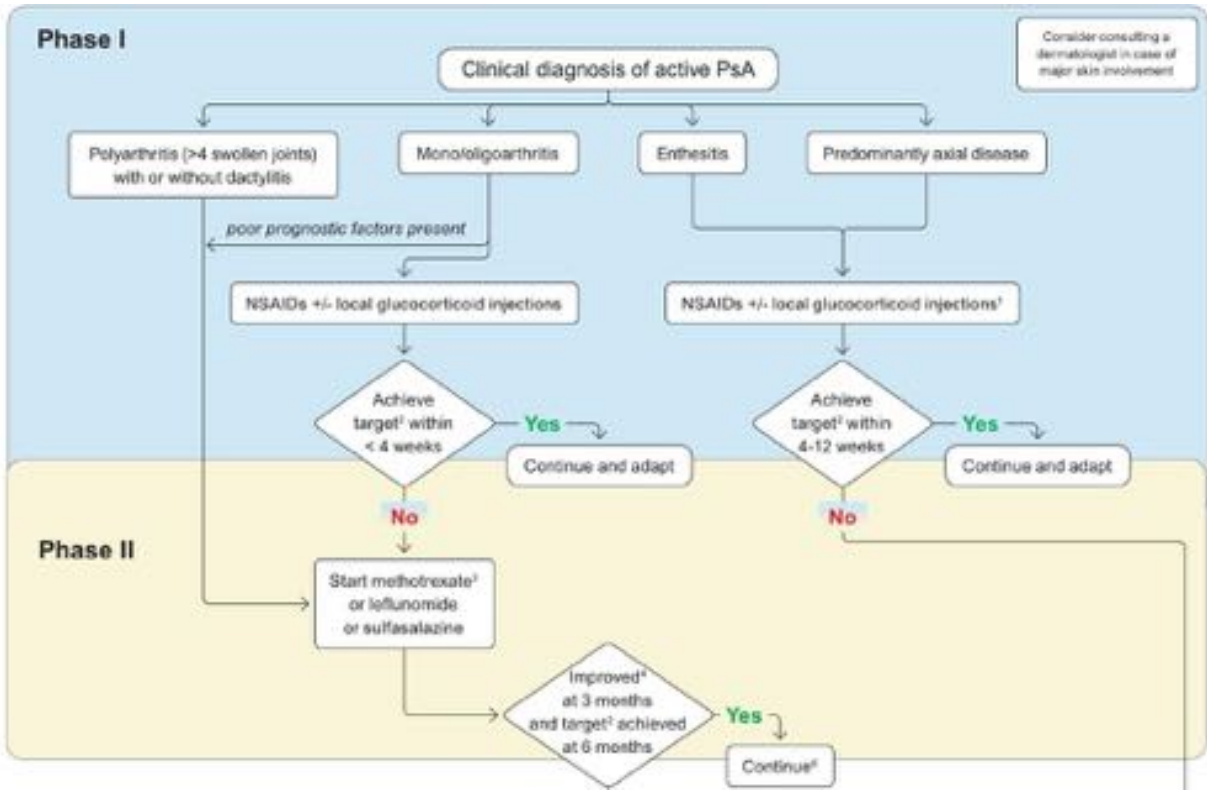
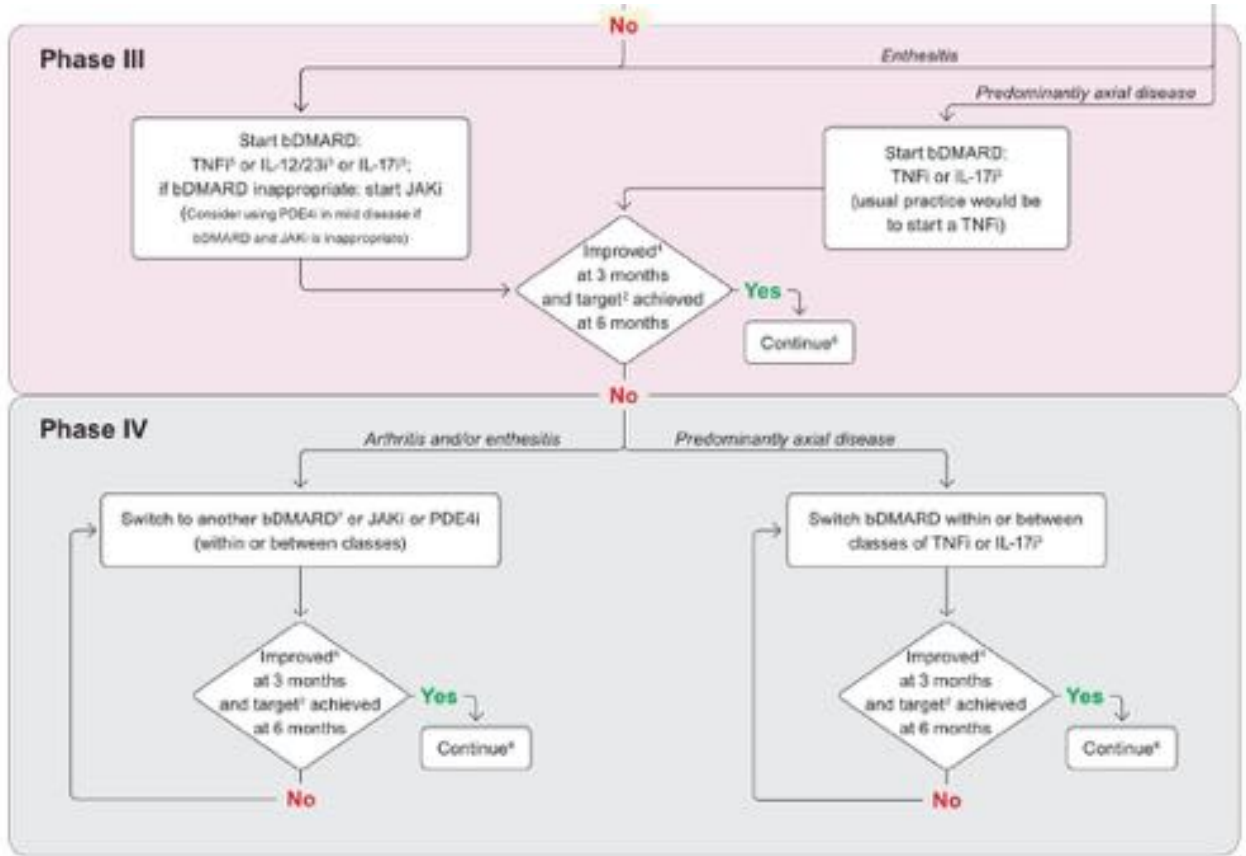
Nouvelles recommandations de la SPA et stratégies des différents traitements ciblés dans le rhumatisme psoriasique

Anne Tournadre

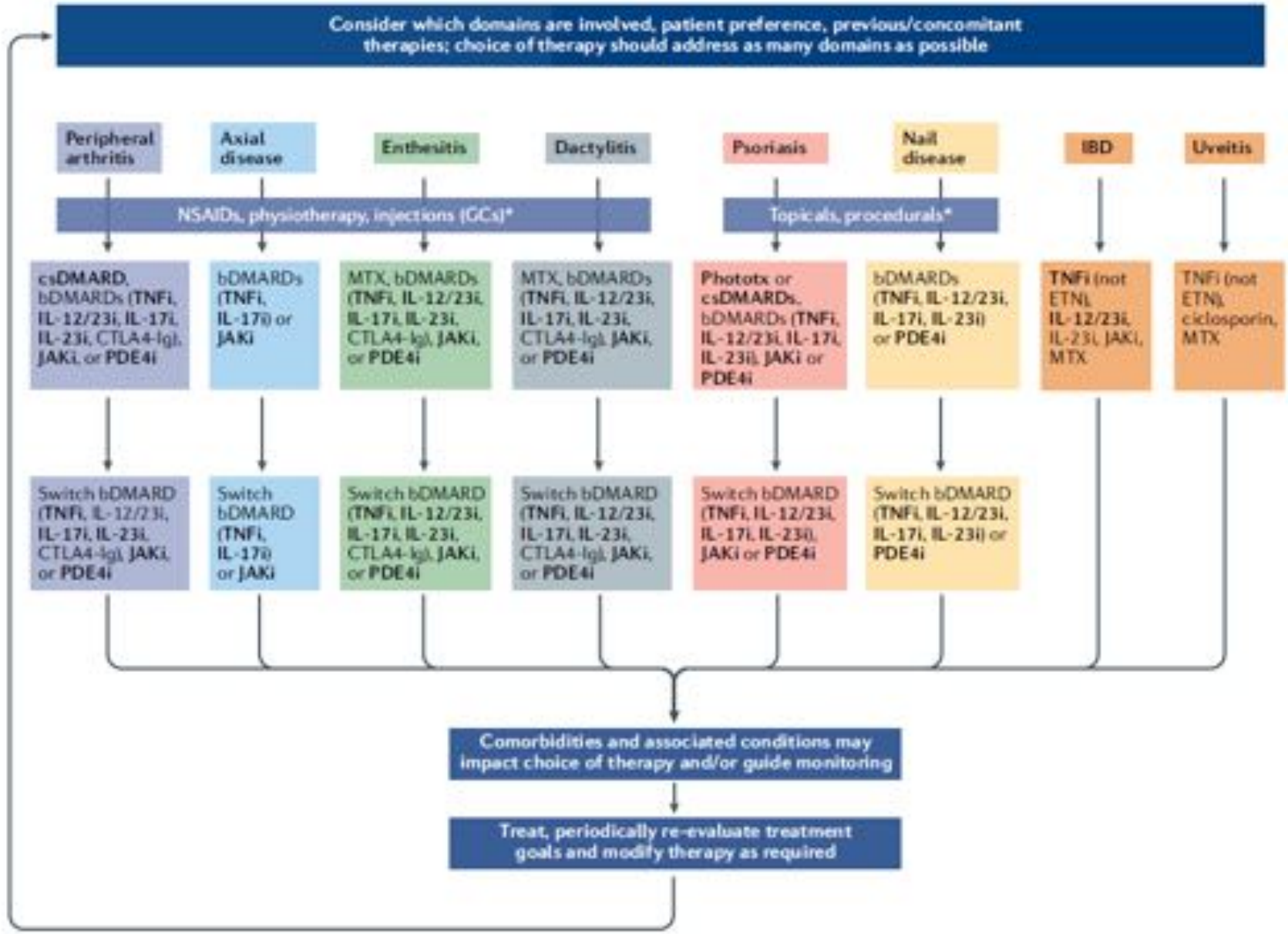
EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update





