for 2 weeks, then 10mg for 1 month, with 1mg per month taper thereafter

Date	ESR mm/hr (0-20)	CRP mg/L (<4)	
8/9/20	115	16	Could not tolerate taper to 12.5mg Plan to continue 15mg for the full month and then taper to 12.5mg
11/30/20	69	26	Tolerating 12.5mg over one month, feels well Still reports slight stiffness in her shoulders in AM Plan taper to 10mg for 1 month, then to 9mg
1/13/21	53	14	On prednisone 8mg x1 week, to taper by 1mg/month Started alendronate for OP She reports significant fatigue upon waking Fingerstick glucose levels in the 300s, adjusting her insulin
2/4/21	67	21	Body aches for 3-4 hours in AM on prednisone 7mg
3/19/21	58	8	Taper from 6mg to 5mg with further taper by 1mg/month
6/11/21	58	21	Tapered from 4mg to 3mg but developed recurrence of shoulder, hand pain and stiffness Increased back up to 4mg today

The Overlapper

- 6/22/21- pt complaining of peripheral arthritis on tapering prednisone. RF/CCP negative
- Increased prednisone to 10mg and started on MTX due to new onset of peripheral arthritis on tapering prednisone and uncontrolled diabetes
- 10/7/21- reports significant fatigue after taking MTX and continues to have high blood glucose levels on Prednisone 10mg

- **WHAT DO YOU DO???**



New Therapies

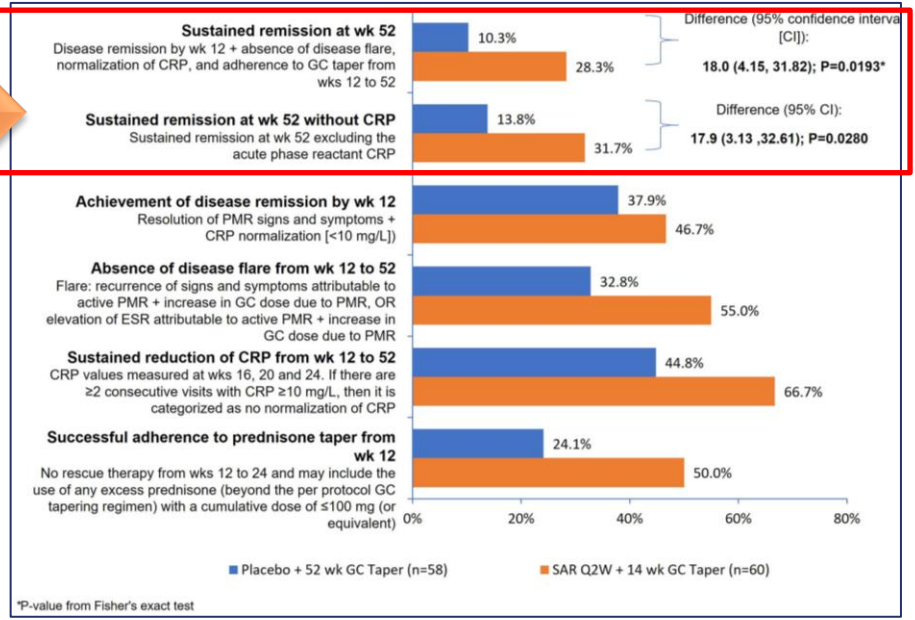
Sarilumab

Approved for
PMR Feb. 2023

Sarilumab (Kevzara®) Phase 3 **SAPHYR TRIAL**

- PMR with inadequate response to GC or could not tolerate GC taper
- 1:1, 52 weeks, SAR 200mg Q2W + 14 Wk GC taper or PBO
- 117 (SAR 59, PBO 58)

Primary Endpoint



SAR

- 44% less flares after clinical remission (16.7% vs 29.3%; P=0.0153)
- Improved PMR activity scores (P=0.0002)
- Favorable GC toxicity scores
- Pt reported outcomes

Treatment-emergent AEs

- SAR: Neutropenia (15.3%), arthralgia (15.3%)
- PBO: Insomnia (15.5%)
- Serious AEs PBO (20.7%) vs SAR (13.6%)

Spiera R, et al., SAPHYR. *Arthritis Rheumatol.* 2022; 74 (suppl 9).

