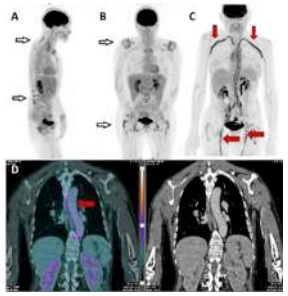
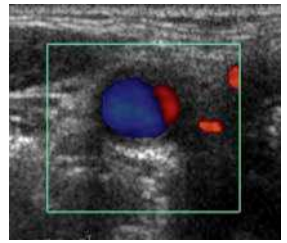


La PPR en 2025



Pr Alain Saraux

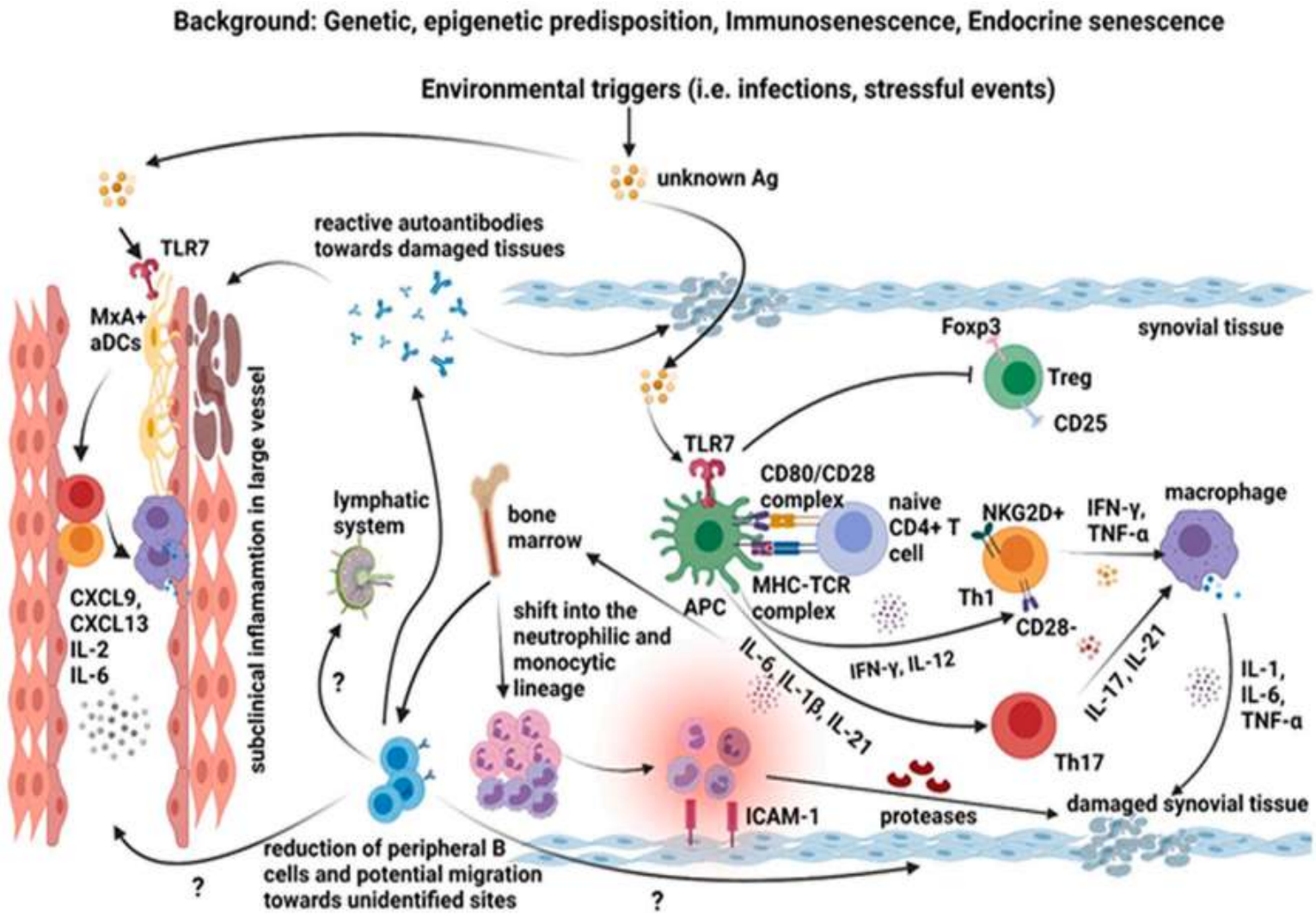
Service de rhumatologie, Pôle PHARES, CHU Brest, univ Brest

Inserm UMR 1227 Lymphocytes B et auto-immunité

Centre de référence maladies rares auto-immunes de l'ouest CERAINO

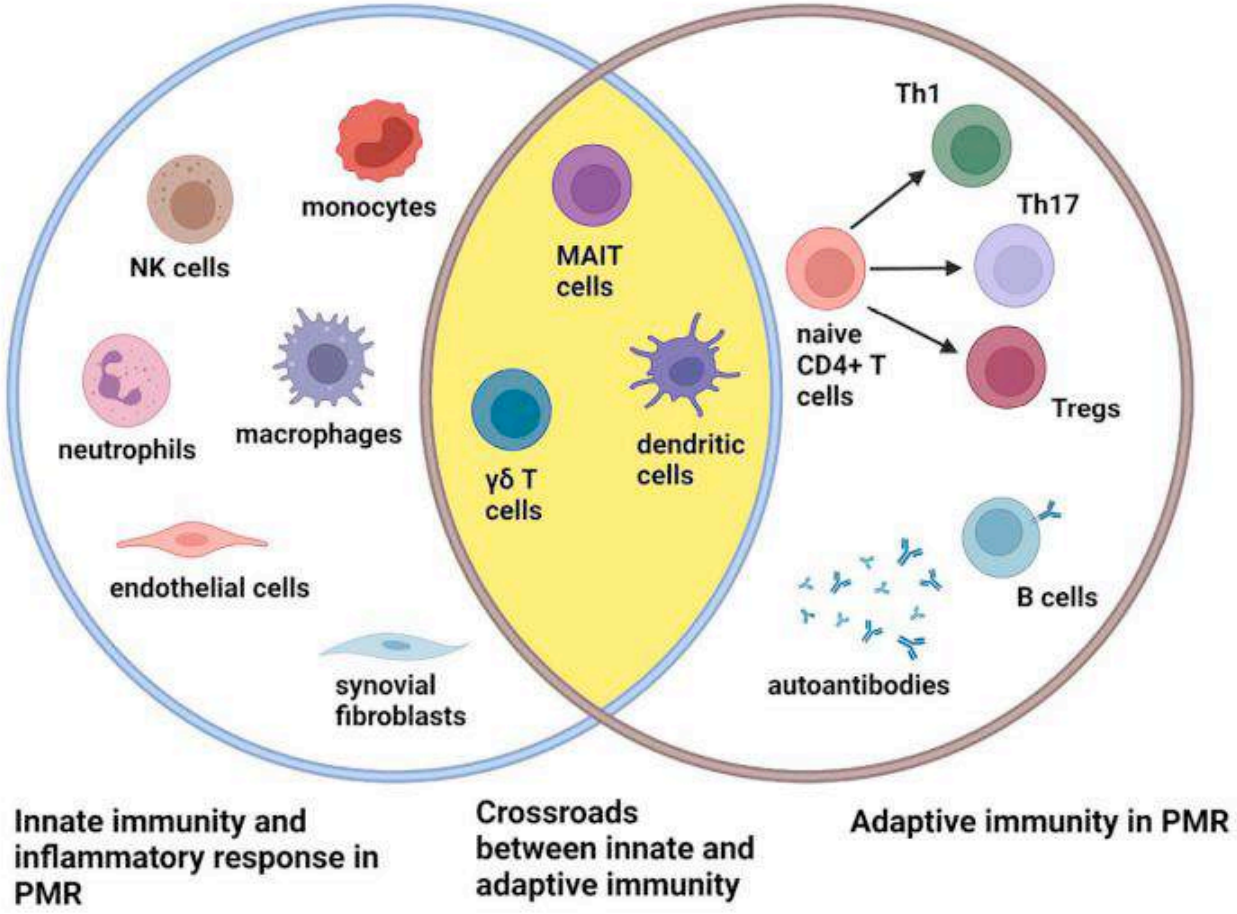
EULAR
BREST: Center of excellence in rheumatology research
EULAR 2024-2029

