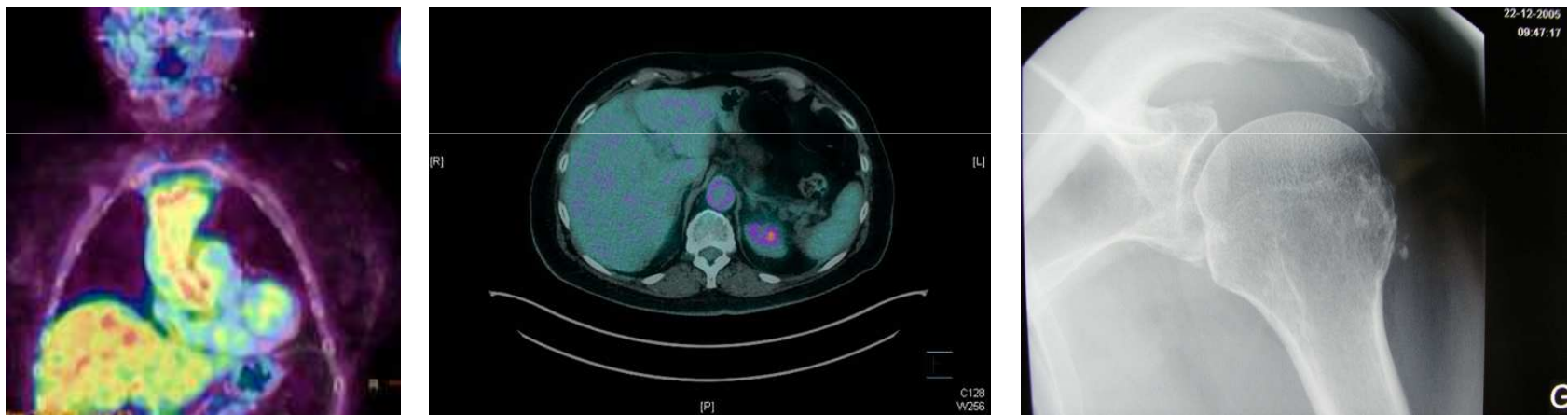


La PPR en 2016



A Saraux, CHU Brest

Cas clinique

- Femme 61 ans
- Douleur inflammatoire des ceintures
- Vague gêne de la région temporale
- Vous faites une CRP qui est élevée
- A peur d'avoir un cancer.....

Quel diagnostic évoquez vous?

Quelle comorbidité recherchez vous?

Quels examens faites vous?

Quels traitements proposez vous?

Des critères de classification actualisés

Critères ACR/EULAR

age ≥ 50 years, douleur d'épaule bilatérale, et VS ou CRP

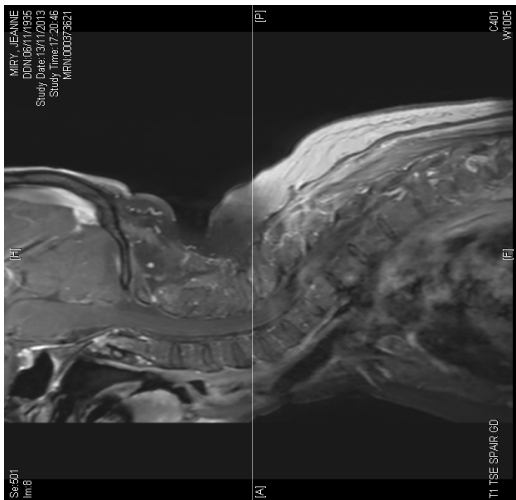
	Points sans échographie (4)	Points avec échographie (5)
Raideur matinale > 45 min	2	2
Douleur des hanches ou limitation de la mobilité	1	1
Absence de facteurs rhumatoïdes ou d'anticorps anti CCP	2	2
Absence d'autre atteinte articulaire	1	1
Atteinte d'au moins une épaule avec bursite deltoïdienne et/ou ténosynovite du long biceps et/ou synovite gléno-humérale ou d'au moins une hanche avec synovite ou ténosynovite trochantérienne	NA	1
Atteinte des 2 épaules avec bursite deltoïdienne, ténosynovite du long biceps ou synovite gléno-humérale	NA	1











MIRY, JEANNE
DDN:06/11/1935
Study Date:13/11/2013
Study Time:17:20:46
IMRN:000373621

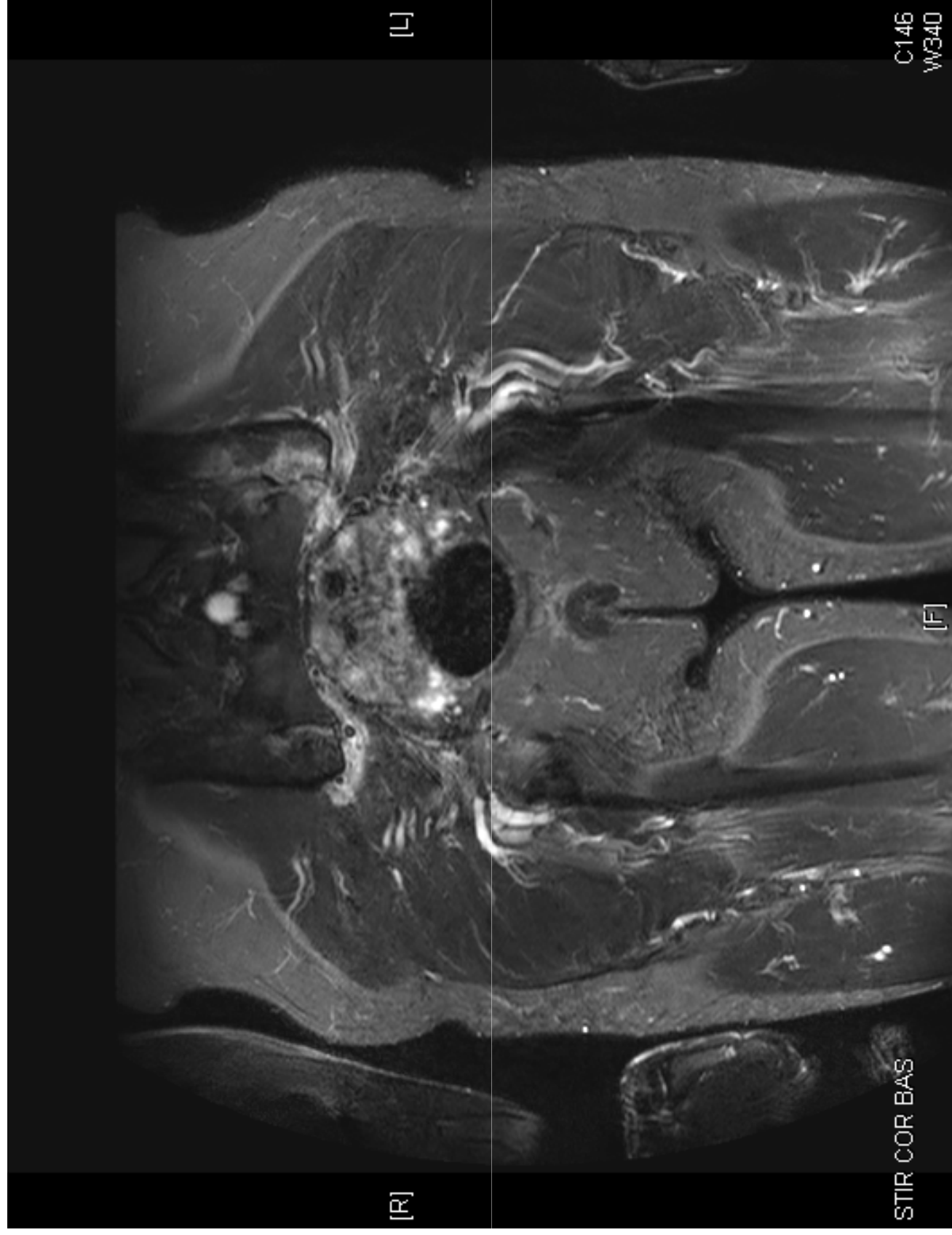


T1_TSE_SAG

C340
W591







Des diagnostics différentiels

- Rhumatismes inflammatoires microcristallins et primitifs
 - Chondrocalcinose
 - Hydroxyapatite
 - Spondyloarthrite
 - Polyarthrite rhumatoïde
- Mais éventuellement, surtout si signes associés:
 - Polymyosite, Connectivites
 - Paranéoplasique (myélodysplasie)
 - néoplasique (myélome, lymphome...)
 - Infection
 - Médicamenteux (rare, ex ipilimumab)
- Et si pas de syndrome inflammatoire
 - Mécanique (« fibromyalgie », arthrose, coiffe, capsulite...)
 - Parkinson, myélome, hypothyroïdie



