Réunion bibliographique
Septembre 2019
Rhumatisme psoriasis et psoriasis

Emmanuelle DERNIS

Un grand merci aux internes du semestre :
Emeline Vignaud , Hélène Racapé, Samuel Rocour et Quentin Grudé

Rhumatologie

Epidémiologie

Prevalence of psoriatic arthritis in patients with psoriasis: A systematic review and meta-analysis of observational and clinical studies

Farzad Alinaghi, MD,[a] Monika Calov, MD,[a] Lars Erik Kristensen, MD, PhD,[b] Dafna D. Gladman, MD, FRCPC,[c] Laura C. Coates, MBChB, MRCP, PhD,[d] Denis Jullien, MD, PhD,[e] Alice B. Gottlieb, MD, PhD,[f] Paolo Gisondi, MD,[g] Jashin J. Wu, MD,[h] Jacob P. Thyssen, MD, PhD, DMSc,[a] and Alexander Egeberg, MD, PhD[a]

Copenhagen, Denmark; Toronto, Ontario, Canada; Oxford, United Kingdom; Lyon, France; New York, New York; Verona, Italy; and Los Angeles, California

Published online June 18, 2018.
0190-9622/$36.00

https://doi.org/10.1016/j.jaad.2018.06.027

Epidémiologie

- Rhumatisme psoriasique (*Psoriatic arthritis*, PsA)
- Critères diagnostiques :
  - **Moll & Wright**, 1973 : Semin Arthritis Rheum 1973;3:55-78.
  - **CASPAR** , 2006 :
  - Et bien d'autres …

- Manque de critères validés et largement acceptés → grande variabilité d'estimation du PsA, notamment parmi patients avec pso.
- Objectif : estimer la prévalence exacte du PsA parmi les patients ayant un psoriasis cutané

Méthodes

- Méta-analyse conduite selon les critères **PRISMA**
- Protocole *a priori*
- Articles éligibles :
  - < Novembre 2017
  - 3 bases de données : PubMed / Web of Science / EMBASE
  - Mots-clés : psoriasis / psoriasis arthritis *or* arthropathy / incidence / prevalence
- Critères :

INCLUSION	EXCLUSION
Article **original**	Rhumatisme non spécifié
En **anglais**	Etudes portant sur AJI
Pop. source de patients avec **pso. cutané**	
Nb absolu ou % de cas de **PsA**	

Résultats

- Au total :
  - 266 études incluses dans la MA
  - Soit **976 408 patients**

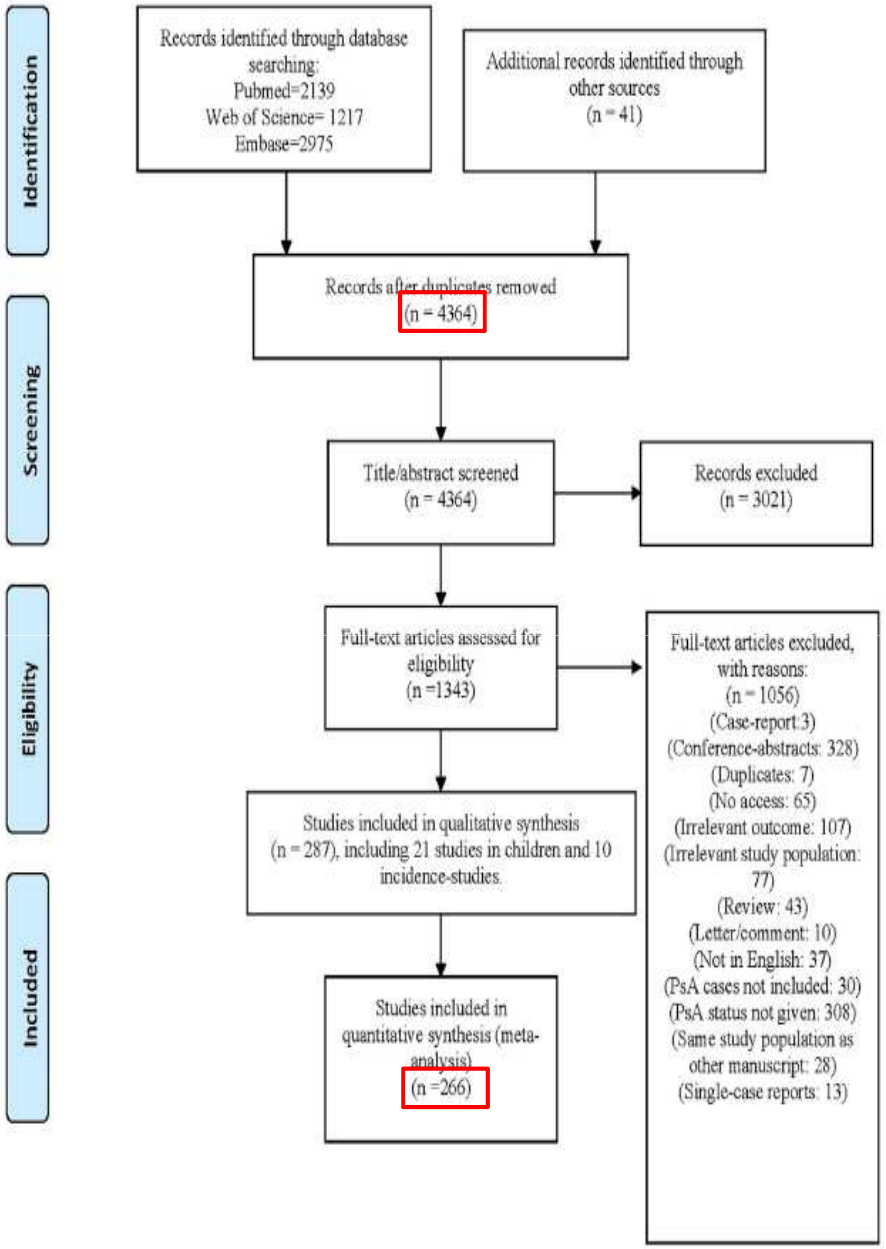


Fig 1. PRISMA flow chart.