Une physiopathogénie connue

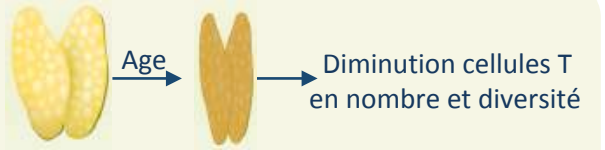


Hysa E et al , autoimmunity Rev, 2022

Immunité innée et adaptative



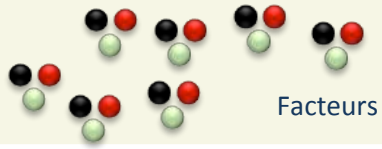
Sénescence = blocage partiel du cycle cellulaire et apparition d'un phénotype sécrétoire appelé SASP



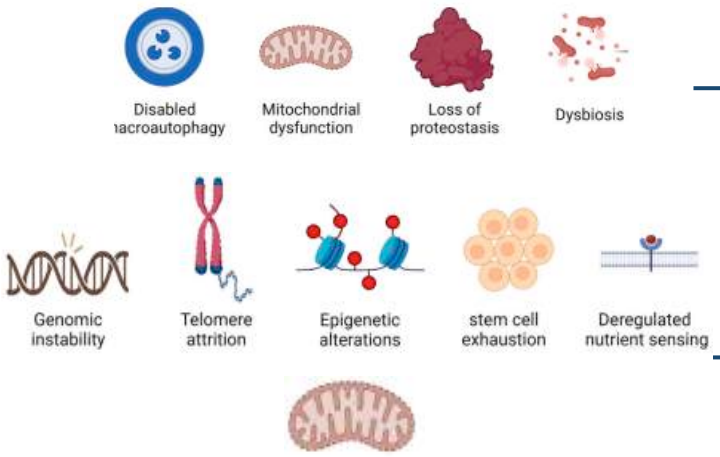
Involution thymique

Environnement proinflammatoire

IL-6, IL-8
CXCL1, CXCL2
AERG, EREG
VEGF, ANGPTL4
etc.



Facteurs SASP



Dysfonction mitochondriale

Immunosénescence

Réponse immune altérée

T cells NK cells B cells
Macrophages
MDSC …

- **SASP (senescence associated secretory phenotype)**
  - Cytokines inflammatoires
  - Facteurs de croissance
  - Protéases

Tumorigenèse
Plus d'infections
Auto-immunité
Mortalité accrue

Lian, J.et al. J Hematol Oncol 13, 151 (2020)
Diekman et al, Osteoarthritis and Cartilage, (2024)

Concepts d'Immunosénescence et MAI

- **Le modèle de l'ACG/PPR**
  - T cell aging-associated phenotype: les cellules T âgées
  - Mobilité et invasion du tissu cible
  - Production de cytokines inflammatoires

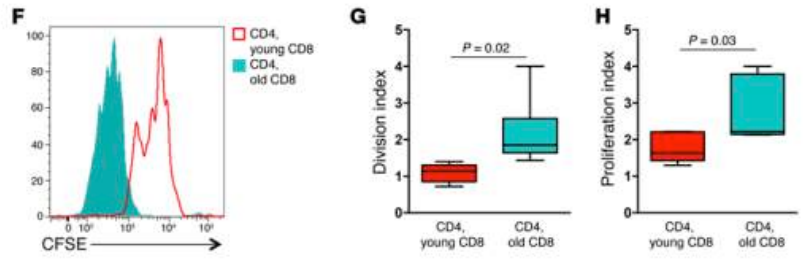


Figure 3. The suppressive function of CD8 Tregs is deficient in older individuals. (**A**) CD8 Tregs induced from young (age < 30 yrs) and older (age > 60 yrs)

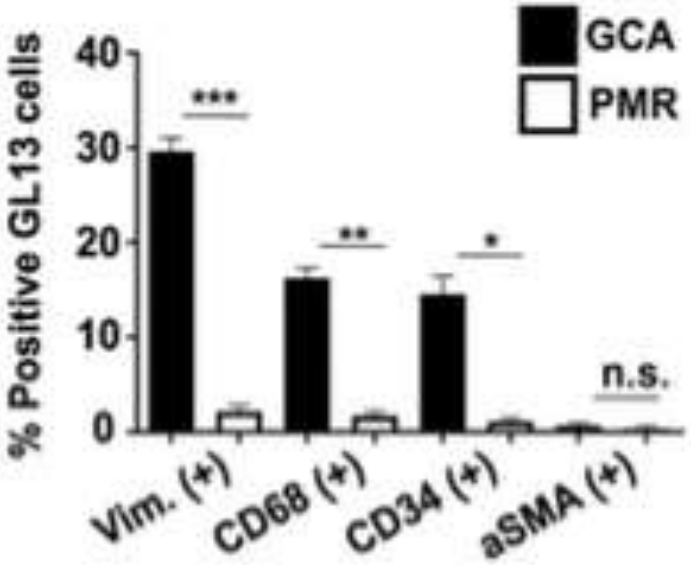
When Z etal, JCI 2016.