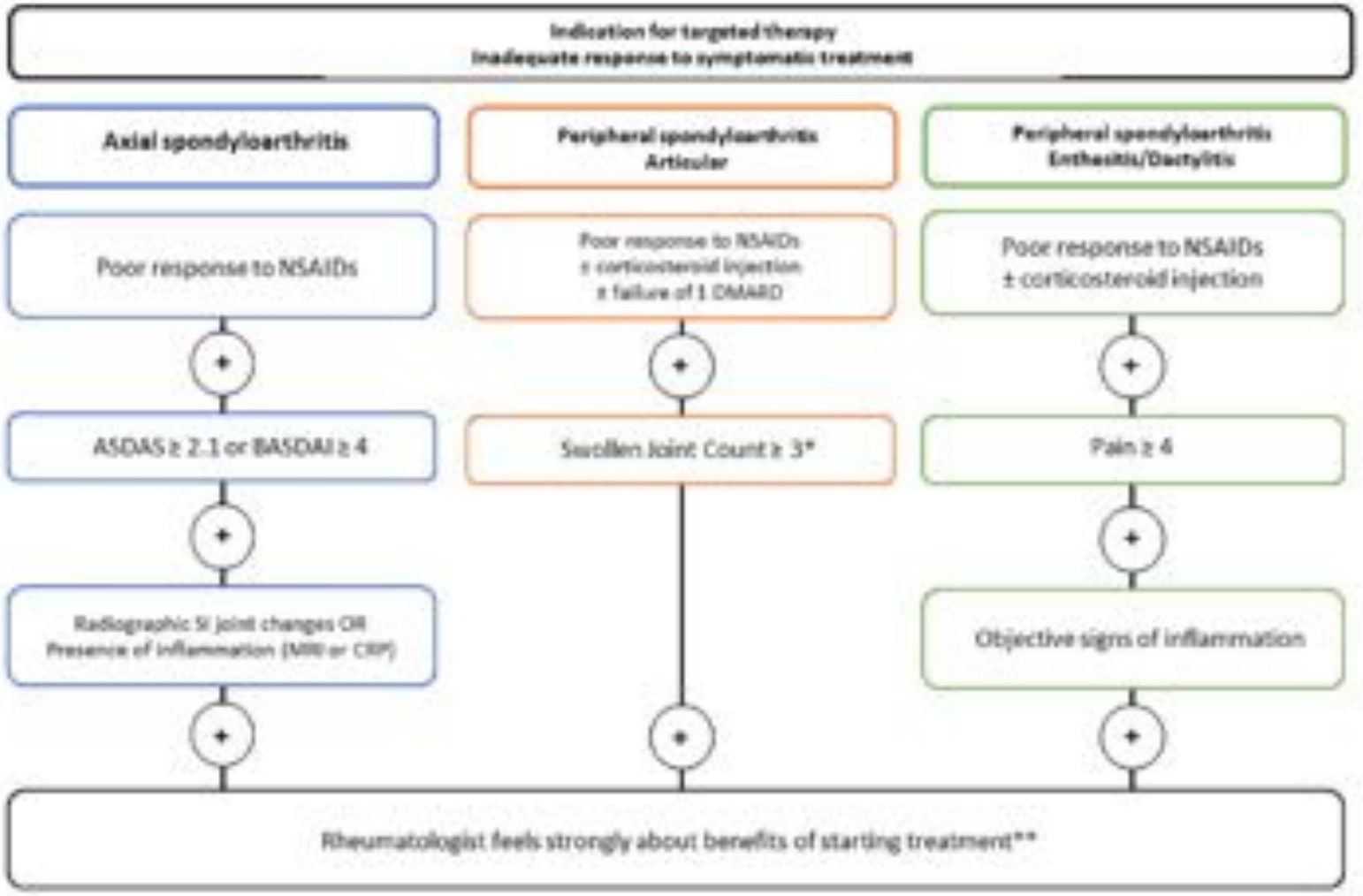
1. No glucocorticoids for axial disease.
2. The target is remission or low disease activity (especially with long standing disease) in accordance with the treat-to-target recommendations.
3. Preferred in the presence of relevant skin involvement, however in case of concomitant inflammatory bowel disease or uveitis, an anti-TNF antibody would be preferred.
4. Improvement means at least 50% reduction in disease activity.
5. As add-on to methotrexate.
6. Consider cautious tapering in sustained remission.
7. Including biosimilars.
8. For definition of individual items see text.
Phase I recommendations 1, 2, 3, 4, 5;
Phase II recommendations 1, 3, 4, 5, 12;
Phase III recommendations 6, 8, 9, 10, 12;
Phase IV recommendations 7, 11,12

Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021



Coates, Laura C., *Nature Reviews. Rheumatology* 18, nº 8 (août 2022): 465-79.

Recommandations 2022 SFR



*Lower number if coccydynia is refractory to corticosteroid injections or radiological progression
**Takes into account extra-articular manifestations

Fig. 1. Indication for a targeted therapy.

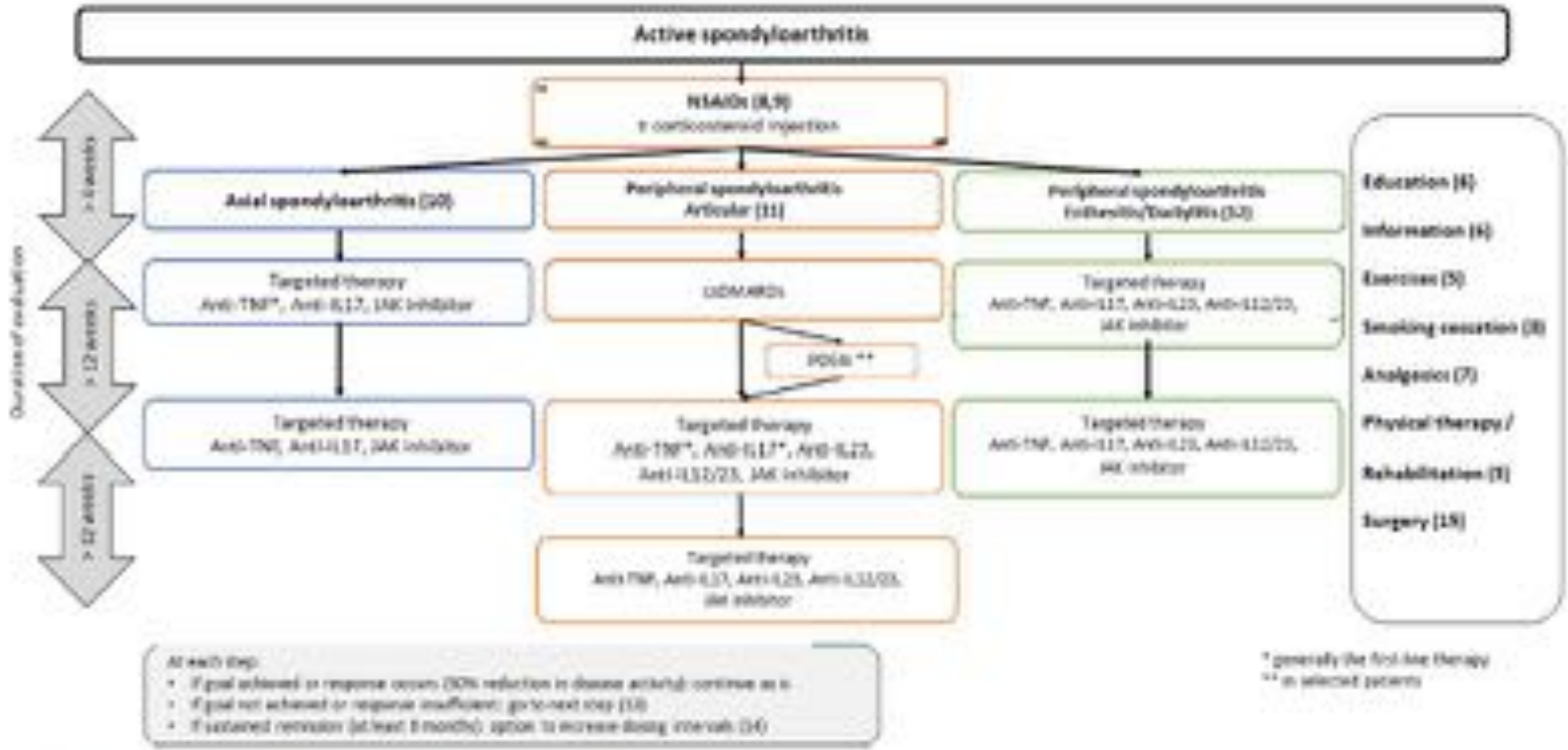


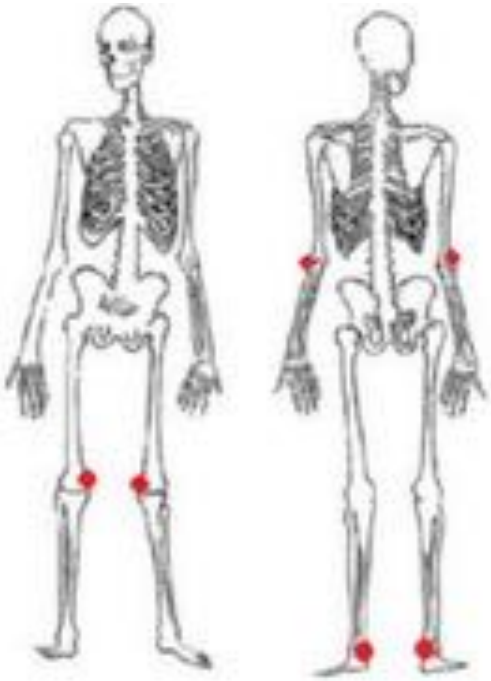
Fig. 2. Overall treatment strategy for spondyloarthritis, including psoriatic arthritis. The numbers in parentheses refer to specific recommendations. At each step: if goal achieved or response occurs (50% reduction in disease activity): continue as is; if goal not achieved or response insufficient: go to next step [13]; if sustained remission (at least 6 months): option to increase dosing interval [14].

Scores d'évaluation du rhumatisme psoriasique

Score	Critères	Rémission	Faible activité
VLDA **MDA**	Articulations douloureuses (≤ 1/68) Articulations gonflées (≤ 1/66) Psoriasis (PASI ≤ 1 ou BSA ≤ 3) Enthèses (≤ 1/13) Douleur patient (≤ 15/100) EVA global patient (≤ 20/100) HAQ (≤ 0,5)	**VLDA** 7 / 7 critères	**MDA** 5 / 7 critères
DAPSA	Articulations douloureuses (≤ 1/68) Articulations gonflées (≤ 1/66) Douleur patient (EVA/10) EVA global patient (EVA/10) CRP (mg/dl)	Somme **≤ 4**	Somme **5-14**

Scores	Psoriasis
Surface corporelle (BSA)	< 5 % : léger > 10 % : sévère
PASI Erythème Induration Desquamation Surface	< 5 : léger > 10 : sévère
Réduction PASI	PASI 75: 75 % PASI 90 : 90 % PASI 100 : 100 %

Enthèses Leeds (/6)



Les cibles


Blood
Synovium
Bone
Cytokines
Macrophages
Anti-TNF
JAKi
Enthesis
Th1 cell
Anti-
IL12/IL23
Anti-IL17
Anti-IL23
Activated T cell
Naive T cell
Th17 cell
Activated FLS
Osteoblast
Osteoclast progenitor cells
Osteoclast
Bone
resorption
Inhibiteur
PDE4

Classe	DCI	Nom Commercial	Essai III, PsA (PsO)	PsA	PsO	axSpA	MICI	Uveite
TNFi	Etanercept		2004					
	Adalimumab		2005					
	Infliximab		2005					
	Golimumab		2009					
	Certolizumab		2014					
IL12/IL23i	Ustékinumab	*Stelara SC/12 sem*	2013, 2014					
IL17i	Secukinumab (IL17A)	*Cosentyx SC/4sem*	2015					
	Ixekizumab (IL17A)	*Taltz SC/4sem*	2017					
	Brodalumab (IL17RA)	*Kyntheum SC/2sem*	2021 (2015)	Phase III				
	Bimekizumab (IL17A,F)	*Bimzelx SC/4sem*	2022 (2021)	EMA				
IL23i	Guselkumab	*Tremfya SC/4-8 sem*	2020, (2019)				Phase III	
	Risankizumab	*Skyrizi SC/0-4-12 sem*	2022, (2018)				Phase III	
	Tildrakizumab	*Ilumetri*	En cours, (2017)	Phase III				
JAKi	Tofacitinib	*Xeljanz 5*	2017					
	Upadacitinib	*Rinvoq 15*	2021					
	Filgotinib	*Jyseleca 200*	En cours	Phase III				
PDE4i	Aprémilast	*Otezla*	2014, 2016, 2017					