Tocilizumab

Already Approved for GCA

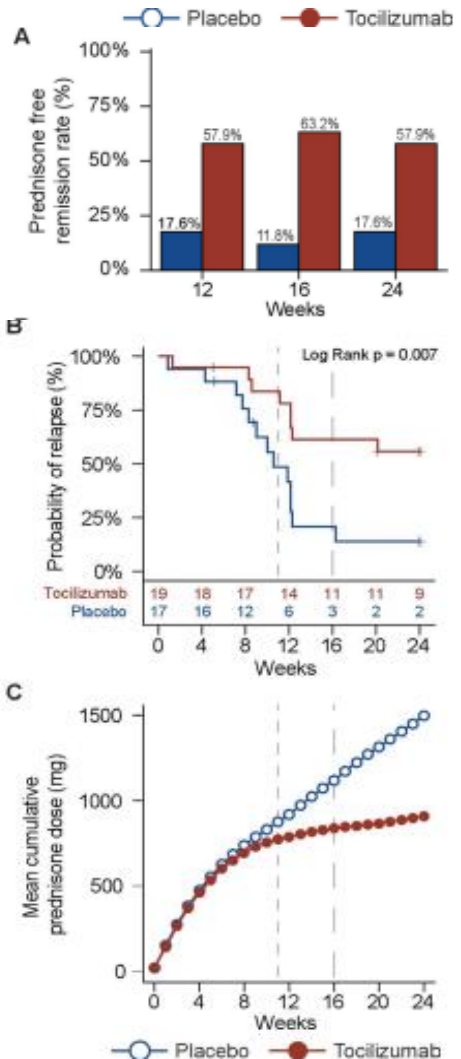
Phase 2/3 PMR-**SPARE** Trial

- Double-blind, multi-center, randomized
- 1:1, Tocilizumab 162mg/week) vs. PBO 16 weeks
- 36 new onset PMR, TOC (19), PBO (17)
- All received 11 week oral prednisone, tapered from 20 mg to 0mg

- **Primary Endpoint:**
  - GC-free remission at week 16, TOC (63.2%) vs PBO (11.8%, p=0.002)

- **Secondary Endpoints:**
  - Time to first relapse, TOC (130±13), PBO (82±11) days (p=0.007)
  - Cumulative GC dose at weeks 16 and 24, TOC 727 (721–842) mg, PBO 935 (861–1244) mg (p=0.003)

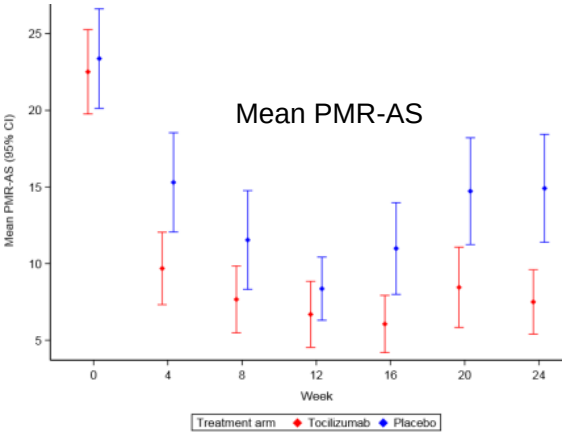
- **Serious AE:** TOC (1), PBO (5)
  - Infection, GI disorder

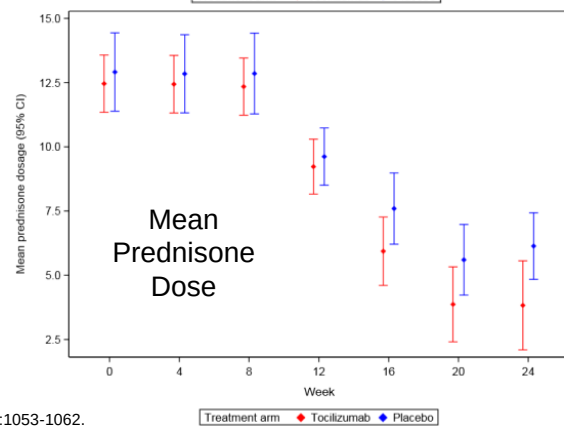


Effect of Tocilizumab on Disease Activity in Patients With Active Polymyalgia Rheumatica Receiving Glucocorticoid Therapy: A Randomized Clinical Trial