In the Clinic®

Polymyalgia Rheumatica

Physician Writers

Eric L. Matteson, MD, MPH

Division of Rheumatology

Mayo Clinic

Rochester, Minnesota

Christian Dejaco, MD, PhD,

MBA

Department of Rheumatology

Medical University of Graz

Graz, Austria

Differential Diagnosis of Polymyalgia Rheumatica

Inflammatory arthritis, myositis, vasculitis

Elderly-onset rheumatoid arthritis

Spondyloarthropathy

Vasculitis (giant cell arteritis;

antineutrophil cytoplasmic

antibody-associated

vasculitis, including

microscopic polyangiitis and

granulomatous polyangiitis)

Inflammatory myopathies

(dermatomyositis,

polymyositis)

Crystalline arthritis (gout, calcium

pyrophosphate dihydrate

deposition disease)

Noninflammatory musculoskeletal

disorders

Rotator cuff disease

Adhesive capsulitis

Degenerative joint disease of the

glenohumeral joint

Fibromyalgia

Endocrinopathies

Thyroid diseases

Disorders of the parathyroid

gland

Infection

Viral syndromes, such as

parvovirus B19, hepatitis B,

HIV

Bacterial infections, such as

endocarditis or disk space

infection

Mycobacterial infections, such as

tuberculosis

Cancer

Other

Parkinsonism

Depression

Vitamin D deficiency

Drug-induced myopathy, such

as from statins

Annals of Internal Medicine®

In the Clinic®

Polymyalgia Rheumatica

Table 2. Clinical Features of Polymyalgia Rheumatica and Giant Cell Arteritis*

Sign/Symptom	Polymyalgia Rheumatica	Cranial Giant Cell Arteritis	Large Vessel Giant Cell Arteritis
Polymyalgia symptoms of shoulder and hip; neck stiffness	++	+	++
Elevated CRP/ESR	++	++	++
Peripheral arthritis/RS3PE syndrome	++	+	+
Wasting syndrome (fever, anorexia, weight loss, night sweats, depression)	++	++	++
Headache	-	++	-
Scalp tenderness	-	++	-
Arterial swelling/tenderness, bruits	-	+	+
Jaw claudication/tongue pain and claudication	-	++	-
Vision symptoms/complications	-	++	-
Painful dysphagia	-	++	-
Limb claudication, absent or asymmetrical pulses, asymmetrical blood pressure readings, Raynaud phenomenon	-	+	++
Aortic regurgitation	-	+	++

CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; RS3PE = remitting seronegative symmetrical synovitis with pitting edema.
 * ++ = Very common; + = common; - = uncommon.

Quel bilan selon ACR/EULAR?

- Hémogramme,
- VS ou préférentiellement CRP,
- ionogramme plasmatique, urée et créatininémie,
- bilan hépatique,
- électrophorèse des protéines sériques,
- CPK,
- TSH,
- Radiographie de thorax,
- bandelette urinaire,
- Facteurs rhumatoïdes, anti-CCP/ACPA et anticorps antinucléaires.

Table 3. Tests for Evaluation of Patients With Polymyalgia Rheumatica	
Type of Test/Disorder	Name of Test
Laboratory tests to assess inflammatory activity (i.e., tests helpful in differential diagnosis)	
General	Complete blood count; liver function tests, including alkaline phosphatase, age- and sex-appropriate cancer screening
Thyroid disease	Thyroid-stimulating hormone
Rheumatoid arthritis	Rheumatoid factor, anti-citrullinated peptide, radiographs of hands, shoulders, feet
Connective tissue diseases, lupus, myositis, vasculitis	Antinuclear antibody, anticytoplasmic neutrophil antibodies
Gout	Uric acid
Pseudogout	Calcium and phosphorus
Prostate cancer	Prostate-specific antigen (men)
Myositis/myopathy	Creatine kinase
Multiple myeloma, dysproteinemia	Protein electrophoresis
Procedures and imaging tests for diagnosis	
Giant cell arteritis	Ultrasonography or other imaging, alternatively temporal artery biopsy
Polymyalgia rheumatica	Musculoskeletal ultrasonography of the shoulders and hips
Assessment of treatment-related adverse events	
Diabetes mellitus	Serum glucose
Osteoporosis	Bone densitometry
Latent tuberculosis	Tuberculosis testing according to national guidelines

Quel bilan selon ACR/EULAR?

Une des meilleures preuves...

l'effet spectaculaire de la corticothérapie
d'épreuve

Elle fait passer de PPR syndrome à PPR maladie

Des pathologies associées

Horton: Examens complémentaires
que si orientation car seulement
15% des PPR...et traitement
identique sans symptôme

- Echo (plus pour guider) mais peut éventuellement suffire si halo typique
- Biopsie reste référence
- TEP si biopsie négative ou impossible

Cancer: Non sauf point d'appel si
typique

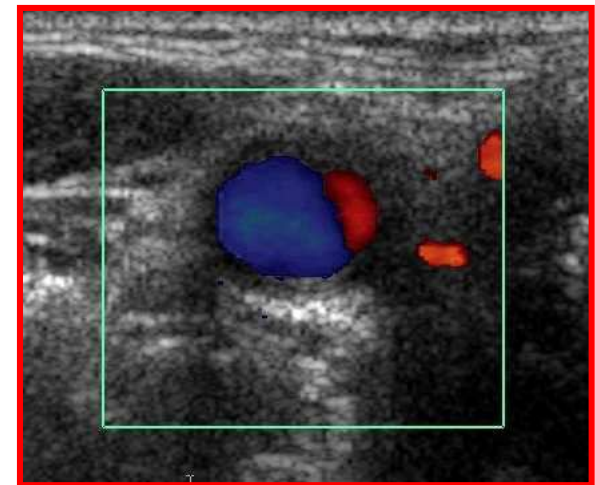
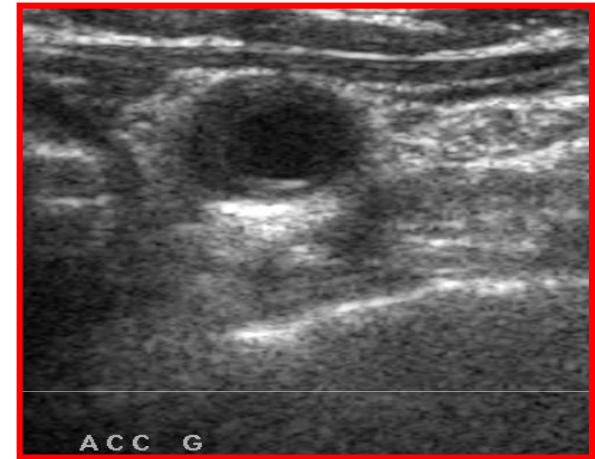
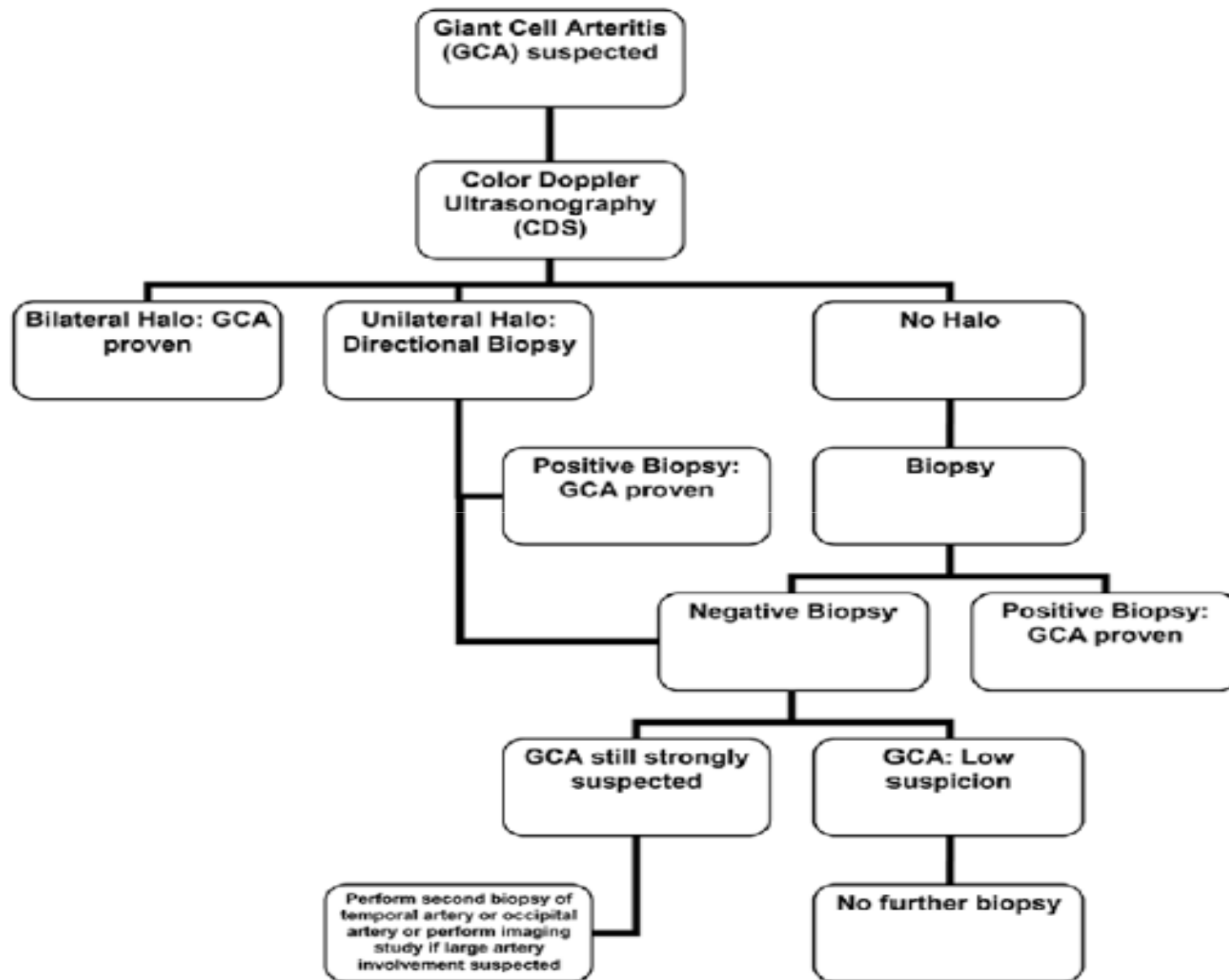