Variation de la prévalence

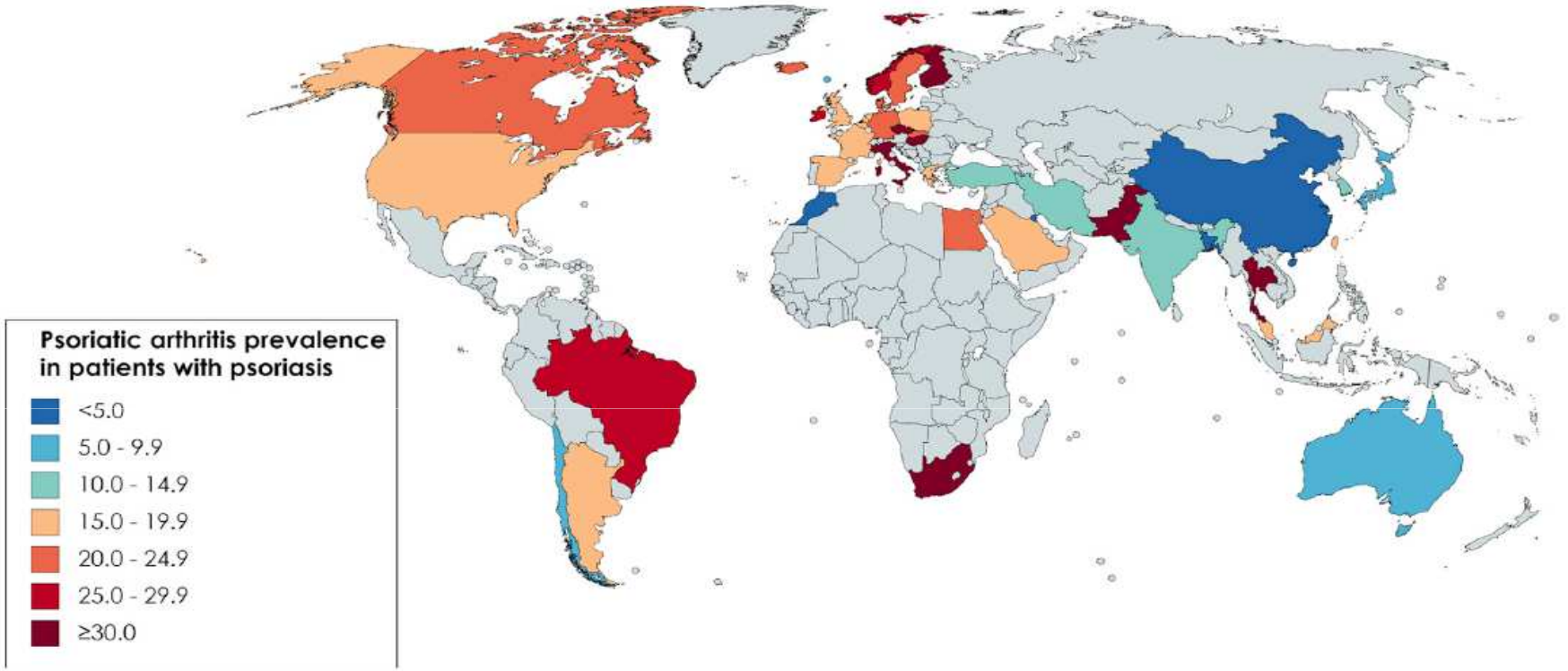


Fig 2. Worldwide prevalence of psoriatic arthritis among patients with psoriasis. Number of studies included per country: Argentina (n = 2), Australia (n = 1), Bangladesh (n = 1), Belgium (n = 1), Brazil (n = 7), Canada (n = 8), Chile (n = 1), China (n = 5), Czech Republic (n = 1), Denmark (n = 5), Egypt (n =1), Faroe Islands (n = 1), Finland (n = 2), France (n = 7), Germany (n = 12), Greece (n = 5), Hungary (n = 1), Iceland (n = 2), India (n = 15), Iran (n = 2), Ireland (n = 1), Israel (n = 1), Italy (n = 36), Japan (n = 5), Kuwait (n = 1), Macedonia (n = 1), Malaysia (n = 1), Morocco (n = 1), Netherlands (n = 11), Norway (n = 2), Pakistan (n = 2), Poland (n=4), Saudi Arabia (n = 1), Scotland (n = 1), Slovakia (n = 1), South Africa (n = 1), South Korea (n = 3), Spain (n = 17), Sweden (n = 8), Taiwan (n = 3), Thailand (n = 4), Turkey (n = 15), United Kingdom (n = 10), United States (n = 36).

Prévalence

Résultats - **Prévalence**

Prévalence globale du PsA : **19,7%** [18,5 – 20,9]

Table I. Prevalence estimates according to different population characteristics

Group	Number of studies	Prevalence	95% CI
All studies	266	19.7%	18.5%-20.9%
Men	36	23.3%	19.4%-27.5%
Women	36	24.0%	20.1%-28.1%
Children	21	3.3%	2.1%-4.9%
Adults	245	21.6%	20.3%-22.9%
Studies using CASPAR	45	23.8%	20.1%-27.6%
Studies using Moll and Wright	20	24.1%	15.0%-34.5%
Mild disease*	58	15.8%	14.3%-17.2%
Moderate-to-severe disease**	122	24.6%	22.9%-26.4%
Population size: < 500	173	22.2%	20.0%-24.4%
Population size: 500-1000	35	18.5%	15.0%-22.3%
Population size: ≥ 1000	57	14.4%	12.5%-16.3%
Publication year (pre-2000)	13	22.0%	16.1%-28.5%
Publication year (2000-2009)	51	16.5%	13.1%-20.3%
Publication year (2010-2017)	202	20.4%	19.1%-21.8%
Study design (clinical)	34	22.9%	20.7%-25.2%
Study design (observational)	160	20.7%	18.3%-23.2%
Study design (register-based)	48	15.1%	13.3%-17.1%
Study design (population-based)	46	15.6%	13.7%-17.7%
Continent (Europe)	119	22.7%	20.6%-25.0%
Continent (Asia)	59	14.0%	11.7%-16.3%
Continent (North America)	47	19.5%	17.1%-22.1%
Continent (South America)	10	21.5%	15.4%-28.2%
Continent (Africa)	3	15.5%	0.009%-51.5%

*BSA/PASI < 10
**BSA/PASI ≥ 10

Incidence

Résultats – Incidence

Seulement 10 études

Hétérogénéité des résultats

- Wilson et al, 2009 [1] :
  - Taux d'incidence : 2,7/1000 personnes-années
  - I cumulées : 1,7% 5 ans / 3,1% 10 ans / 5,1% 20 ans
- Li et al, 2012 [2] : I annuelle = 2,1%
- Love et al, 2012 [3] : taux d'I = 26,5/10 000 PA
- Christophers et al, 2010 [4] : I cumulée = 13% à 20 ans
- Eder et al, 2011 [5] : taux d'I = 1,9/100 PA
- De Marco et al, 2012 [6] : I moyenne = 1,7% (à 3 ans)
- Tinazzi et al, 2012 [7] : I cumulée = 8,4% à 1 an
- Brunasso et al, 2011 [8] : taux d'I = 22,7/1000 PA
- Abji et al, 2016 [9] : I cumulée = 8,4% à 8 ans
- Eder et al, 2016 [10] : taux d'I = 2,7/100 PA

(1)Arthritis Care Res. 2009;61(2):233-239.
(2)Ann Rheum Dis. 2012;71(8):1267-1272.
(3)Ann Rheum Dis. 2012;71(8):1273-1277.
(4)J Eur Acad Dermatol Venereol. 2010;24(5):548-554.
(5)Arthritis Care Res. 2011; 63(4):619-622.
(6)Arch Dermatol Res. 2012;304(9):719-726.
(7)Rheumatology. 2012; 51(11):2058-2063.
(8)Acta Derm Venereol. 2011;91(1):44-49.
(9)Arthritis Rheum. 2016;68(12):2911-2916.
(10)Arthritis Rheum. 2016;68(4):915-923.

Conclusion de la méta analyse

- Prévalence globale du PsA si psoriasis := **19,7% (1/5)** sur presque 1M de pts
  Equivalente dans les deux sexes
  - Bien + faible si < 18 ans : 3,3% (diagnostic entre PsA et AJI / PsA avant pso.)
  - ↗ avec la sévérité du psoriasis
  - Variations géographiques (HLA / peu d'études Africaines)

- Estimation de **l'incidence** du PsA chez les patients pso :
  - Peu d'études : seulement 10 … sur 266 sélectionnées
  - Hétérogénéité des résultats : **0,27 à 2,7/100 PA ….**

- Haut degré d'hétérogénéité *inter*-études (I^2 = 99,5%)
  - Manque de critères de classification validés par le passé ?
  - Variations de dessin, origines géographiques **…**

ORIGINAL ARTICLE

Metabolic syndrome and psoriatic arthritis among patients with psoriasis vulgaris: Quality of life and prevalence

Cacilda S. SOUZA,[1] Caio C. S. de CASTRO,[2] Francisca R. O. CARNEIRO,[3] Jane M. N. PINTO,[4] Lincoln H. Z. FABRICIO,[5] Luna AZULAY-ABULAFIA,[6] Ricardo ROMITI,[7] Tania F. CESTARI,[8] Cláudia E. SUZUKI,[9] Priscila M. BIEGUN,[9] Luciana S. GUEDES,[10] Luiza K. M. OYAFUSO[11]

This was a cross-sectional observational study conducted in nine tertiary centers, located in southeastern, southern and northern Brazilian regions, specializing in PsO treatment, in the following Brazilian cities (with respective states): São Paulo, Santo André and Ribeirão Preto (state of São Paulo); Rio de Janeiro and Niterói (state of Rio de Janeiro); Curitiba (state of Paraná); Porto Alegre (state of Rio Grande do Sul); and Belém

Table 1. Sociodemographic and clinical characteristics of patients with plaque-type psoriasis in a Brazilian population (n = 293)

Characteristics	n	%
Age		
Mean ± SD	52.0 ± 12.8	–
Sex		
Male	152	51.9
Female	141	48.1
Race		
Caucasian/white	199	67.9
Brown	79	27.0
Black	13	4.4
Asian	1	0.3
Indigenous	1	0.3
Educational level		
No education	3	1.0
Incomplete elementary school	75	25.6
Complete elementary school	33	11.3
Incomplete high school	31	10.6
Complete high school	83	28.3
Incomplete college and/or university degree	21	7.2
Complete college and/or university degree	36	12.3
Post-graduate	11	3.7
Family history		
MetS	46	15.7
PsA	13	4.4
Employment status		
Employed	92	31.4
Retired	87	29.7
Autonomous worker	66	22.5
Unemployed	22	7.5
Housewife	13	4.4
Student	9	3.1
Other[†]	4	1.4
Monthly household income ($US)		
Mean ± SD	774.29 ± 687.85	–
PASI		
PASI score, mean ± SD	7.3 ± 8.4	–
PASI score >10	219	74.7
BSA		
BSA involvement %, mean ±SD	12.7 ± 15.8	–
BSA involvement >10	212	72.4
DLQI score		
DLQI score, mean ± SD	6.5 ± 6.9	–
DLQI score >10	65	22.2
Severity of psoriasis (defined as Finlay's Rule of Tens)		
Severe psoriasis (PASI score >10 and/or DLQI score >10 or BSA involved >10%)	244	83.3
Mild to moderate psoriasis	49	16.7
Smoking		
Non-smokers	131	44.7
Current	49	16.7
Past	113	38.6
Length of abstinence in years (n = 113), mean ± SD	15 ± 10.4	–
No. of cigarettes per day (n = 162), mean ± SD	19.3 ± 18.5	–
"How long have you been smoking?", years (n = 162), mean ± SD	22.3 ± 13.9	–
Alcoholism		
Non-drinkers	188	64.2
Drinkers	105	35.8
Frequency of alcohol consumption (n = 105)		
<1 per week	57	54.3
Once per week	20	19
Twice per week	16	15.2
3 times a week	5	4.8
4 times a week	1	1.0
5 times a week	1	1.0
6 times a week	1	1.0
7 times a week	3	2.9
No information	1	1.0
"How long have you been drinking?", years (n = 105), mean ± SD	28.6 ± 14	–
Physical activity		
Sedentary	98	33.4
Currently physically active	101	34.5
Physically active in the past	94	32.1
Time (years) without practicing (n = 94), mean ± SD	7.2 ± 7.8	–
Frequency of physical activity (n = 195)		
Once per week	26	13.3
Twice per week	39	20
3 times a week	47	24.1
4 times a week	15	7.7
5 times a week	40	20.5
6 times a week	5	2.6
7 times a week	23	11.8
"How long have you been practicing physical activity?", years, mean ± SD	10 ± 12.5	–

[†]Off work (n = 2) and pensioner (n = 2). BSA, body surface area; DLQI, Dermatology Life Quality Index; MetS, metabolic syndrome; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; SD, standard deviation.