SEMAPHORE

- Double-blind, parallel-group, placebo-controlled randomized clinical trial of 101 PMR patients
- Randomly assigned to IV tocilizumab (8 mg/kg; n = 51) or PBO (n = 50) every 4 weeks for 24 weeks, with predefined standardized tapering of oral prednisone
- **Primary efficacy end point** was CRP PMR-AS < 10 (range, 0-100) combined with either prednisone dose ≤ 5 mg/day or a decrease in prednisone dose ≥10 mg from baseline at week 24
  - 67.3% TOC vs 31.4% PBO P < .001
- **11 reported secondary end points** at 24 weeks
  - Mean CRP PMR-AS score (7.5 TOC vs 14.9 PBO) P < .001
  - % no longer receiving prednisone (49.0% TOC vs 19.6% PBO) P <.001
- ADE: 46.9% TOC vs 39.2% PBO, infection





Devauchelle-Pensec V, et al. JAMA. 2022 Sep 20;328(11):1053-1062.

To Summarize

TABLE 3: RANDOMIZED CONTROLLED, CLINICAL TRIALS OF IL-6 INHIBITION IN PMR

STUDIES	STUDY DESIGN	PATIENTS STUDIED (N)	RESULTS
PMR-SPARE study[18]	Tocilizumab (SC, 162 mg weekly) with 11 weeks glucocorticoid taper vs. glucocorticoid alone (with same glucocorticoid regimen until week 11)	New onset PMR patients (n=36)	Primary end point of steroid-free remission at week 16 is achieved by 60% in tocilizumab group vs. 11% in glucocorticoid alone group
SEMAPHORE study (A phase 2/3 study)[19]	Tocilizumab (IV, 8 mg/kg) every 4 weeks vs. placebo up to week 24	Glucocorticoid-dependent PMR patients (at 10 mg/day or higher) (n=101)	Primary end point of low disease activity based on a composite score of CRP PMR-AS of less than 10 in addition to either prednisone <5 mg/day or 10 mg lower than at the study entry is achieved by 67.3% in tocilizumab group vs. 31.4% in placebo; 49% in tocilizumab group were able to stop prednisone compared with 19.6% in placebo group
SAPHYR study[20]	Sarilumab (SC, 200 mg every 2 weeks) with 14-wk prednisone taper (treatment arm) vs. placebo with 52-wk prednisone taper (comparator arm)	Glucocorticoid-refractory PMR patients (disease relapse at prednisone dose at or more than 7.5 mg/day (n=117)	Primary end point of sustained disease remission at week 52 was achieved by 28.3 % in treatment arm vs. 10.3% in comparator arm

Key: SC: subcutaneous; IV: intravenous; CRP PMR-AS: C-reactive protein polymyalgia rheumatica activity score

Back To The Overlapper

Date	ESR mm/hr (0-20)	CRP mg/L (<4)	
09/21/21	53	25	
03/29/22	66	57	
10/06/22	75	25	Started Adalimumab
1/12/23	97	30	Unable to taper prednisone, return of symptoms on 2.5mg prednisone On Adalimumab since 10/13/2022 but hospitalization for UTI
3/15/23	83	15	Pt agreeable to IV Tocilizumab
4/20/23	82	10	
5/9/23	59	6	
6/7/23	46	4	Feeling better, improvement in joint pain, hand pain, swelling, able to walk Down to prednisone 3mg daily, but recurrent wrist stiffness and swelling on 2mg
7/5/23	35	<3	
8/2/23	38	<3	Bilateral wrist swelling R>L, worse at time of next Tocilizumab dose Currently on prednisone to 2 mg daily Increase dose of Tocilizumab to 350 mg

RITUXIMAB

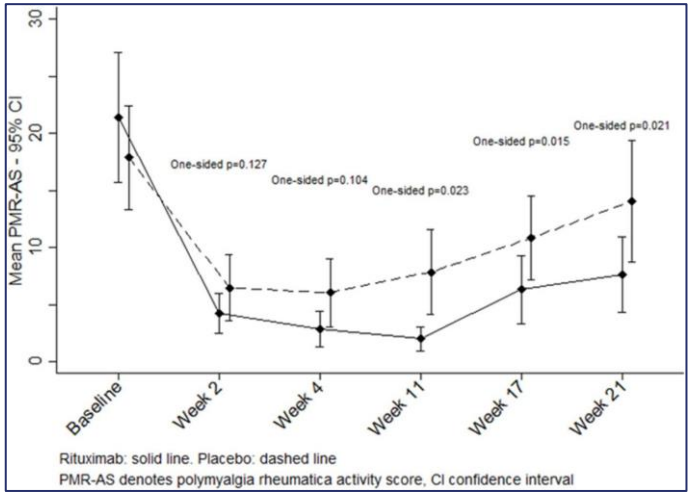
POS0343: Rituximab Is Superior To Placebo In Polymyalgia Rheumatica, Proof-of-Concept **BRIDGE-PMR** trial