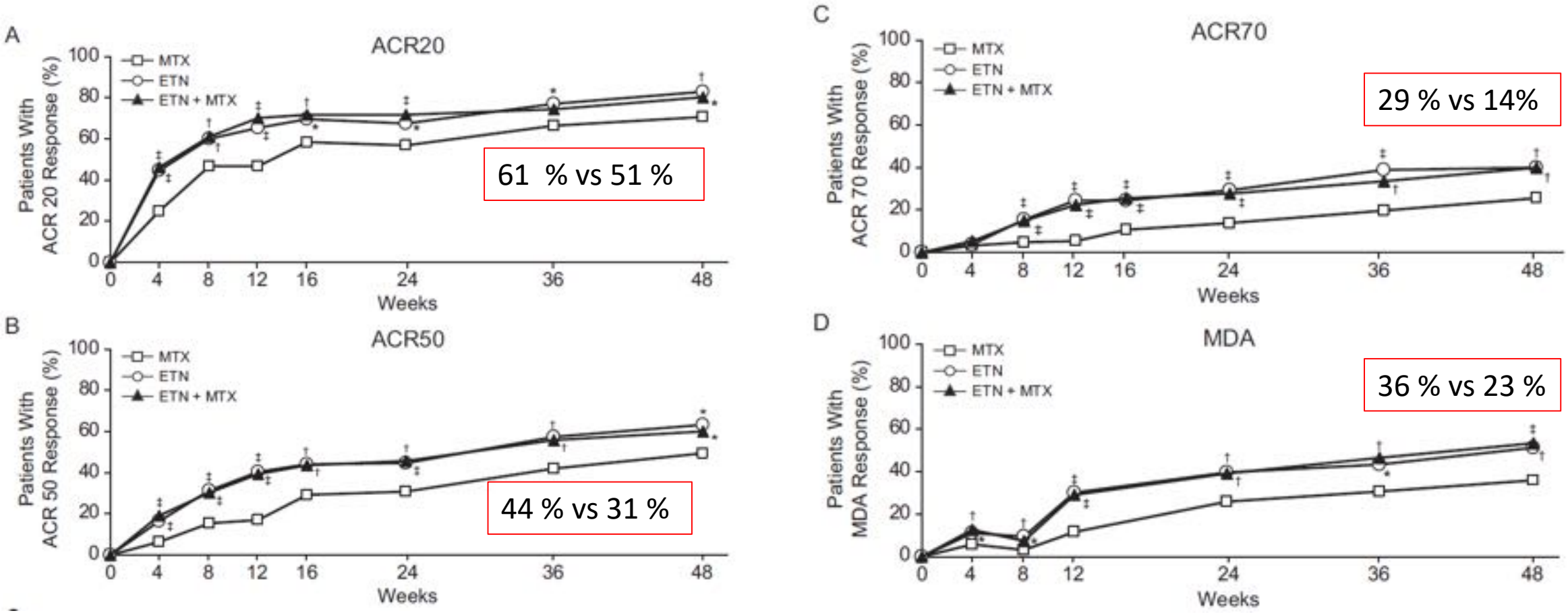
Cs DMARDs : peu de données positives

- **MTX**
  - RCT contre PBO (n=221 PsA) *(Kingsley GH Rheumatolgy 2012)* :
  - Pas de différence MTX 15 mg/semaine vs PBO à S24 semaines (PsARC, ACR20, DAS28)
  - Efficacité uniquement sur le PASI

- **Léflunomide**
  - RCT contre PBO (n=190) *(Kaltwasser JP Arthritis Rheum 2004)*
    - Réponse PsARC S24: 59 % vs 30 %.
    - Meilleure réponse PASI, pas de données structurales
  - Etude observationnelle *(Behrens F ACR 2013)* : réponse PsARC à S24 chez 86 % des 514 patients, diminution % de psoriasis sévère

- **Salazopyrine**
  - 43 SLZ vs 48 PBO: amélioration EVA douleur *(Dougados et al Arthritis Rheum 1995)*
  - 24 SLZ vs PBO, amélioration EVA globales patient et médecin *(Gupta et al. J Rheum 1995)*
  - SLZ vs PBO chez 221 RPso étant en échec des AINS: tendance à la supériorité à S 36 pour EVA douleur et globale, gonflements articulaires, pas d'effet cutané *(Combe et al. en 1996 Br J Rheumatol)*

MTX vs ETA vs ETA+MTX (SEAM)



Mease, P. J. et al. *Arthritis Rheumatol.* **71**, 1112–1124 (2019).

2022 French Society for Rheumatology (SFR) recommendations on the everyday management of patients with spondyloarthritis, including psoriatic arthritis

Recommendation 11. In cases of peripheral arthritis unresponsive to symptomatic therapy.

Recommendation 11A. Treatment with csDMARDs should be considered if NSAIDs have failed, along with local interventions. In cases of psoriasis, methotrexate is the preferred treatment.

Recommendation 11H. Methotrexate should not be used routinely with targeted therapies.

Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021

For treatment-naive patients, there remains a low level of evidence to support the use of csDMARDs for the treatment of peripheral arthritis. However, in view of supportive observational data and universal accessibility, the use of csDMARDs (methotrexate, sulfasalazine or leflunomide) is strongly recommended.

In many circumstances, csDMARDs can be used as first-line therapy, with regular assessment of clinical response (every 12–24 weeks) and early escalation of therapy (between 12 and 24 weeks) advised as necessary.

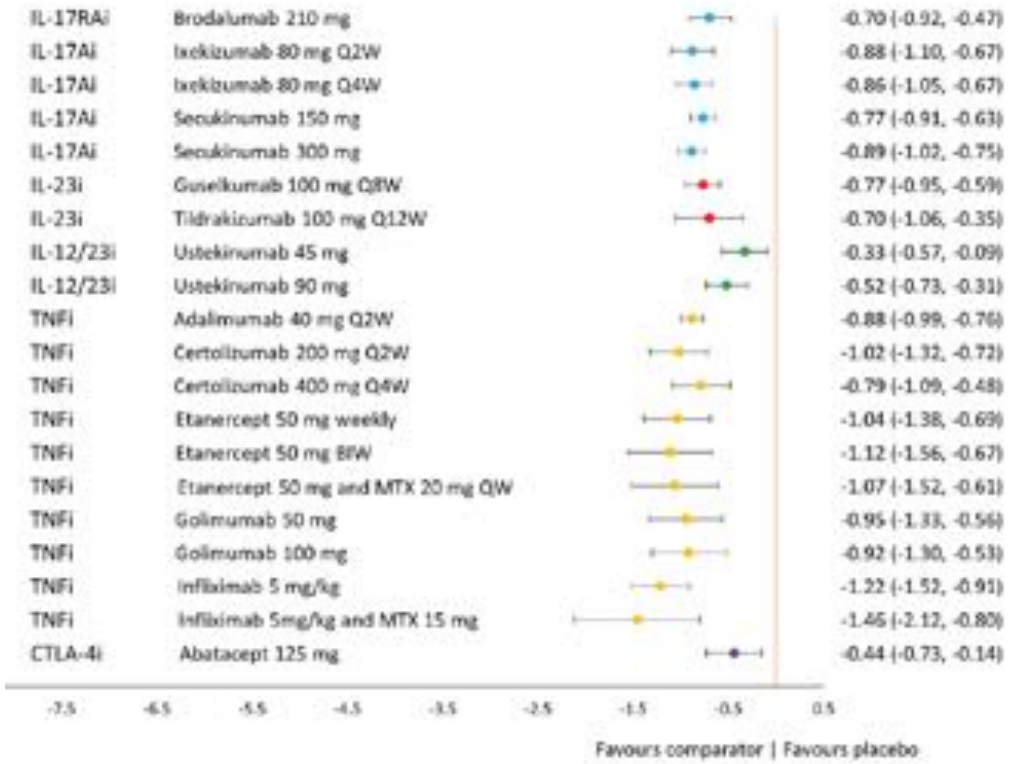
Données des essais randomisés contre placebo bDMARDs

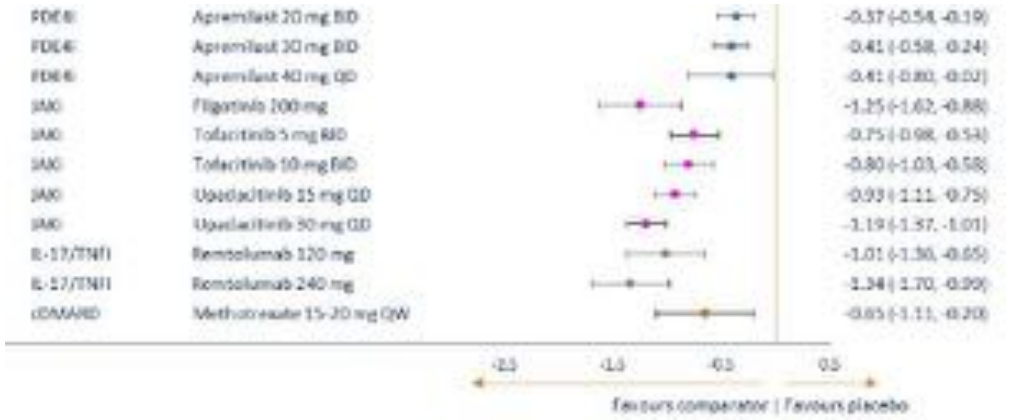
- **Efficacité comparable à S16-S24 pour anti-TNF, anti-IL17, anti-IL23, JAKi**
  - ACR20 60%, ACR50 40 %, ACR70 20 %
  - Un peu moins bien chez IR-bDMARD (- 5 %)

- **Efficacité moindre pour Ustekinumab**
  - ACR20 50 %, ACR50 30 %, ACR70 15 %

- **Apremilast**
  - ACR20 30 %, ACR50 10 %, ACR70 <5 %
  - Pas d'effet structural

Méta-analyse tsDMARDs: réponse ACR



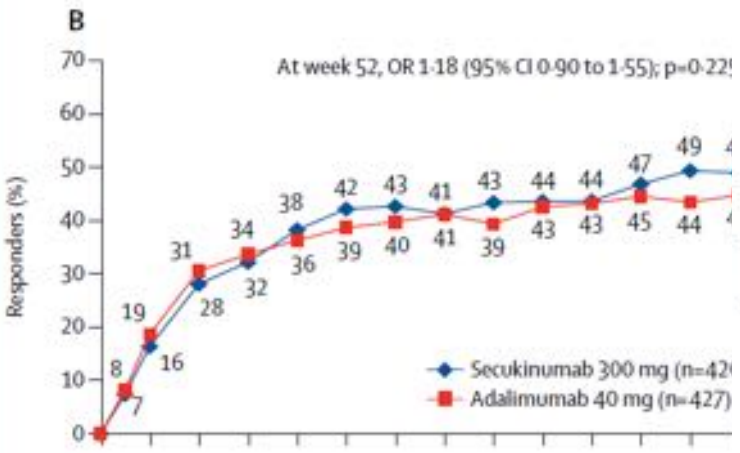


McInnes, Iain B., *RMD Open* 8, nº 1 (mars 2022): e002074.