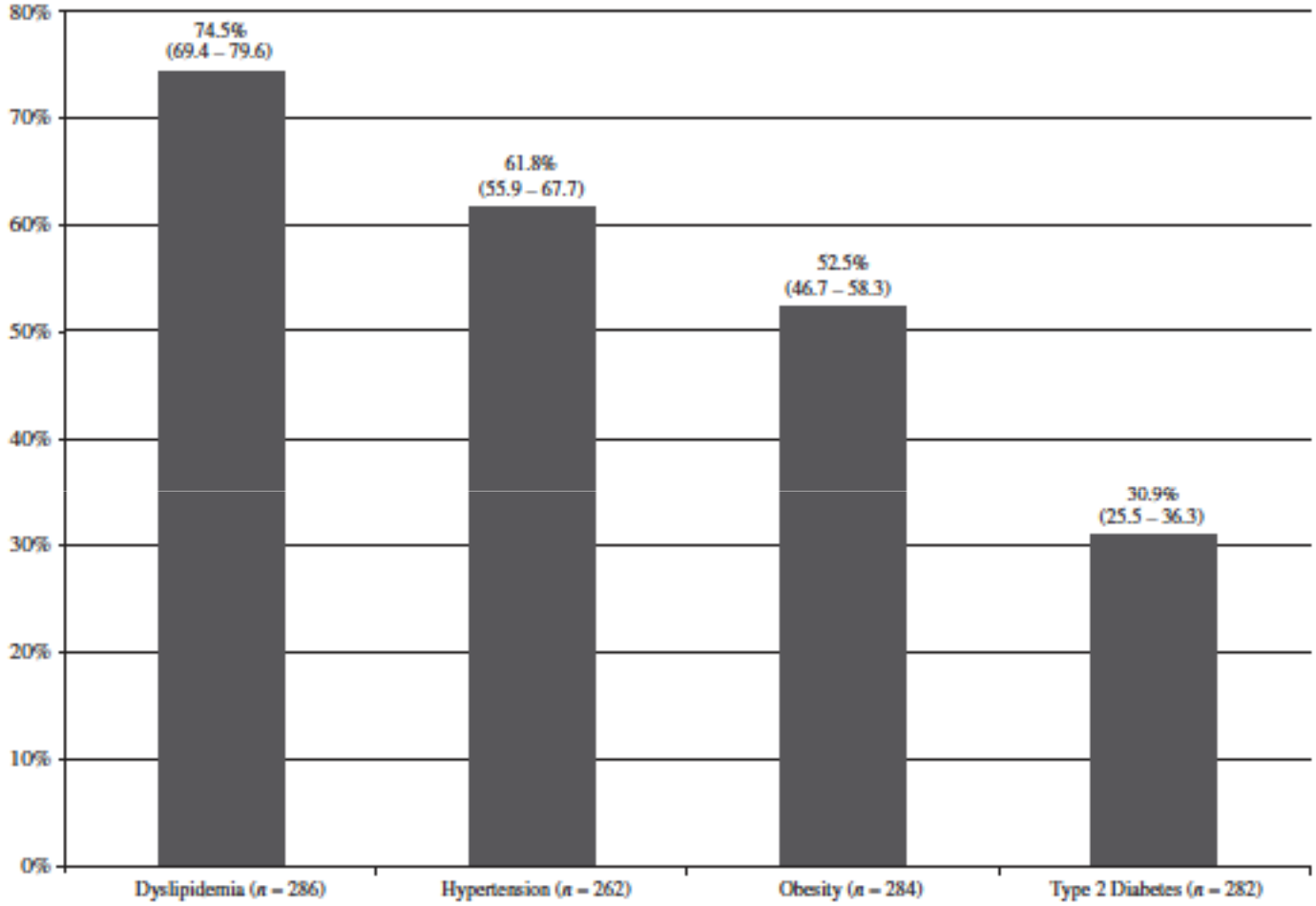


Figure 1. Prevalence of comorbidities assessed as secondary outcomes among patients with plaque-type psoriasis.

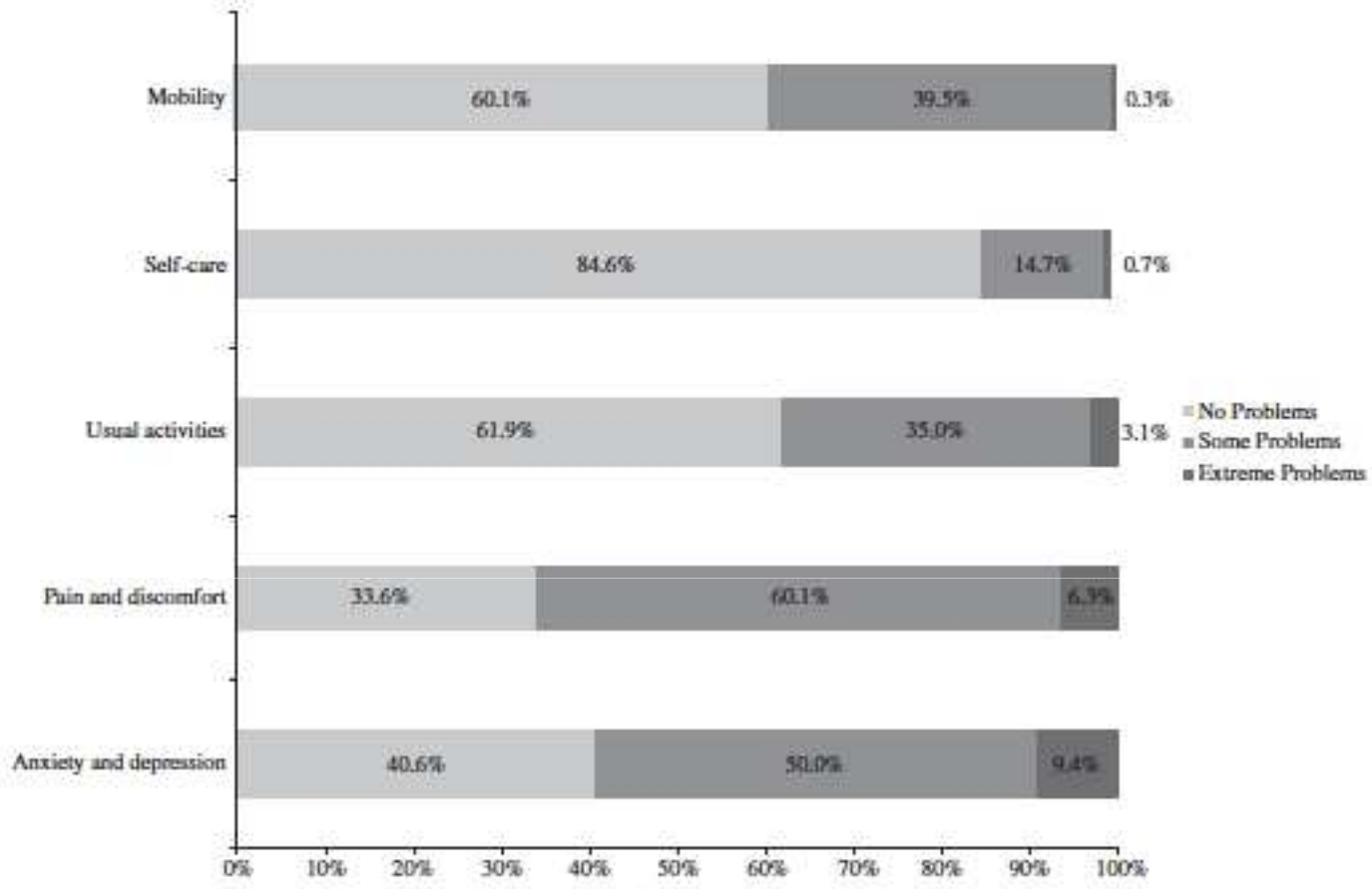


Figure 3. Limitations in health-related quality of life in each dimension of the EuroQol Five-Dimension Questionnaire Three-Level version questionnaire among patients with plaque-type psoriasis (n = 286).

EDITORIAL

BJD
British Journal of Dermatology

Increased risk of death in patients with psoriasis: disease or lifestyle?