Image Sandrine Jousse-Joulin



Algorithme décisionnel en cas de suspicion de MH. Karahaliou M (Arthritis Res Ther. 2006;8(4):R116).

La TEP

- **La TEP: imagerie isotopique.**

Radio traceur = vecteur + isotope radio-actif

- **La TEP: imagerie fonctionnelle in vivo.**

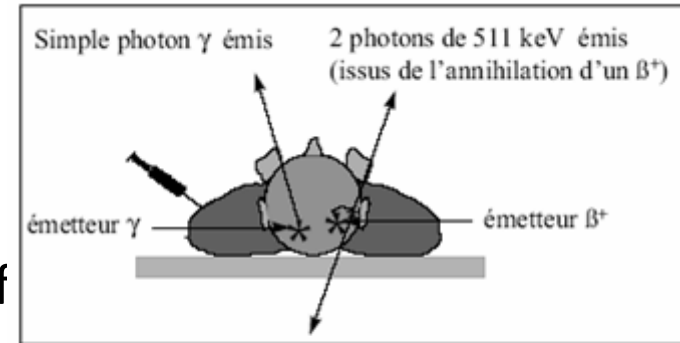
Selon le vecteur, une fonction de l'organisme va être explorée

- **La TEP : imagerie quantitative.**

Détection du rayonnement gamma issu de l'annihilation du positon émis par ces isotopes.

- **La TEP : imagerie tomographique 3D.**

Image = empilement de coupes sur 15 cm de longueur, Précision de quelques millimètres cube.