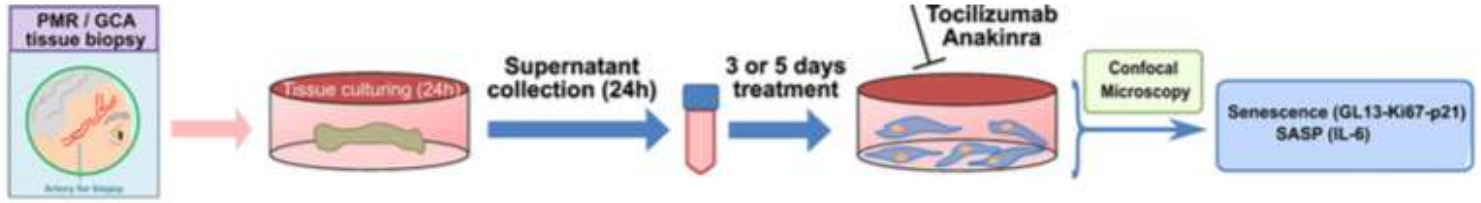
L’immunoscenesence de PPR/ACG

Senescent cells in giant cell arteritis display an inflammatory phenotype participating in tissue injury via IL-6-dependent pathways

Dimitris Veroutis ,[1] Ourania D Argyropoulou,[2] Andreas V Goules,[2,3,4] Konstantinos Kambas,[5] Dimitris Anastasios Palamidas,[2,3] Konstantinos Evangelou,[1] Sophia Havaki,[1] Aikaterini Polyzou,[1] Dimitrios Valakos,[6] Evangelia Xingi,[7] Elli Karatza,[8] Kyriaki A Boki,[9] Alberto Cavazza,[10] Christos Kittas,[1] Dimitris Thanos,[6] Caterina Ricordi,[11,12] Chiara Marvisi,[11,13] Francesco Muratore ,[11,12] Elena Galli,[11,12] Stefania Croci,[14] Carlo Salvarani ,[11,12] Vassilis G Gorgoulis,[1,15,16,17] Athanasios G Tzioufas [2,3,4,18]

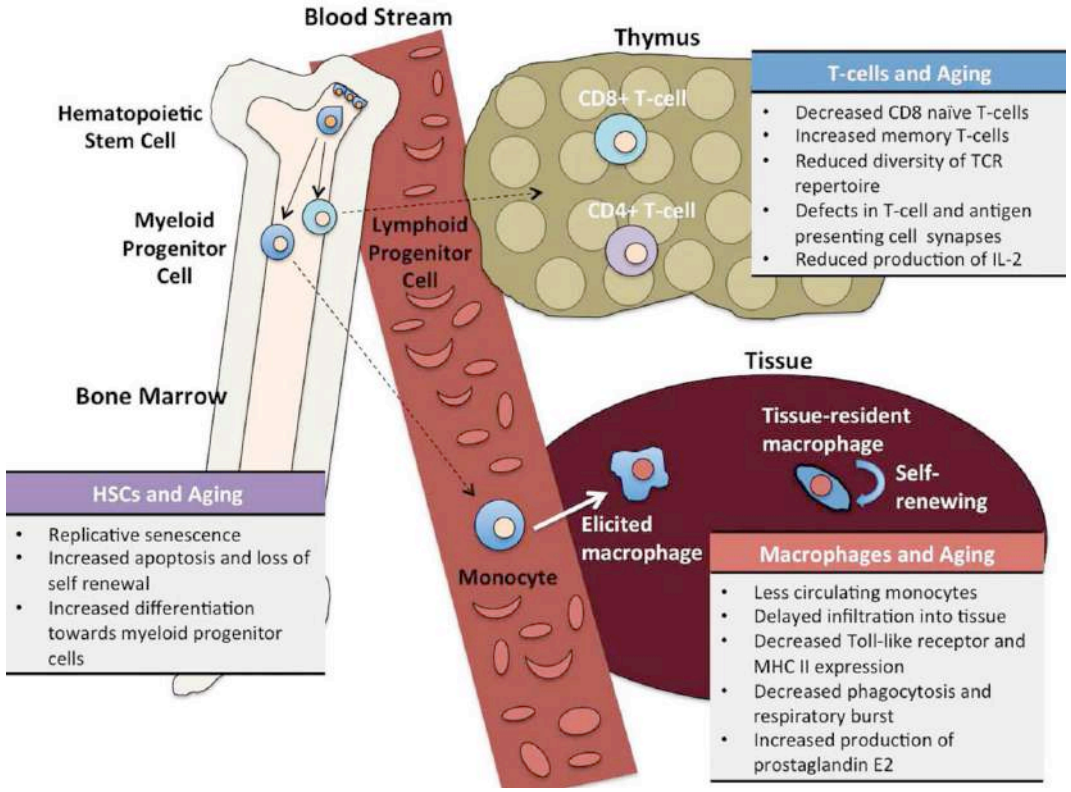
Nombreuses cellules (fibroblastes vimentine, macrophages CD68, endothéliales CD34) sont sénescentes (GL13) dans l’artère temporale d’ACG plus que de PPR et c’est induit par l’IL6, aggravé par l’IL6, réversible en partie sous anti IL6





Consequences?

- **Infections**
  - Virus : grippe, hepatite B
  - Bacterial : pneumococcus, tuberculose
- **Vaccin** (ex: grippe)
  - <65 ans : 70-90%
  - >65 ans : 17-53%
- **Covid:** Age > 65
- **Cancer**
  - **immuno-surveillance**
- **clones auto-réactifs**
  - **Autoantianticorps** (RF, AAN)

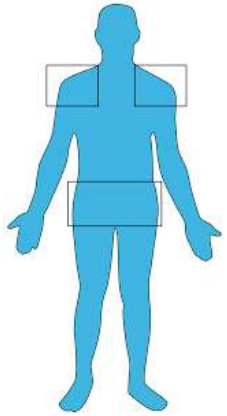


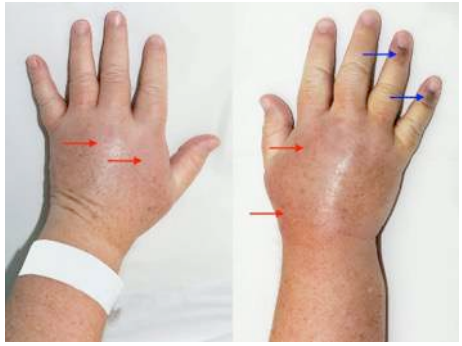
Stahl E et al. Organogenesis (2015)
Candel FJ et al. Viruses (2023)

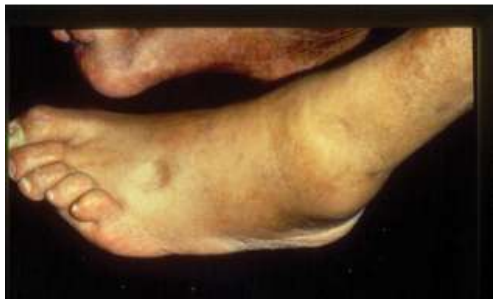
Rhumatismes inflammatoires du sujet âgé

Caractéristiques des principaux rhumatismes inflammatoires du sujet âgé

	PPR	Polyarthrite	RS3PE	LOPS
Localisation Œdèmes Évolution HLA Traitement Délai guérison	Proximale + 0 séquelle DR 4 Corticoïdes 18 mois	Proximale et périph. + Destruction articulaire DR 4 Corticoïdes + Tt de fond Années	Périphérique +++ mains Possibilité contractures B7 Corticoïdes 12 mois	Périphérique + axiale +++ pieds Possibilité destruction B 27 Inefficacité corticoïdes Années







D. Wendling et al. Revue du rhumatisme monographies 86 (2019) 195–198.
J.-J. Dubost et al. Revue du rhumatisme monographies 86 (2019) 190–194.
Laidler NK, Delaney T. BMJ Case Rep. 2020 Apr 22;13(4):e234197.