- 21-week double-blind placebo controlled exploratory study, 47 new PMR, relapsing on prednisolone ≥7.5mg/day

- 1:1, RTX IV 1 x 1000 mg (n=23) or PBO (n=24), with a 17-week long glucocorticoid co-treatment

- **Primary Outcome:** GC-free remission at week 21
  - 48% (RTX) vs 21% (PBO) p=0.049
  - Post-hoc analysis: 58% (RTX) vs 21% (PBO) p=0.02

- **Secondary Outcome:** GC≤5mg/day
  - 100% (RTX) vs 54% (PBO) p=0.005
  - Post-hoc analysis:100% (RTX) vs 47% (PBO) p<0.001



PBO

RTX

Marsman D, *et al.*, POS0343.*Annals of the Rheumatic Diseases* 2021;80:399-400.

POS0269: Results Of One Year Observational Extension Of The **Bridge-PMR** Study, A Randomized Double-blind Placebo Controlled Trial With Rituximab In PMR

- After the 21-week study, patients were followed in a double-blind extension until 1 year after infusion during which standard-of-care treatment was provided
- **Primary Outcome:** GC-free remission 1 year
  - 48%(RTX) vs 17% (PBO) p=0.03
- **Secondary Outcome:** GC cumulative dose
  - 1595 mg (RTX) vs 2302 mg (PBO) p = 0.04
- **To Be Continued:**
  - Short study duration, small sample size and only few relapsing patients included
  - Larger, longer, RCT will be performed on RTX efficacy on GC free remission in relapsing PMR patients during GC taper
  - **REDUCE-PMR-2:** RTX Effect on Decreasing GC Exposition in PMR Patients Experiencing a PMR Relapse

Bolhuis T, *et al*. POS0269. *Annals of the Rheumatic Diseases* 2022;81:377-378.

ABBV-154

ABBV-154: Abbvie -NCT04972968
End Date: Apr 9, 2024

- **A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study to Evaluate the Safety and Efficacy of ABBV-154 in Subjects With Polymyalgia Rheumatica Dependent on Glucocorticoid Treatment (AIM-PMR)**
  - anti-TNF steroid conjugate (Abbv154)
  - 52 week double-blind, placebo-controlled
  - Must have had at least 2 episodes of unequivocal PMR flare
  - All participants will receive a GC taper along with the assigned dose (3) of ABBV-154 or PBO, SQ every other week

- **While the drug looked effective, AbbVie halted due to concerns about the benefit-risk profile at higher doses, stating safety profile "consistent with systemic steroid exposure at the higher doses"**

Centerwatch.com:clinical-trials: NCT04972968. August 2023; Clinicaltrials.gov: NCT04972968; Phil Taylor. Pharmaphourum. 28 April, 2023

SPI-62

End Date: Dec 29, 2023
Sparrow Pharmaceuticals

A Trial of Prednisolone in Combination With SPI-62 or Placebo in Subjects With PMR

- Will be a single-blind, placebo-controlled phase 2 trial to compare prednisolone effects with and without SPI-62 in subjects with PMR
- Potent, selective investigational HSD-1 inhibitor, targeting 11 beta-hydroxysteroid dehydrogenase type 1 (HSD1)
- Screening period up to 28 days (Day -28 to Day-1)
- 4-week treatment period (Day 1 to Day 28)
  - **First Cohort:** All receive prednisolone 10mg/day for 4-weeks plus SPI-62 for 2-weeks and matching PBO for 2-weeks
  - **Second Cohort** 2-4: prednisolone dose co-administered with SPI-62 could be adjusted
- Follow up Period (Day 29 to Day 56)
- A fixed-dose combination of prednisolone and SPI-62 will be referred to as SPI-47

JAK-Inhibitor

Tofacitinib (Xeljanz)

Phase II Study of Efficacy and Safety of Tofacitinib in Patients With PMR

14 patients (3 relapsed after cDmard, 11 newly diagnosed)

Tofacitinib 10mg/day for 24 weeks

Prednisone 15mg daily (or eq) at baseline and tapered ≤2.5mg/day within 20 weeks

Primary Endpoint: sustained LDA (low disease activity) (PMR-AS<7) with GC independence (prednisone≤2.5mg daily or eq) for 4 weeks from week 20