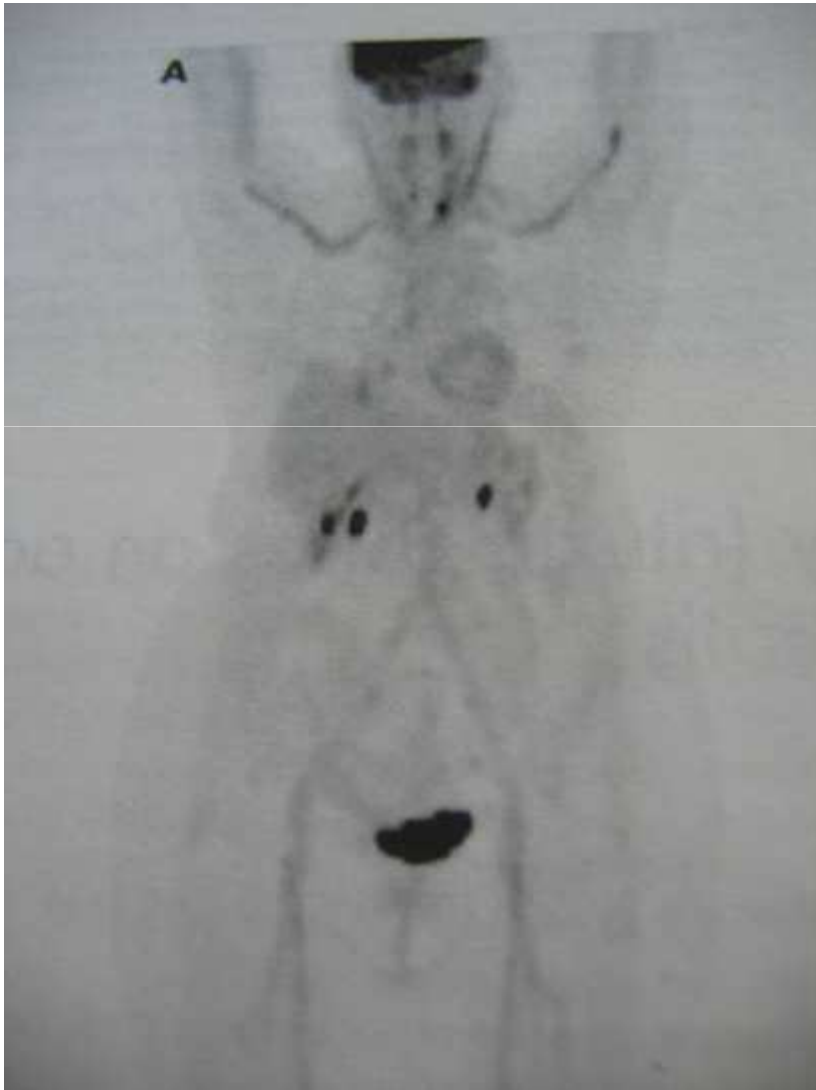


- FIGURE 1 -

Différence entre émetteur de positons et émetteur simple photon

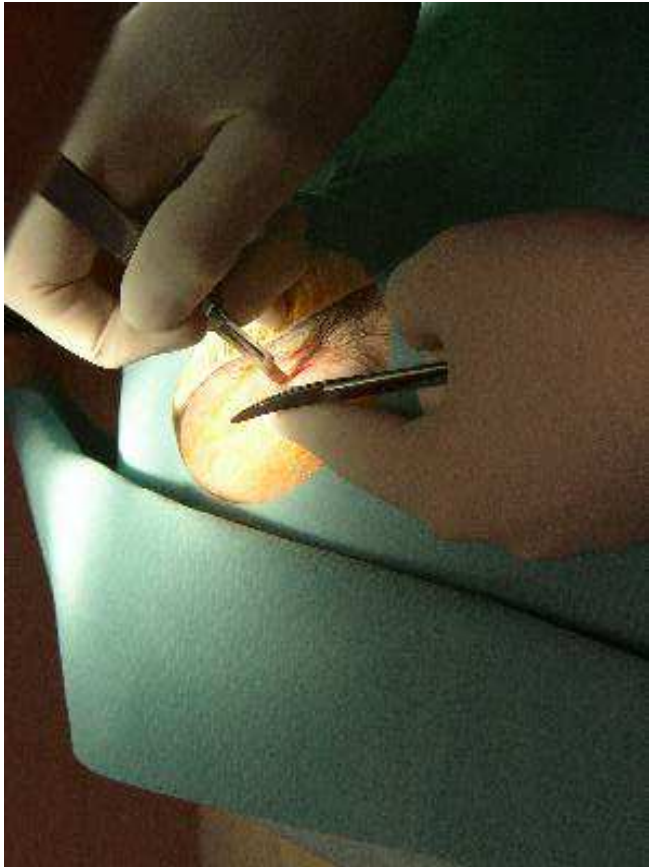


Des pathologies associées

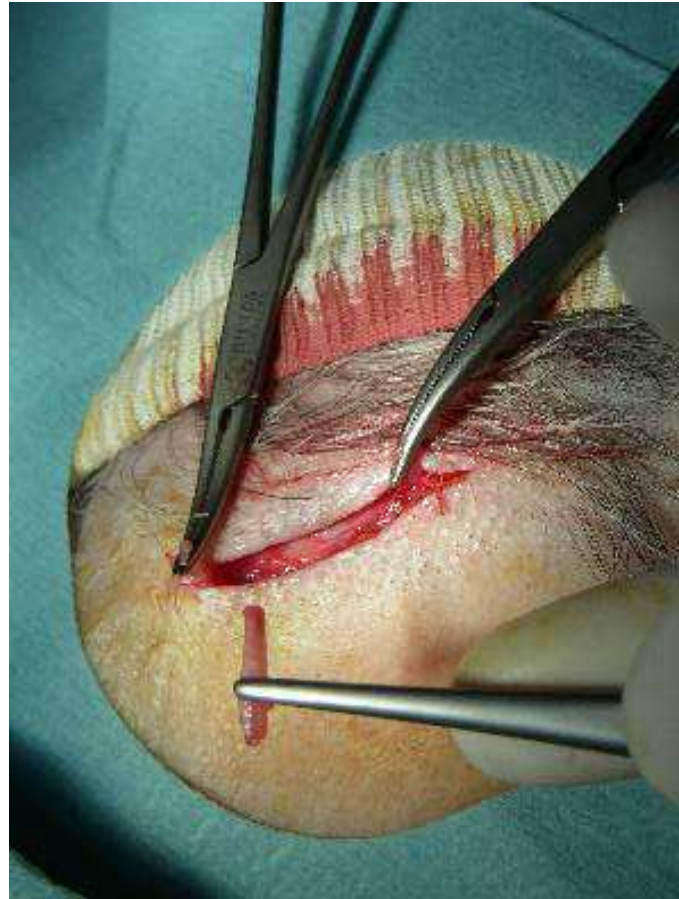


Biopsie d'artère temporale











Risk of malignancy in patients with giant cell arteritis and polymyalgia rheumatica: A systematic review and meta-analysis

Patompong Ungprasert, MD^{a,b,*}, Anawin Sanguankeo, MD^c, Sikarin Upala, MD^c,
Eric L. Knight, MD, MPH^a

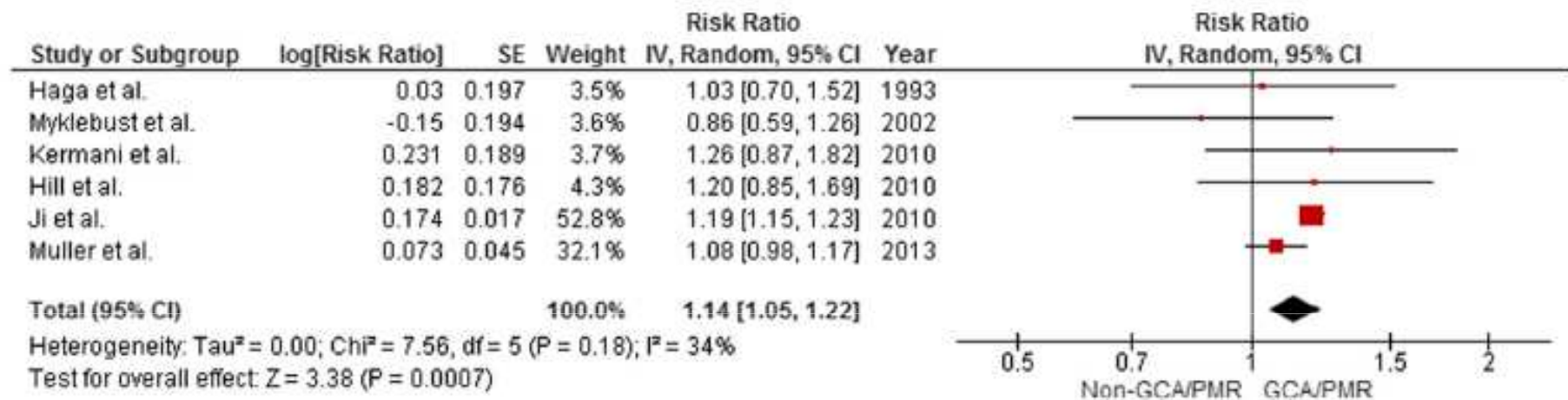


Fig. 2. A forest plot of overall malignancy risk.

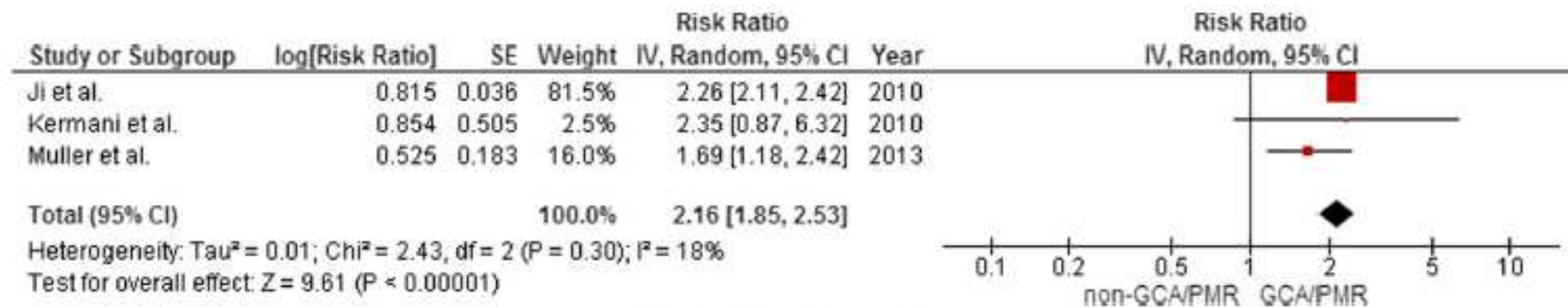
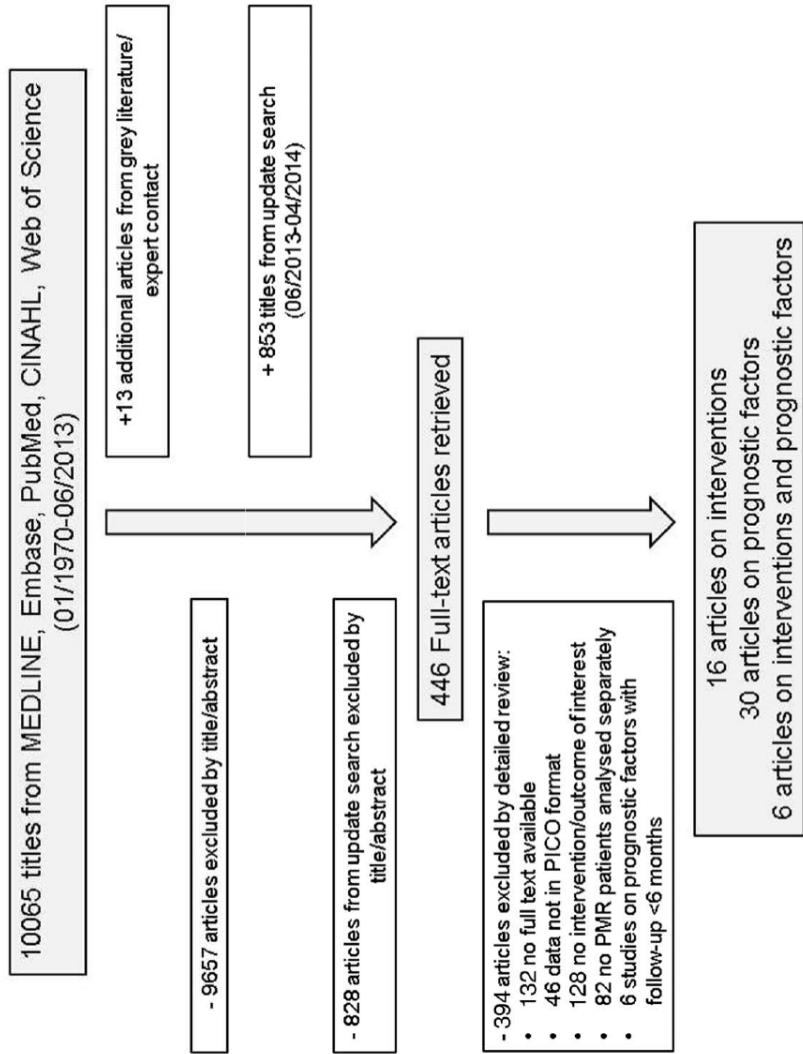


Fig. 3. A forest plot of malignancy risk in the first 6-12 months.