Des recommandations européennes

Recommendations for early referral of individuals with suspected polymyalgia rheumatica: an initiative from the international giant cell arteritis and polymyalgia rheumatica study group

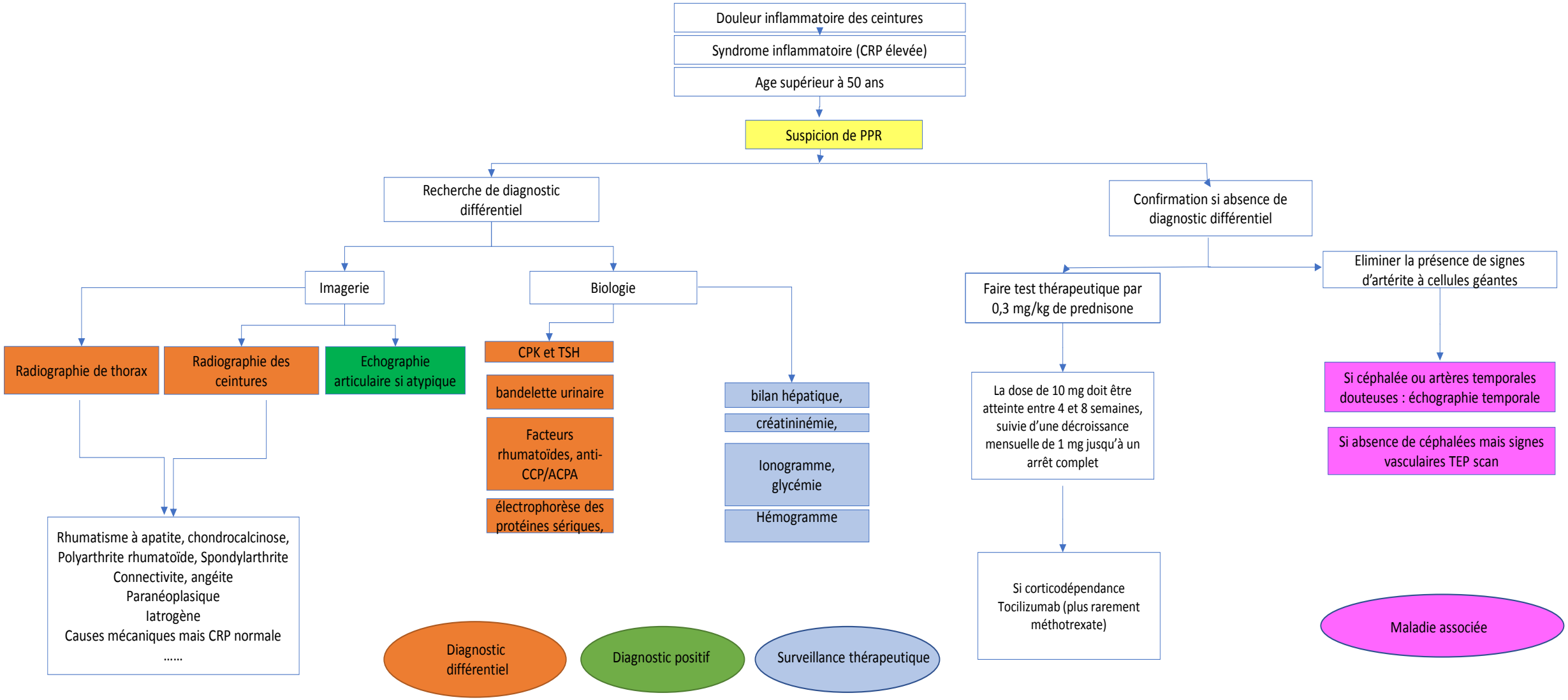
Kresten Krarup Keller ,[1,2] Chetan B Mukhtyar ,[3] Andreas Wiggers Nielsen ,[1,2]

Table 1 Recommendations for early referral of individuals with suspected polymyalgia rheumatica

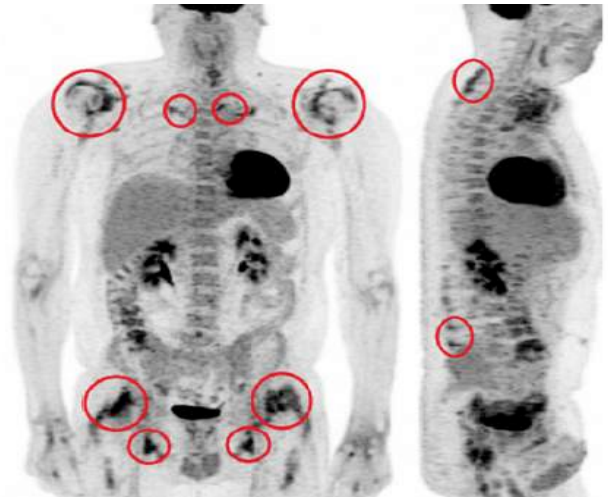
	LOE	FV	LOA
Overarching principle			
1. Management of individuals with suspected PMR should be based on shared decision between the healthcare provider and patient and take severity of symptoms into consideration	–	100	9.7 (0.64)
2. All individuals with suspected PMR should be informed (preferably written) about the potential overlap with GCA. They should be counselled about the need to seek urgent attention if they develop symptoms of GCA	–	100	9.4 (1.4)
Recommendations			
1. Each individual with suspected or recently diagnosed PMR should be considered for specialist evaluation	5	100	9.3 (1.2)
2. Before referring an individual with suspected PMR to specialist care, a thorough history and clinical examination should be performed and preferably complemented with urgent basic laboratory investigations (box 1)	4	100	9.4 (1.0)
3. Individuals with suspected PMR with severe symptoms should be referred for specialist evaluation using rapid access strategies	4	100	9.2 (1.3)
4. In individuals with suspected PMR who are referred via rapid access, the commencement of glucocorticoid therapy should be deferred until after specialist evaluation	5	100	8.6 (1.6)
5. Individuals diagnosed with PMR in specialist care with a good initial response to glucocorticoids and a low risk of glucocorticoid related adverse events can be managed in primary care; they should be referred back to specialist care if glucocorticoids can not be tapered or GCA is suspected	5	100	8.5 (2.3)

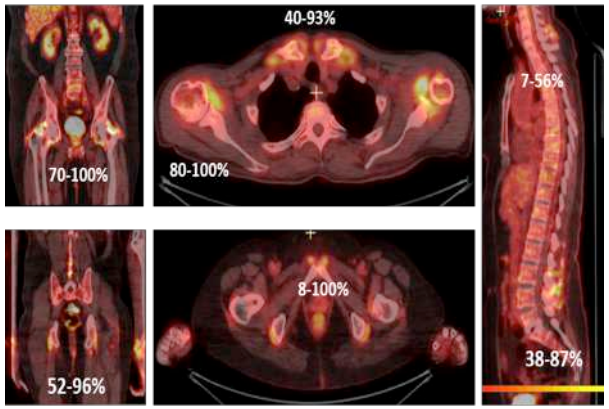
LOA was evaluated on a 0–10 scale and demonstrated as mean (SD).