The increased mortality among persons with more severe psoriasis found in the Danish study confirms similar findings in other studies.[1,6] So, is the increased mortality seen in patients with psoriasis related to disease-specific biological factors causing systemic inflammation, as suggested by Skov and colleagues? The hypothesis that psoriasis-related systemic inflammation may drive excess comorbidity and mortality is biologically plausible and has been indicated in some studies.[9,10] Should this be the case, it warrants more aggressive therapy of the condition. However, an association does not automatically mean causality.

Suivi de l’activite RhPso

Rhumatisme psoriasique et activité de la maladie

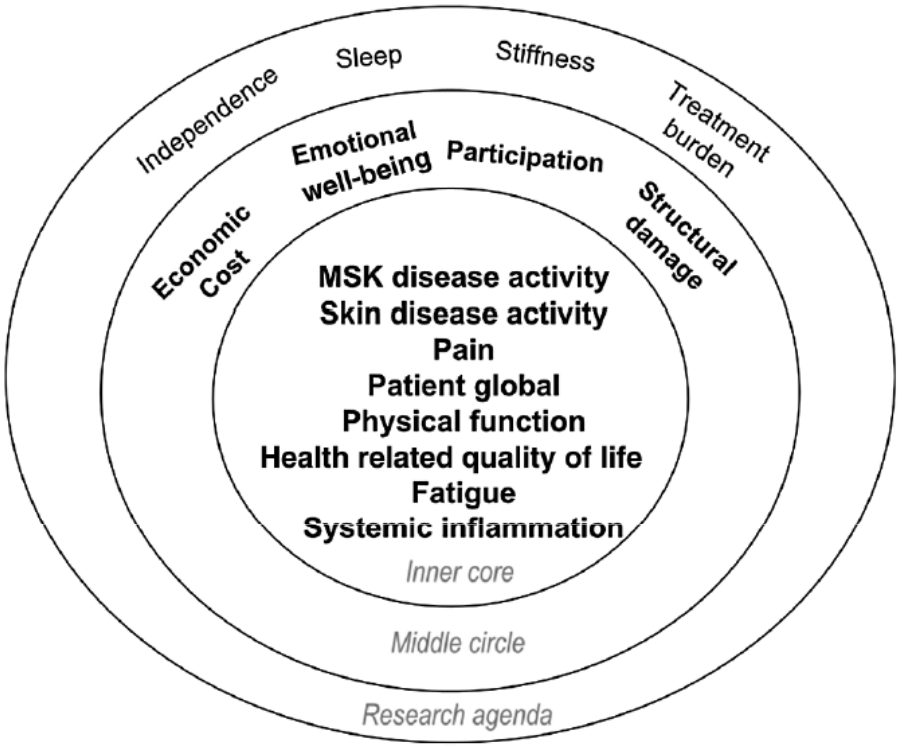


Figure 3 Updated 2016 psoriatic arthritis (PsA) core domain set. Musculoskeletal (MSK) disease activity includes peripheral joints, enthesitis, dactylitis and spine symptoms; skin activity includes skin and nails; patient global is defined as patient-reported disease-related health status. The inner circle (core) includes domains that should be measured in all PsA randomised controlled trials (RCTs) and longitudinal observational studies (LOS). The middle circle includes domains that are important but may not be feasible to assess in all RCTs and LOS. The outer circle or research agenda includes domains that may be important but need further study.

Consensus OMERACT

Core set central : RCT et LOS

Cercle moyen :
difficile à appliquer dans les études mais important

Cercle périphérique

Orbai A-M, *et al. Ann Rheum Dis* 2017;**76**:673–680.

PsAID12 Provisionally Endorsed at OMERACT 2018 as Core Outcome Measure to Assess Psoriatic Arthritis-specific Health-related Quality of Life in Clinical Trials

Objective. The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) and Outcome Measures in Rheumatology (OMERACT) psoriatic arthritis (PsA) working group is developing a Core Outcome Measurement Set for PsA clinical trials [randomized controlled trials (RCT) and longitudinal observational studies (LOS)] using the OMERACT Filter 2.1 instrument selection algorithm. Our objective was to assess the Psoriatic Arthritis Impact of Disease questionnaire (PsAID12) for the measurement of the core domain PsA-specific health-related quality of life (HRQOL).

Conclusion. At OMERACT 2018, PsAID12 was the first patient-reported outcome measure provisionally endorsed as a core outcome measure for disease-specific HRQOL in PsA clinical trials. PsAID12 discrimination and improvement thresholds will be studied in future RCT. (J Rheumatol First Release December 15 2018; doi:10.3899/jrheum.181077)

PSAID est le premier outil de mesure des PRO au cours du Rh Pso (HRQOL)
Utilisable dans les RCT

The Journal of Rheumatology 2019; 46:

Psoriatic Arthritis Impact of Disease (PsAID12) OMERACT SOMP

Author	Truth Domain Match	Feasibility	Truth	Discrimination			
			Construct Validity	Test Retest Reliability	Longitudinal Construct Validity	Clinical Trial Discrimination	Thresholds of Meaning
Working Group Appraisal	+	+					
Gossec L, *et al*[6]	+	+	+	+	+		+
de Wit M, *et al*[12]	+						
Salaffi F, *et al*[13]			+				
Di Carlo M, *et al*[14]			+				
Queiro R, *et al*[15]			+				
Holland R, *et al*[10]			+	+	+	+	+
Holland R, *et al*[11]	+	+					
Gorlier C, *et al*[16]			+				
Total Available Studies for Each Property	4	3	6	2	2	1	2
Total Studies Available for Synthesis	4	3	6	2	2	1	2
Rating (green = good to go, amber = caution but go)	GREEN	GREEN	GREEN	GREEN	GREEN	AMBER	AMBER

Overall rating for instrument across properties

Working group and TAG are recommending **provisional (amber) endorsement** of this instrument. Specific research agenda is set to complete full endorsement.

The Journal of Rheumatology 2019; 46:

PSAID

12 domaines

Each domain is scored using a NRS, 0–10,

Le questionnaire EULAR Psoriatic Arthritis Impact of Disease: PsAID12 pour la pratique

Nous vous demandons d'indiquer quel impact le rhumatisme psoriasique a eu sur votre santé. Veuillez indiquer comment vous vous sentez depuis 8 jours.

1. Douleur
Entourez le chiffre qui correspond le mieux à la douleur causée par votre rhumatisme psoriasique au cours des 8 derniers jours :

Aucune | 0 1 2 3 4 5 6 7 8 9 10 | Extrême

Ne pas remplir
Résultat x3 ☐

2. Fatigue
Entourez le chiffre qui correspond le mieux à la fatigue causée par votre rhumatisme psoriasique au cours des 8 derniers jours :

Aucune fatigue | 0 1 2 3 4 5 6 7 8 9 10 | Complètement épuisé(e)

Résultat x2 ☐

3. Problèmes de peau
Entourez le chiffre qui correspond le mieux aux problèmes de peau, y compris les démangeaisons, causés par votre rhumatisme psoriasique au cours des 8 derniers jours :

Aucun | 0 1 2 3 4 5 6 7 8 9 10 | Extrêmes

Résultat x2 ☐

4. Travail et/ou activités de loisirs
Entourez le chiffre qui correspond le mieux aux difficultés causées par votre rhumatisme psoriasique, pour exercer pleinement votre travail et/ou vos activités de loisirs, au cours des 8 derniers jours :

Aucune | 0 1 2 3 4 5 6 7 8 9 10 | Extrême

Résultat x2 ☐

5. Capacité d'activités physiques
Entourez le chiffre qui correspond le mieux à la difficulté causée par votre rhumatisme psoriasique pour accomplir vos activités physiques quotidiennes au cours des 8 derniers jours :

Aucune difficulté | 0 1 2 3 4 5 6 7 8 9 10 | Difficulté extrême

Résultat x2 ☐

6. Inconfort
Entourez le chiffre qui correspond le mieux à la sensation d'inconfort ou de désagrément causée par votre rhumatisme psoriasique, pour les tâches quotidiennes, au cours des 8 derniers jours :

Aucun | 0 1 2 3 4 5 6 7 8 9 10 | Extrême

Résultat x2 ☐

7. Sommeil
Entourez le chiffre qui correspond le mieux à la difficulté pour dormir (vous reposer la nuit), causée par votre rhumatisme psoriasique, au cours des 8 derniers jours :