Current evidence for therapeutic interventions and prognostic factors in polymyalgia rheumatica: a systematic literature review informing the 2015 European League Against Rheumatism/American College of Rheumatology recommendations for the management of polymyalgia rheumatica

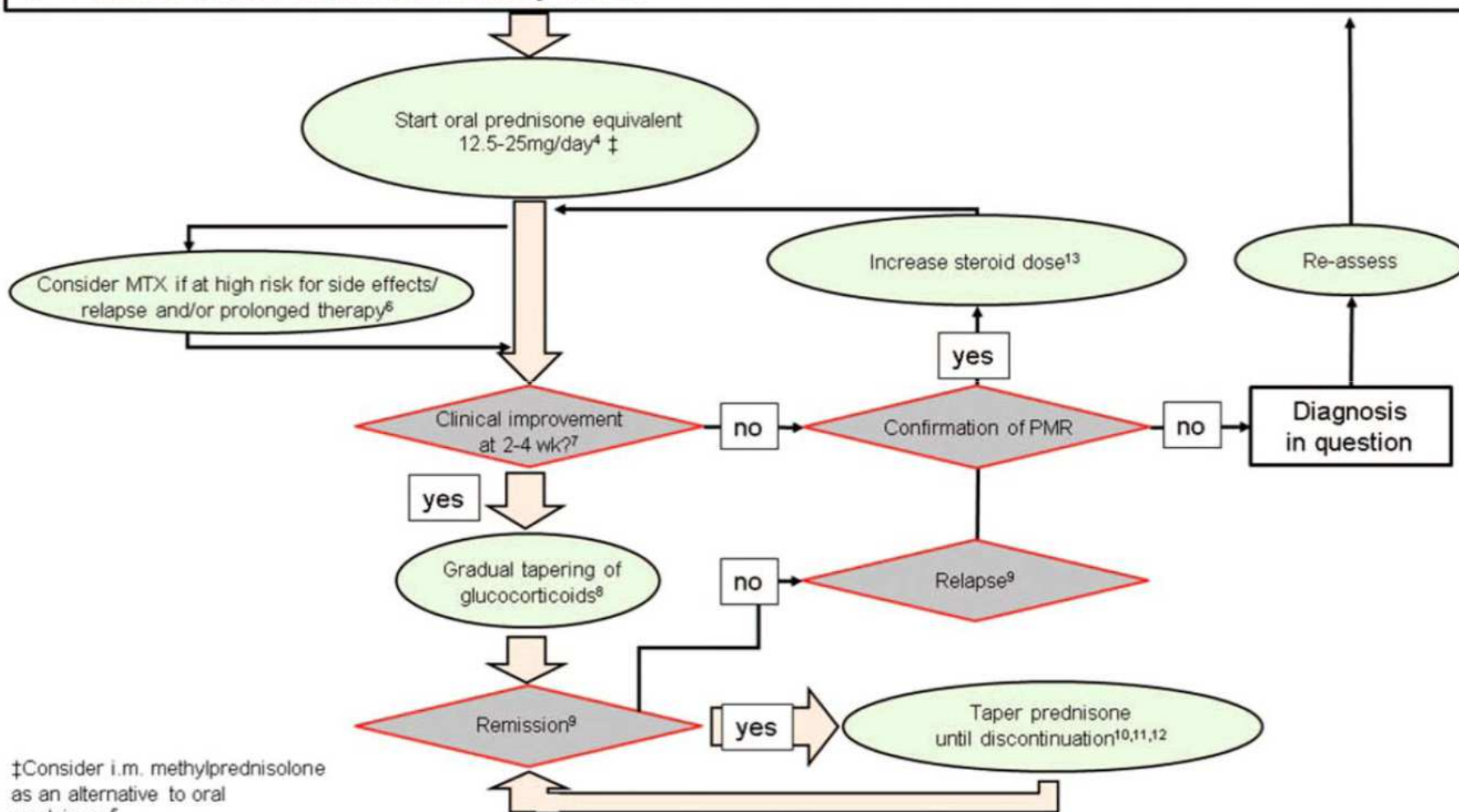
Christian Dejaco,^{1,2} Yogesh P Singh,² Pablo Perel,³ Andrew Hutchings,⁴ Dario Camellino,⁵ Sarah Mackie,⁶ Eric L Matteson,⁷ Bhaskar Dasgupta²

Figure 1 Study flow diagram detailing the literature search. PICO, Population, Intervention, Comparator, Outcome; PMR, polymyalgia rheumatica.



Patient fulfilling PMR case definition (primary or secondary care)

1. Assess comorbidities¹, other relevant medications and other risk factors for steroid related side effects²
2. Assess possible risk factors for relapse/prolonged therapy³
3. Consider specialist referral (experience or risk of side-effects, relapse/prolonged therapy and/or atypical presentation)
4. Document minimal clinical and laboratory dataset



Un traitement codifié

Instauration de la corticothérapie dans la PPR

- 15-25 mg/j pendant 3 semaines (predinone=prednisolone)*
- Methotrexate à discuter si risque de corticothérapie, risque de traitement prolongé, risque de récurrence

Modalités de décroissance de la corticothérapie dans la PPR

- Descendre à 10 mg en 4 à 8 semaines
- Décroissance de 1 mg toutes les 4 semaines

Modalités en cas de rechute clinique lors de la décroissance

- Réaugmenter à la posologie précédente

Un suivi simplifié

- **DAS PPR: 5 paramètres**

1. Protéine C réactive (CRP, mg/dl)
2. Echelle visuelle analogique du patient (EVAp, 0 à 10)
3. Echelle visuelle analogique du médecin (EVAm, 0 à 10)
4. Dérouillage matinal (DM, minutes)
5. Capacité d'élévation des épaules (CAE; 0 $\geq$ 90°, 1=90°, 2 $\leq$ 90°, 3=pas d'élévation des épaules).

- **Calcul selon la formule de Leed et Bird (2004)**

DAS-PPR= CRP (mg/dl) + EVAp (0-10)+ EVAm (0-10) + DM (min $\times$ 0,1)+
CAE (3-0)

Un suivi simplifié

- Score d'activité de la maladie de 0 à 50
- Activité ≥ 7 (<7 = faible activité, de 7 à 17=activité modérée, >17 forte activité)
- Rémission de la maladie: 0 à 1,5
- Rechute: $>9,35$ ou ayant augmentation $\geq 6,6$ entre 2 visites

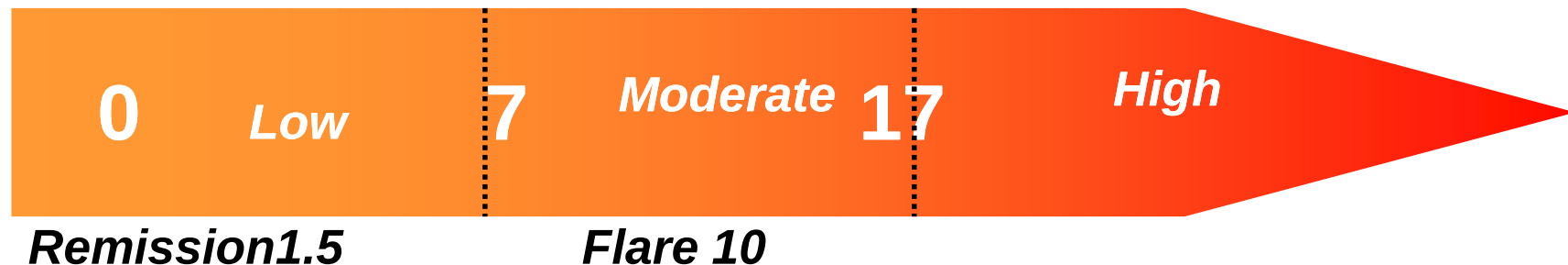


Table 5. Calculation of the Polymyalgia Rheumatica Activity Score* and Suggested Cutoffs for Disease Activity States

*CRP (mg/dL) + patient’s pain assessment (visual analogue scale, 0-10)† + physician’s global assessment (visual analogue scale, 0-10)‡ + [morning stiffness (min) × 0.1] + EUL (0-3)§		
Disease Activity	Suggested Cutoff	
Remission	0-1.5	
Low	1.6-6.9	
Medium	7.0-17.0	
High	>17.0	
Relapse	Actual score ≥9.35 or change in score ≥6.6	

CRP = C-reactive protein; EUL = ability to elevate the upper limbs.
 † 0 = no pain; 10 = unbearable pain.
 ‡ 0 = no disease activity; 10 = highest activity possible.
 § 0 = above shoulder girdle; 1 = up to shoulder girdle; 2 = below shoulder girdle; 3 = no elevation possible.