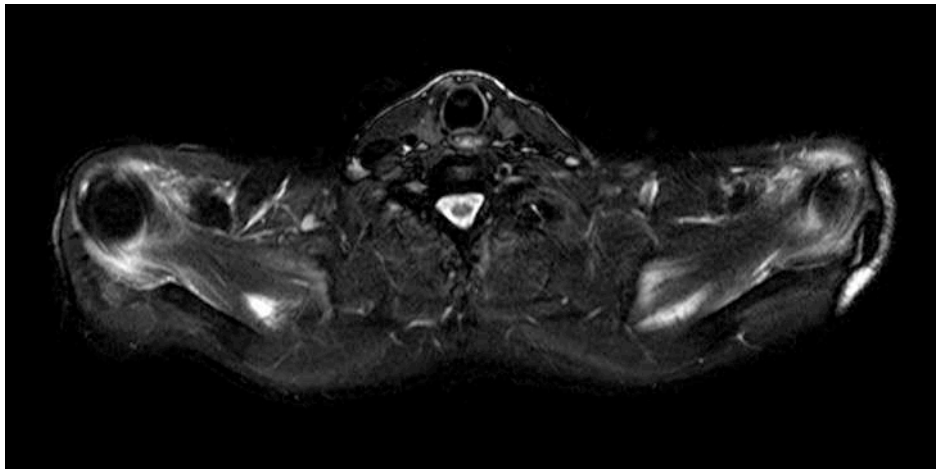
Prise en charge de la PPR

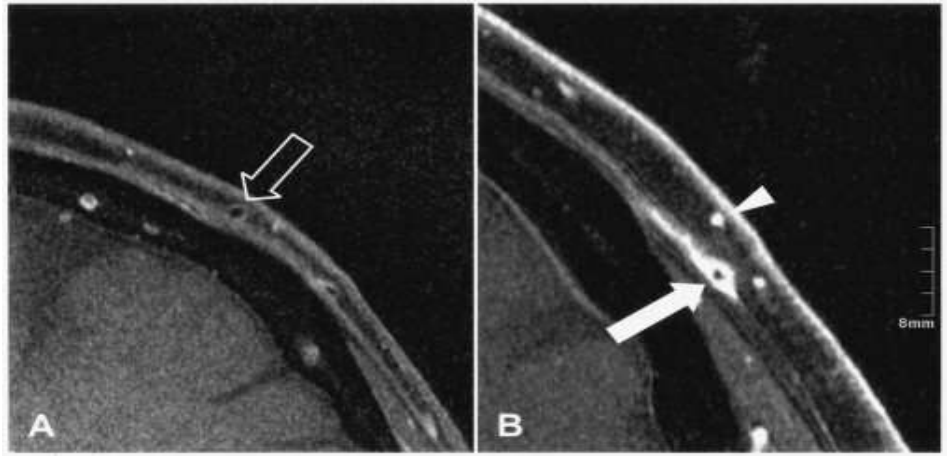


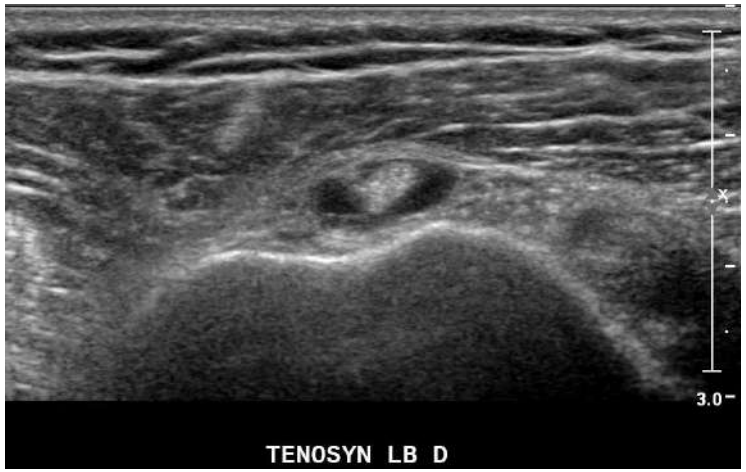
Imagerie du diagnostic positif

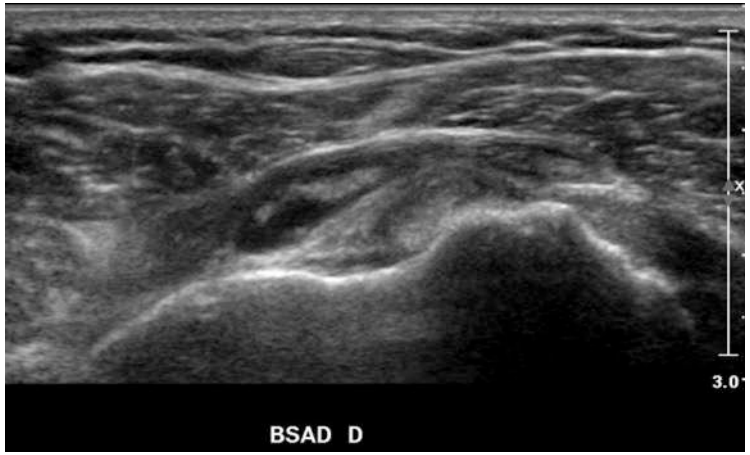


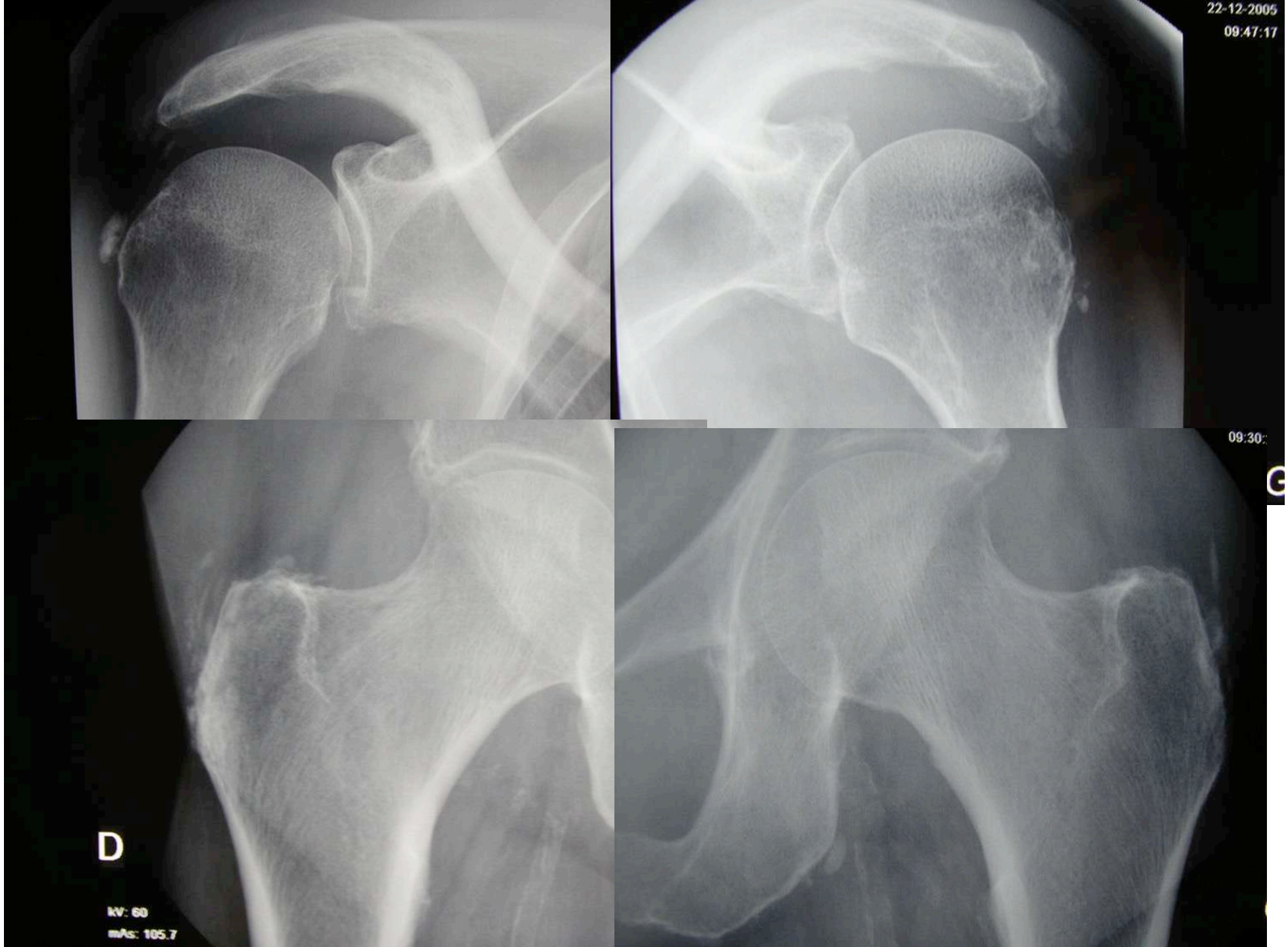











22-12-2005
09:47:17
09:30:
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kV: 60
mAs: 105.7

Contents lists available at ScienceDirect

Joint Bone Spine

journal homepage: www.elsevier.com

Recommendations and metaanalyses

Recommendations of the French Society of Rheumatology for the management in current practice of patients with polymyalgia rheumatica

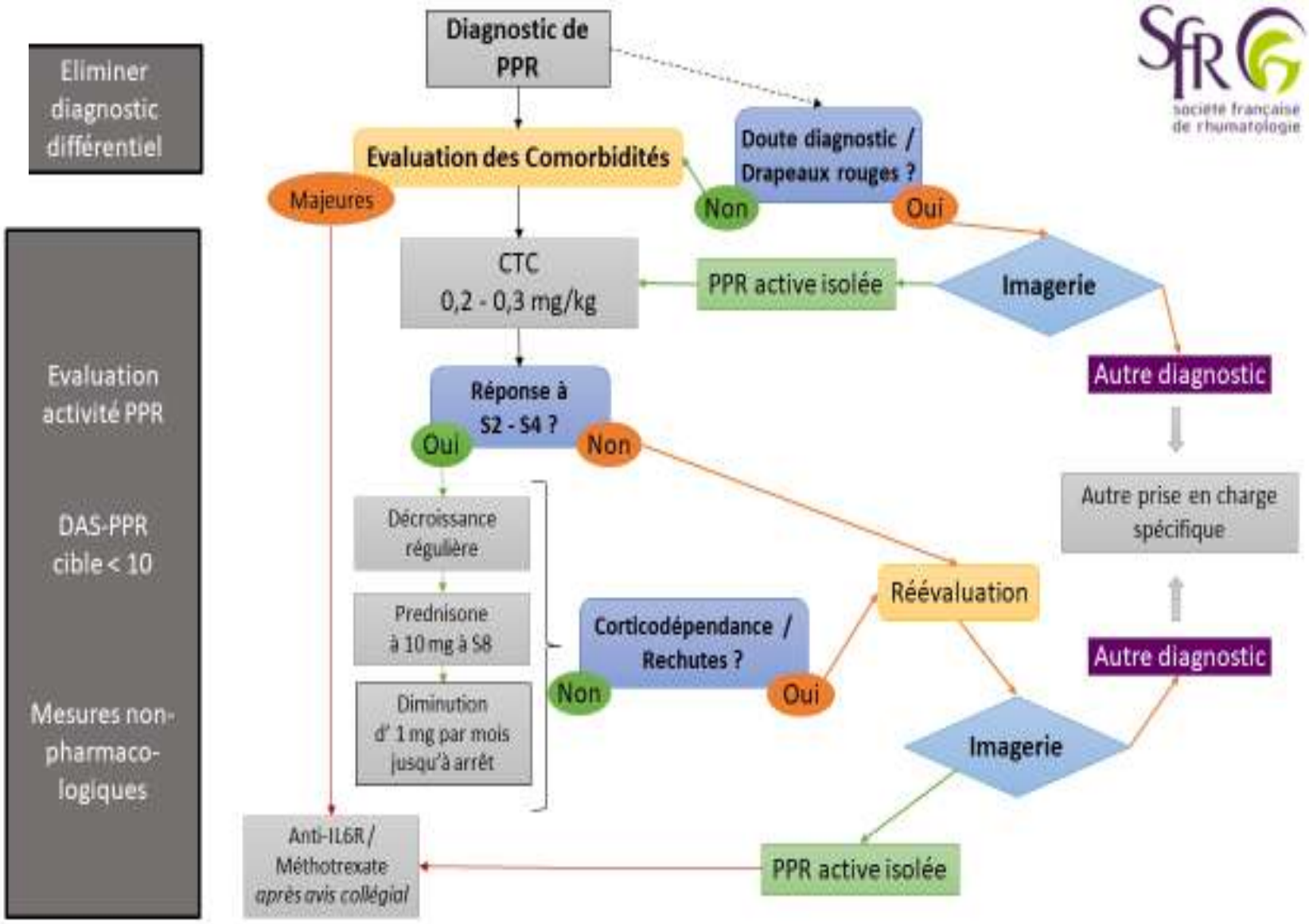
Daniel Wendling[a,*], Omar Al Tabaa[b,c,1], Baptiste Chevet[d,1], Olivier Fakih[a,1], Roba Ghossan[b,1], Sophie Hecquet[b,1], Emmanuelle Dernis[e], Emmanuel Maheu[f], Alain Saraux[d], Florent L. Besson[g], Guillermo Carvajal Alegria[h], Bernard Cortet[i], Bruno Fautrel[j], Renaud Felten[k], Jacques Morel[l], Sébastien Ottaviani[m], Solène Querellou-Lefranc[n], André Ramon[o], Adeline Ruyssen-Witrand[p], Raphaèle Seror[q], Anne Tournadre[r], Nathan Foulquier[s], Bernard Verlhac[t], Frank Verhoeven[a], Valérie Devauchelle-Pensec[d,**]

Corticothérapie 12 à 18 mois (<0.3 mg/kg/j),
10 mg doit être atteint entre 4 et 8 semaines
Suivie d'une décroissance mensuelle de 1 mg jusqu'à arrêt complet

Au diagnostic, le tocilizumab peut être utilisé en cas de nécessité d'un sevrage rapide ou exceptionnellement en monothérapie après discussion collégiale.