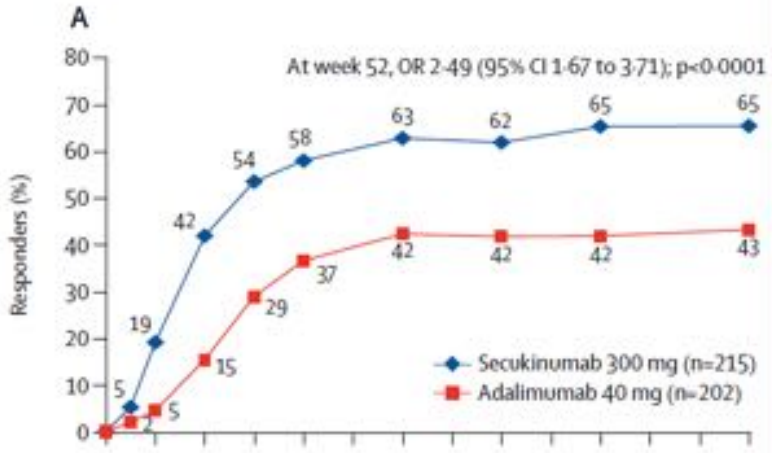
Etudes Face-Face : critère articulaire

- **anti-IL17 (Secukinumab 300) vs TNFi (Adalimumab 40)**

ACR50



PASI

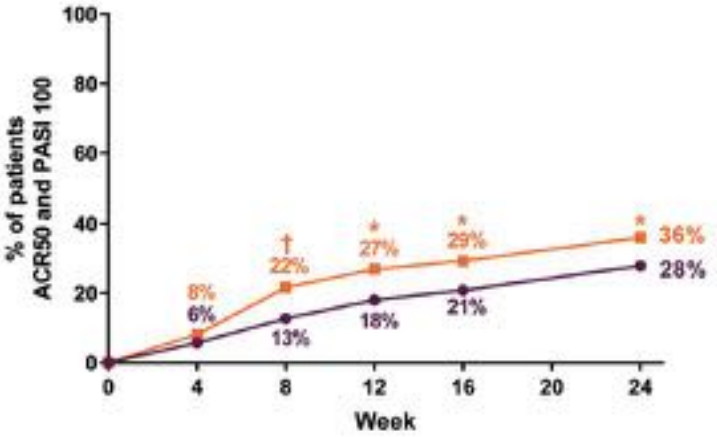


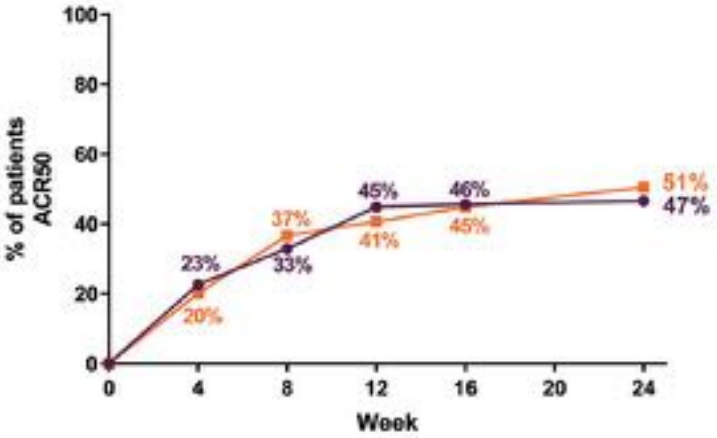
	Secukinumab 300 mg	Adalimumab 40 mg	Odds ratio (95% CI)	p value (unadjusted)*
Primary endpoint				
ACR20	67% (426)	62% (427)	1·30 (0·98 to 1·72)	0·0719
Prespecified sensitivity analysis using non-responder imputation				
ACR20	67% (426)	59% (427)	1·38 (1·04 to 1·83)	0·0239
Key secondary endpoints				
PASI 90	65% (215)	43% (202)	2·49 (1·67 to 3·71)	<0·0001
ACR50	49% (426)	45% (427)	1·18 (0·90 to 1·55)	0·2251
HAQ-DI score, change from baseline, mean (SE) [n]	−0·58 (0·03) [363]	−0·56 (0·03) [318]	−0·02† (−0·10 to 0·05)	0·5465
Resolution of enthesitis (based on Leeds Enthesitis Index)	61% (234)	54% (264)	1·30 (0·91 to 1·87)	0·1498
Combined endpoint				
ACR50 plus PASI100‡	31% (215)	19% (202)	1·85 (1·17 to 2·92)	0·0087
Exploratory endpoints				
Psoriatic arthritis endpoints				
Minimal disease activity (78/76 joints)	43% (426)	38% (427)	1·22 (0·93 to 1·61)	0·1498
Very low disease activity (78/76 joints)	18% (426)	17% (427)	1·10 (0·77 to 1·57)	0·6107
Resolution of dactylitis	75% (130)	70% (137)	1·29 (0·75 to 2·22)	0·3560
Resolution of enthesitis	53% (301)	50% (330)	1·11 (0·81 to 1·52)	0·5117

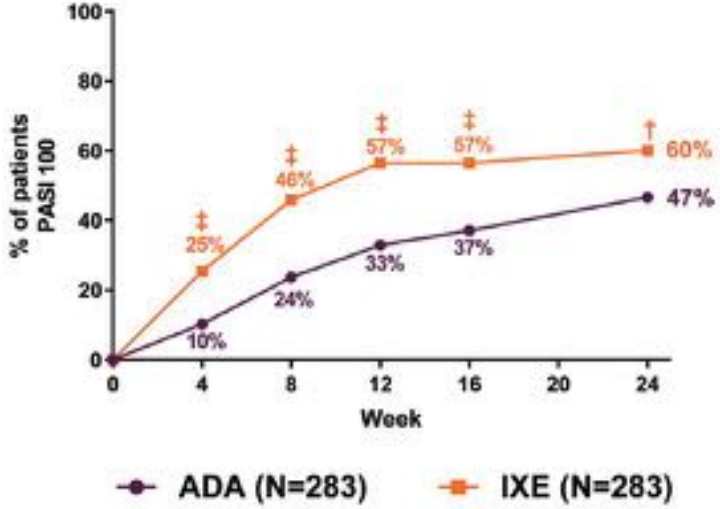
McInnes, Iain B, *The Lancet* 395, nº 10235 (9 mai 2020): 1496-1505.

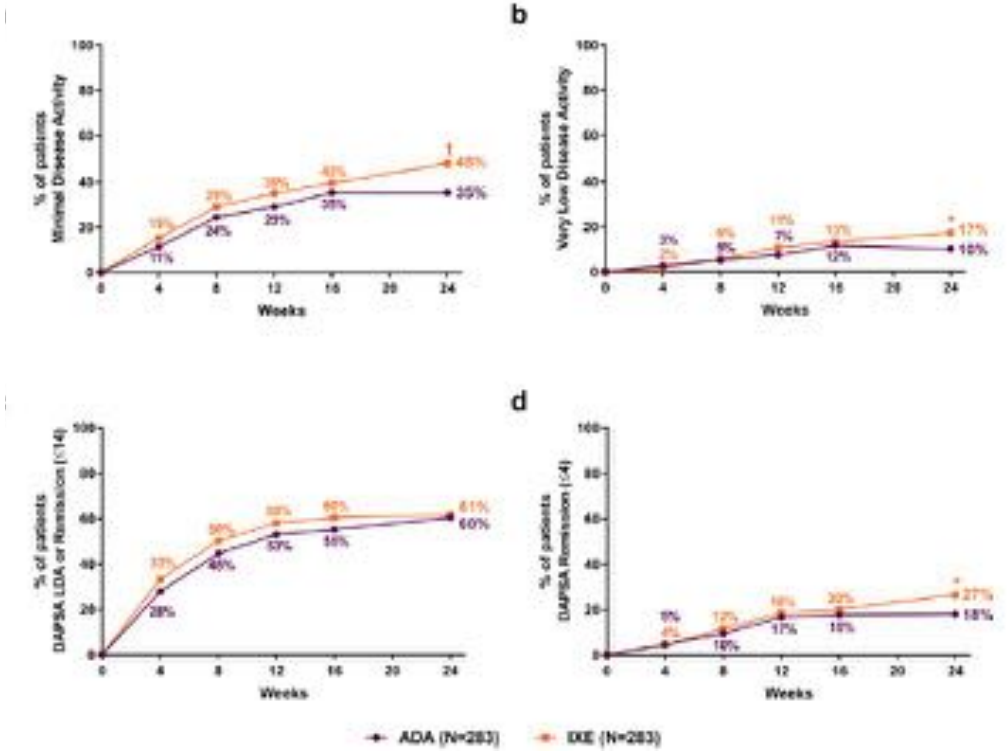
Etudes Face-Face : critère articulaire

- **anti-IL17 (Ixekizumab) vs TNFi (Adalimumab 40)**









Mease, Philip J*Annals of the Rheumatic Diseases* 79, nº 1 (janvier 2020): 123-31.

Etudes Face-Face : critère articulaire

- **JAKi (Upadacitinib) vs TNFi (Adalimumab 40)**

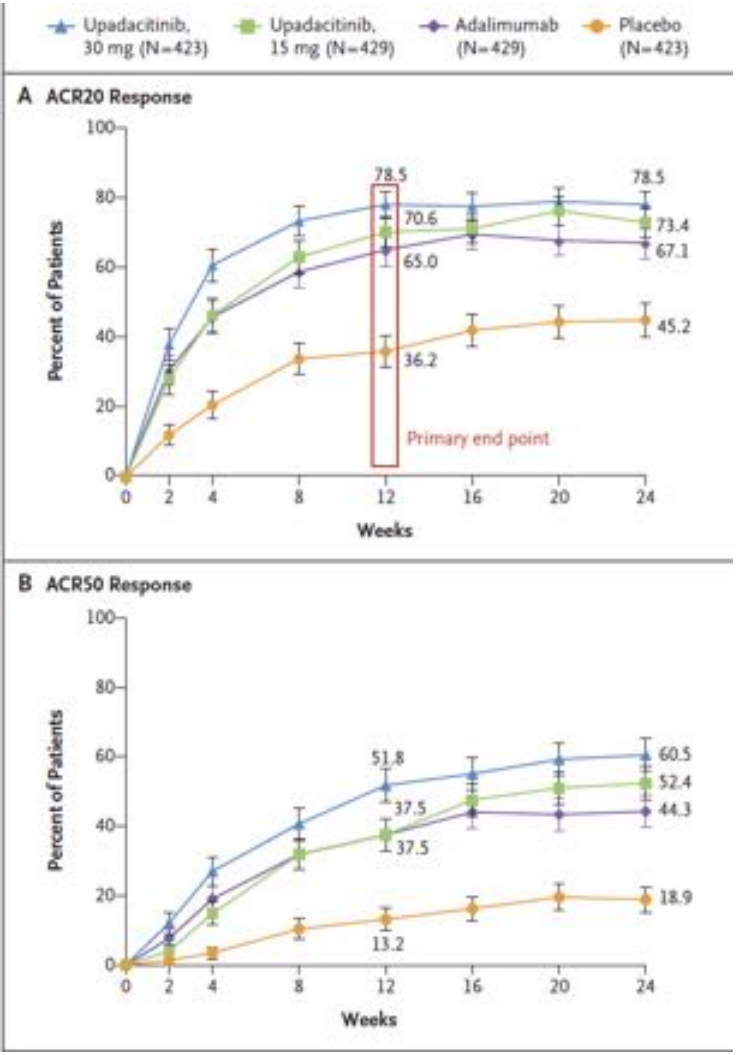


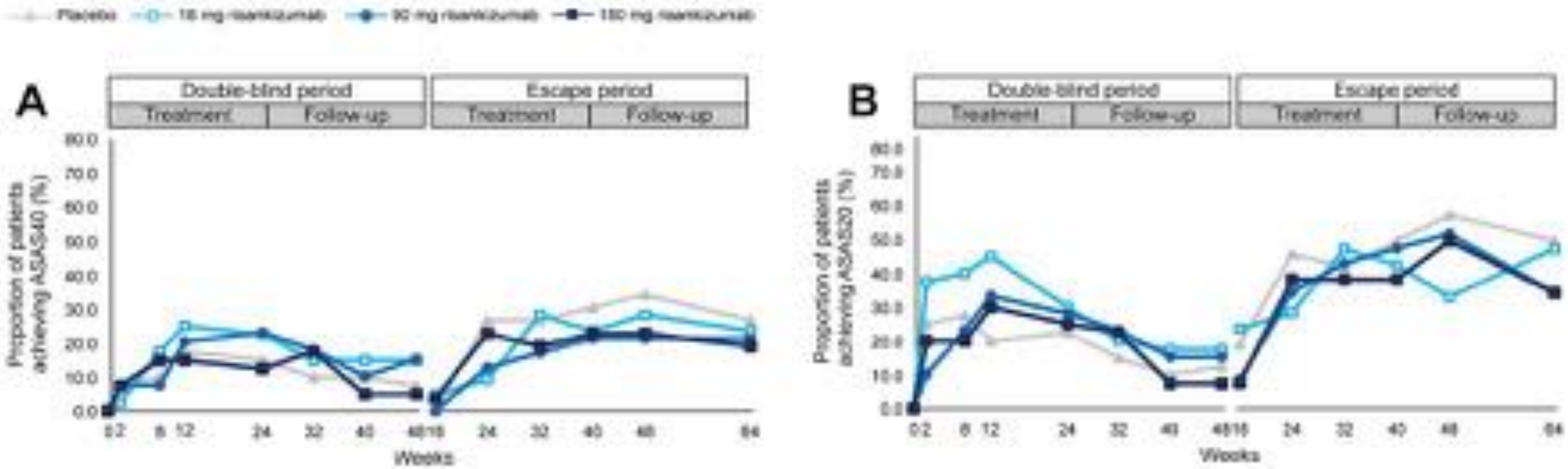
Table 2. Primary and Secondary End Points.*

End Point	Upadacitinib, 15 mg (N=429)	Upadacitinib, 30 mg (N=423)	Placebo (N=423)	Adalimumab (N=429)
PASI75 response at wk 16 — no./total no. (%) §	134/214 (62.6)	131/210 (62.4)	45/211 (21.3)	112/211 (53.1)
Difference vs. placebo — percentage points (95% CI)	41.3 (32.8 to 49.8); P<0.001	41.1 (32.5 to 49.6); P<0.001		
Minimal disease activity at wk 24 — no. (%)‖	157 (36.6)	192 (45.4)	52 (12.3)	143 (33.3)
Difference vs. placebo — percentage points (95% CI)	24.3 (18.8 to 29.8); P<0.001	33.1 (27.4 to 38.8); P<0.001		
Resolution of enthesitis at wk 24 — no./total no. (%)**	145/270 (53.7)	154/267 (57.7)	78/241 (32.4)	125/265 (47.2)
Difference vs. placebo — percentage points (95% CI)	21.3 (13.0 to 29.7); P<0.001	25.3 (16.9 to 33.7); P<0.001		
Resolution of dactylitis at wk 24 — no./total no. (%)‖‖	104/136 (76.5)	101/127 (79.5)	50/126 (39.7)	94/127 (74.0)
Difference vs. placebo — percentage points (95% CI)	36.8 (25.7 to 47.9)	39.8 (28.8 to 50.9)		

McInnes, Iain B., *New England Journal of Medicine* 384, nº 13 (avril 2021): 1227-39. https://doi.org/10.1056/NEJMoa2022516.