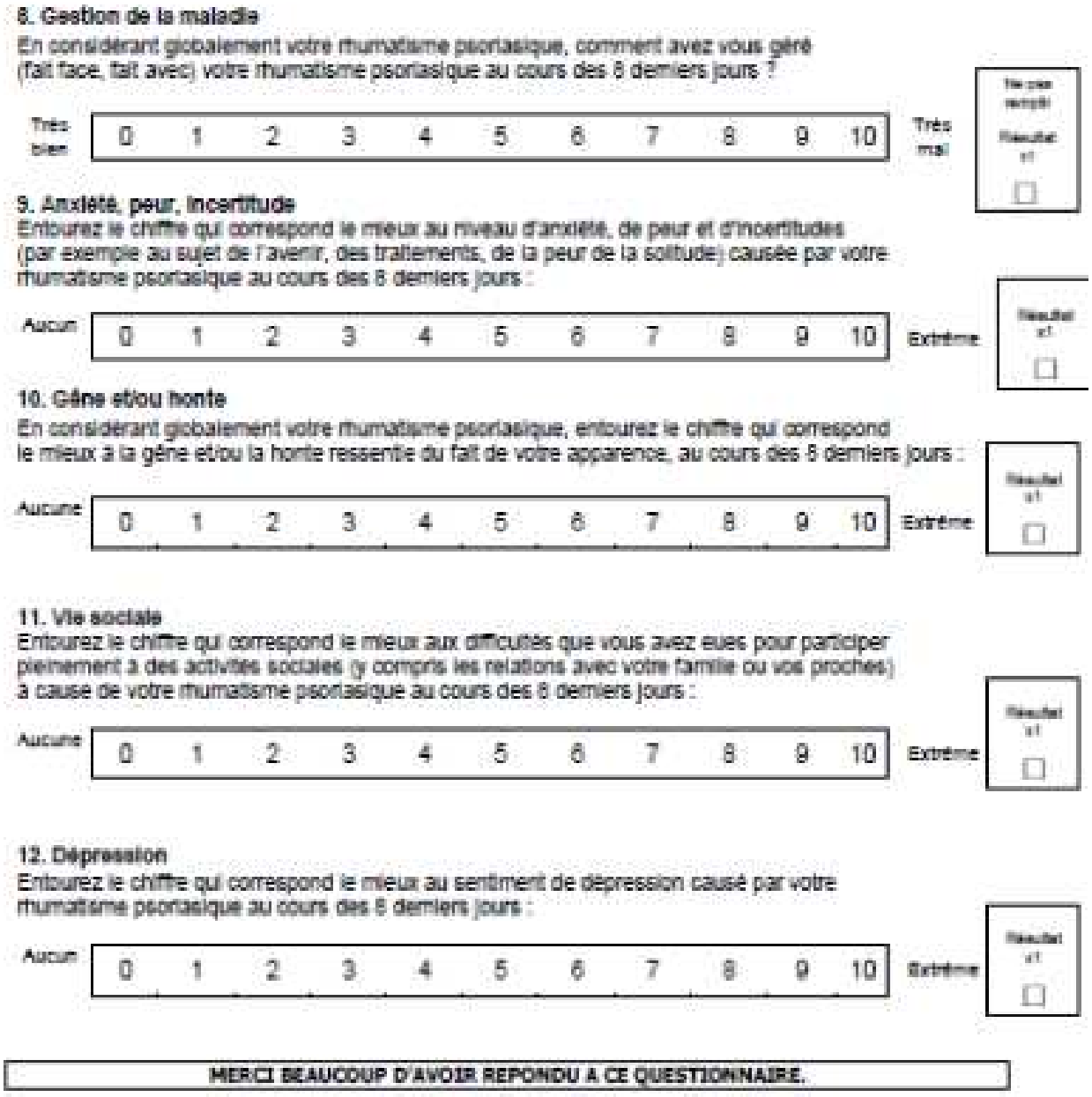
Aucune difficulté | 0 1 2 3 4 5 6 7 8 9 10 | Difficulté extrême

Résultat x2 ☐

PSAID

12 domaines

Each domain is scored using a NRS, 0–10,



8. Gestion de la maladie

En considérant globalement votre rhumatisme psoriasique, comment avez vous géré (fait face, fait avec) votre rhumatisme psoriasique au cours des 6 derniers jours ?

Très bien 0 1 2 3 4 5 6 7 8 9 10 Très mal

9. Anxiété, peur, incertitude

Entourez le chiffre qui correspond le mieux au niveau d'anxiété, de peur et d'incertitudes (par exemple au sujet de l'avenir, des traitements, de la peur de la solitude) causée par votre rhumatisme psoriasique au cours des 6 derniers jours :

Aucun 0 1 2 3 4 5 6 7 8 9 10 Extrême

10. Gêne et/ou honte

En considérant globalement votre rhumatisme psoriasique, entourez le chiffre qui correspond le mieux à la gêne et/ou la honte ressentie du fait de votre apparence, au cours des 6 derniers jours :

Aucune 0 1 2 3 4 5 6 7 8 9 10 Extrême

11. Vie sociale

Entourez le chiffre qui correspond le mieux aux difficultés que vous avez eues pour participer pleinement à des activités sociales (y compris les relations avec votre famille ou vos proches) à cause de votre rhumatisme psoriasique au cours des 6 derniers jours :

Aucune 0 1 2 3 4 5 6 7 8 9 10 Extrême

12. Dépression

Entourez le chiffre qui correspond le mieux au sentiment de dépression causé par votre rhumatisme psoriasique au cours des 6 derniers jours :

Aucun 0 1 2 3 4 5 6 7 8 9 10 Extrême

MERCI BEAUCOUP D'AVOIR REPONDU A CE QUESTIONNAIRE.

Ixekizumab improves patient-reported outcomes in patients with active psoriatic arthritis and inadequate response to tumour necrosis factor inhibitors: SPIRIT-P2 results to 52 weeks

A. Kavanaugh[1], H. Marzo-Ortega[2], R. Vender[3], C.-C. Wei[4], J. Birt[5], D.H. Adams[6], O. Benichou[6], C.-Y. Lin[7], P. Nash[8]

Conclusion

In patients with PsA and an IR or intolerance to TNFi, ixekizumab significantly improved disease activity, skin symptoms, HRQOL, and work productivity to 52 weeks.

Études pivot SPIRIT-P1 et SPIRIT-P2

SPIRIT P1

Patients naïfs de traitements biologiques (bDMARD)
N=417

- Étude contrôlée vs placebo
- Double aveugle
- 24 semaines

Groupes de traitement
Taltz 80 mg toutes les 4 sem. ou
Taltz 80 mg toutes les 2 sem. ou
adalimumab 40 mg toutes les 2 sem., ou placebo

Critère de jugement principal
ACR20 à 24 sem.

SPIRIT P2

Patients préalablement traités par au moins un anti-TNF
N=363

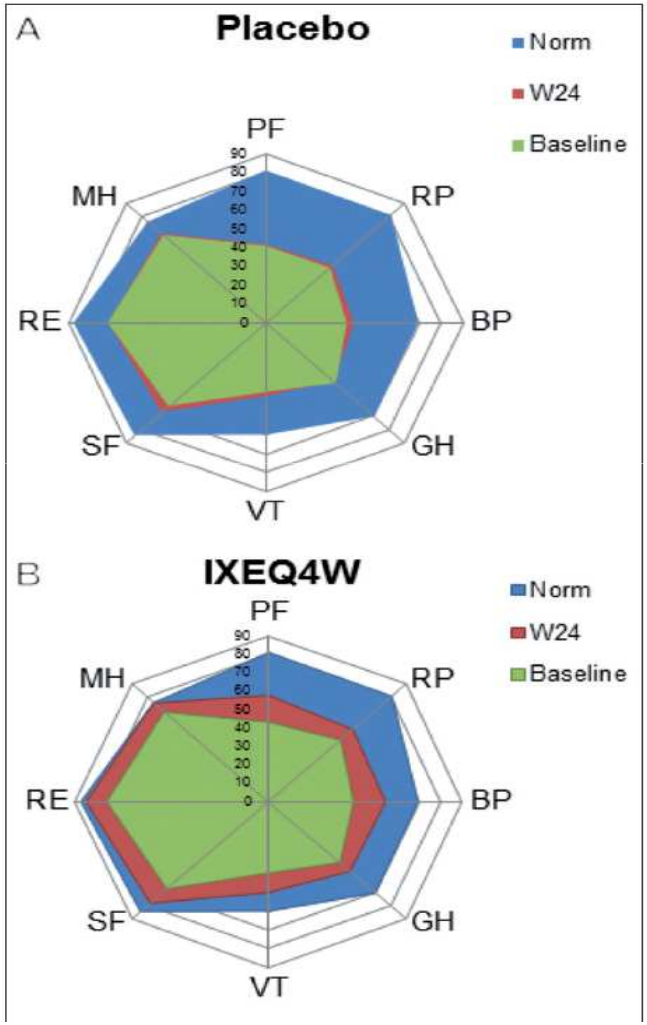
- Étude contrôlée vs placebo
- Double aveugle
- 24 semaines

Groupes de traitement
Taltz 80 mg toutes les 4 sem. ou
Taltz 80 mg toutes les 2 sem. ou
placebo

Critère de jugement principal
ACR20 à 24 sem.

- Après la sem. 24, extension en ouvert durant laquelle tous les patients recevaient Taltz
- Durée totale de l'étude: 3 ans

Mease PJ, et al. Ann Rheum Dis. 2017;76:79-87; Nash P, et al. Lancet. 2017;389:2317-2327.