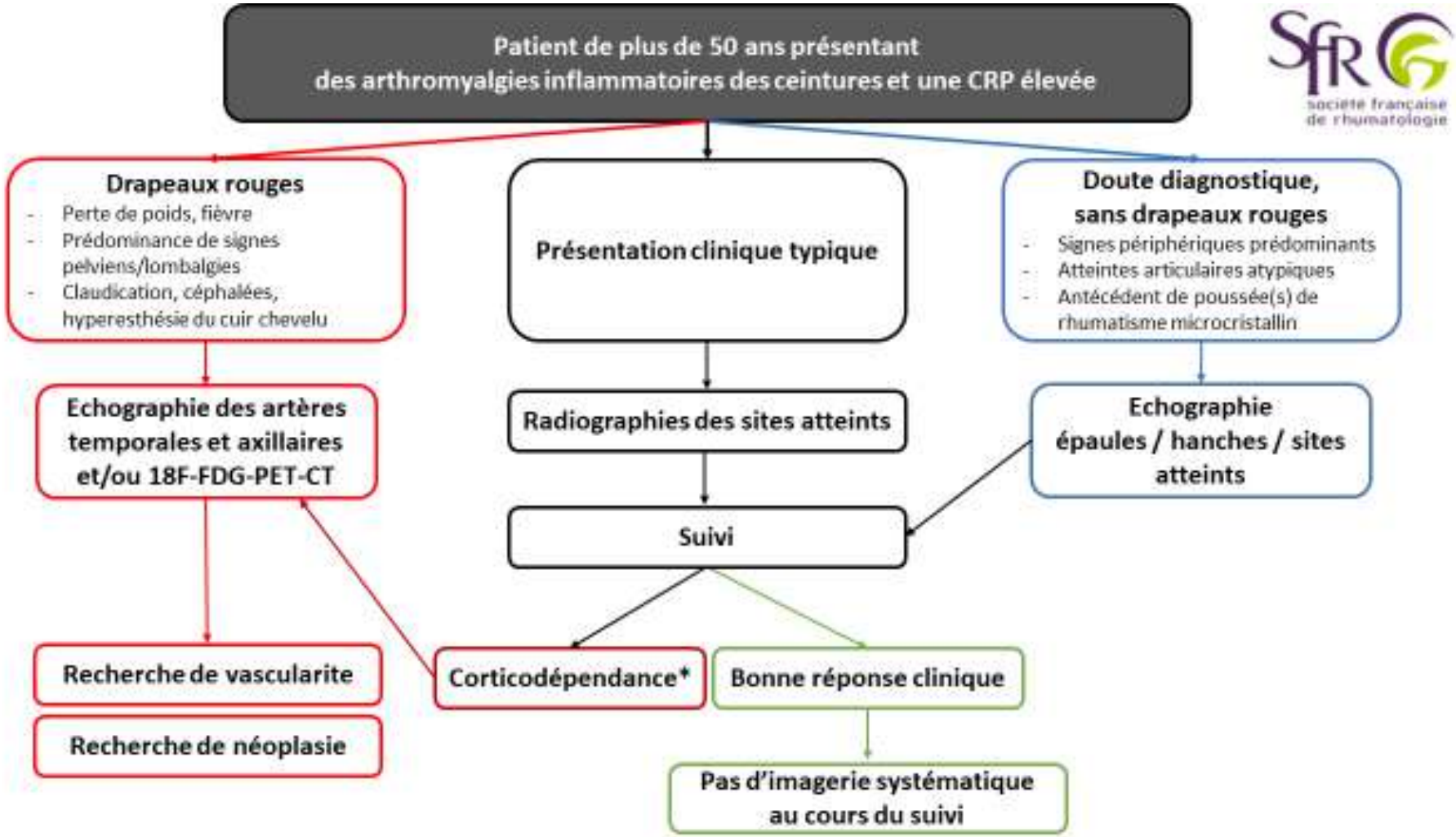
A défaut, le méthotrexate est une alternative

Evaluation sur le DAS-PPR (PMR-AS) <10



Recommandations de la Société Française de Rhumatologie pour la prise en charge en pratique courante des patients atteints de Pseudo Polyarthrite Rhizomélique.

Daniel Wendling, Omar Al Tabaa, Baptiste Chevet, Olivier Fakih et coll



Score d'activité de la PPR: DAS-PPR

- EVA douleur du patient
- CRP (mg/l) ou VS mm/1h
- Dérouillage matinale (mn)
- Elévation des bras (0-3: 180°, 120°, 60°, 0°)
- EVA du médecin

DAS-PPR < 7 — Faible activité

7≤DAS-PPR < 17 — Activité moyenne

DAS-PPR> 17 — Forte activité

DAS-PPR ≤ 10 — Faible activité

7DAS-PPR> 10 — Forte activité

Comment baisser les corticoïdes en pratique

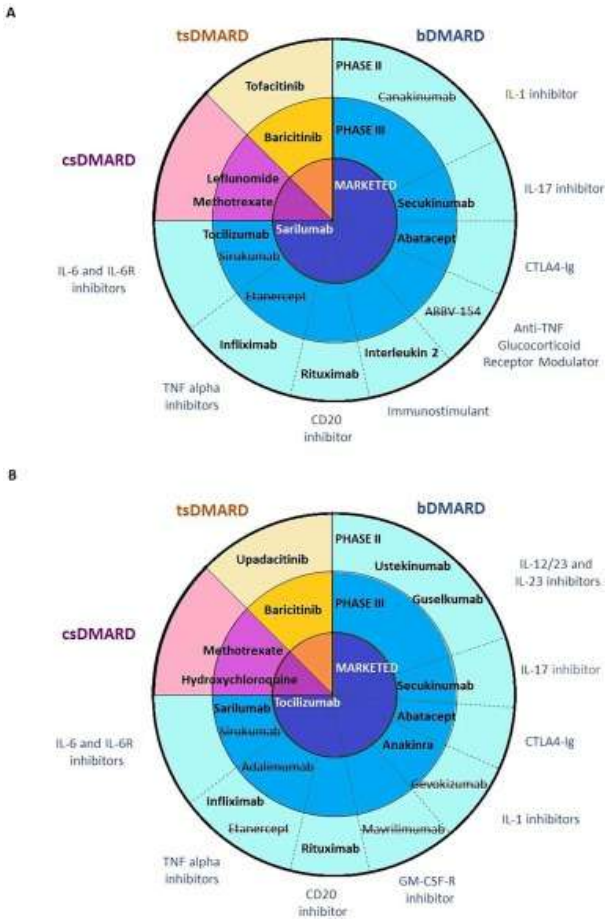
S0	S2	S4	S6	S8	S12	S16	S20	S24	
30	25	20	15	10	9	8	7	6	**Puis diminution d' 1 mg tous les mois**
25	20	15	12,5	10	9	8	7	6	
20	15	12,5	10	9	8	7	6	5	
17,5	15	12,5	10	9	8	7	6	5	
15	12,5	10	9	8	7	6	5	4	
12,5	10	9	8	7	6	5	4	3	
10	9	8	7	6	5	4	3	2	

Saraux A, Le Henaff C, Dernis E et coll, Lancet Rheumatol 2023

Traitements de la PPR et de l'ACG

PPR

GCA



Samson M et al. Targeting interleukin-6 pathways in giant cell arteritis managementrrative review of evidence. Autoimmunity review 2024

Marco A. Expert perspective: management of relapses in giant cell arteritis Arthritis Rheum jan 2024

de Boysson H et al. French protocol for GCA. Rev Med Interne. 2025

Kawka L. The pipeline of immunomodulatory therapies in polymyalgia rheumatica and giant cell arteritis: A systematic review of clinical trials. Autoimmune rev. 2024

Méthotrexate dans la PPR

- On l'utilise comme dans la polyarthrite rhumatoïde
- Pour une durée de l'ordre de un à deux ans

Premier auteur	Journal	Année	Patients (n)	Période évaluée (Semaines)	Posologie de MTX	Posologie initiale de CTC	Posologie cumulée groupe MTX	Posologie cumulée groupe témoin	p
Caporali	Ann Intern Med	2004	72	76	10 mg	25 mg	2100 mg (Médian)	2970 mg (Médian)	0,03
Ferraccioli	J. Rheumatol	1996	24	52	10 mg (IM)	25 mg (MTX) 15 mg (Contrôles)	1840 mg	3200 mg	< 0,01
Nazarinia	Koomesh	2013	58	44	10 mg (PO)	15 mg	3225 mg	3715 mg	0,026
Van Der Veen	Ann Rheum Dis	1996	40	52	7,5 mg (PO)	20 mg	2052 mg	2286 mg	NS

Caporali R, Ann Intern Med. 2004 Oct 5;141(7):493-500
Ferraccioli J, J Rheumatol. 1996 Apr;23(4):624-8.
Nazarinia AM, Koomesh 2013-14(3)
Van Der Veen MJ, Ann Rheum Dis 1996 Aug;55(8):218-23.