SpA axiale : pas d'efficacité des anti-IL23

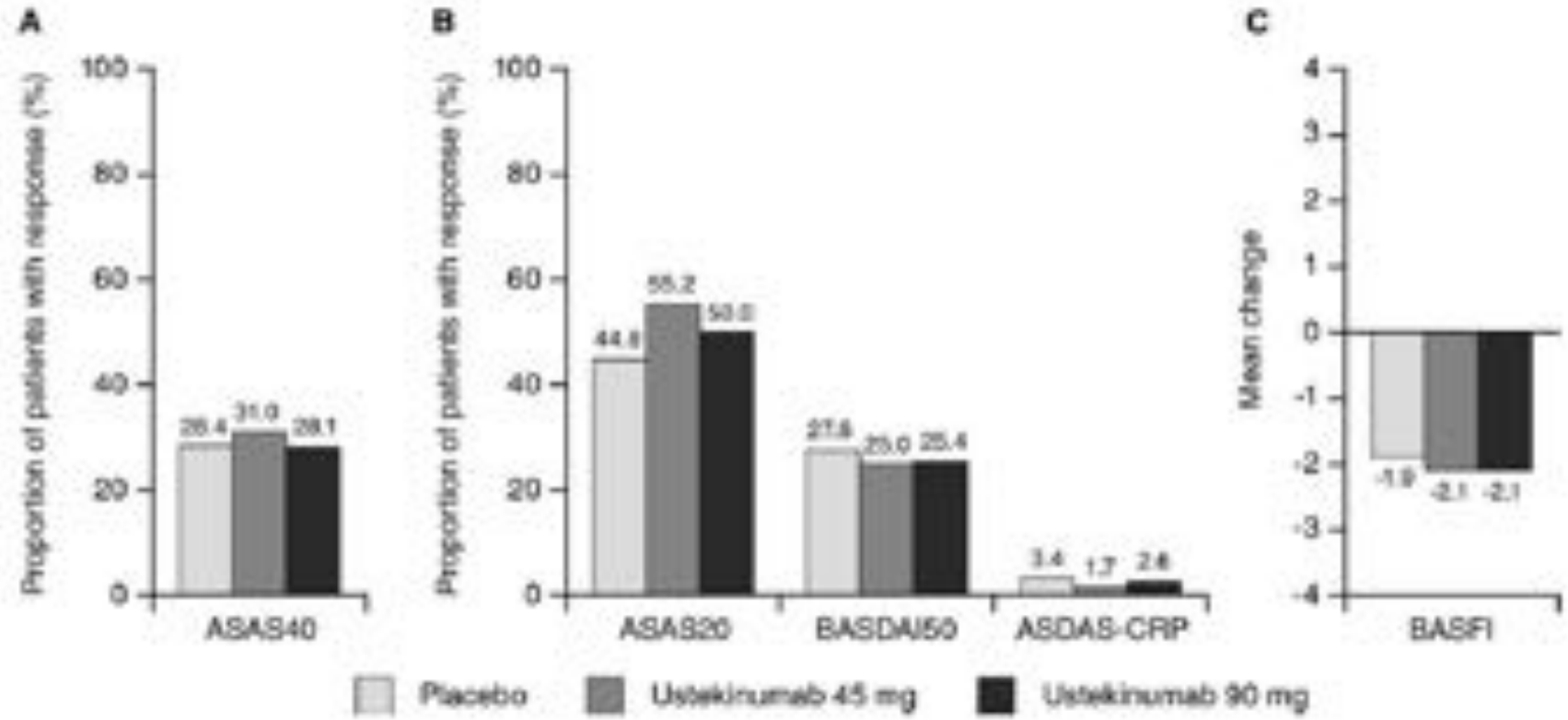
- **Risankizumab : SA radiographique naïve antiTNF**



Baeten, Dominique, *Annals of the Rheumatic Diseases* 77, nº 9 (septembre 2018): 1295-1302.

SpA axiale : pas d'efficacité des anti-IL12/23

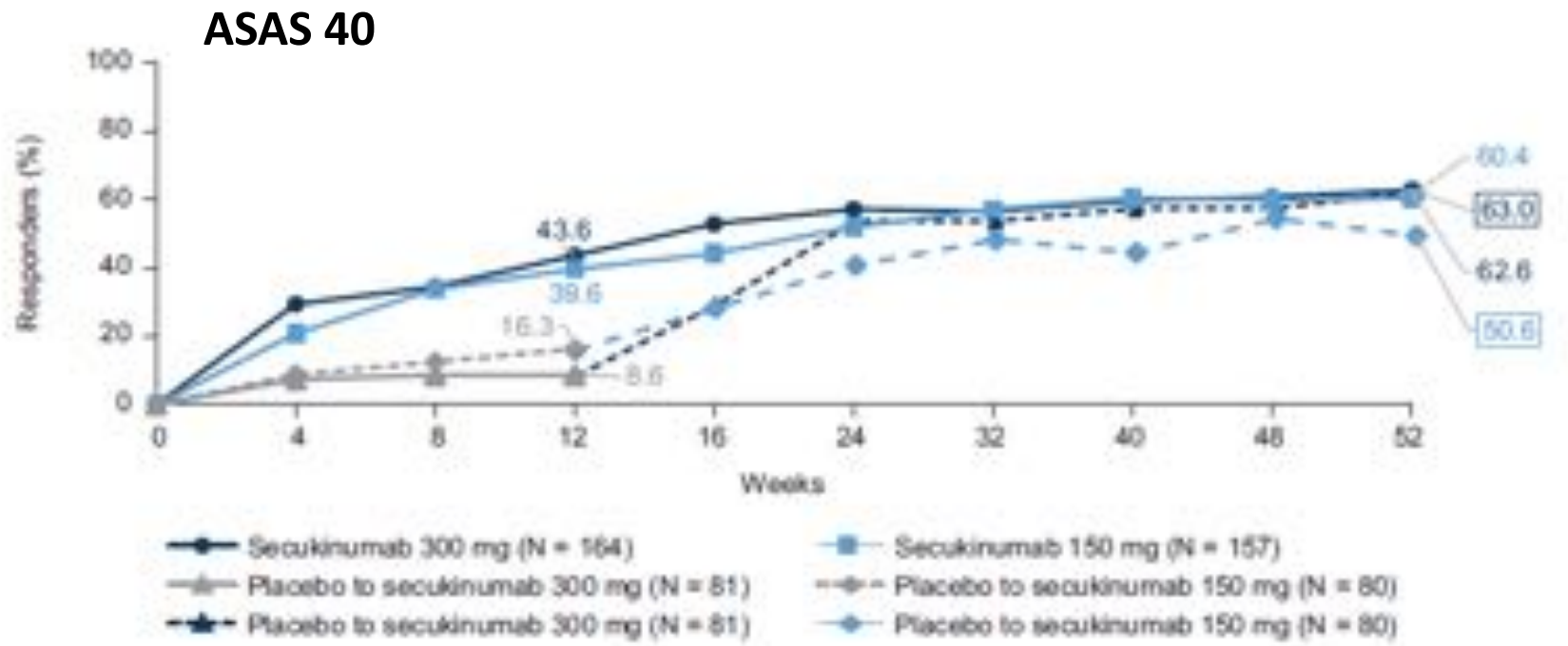
- Ustekinumab : Ax SpA radiographique et non-radiographique, naïve antiTNF



Deodhar, A. et al. Three multicenter, randomized, double- blind, placebo- controlled studies evaluating the efficacy and safety of ustekinumab in axial spondyloarthritis. Arthritis Rheumatol. 71, 258–270 (2019)

Atteinte axiale du rhumatisme psoriasique

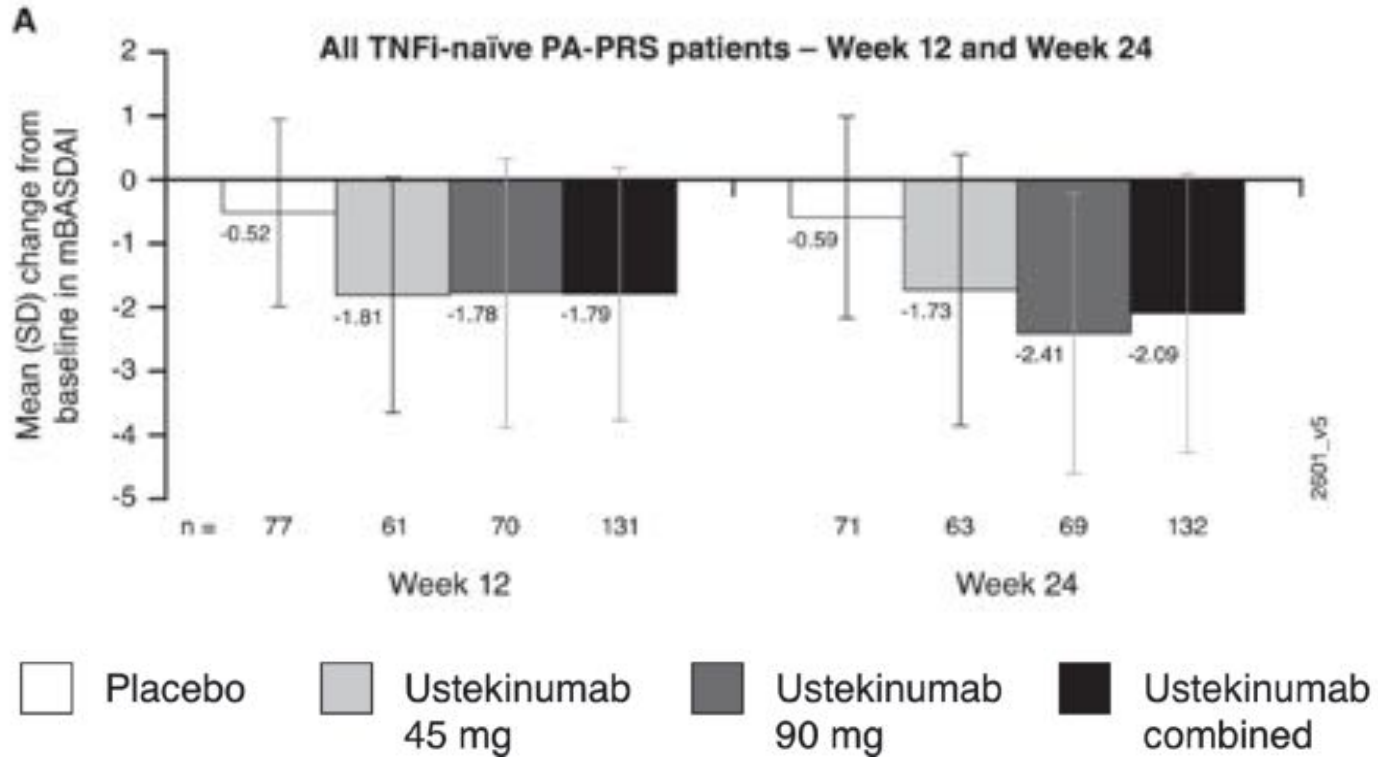
- Une seule étude spécifiquement dans le PsA avec atteinte axiale
  - Caspar, BASDAI≥40, EVA rachis > 40/100, réponse AINS insuffisante
- **Anti-IL17 : Secukinumab**