- 12/14 reached remission response (p=0.014), other 2 by week 48
- Significant reduction in PMR-AS at week 2 from baseline and maintained throughout study
- All achieved LDA at week 24 with a median VAS-pain of 5 (0–17.5) at a prednisone dose of 2.2 (1.1) mg/ day
- Improved QOL: Significantly improved MHAQ and EQ-5D-3L (p<0.001)
- Significant decrease in inflammatory/disease activity Biomarkers IL-6, TNF-α, BAFF and IL-1Ra (p<0.05)
- LDA persisted in extension

Zhang L, *et al*. *Annals of the Rheumatic Diseases* 2023;82:722-724.
ClinicalTrials.gov: NCT04799262

Efficacy and Safety of Tofacitinib in Patients with PMR **(EAST PMR):** A Prospective Study

First cohort

- 11 treatment-naive PMR and 20 healthy controls
- Significantly different gene expression in peripheral blood mononuclear cells (PBMCs) by RNA sequencing
- Observed marked increases in IL6R, IL1B, IL1R1, JAK2, TLR2, TLR4, TLR8, CCR1, CR1, S100A8, S100A12, and IL17RA, which could trigger JAK signaling
- TOF suppressed the IL-6R and JAK2 expression of $CD4^{+}$T cells from patients with PMR *in vitro*

Second cohort

- 76 PMR randomly assigned to TOF (39) or GC (37) in an open-label, 24 week trial, with 67 completing
- **Primary Endpoint:** PMR-AS ≤10 at weeks 12 and 24
- **Secondary endpoints:** PMR-AS score, CRP, ESR at weeks 12 and 24
- No statistically significant differences in primary/ secondary outcomes
- At weeks 12 and 24, all patients in both groups had PMR-AS <10
- PMR-AS, CRP, ESR were all significantly decreased in both groups with no severe adverse events

Ma X, et al., *Arthritis Rheumatol.* 2022; 74 (suppl 9).

GM

- 65 year old woman sent from ortho due to ongoing hip pain and elevated ESR.
- Reports pain as achy, disrupting her sleep and preventing her from sleeping on either side.
- She has moderate morning stiffness with pain radiating down her leg.
- Inflammatory markers were elevated

Date	ESR mm/hr (0-20)	CRP mg/L (<4)	
4/21/22	47	7	Started on Prednisone 20mg for 2 weeks then decrease to 10mg, feeling really well hip pain is pretty much gone 7/5/22- feeling well. Symptoms controlled, decreased by 1 mg every week, will stop at 5 mg daily
8/16/22	30	8	On prednisone 5 mg/day – Feeling well, no pain in hips, shoulder and able to sleep, consider decreasing by 1 mg daily
10/4/22	35	8	On prednisone 5 mg/day - now with overall stiffness/achiness, no weakness The patient is currently experiencing arthralgias
12/6/22	22	8	On prednisone 5 mg/day - ongoing achiness/stiffness over the hands, feet, hips and shoulders. Worse over the shoulders/knees. No swelling. ESR and CRP remain elevated. 1/17/23-stable on prednisone 5 mg/day with ongoing achiness - but stable - will try to taper - 1 mg every month 3/21/23- on prednisone 3 mg/day – On Celebrex as well with no hand pain, continue to taper prednisone as tolerated
6/14/23	14	8	Was able to taper down, but now having a recurrence - difficulty movement with overall achiness. Bilateral shoulder and hip girdle involvement with stiffness and pain. PMR with features of RA

What Would You Do?

A. Restart Prednisone
B. Start Sarilumab
C. Restart Prednisone and start Adalimumab
D. Restart Prednisone and start Sarilumab

Date	ESR mm/hr (0-20)	CRP mg/L (<4)	
6/14/23	14	8	Re-start prednisone 1 day of 20 mg and then 5 mg Start Sarilumab to decrease exposure to prednisone
7/25/23			Flare has resolved - now on Sarilumab every 2 weeks and prednisone 5 mg with no active symptoms of PMR Will wait until 4 th injection and will try to taper off prednisone 1 mg every 2 weeks

Follow-up

Every 4–8 weeks in the first year

Every 8–12 weeks in the second year

As indicated in case of relapse or as prednisone is tapered off

No recommendation can be made for minimal/optimal duration of therapy

Thank You!