Les anti-TNF ne sont pas supérieurs au placebo

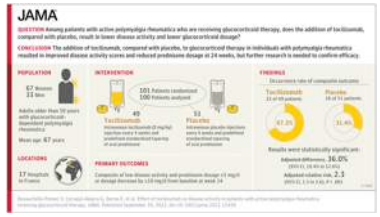
Auteur	Pathologie	Traitement	Méthode	Critère	p
Salvarani	PPR	IFX-51 pts	+CTC	sans rechute	NS
Kreiner	PPR	ETA- 20 pts	seul	DAS PPR	NS (0,01 vs inclusion)

Les autres traitements ciblés

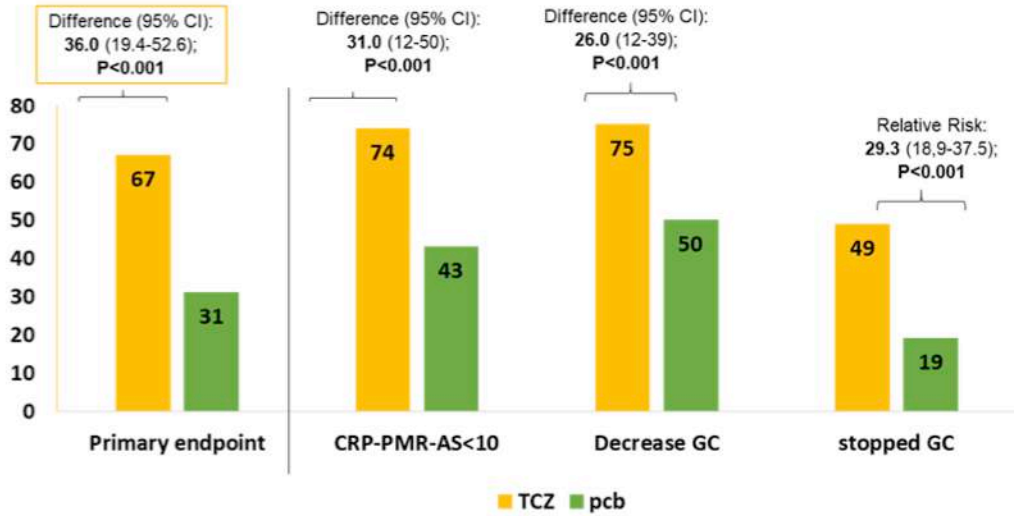
Nom de l'étude	Molécule	Phase	Avancée
SEMAPHORE	Tocilizumab	III	Efficace
PMR SPARE	Tocilizumab	III	Efficace
EFC15160 (Saphyr)	Sarilumab	III	Efficace
Rituximab	Rituximab	III	Efficace
ALORS	Abatacept	II	Inefficace (ou pas assez)
BACHELOR	Baricitinib	II	Efficace
NOVARTIS	antiIL17/antiIL1	II	Inclusions terminées
ABBVIE	ABBV154 (TNFi-corticoïdes)	II	Abandonnée

Salvarani et al Ann intern Med. 2007 May 1; 146 (9) : 631-9 Kreiner et al, A Res Ther 2010; 12(5) R176. Devauchelle-Pensec JAMA 2022 De Marsan Lancet Rheumatol 2021

Anti IL6



SEMAPHORE, W 24
100 pts planned, 100 treated



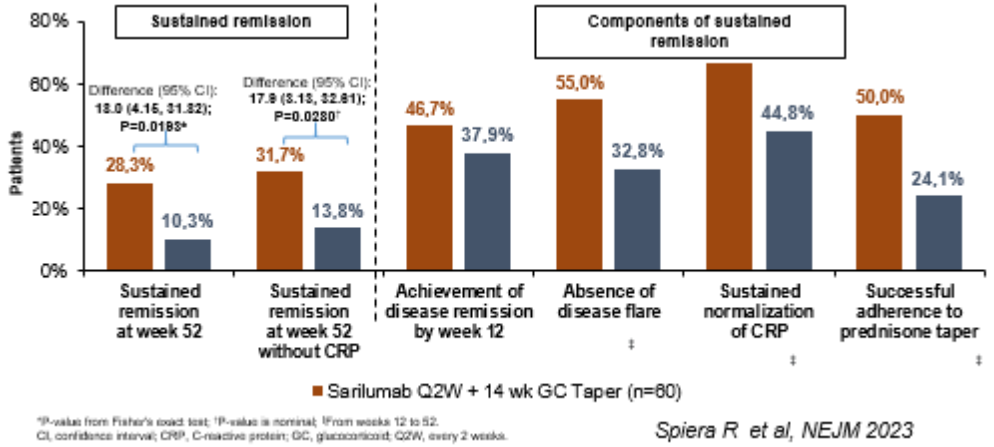
*P-value from Fisher's exact test.
CI, confidence interval; CRP, C-reactive protein; GC, glucocorticoid.

Devauchelle-Pensec V et al, JAMA 2022

Sarilumab for Relapse of Polymyalgia Rheumatica during Glucocorticoid Taper

Robert F. Spiera, M.D., Sebastian Unizony, M.D., Kenneth J. Warrington, M.D., Jennifer Sloane, M.D., Angeliki Giannelou, M.D., Michael C. Nivens, Ph.D., Bolanle Akinlade, M.D., Wanling Wong, Ph.D., Rafia Bhore, Ph.D., Yong Lin, M.D., Frank Buttgereit, M.D., Valerie Devauchelle-Pensec, M.D., Ph.D., Andrea Rubbert-Roth, M.D., George D. Yancopoulos, M.D., Ph.D., Frederic Marrache, M.D., Ph.D., Naimish Patel, M.D., and Bhaskar Dasgupta, M.D., for the SAPHYR Investigators*

SAPHYR, W 52
250 pts planned, 102 treated



*P-value from Fisher's exact test; †P-value is nominal; ‡From weeks 12 to 52.
CI, confidence interval; CRP, C-reactive protein; GC, glucocorticoid; Q2W, every 2 weeks.

Spiera R et al, NEJM 2023

-Autres cibles en développement: anti-IL-17, JAKi, rituximab

Devauchelle-Pensec V et al. JAMA (2022)
Spiera RF et al. N Engl J Med (2023)
Chevet B, ACR (2024)