Baraliakos, X MAXIMISE trial. *Ann. Rheum. Dis.* 2020

Atteinte axiale du rhumatisme psoriasique

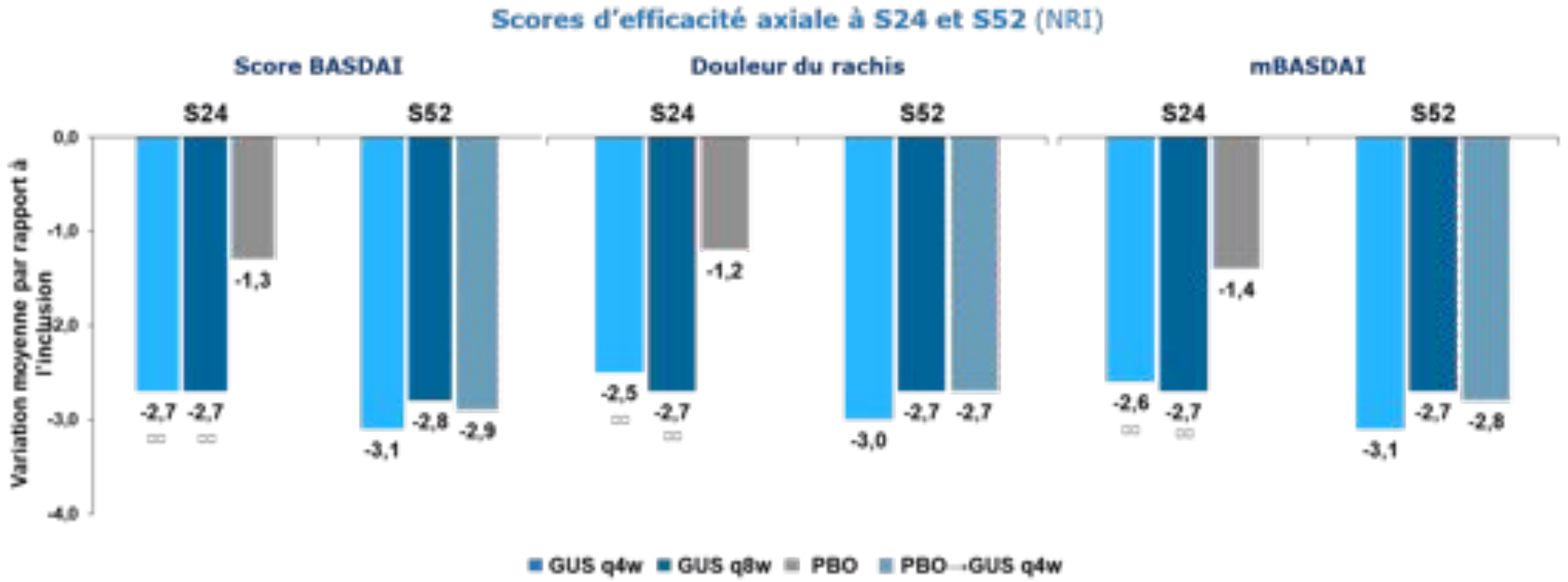
- **Données post-hoc avec Ustekinumab**
  - RCT PSUMMIT dans rhumatisme psoriasique périphérique naif anti-TNF



Helliwell, Philip S., *RMD Open* 6, nº 1 (1 février 2020): e001149.

Atteinte axiale du rhumatisme psoriasique

- **Données post-hoc avec Guselkumab**
  - RCT DISCOVERY dans le rhumatisme psoriasique périphérique, avec sacro-iliite confirmée (n=312, 28 %)



Mease et al. Lancet Rheum 2021;e-pub 29JUN; doi:10.1016/S2665-9913(21)00105-3

Atteinte axiale du rhumatisme psoriasique

- **Etude STAR avec Guselkumab en cours de recrutement**

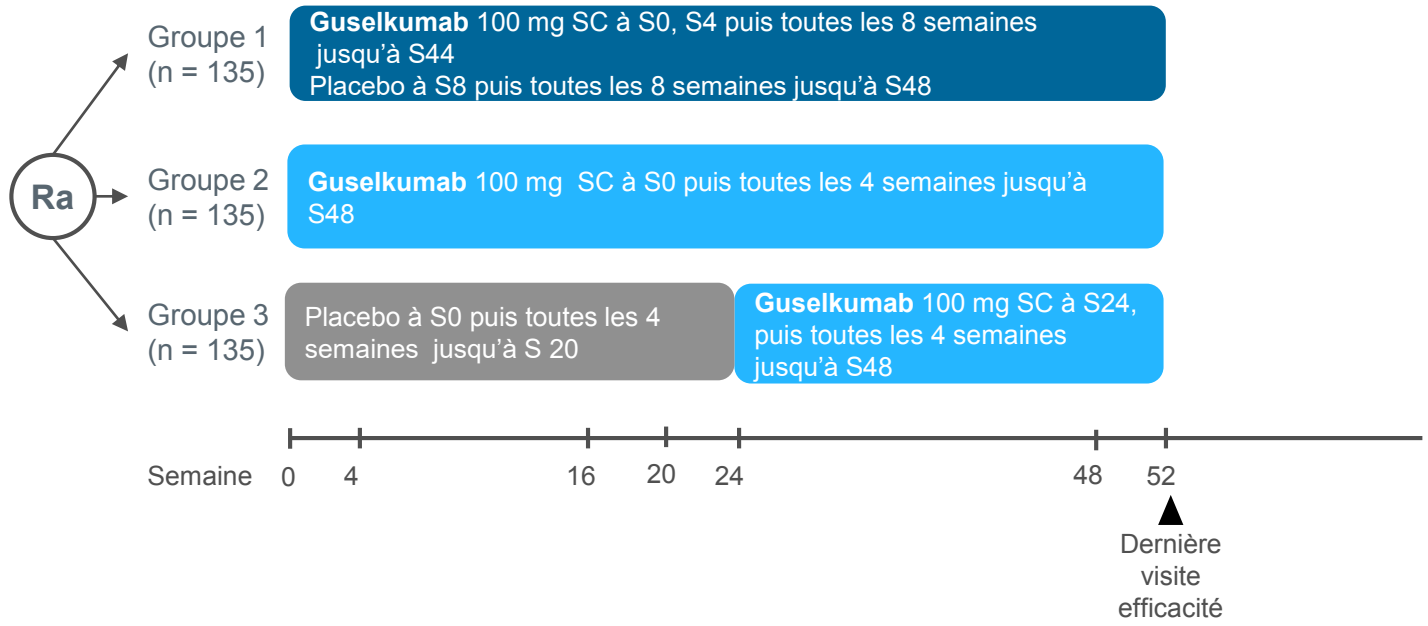
Critères d'inclusion

- **CASPAR***
- **≥ 3 NAG et ≥ 3 NAD**
- **CRP ≥ 0,3 mg/dL**
- **BASDAI ≥ 4**
- **Score EVA rachis ≥ 4**
- **Atteintes axiales du RhPsO confirmée par IRM****
- psoriasis en plaques actif (Ø ≥2cm) ou atteinte de l'ongle ou un historique de psoriasis

405 sujets bio-naïfs avec un RhPsO axial actif

Critère Primaire

Amélioration du BASDAI à S24

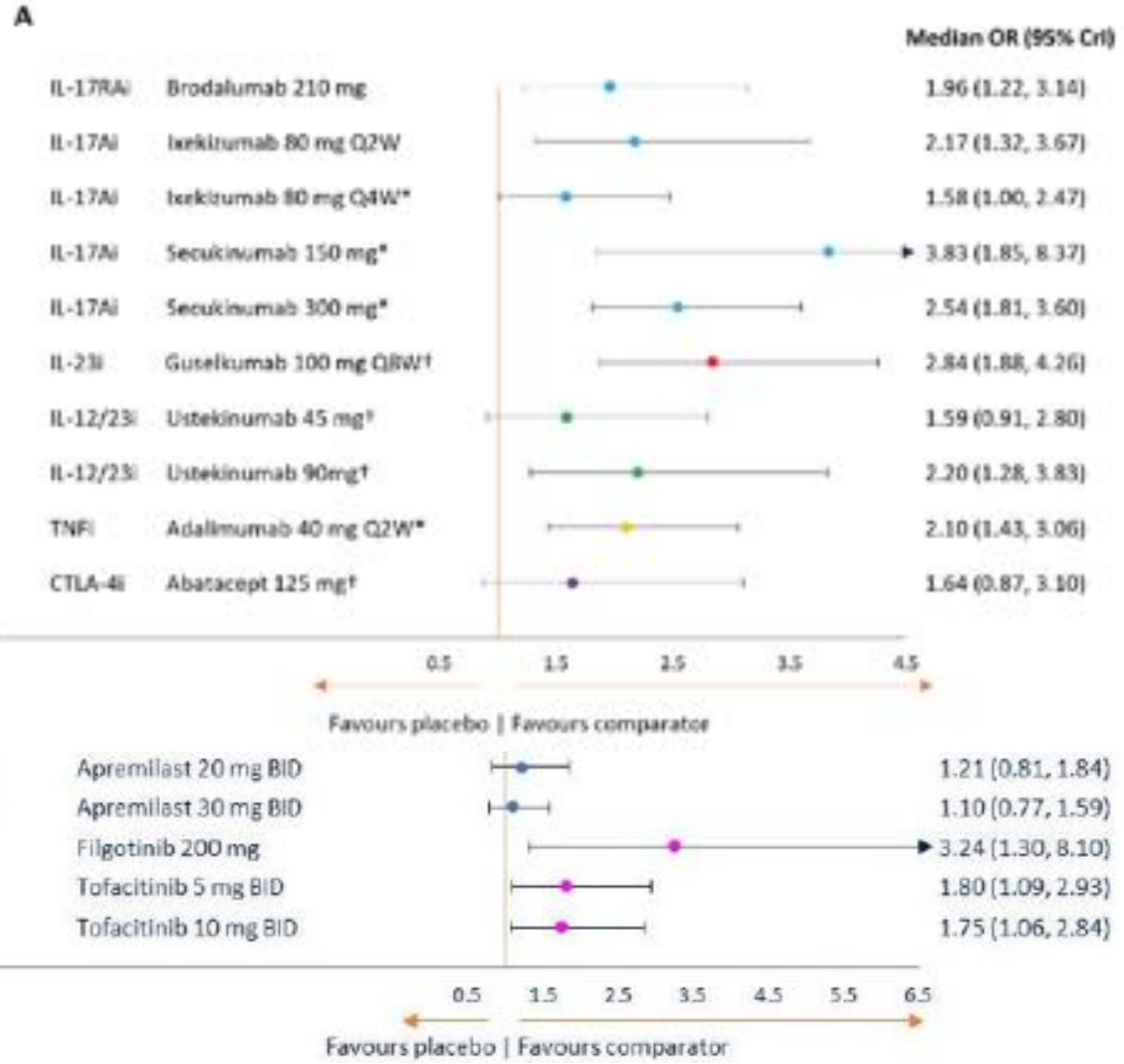


Enthésites, dactylites: Face-Face

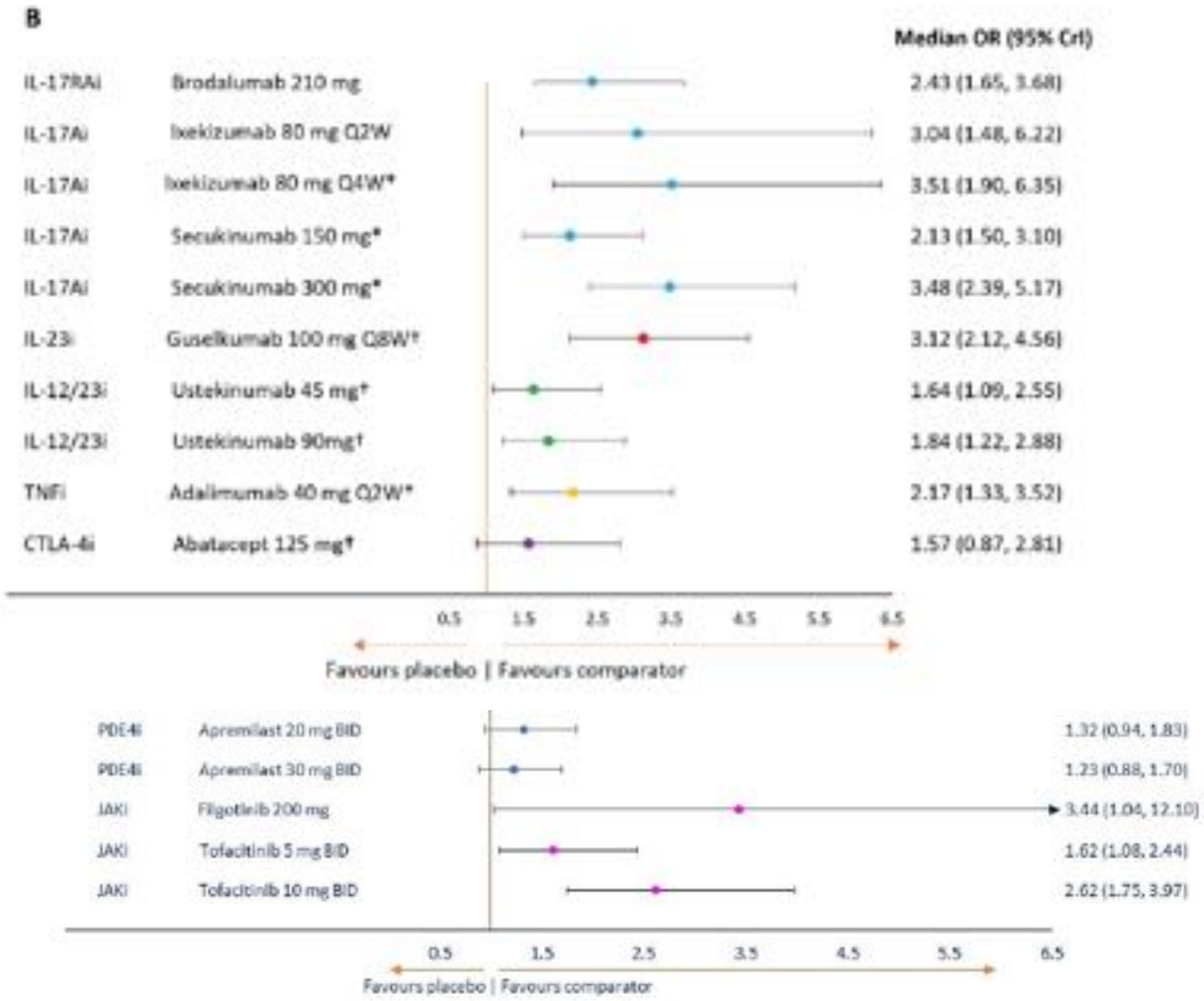
- **Pas de différence: anti-IL17, TNFi, IL12/IL23, upadacitinib**
- **Pas de différence MTX vs ETA (SEAM)**