Efficacy of first-line tocilizumab therapy in early polymyalgia rheumatica: a prospective longitudinal study

Valérie Devauchelle-Pensec^{1,3}, Jean Marie Berthelot², Divi Cornec^{1,3}, Yves Renaudineau³, Thierry Marhadour¹, Sandrine Jousse-Joulin^{1,3}, Solène Querellou⁴, Florent Garrigues⁵, Michel De Bandt⁶, Maelenn Gouillou⁷, Alain Saraux^{1,3} doi:10.1136/annrheumdis-2015-208742

Eur J Nucl Med Mol Imaging
DOI 10.1007/s00259-015-3287-z



ORIGINAL ARTICLE

Value of ¹⁸F-FDG PET/CT for therapeutic assessment of patients with polymyalgia rheumatica receiving tocilizumab as first-line treatment

X. Pakard-Novello¹ · S. Querellou^{1,5} · M. Gouillou² · A. Saraux^{3,6} · T. Marhadour³ · F. Garrigues⁴ · R. Abgral^{1,5} · P. Y. Salaün^{1,5} · V. Devauchelle-Pensec^{3,6}

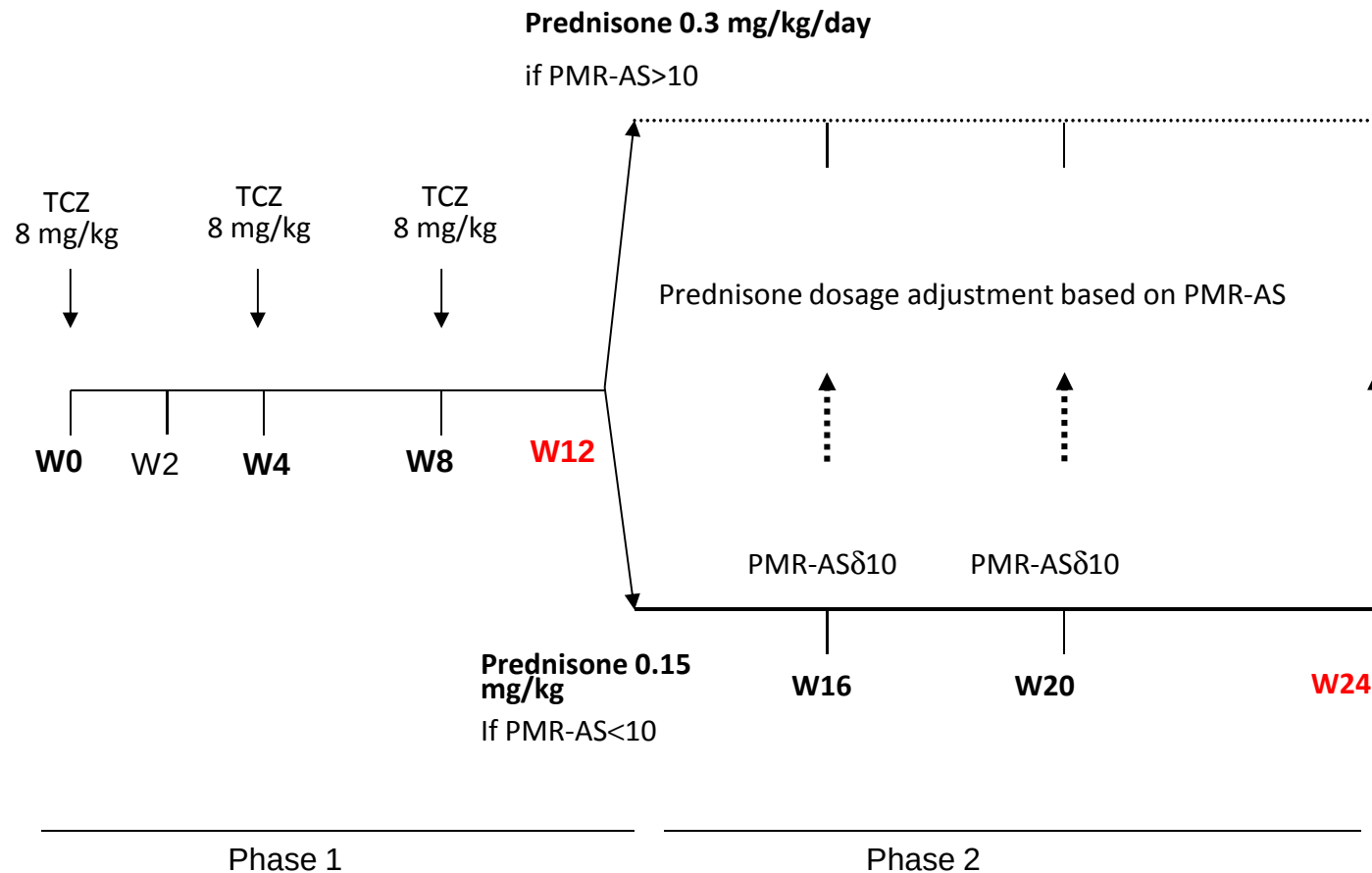


Fig. 1 Maximum intensity projection ¹⁸F-FDG PET/CT images. SUVmax measurements were obtained in the ten regions of interest (red circles)



CONCISE REPORT

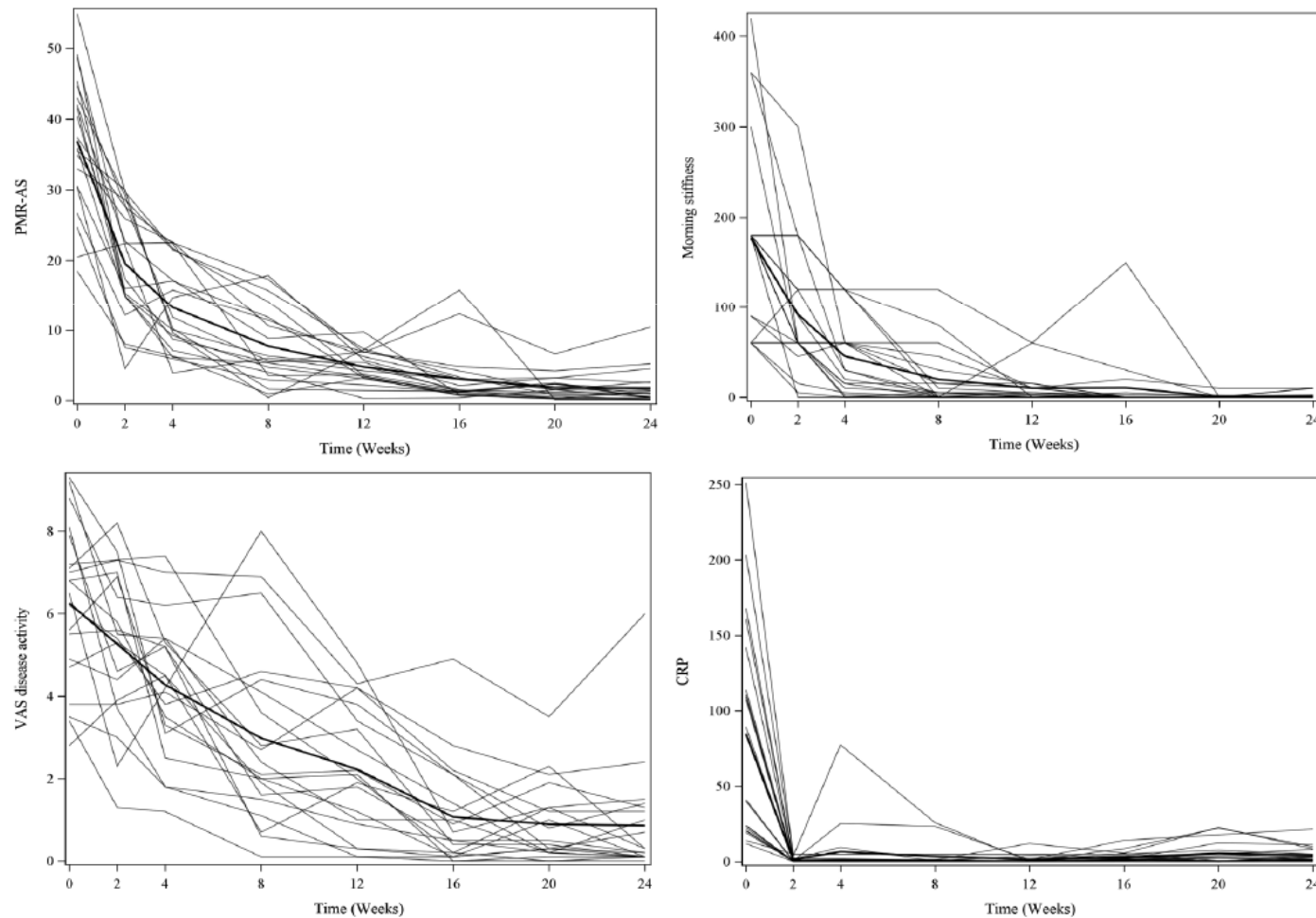
Efficacy of first-line tocilizumab therapy in early polymyalgia rheumatica: a prospective longitudinal study