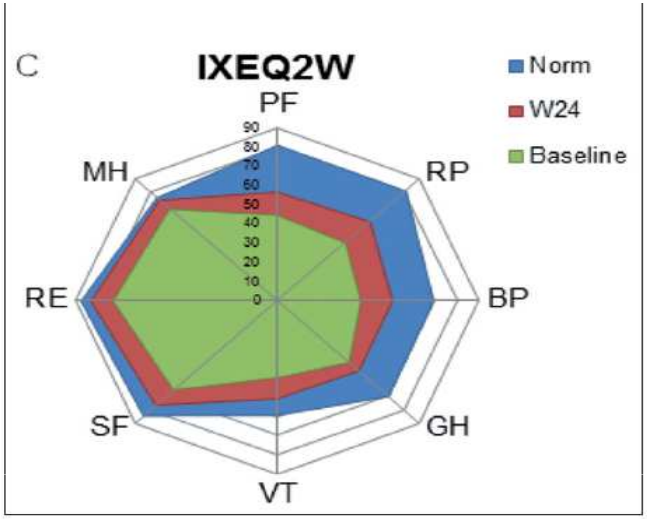


Fig. 2. SF-36. The spydergrams depict mean SF-36 scores in the ITT population during the Placebo-controlled Period (baseline and Week 24) compared with age- and gender- matched normative values. mBOCF was applied for inadequate responders at Week 16 and patients who discontinued at or before Week 24.
BP: bodily pain; GH, general health; ITT: intent-to-treat; IXEQ2W: ixekizumab 80 mg every 2 weeks; IXEQ4W: ixekizumab 80 mg every 4 weeks; mBOCF: modified baseline observation carried forward; MH: mental health; Norm: normative value; PF: physical functioning; RE: role emotional; RP: role physical; SF: social functioning; SF-36: 36-Item Short Form Health Survey version 2; VT: vitality; W24: Week 24.

DLQI

Prurit

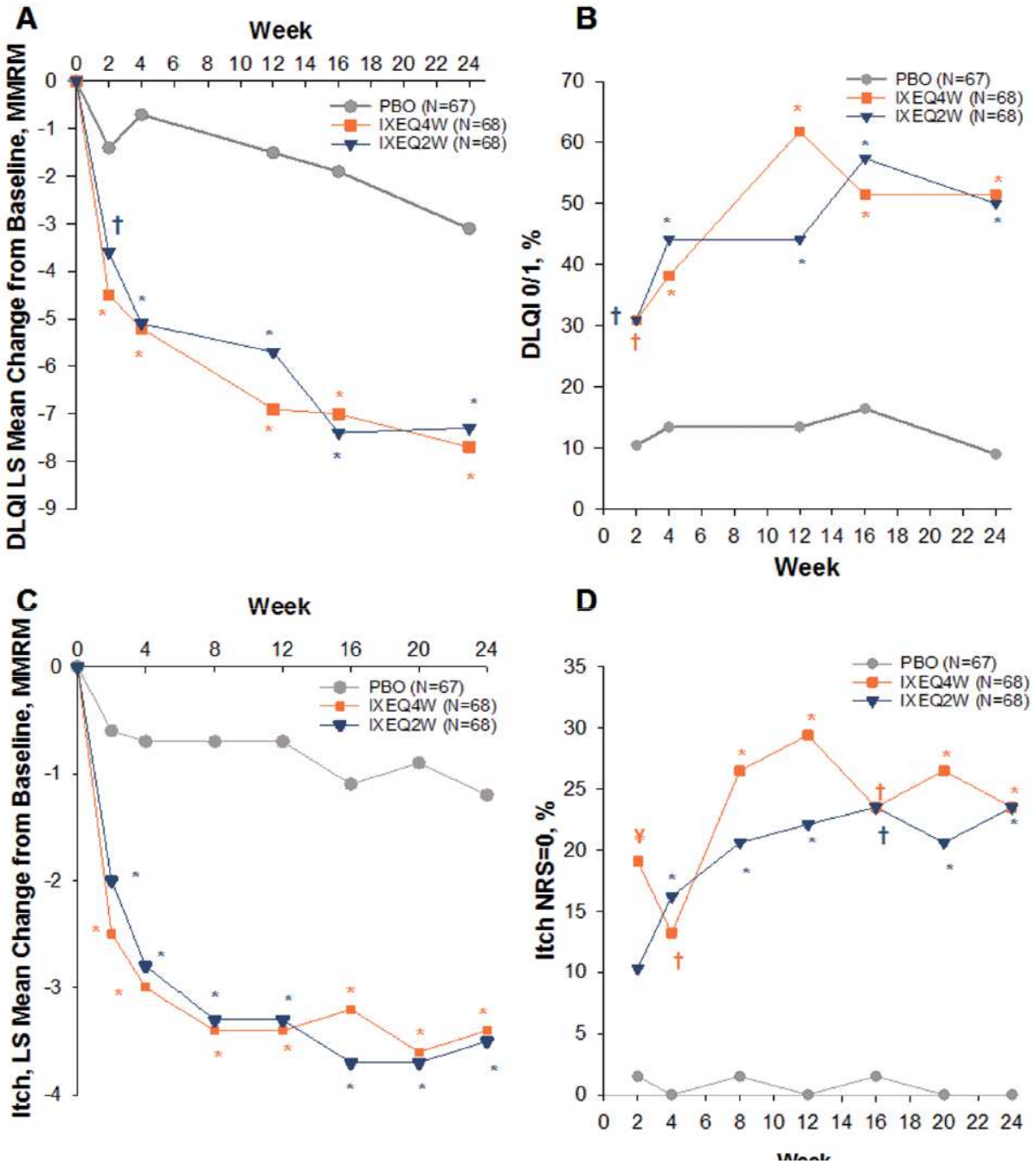


Fig. 1. Dermatology Life Quality Index and Itch.

McInnes et al. Arthritis Research & Therapy (2018) 20:113
https://doi.org/10.1186/s13075-018-1610-3

Arthritis Research & Therapy

RESEARCH ARTICLE Open Access

Secukinumab provides rapid and sustained pain relief in psoriatic arthritis over 2 years: results from the FUTURE 2 study

Iain B. McInnes[1*], Philip J. Mease[2], Georg Schett[3], Bruce Kirkham[4], Vibeke Strand[5], Nicole Williams[6], Todd Fox[7], Luminita Pricop[8], Steffen M. Jugl[7], Kunal K. Gandhi[8], on behalf of the FUTURE 2 Study Group