Méta-analyse tsDMARDs

- **Enthésites**

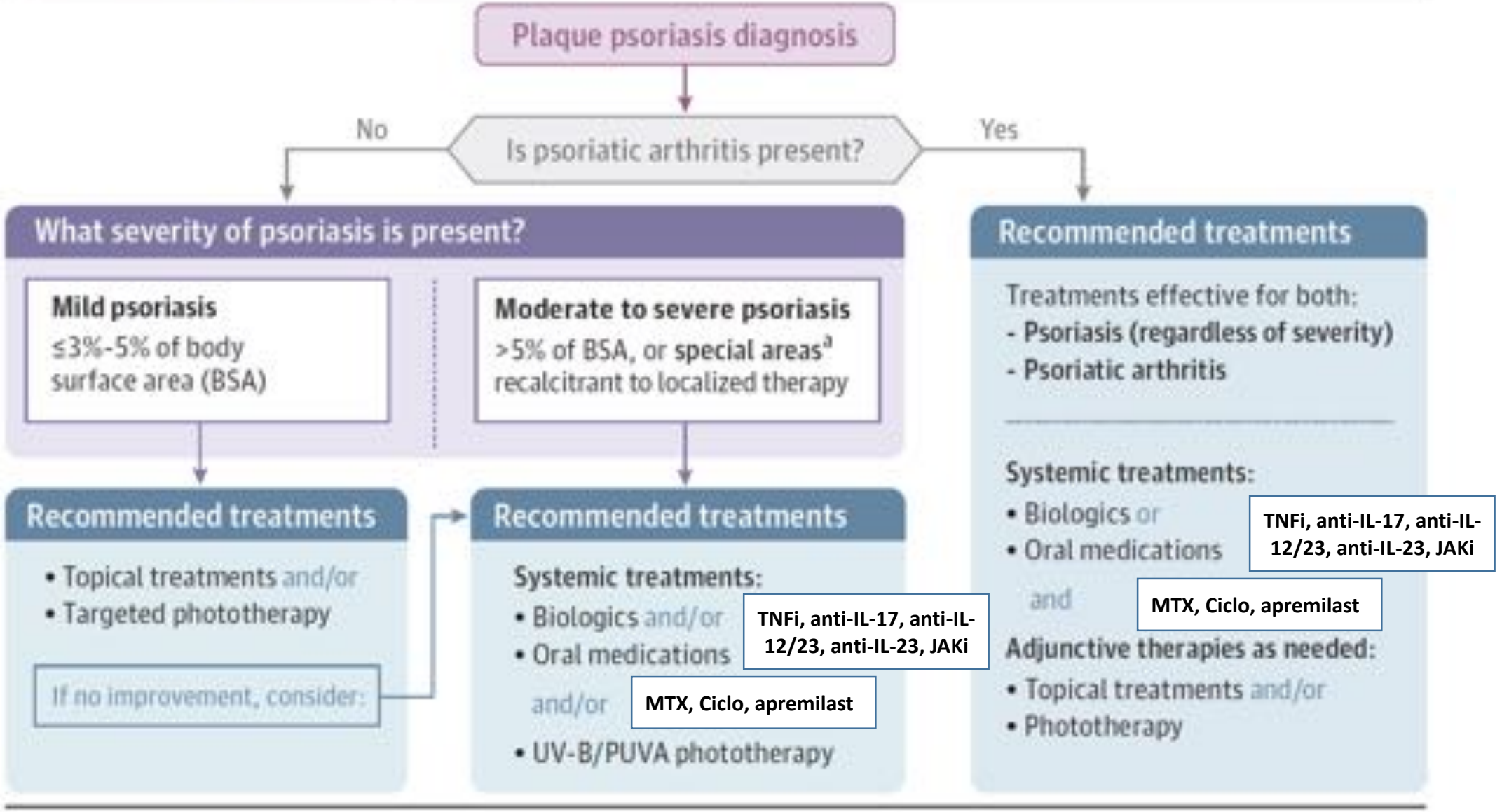


- **Dactylites**



McInnes, Iain B., *RMD Open* 8, nº 1 (mars 2022): e002074.

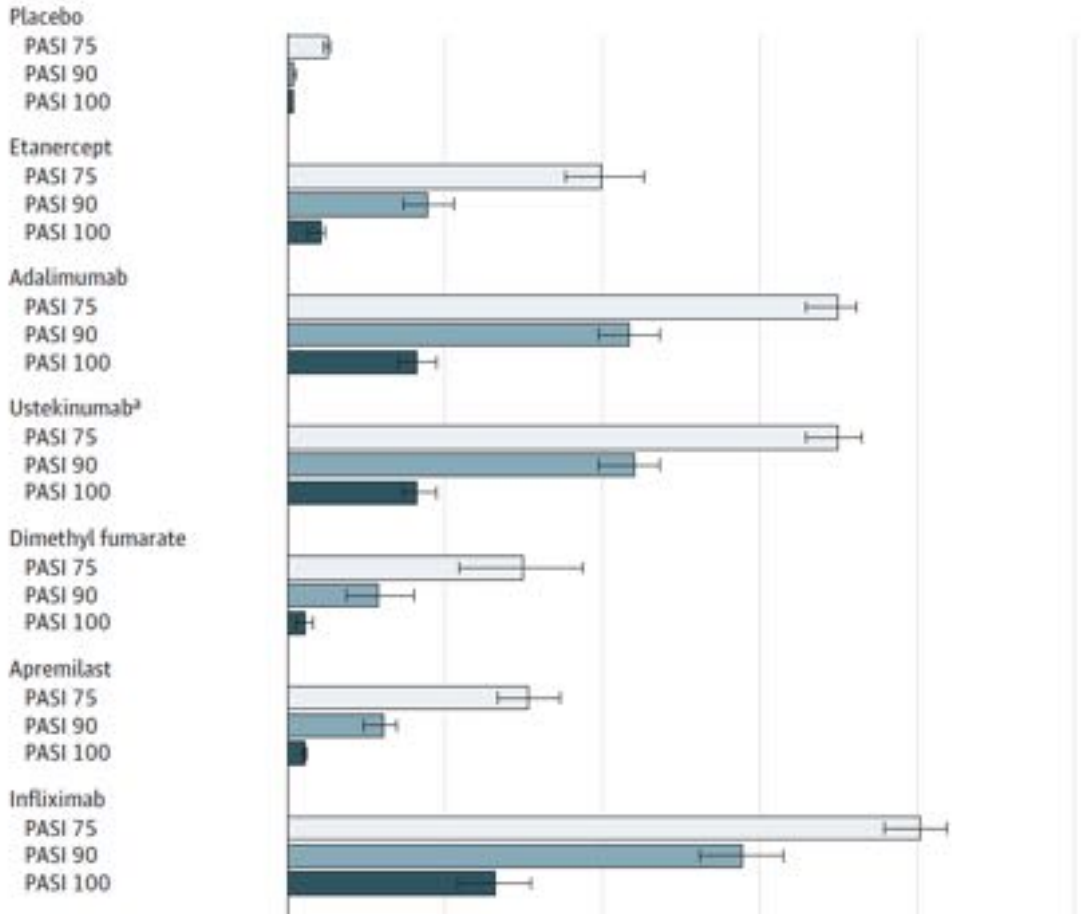
Figure 3. Overall Treatment Approach for Plaque Psoriasis

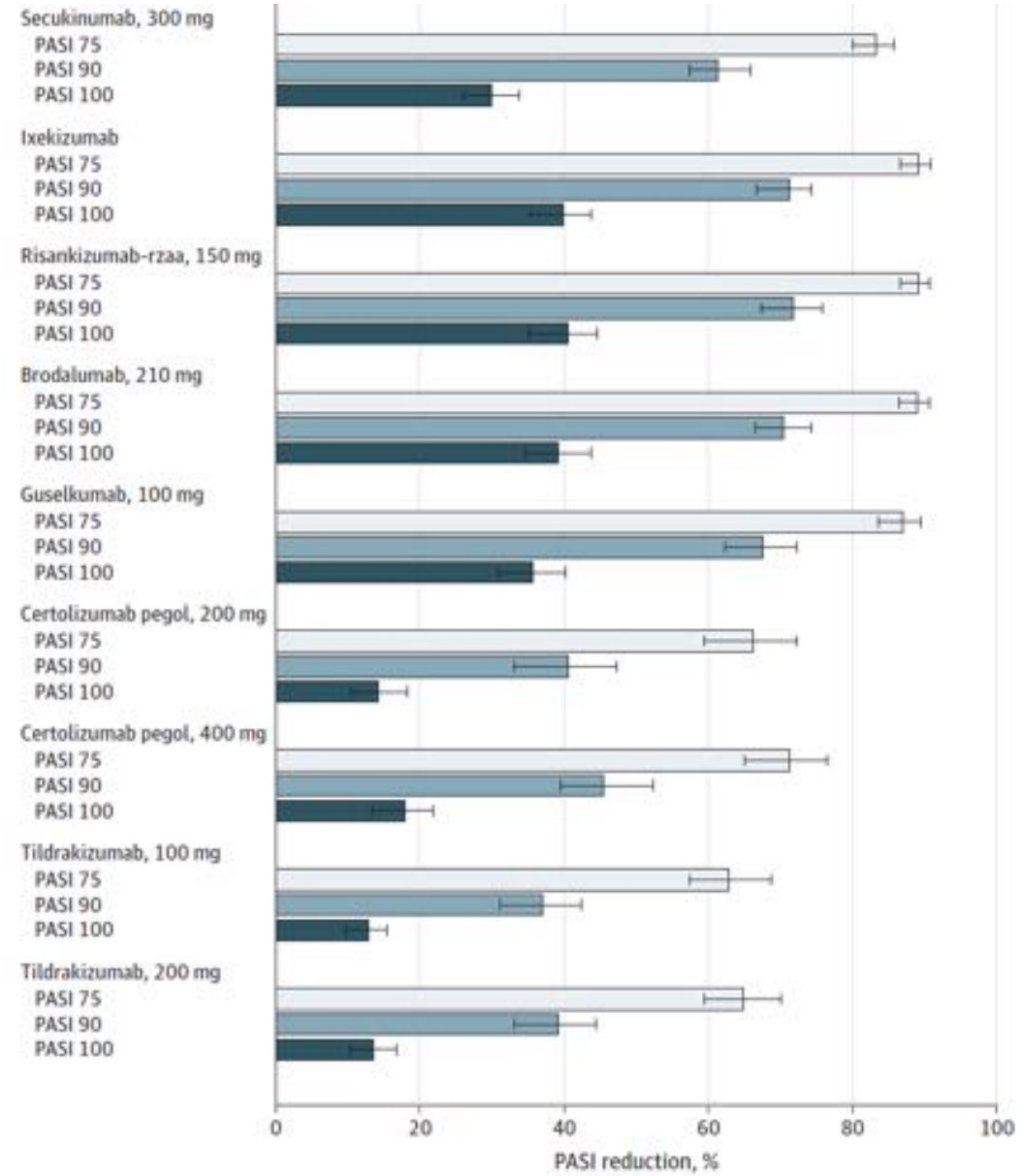


Armstrong, *JAMA* 323, nº 19 (19 mai 2020): 1945. https://doi.org/10.1001/jama.2020.4006.