Median, IQR	Week 0	Week 2	Week 4	Week 8	Week 12	p Value Week 0 vs week 12
PMR-AS	36.6 (30.4–43.8)	19.7 (14.9–27.7)	11.0 (7.9–19.3)	5.8 (3.7–11.6)	4.5 (3.2–6.8)	<0.001*
CRP, mg/dL	65.1 (21.6–127.8)	0.5 (0.3–1.4)	0.6 (0.3–3.5)	0.6 (0.2–1.2)	0.2 (0.1–1.0)	<0.001*
ESR, mm/h	51.0 (34.0–79.5)	7.5 (4.0–9.5)	5.0 (4.0–10.0)	4.5 (2.0–5.0)	2.00 (2.0–4.5)	<0.001*
Patient VAS for pain	6.4 (4.6–7.8)	5.4 (3.8–6.9)	4.5 (3.2–5.4)	2.2 (1.5–4.2)	1.7 (0.6–2.7)	<0.001*
Patient VAS for fatigue	5.4 (2.9–6.9)	5.3 (3.0–6.2)	4.5 (2.0–5.1)	2.8 (1.0–4.8)	2.1 (0.7–4.4)	<0.001*
Patient VAS for disease activity	6.6 (4.8–7.5)	5.45 (3.8–6.9)	4.5 (3.1–5.4)	2.2 (1.5–4.2)	2.0 (0.9–3.6)	<0.001*
Physician VAS for disease activity	6.8 (6.0–7.9)	4.4 (2.8–6.6)	2.7 (1.7–4.5)	2.1 (0.5–3.1)	1.1 (0.8–1.8)	<0.001*
MST (min)	180.0 (75.0–180.0)	60.0 (60.0–120.0)	30.0 (7.50–60.0)	5.0 (0.0–22.5)	4.0 (0.0–10.0)	<0.001*
EUL	0.5 (0.0–2.0)	0.0 (0.0–2.0)	0.0 (0.0–1.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.002*
0	10 (50.0%)	11 (55.0%)	13 (65.0%)	17 (85.0%)	18 (90.0%)	
1	2 (10.0%)	3 (15.0%)	4 (20.0%)	2 (10.0%)	2 (10.0%)	
2	8 (40.0%)	6 (30.0%)	3 (15.0%)	1 (5.0%)	0 (0.0%)	
3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
PMR-AS (ESR)	35.6 (30.4–39.9)	20.8 (15.3–29.4)	13.7 (9.3–22.0)	5.8 (3.5–11.8)	4.7 (3.5–6.6)	<0.001*



CONCISE REPORT

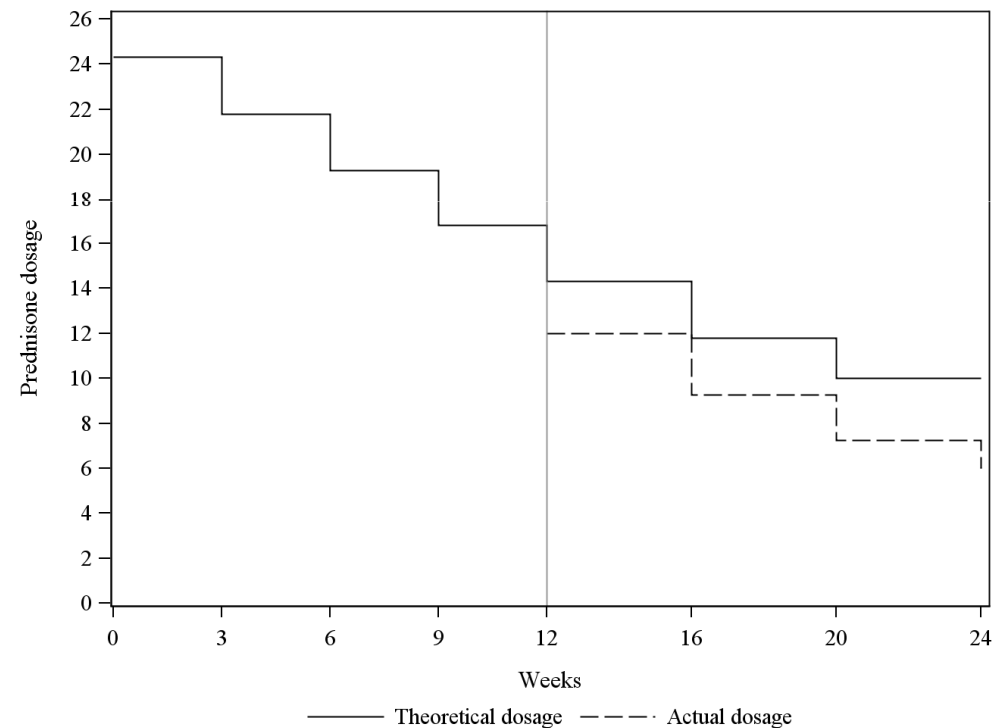
Efficacy of first-line tocilizumab therapy in early polymyalgia rheumatica: a prospective longitudinal study





CONCISE REPORT

Efficacy of first-line tocilizumab therapy in early polymyalgia rheumatica: a prospective longitudinal study



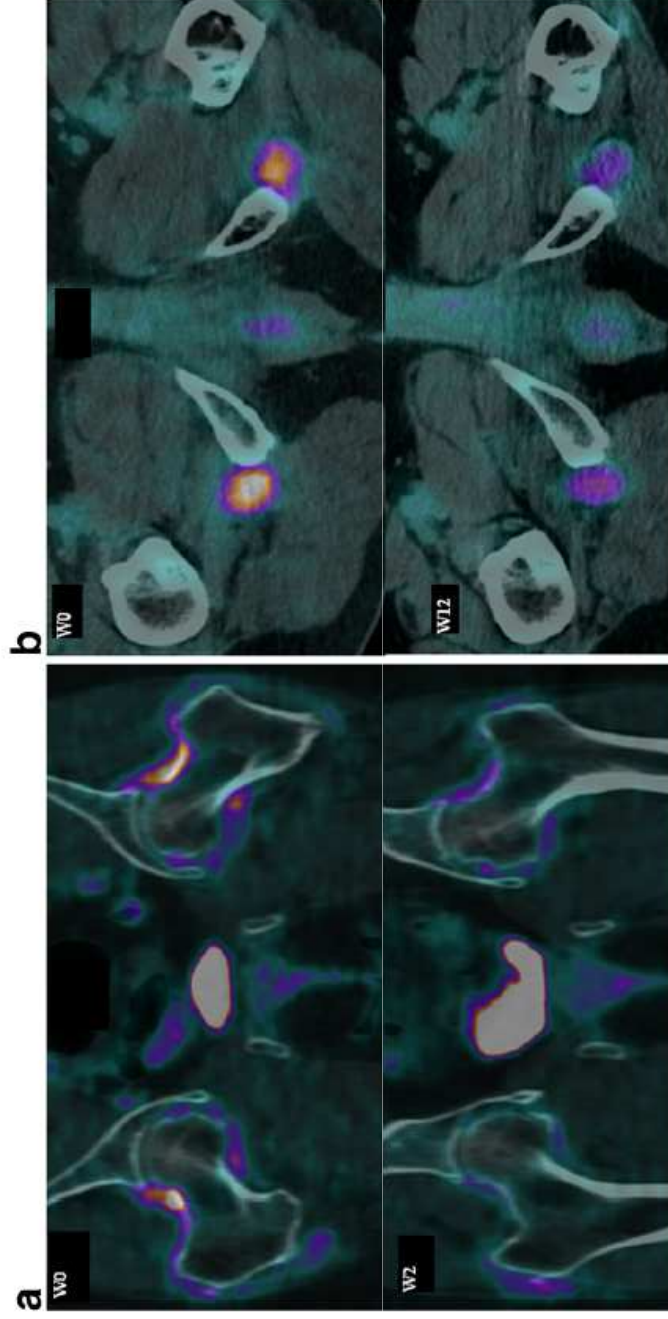


Fig. 2 Changes in FDG uptake on follow-up PET/CT imaging. **a** Coronal images of the hip region before treatment (week 0, *W0*) and after one infusion of tocilizumab (week 2, *W2*) in a 73-year-old woman with polymyalgia rheumatica. At week 0, the right hip SUVmax is 12.3 and the left hip SUVmax is 9.7. At week 2, the right hip SUVmax is 10.1 and the left hip SUVmax is 9.4. **b** Axial images of the ischial tuberosity

region before treatment (week 0, *W0*) and after two infusions of tocilizumab (week 12, *W12*) in a 60-year-old man with polymyalgia rheumatica. At week 0, the right ischial tuberosity SUVmax is 8.5 and the left ischial tuberosity SUVmax is 9.8. At week 2, the right ischial tuberosity SUVmax is 5 and the left ischial tuberosity region SUVmax is 5.5