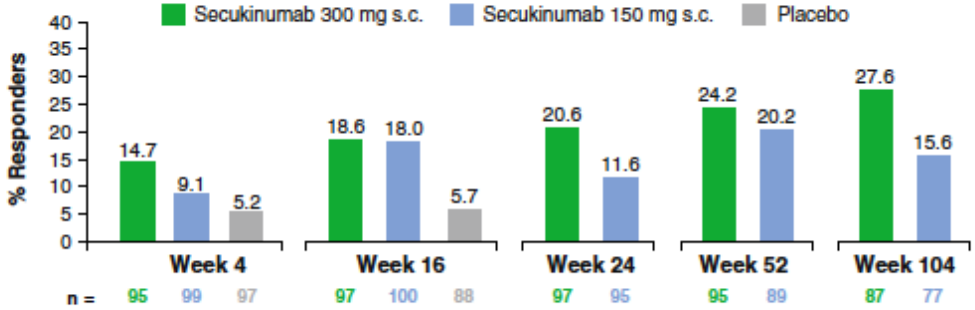


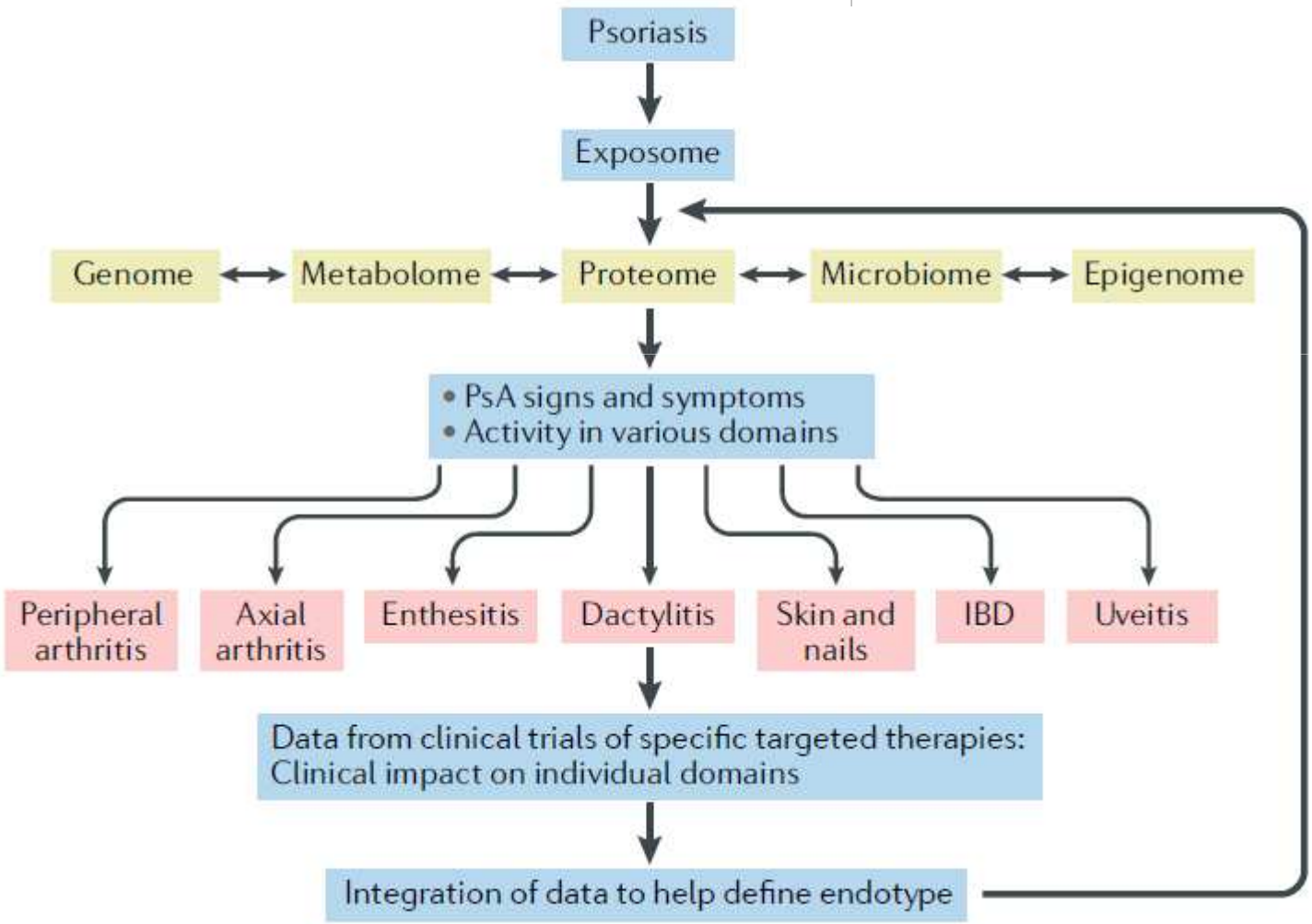
Fig. 3 Proportion of patients with no pain or discomfort in the EuroQoL 5-Dimension (EQ-5D-3 L) domain through week 104
Observed data are presented. Data are presented only for evaluable patients at each time point
s.c., subcutaneous

Revue

Revues

Bedside to bench: defining the immunopathogenesis of psoriatic arthritis

Arlene Bravo and Arthur Kavanaugh *



2019

Traitements de fond des RIC

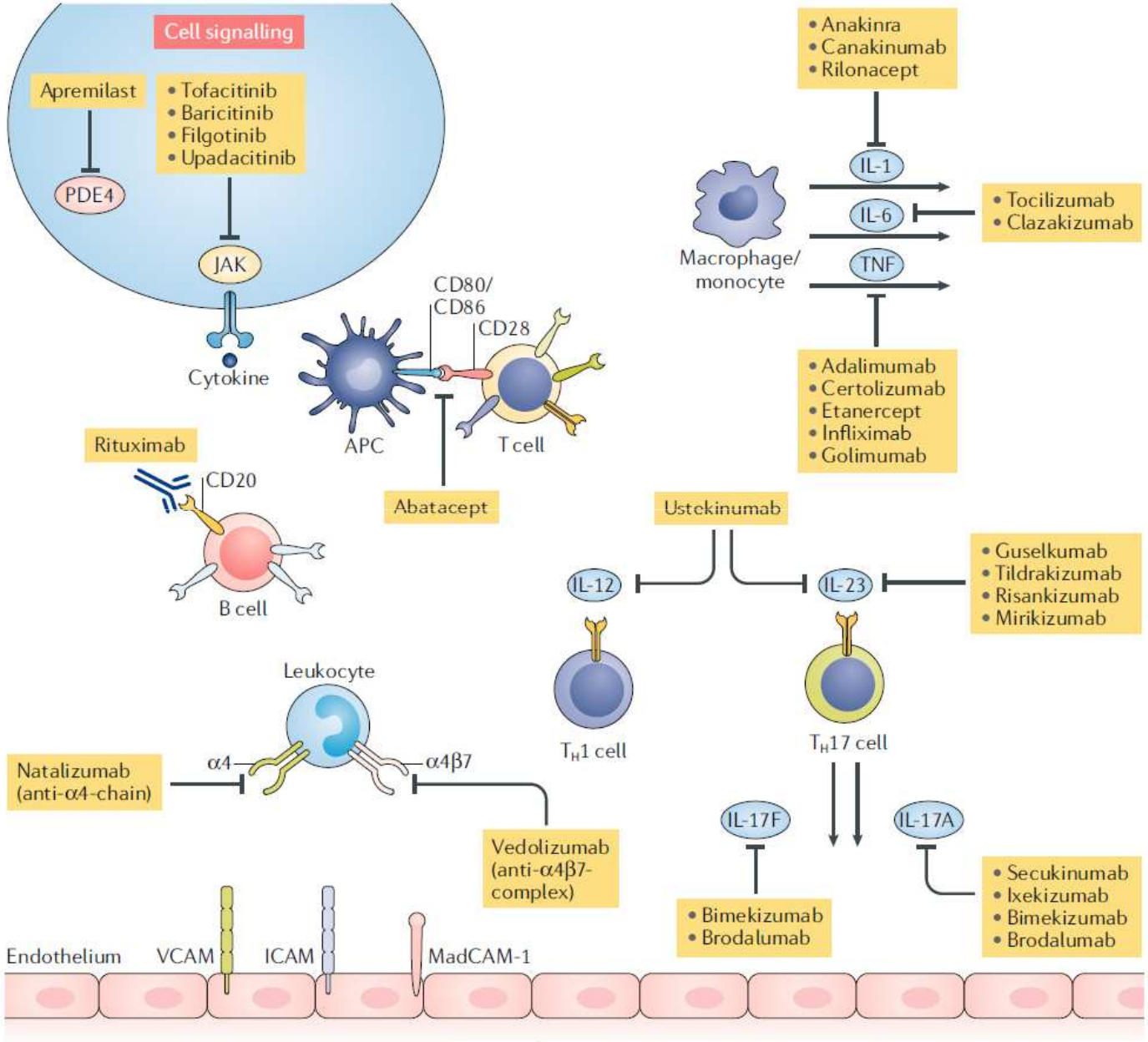


Fig. 2 | **Summary of immune target interactions in PsA.**

Traitements de fond des RIC

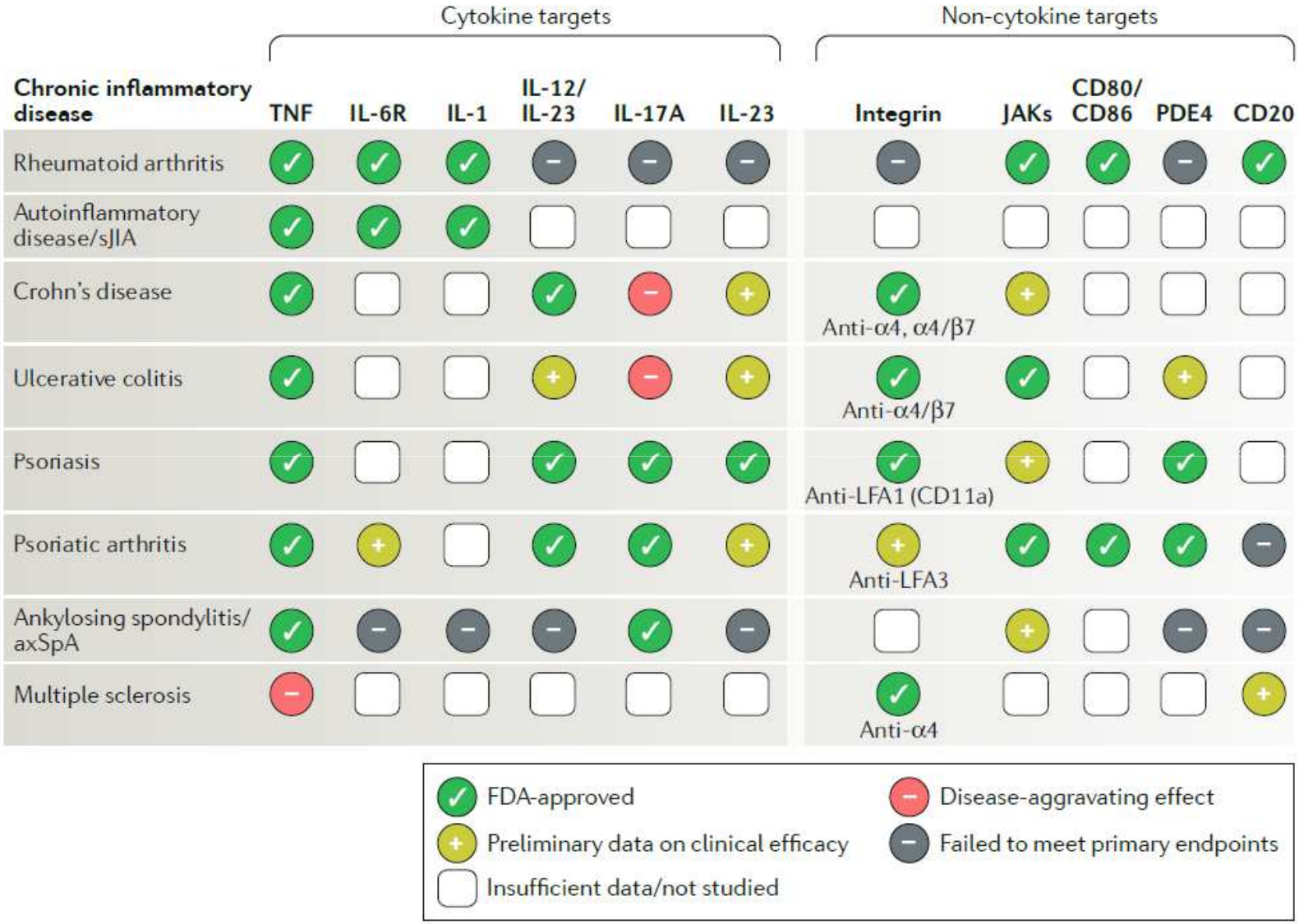


Fig. 3 | **Summary of cytokine and non-cytokine targets in various chronic inflammatory diseases.** This figure