Données des essais randomisés contre placebo
Psoriasis bDMARDs

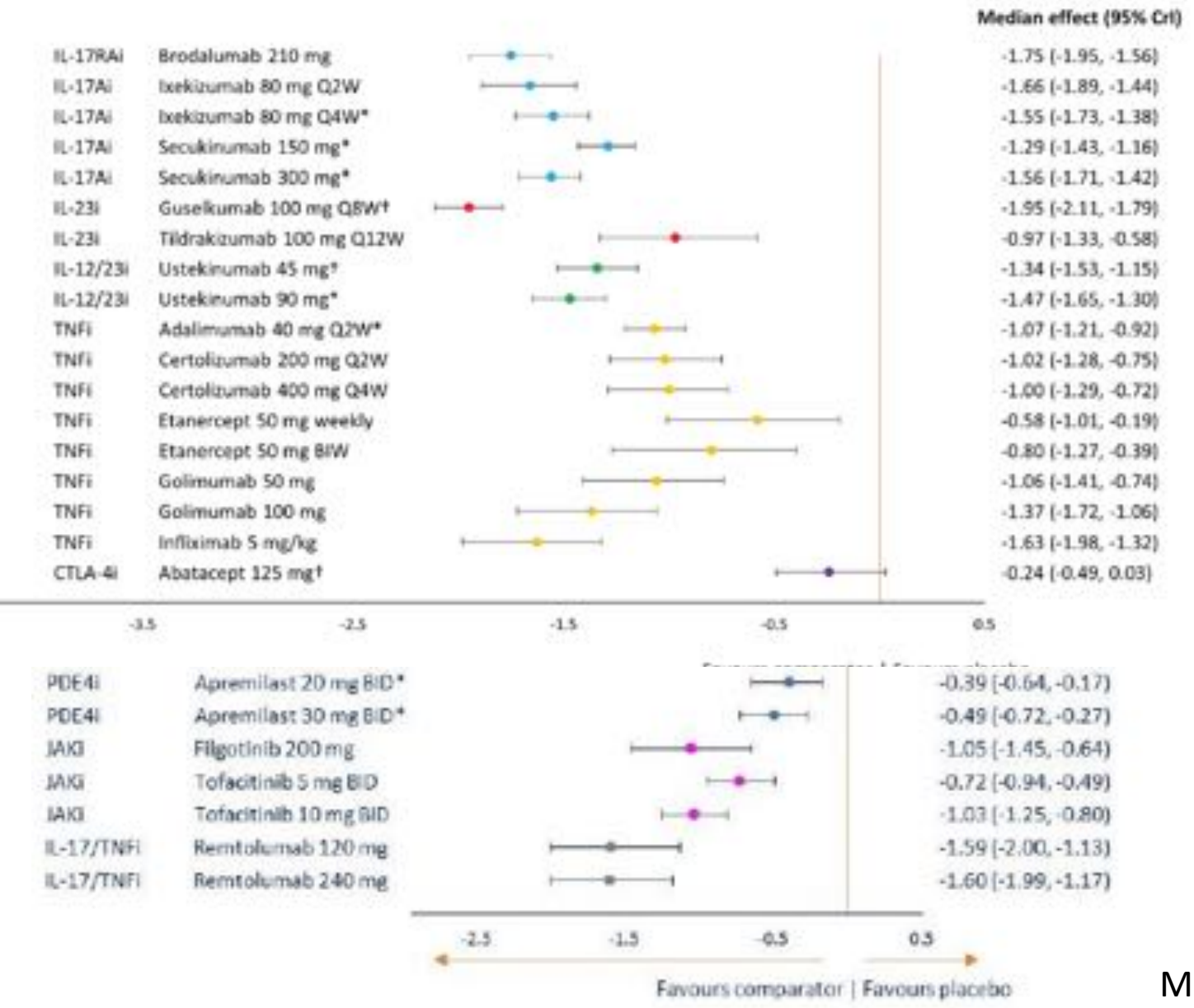
Figure 4. Comparison of PASI 75/90/100 Short-term Response Rates in US FDA-Approved Oral Systemics and Biologics for Psoriasis





Armstrong, *JAMA* 323, nº 19 (19 mai 2020): 1945.

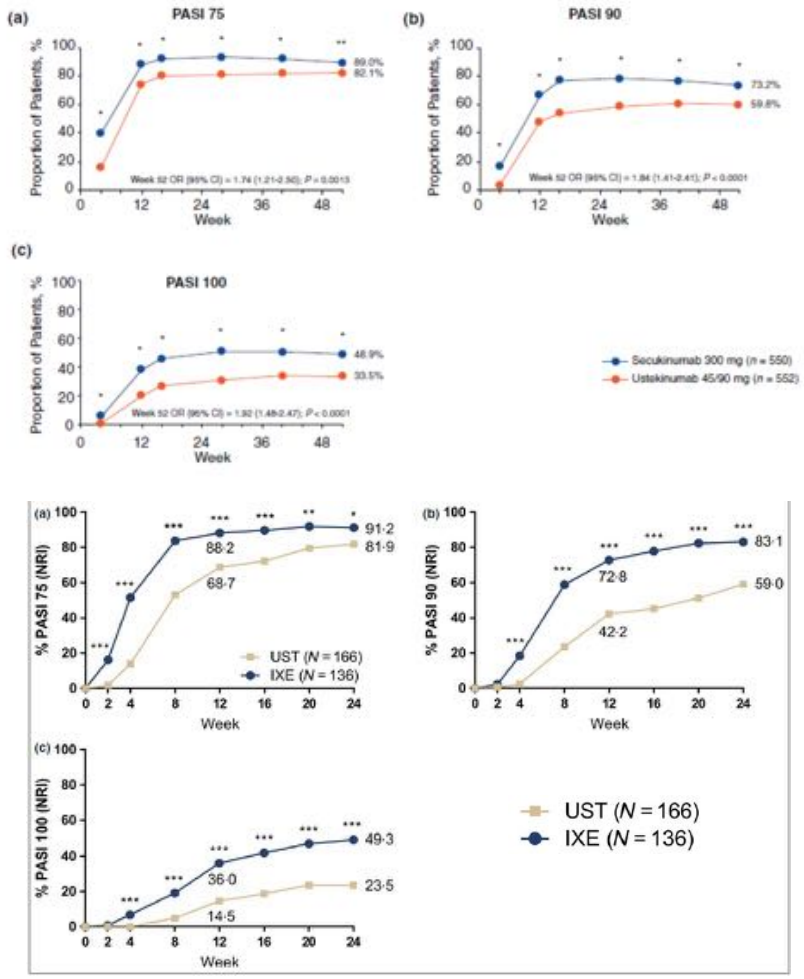
Méta-analyse tsDMARDs - PASI



McInnes, Iain B., *RMD Open* 8, nº 1 (mars 2022): e002074.

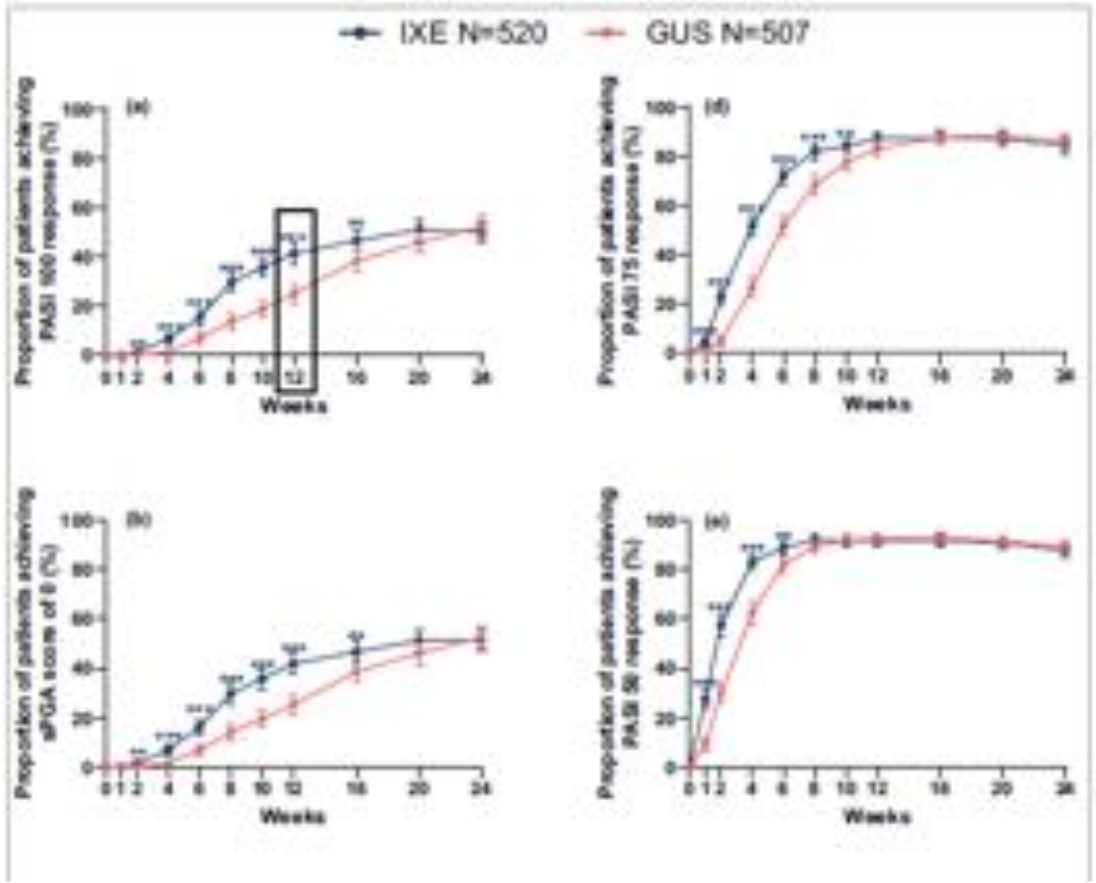
Etudes Face-Face psoriasis

- **Anti-IL17 > Ustekinumab**



Bagel, J., *Journal of the European Academy of Dermatology and Venereology. 2021*: 135-42.
Reich, K., *The British Journal of Dermatology* 177, nº 4 (octobre 2017): 1014-23.

- **Ixekizumab = guselkumab**



Blauvelt, A., C. *The British Journal of Dermatology* 184, nº 6 (juin 2021): 1047-58.

En cas d'autres MEA

- **MICI**
  - Efficacité anti-TNF: RCH, Crohn
  - Anti-IL12/IL23, Ustekinumab : RCH, Crohn
  - JAKi: Tofacitinib (RCH), Upadacitnib (RCH, *Crohn*), Filgotinib (*RCH*)
  - *Anti-IL23 : Guselkumab, risankizumab (Crohn)*

- **Uveites**
  - MTX
  - TNFi hors etanercept: adalimumab

Prise en compte des comorbidités

- **Risque cardiovasculaire**
  - Anti-TNF: rôle protecteur
  - Anti-IL17, anti-IL23 ?
  - JAKi : à éviter

- **PRAC EMA, toute la classe JAKi, utilisation en cas d'absence d'alternative thérapeutique si:**
  - 65 ans ou plus
  - Tabagisme actuel ou ancien de durée longue
  - FDR CV, FDR cancer

Précaution pour risque thrombo-embolique

Conclusions

- **MTX, LEF, SLZ:** 1ére ligne si atteinte articulaire
- **Pour l'atteinte articulaire, enthésites, dactylites**
  - Efficacité similaire: anti-TNF, anti-IL17, anti-IL23, JAKi
    - anti-IL12/IL23, aprémilast, abatacept
  - Association avec MTX non systématique
- **Si atteinte axiale**
  - Anti-TNF, anti-IL17 (Secukinumab, Ixekizumab), JAKi (Tofacitinib, Upadacitinib)
- **Si psoriasis modéré associé**
  - Anti-IL17, anti-IL23
- **Si MICI**
  - Anti-TNF, anti-IL12/IL23, JAKi, anti-IL23
- **Si uvéites**
  - Anti-TNF (sauf etanercept)
- **Précaution d'utilisation pour JAKi**