Tocilizumab is effective against polymyalgia rheumatica: experience in 13 intractable cases

Keisuke Izumi,^{1,2} Harumi Kuda,² Mari Ushikubo,² Masataka Kuwana,^{1,3} Tsutomu Takeuchi,¹ Hisaji Oshima²

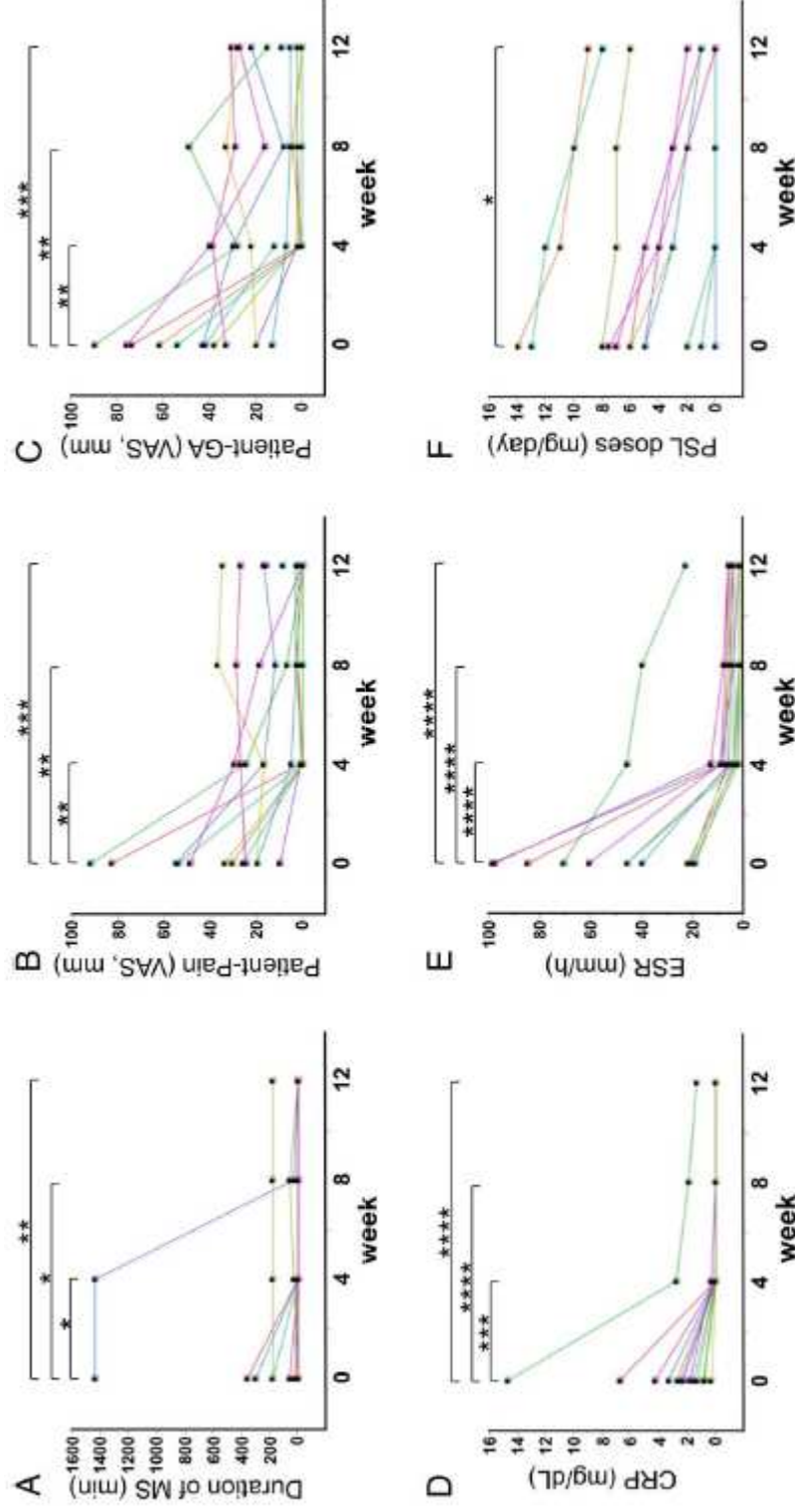


Figure 1 Changes in evaluation indicators from baseline to 12 weeks per visit. (A) Duration of morning stiffness (MS), (B) Patient-Pain, (C) Patient-Global Assessment (GA), (D) C-reactive protein (CRP), (E) erythrocyte sedimentation rate (ESR) and (F) prednisolone (PSL) doses (VAS, visual analogue scale). Asterisks indicate significant differences as compared with baseline analysed by Wilcoxon signed-rank test. *p<0.05, **p<0.01, ***p<0.001 and ****p<0.0001.

Table 4. Medications Available for Treatment of Polymyalgia Rheumatica

Drug	Indication	Dosing/Tapering	Possible Adverse Events	Monitoring
GCs (prednisone equivalent)				
Oral	First-line treatment for all patients with polymyalgia rheumatica	Initial daily dose: 12.5–25 mg; taper to 10 mg daily after 4–8 wk, then reduce daily dose by 1 mg every 4 wk until discontinuation. Relapse: Increase to prerelapse dose	Cushingoid appearance, weight gain, osteoporosis, hypertension, cardiovascular disease, hyperglycemia and diabetes mellitus, infections, skin atrophy, cataracts	Blood pressure at each visit, polyuria, polydipsia, edema, shortness of breath, vision changes, weight gain, urinalysis for glucose levels yearly, regular osteoporosis screening including dual-energy x-ray absorptiometry and bone density measurement
Intramuscular MP	Individualized alternative to oral GCs or when a low cumulative GC dose is desired	Initial dose 120 mg every 3 wk; taper from wk 12: 100 mg at wk 12, then injections at monthly intervals with dose reduced by 20 mg every 12 wk until wk 48; then, dose reduction by 20 mg every 16 wk until discontinuation	Same as for oral GCs	Same as for oral GCs

Immunosuppressive agents

MTX	Individualized first-choice immunosuppressive agent, concomitant with GCs: Early: Risk for relapse and/or GC-related adverse events Follow-up: Relapse, insufficient response to GCs, GC-related adverse events	7.5–10 mg/wk; taper after GC discontinuation	Dizziness, nausea, vomiting, diarrhea, loss of appetite, temporary hair loss, elevated liver enzymes, low leukocyte count, predisposition to infection, teratogenicity, mouth sores	Baseline: Complete blood count, measurement of aminotransferase and serum creatinine levels. Screening for hepatitis B/C in patients at higher risk for these infections Follow-up: Regular testing for complete blood count, measurement of aminotransferase and serum creatinine levels: 0–3 mo: Every 2–4 wk 3–6 mo: Every 8–12 wk >6 mo: Every 12 wk
Tocilizumab	For patients in whom MTX is unavailable or toxic, immunosuppressive agent needed	8 mg/kg of body weight IV at 0, 2, and 4 wk, then every 4 wk, or 162 mg SQ weekly	Infections (particularly respiratory tract and urinary), local injection site reactions, increment of blood lipids, rarely diverticulitis	Baseline: Complete blood count, measurement of aminotransferase and serum creatinine levels, lipids. Exclusion of active or latent infection including screening for hepatitis B/C and tuberculosis (following national guidelines) Follow-up: Clinical exclusion of infections, regular testing for complete blood count, liver aminotransferase levels, serum creatinine: 0–3 mo: Every 4 wk; lipids 4 wk after treatment start >3 mo: Every 8–12 wk
Azathioprine	For patients in whom MTX is unavailable or toxic, immunosuppressive agent needed	150 mg/d	Nausea, vomiting, diarrhea, low leukocyte count, anemia, predisposition to infection, rarely pancreatitis	Same as for MTX
Leflunomide	For patients in whom MTX is unavailable or toxic, immunosuppressive agent needed	10–20 mg/d	Same as for MTX, hypertension	Same as for MTX

GC = glucocorticoid; IV = intravenous; MTX = methotrexate; MP = methylprednisolone; SQ = subcutaneous.

Quand demander un avis spécialisé (ACR/EULAR 2015)

Présentation atypique

- Arthrites périphériques
- Signes systémiques
- Inflammation faible
- Age < 60 ans

Effets secondaires antérieurs sous corticoïdes

Risque prévisible des corticoïdes

Résistance à la corticothérapie

Récidive

Conclusion

Des recommandations claires

Un suivi souvent simple

Eviter les excès de corticothérapie

- erreur de diagnostic
- excès de précaution

Une place pour le méthotrexate

Très probablement un grand avenir pour anti IL6

Inclusions dans Sémaphore