2019

Early and sustained efficacy with apremilast monotherapy in biological-naïve patients with psoriatic arthritis: a phase IIIB, randomised controlled trial (ACTIVE)

Peter Nash,[1] Kamal Ohson,[2] Jessica Walsh,[3] Nikolay Delev,[4] Dianne Nguyen,[4] Lichen Teng,[4] Juan J Gómez-Reino,[5] Jacob A Aelion,[6] on behalf of the ACTIVE investigators

Nash P, *et al*. *Ann Rheum Dis* 2018;**77**:690–698.

Efficacy and safety of filgotinib, a selective Janus kinase 1 inhibitor, in patients with active psoriatic arthritis (EQUATOR): results from a randomised, placebo-controlled, phase 2 trial

Philip Mease, Laura C Coates, Philip S Helliwell, Mykola Stanislavchuk, Anna Rychlewska-Hanczewska, Anna Dudek, Walid Abi-Saab, Chantal Tasset, Luc Meuleners, Pille Harrison, Robin Besuyen, Annegret Van der Aa, Neelufar Mozaffarian, Joy M Greer, Rebecca Kunder, Filip Van den Bosch, Dafna D Gladman

Study design

- A phase 2, 16-week, multicenter, double-blind study of filgotinib 200 mg vs placebo in 131 patients with active PsA and insufficient response or intolerance to csDMARDs
- Primary endpoint: ACR20 response at Week 16
- Secondary endpoints included safety, MDA, HAQ-DI and DAPSA
- The present study evaluated the effects of filgotinib vs placebo on a patient level

www.thelancet.com Published online October 22, 2018

Dessin de l'étude EQUATOR

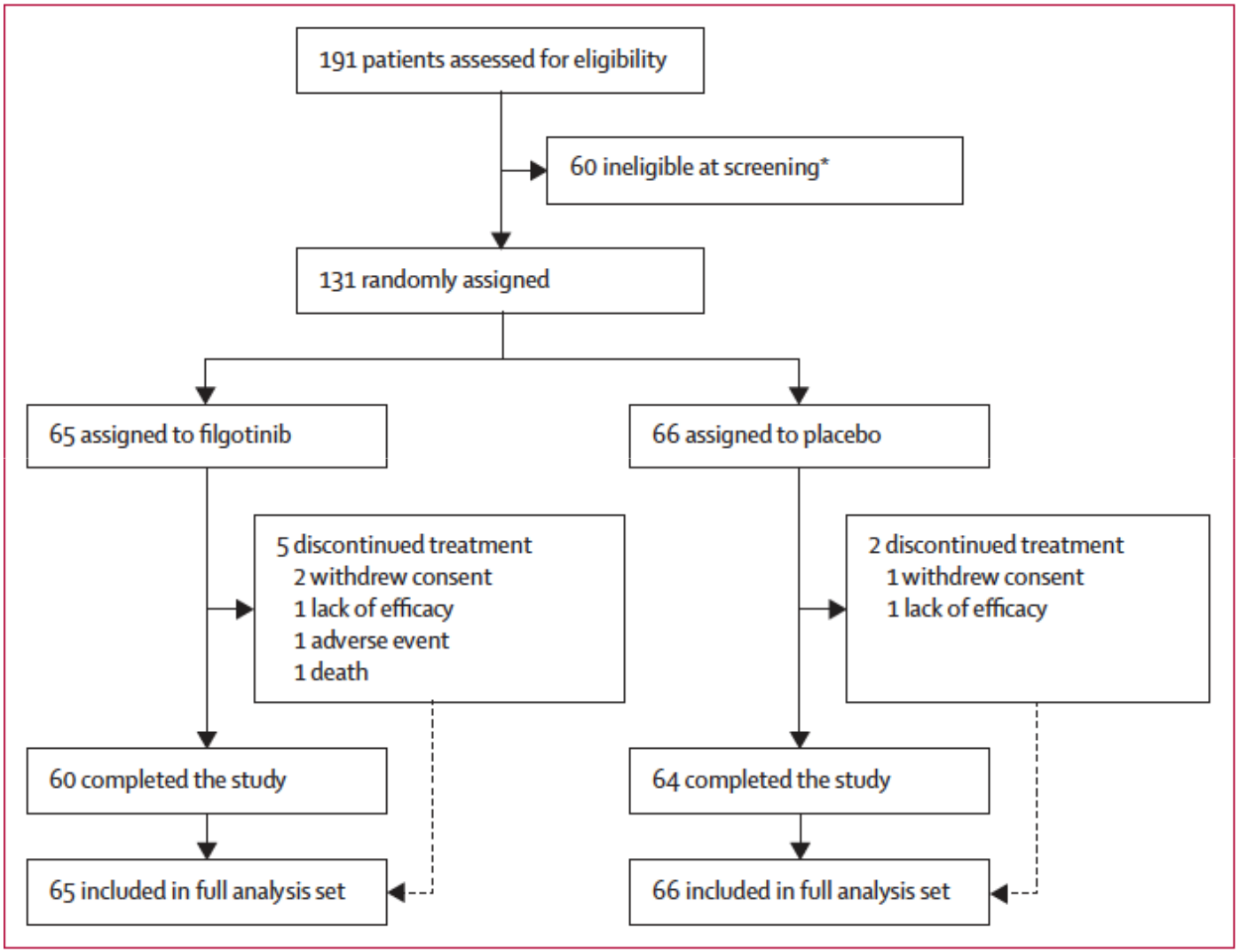


Figure 1: Trial profile

	Filgotinib (n=65)	Placebo (n=66)
Mean age, years	49 (12·2)	50 (10·9)
Sex		
Female	36 (55%)	30 (45%)
Male	29 (45%)	36 (55%)
Mean weight, kg	81 (19·0)	87 (17·5)
Mean body-mass index, kg/m²	28·6 (6·8)	30·1 (5·7)
Mean duration of psoriatic arthritis, years	7 (6·7)	7 (6·2)
Tender joint count 68 score	18·3 (9·2)	21·6 (13·2)
Swollen joint count 66 score	11·6 (5·1)	12·7 (6·7)
Mean Health Assessment Questionnaire-Disability Index score	1·43 (0·5)	1·36 (0·6)
Mean hsCRP, mg/L	13·9 (19·8)	10·9 (17·2)
hsCRP ≥10 mg/L	25 (38%)	17 (26%)
At least 3% body surface area of psoriasis	42 (65%)	40 (61%)
Median PASI*	6·5 (2·6–15·0)	6·9 (3·8–18·6)
Mean PASDAS	6·1 (0·8)	6·2 (1·0)
Mean DAPSA score	44·0 (14·3)	47·8 (19·8)
Enthesitis based on SPARCC Enthesitis Index	37 (57%)	48 (73%)
Mean SPARCC Enthesitis Index score†	4·9 (3·0)	5·5 (3·8)
Enthesitis based on Leeds Enthesitis Index	38 (58%)	49 (74%)
Mean Leeds Enthesitis Index score‡	2·8 (1·4)	2·6 (1·4)
Prior anti-TNF therapy§	11 (17%)	9 (14%)
Concurrent use of csDMARD	47 (72%)	50 (76%)
Leflunomide	2 (3%)	4 (6%)
Sulfasalazine	3 (5%)	3 (5%)
Methotrexate (oral)	36 (55%)	35 (53%)
Mean methotrexate dose (oral)	1·9 (0·6)	2·3 (0·7)
Methotrexate (subcutaneous)	5 (8%)	8 (12%)
Mean methotrexate dose (subcutaneous)	2·9 (0·9)	2·4 (0·8)
Concurrent use of steriods	17 (26%)	16 (24%)
Prednisolone-equivalent dose (oral)	7·8 (2·5)	5·9 (2·6)

Data are mean (SD), n (%), or median (IQR). csDMARD=conventional synthetic disease-modifying anti-rheumatic drug. DAPSA=Disease Activity Index for Psoriatic Arthritis. hsCRP=highly-sensitive C-reactive protein. PASDAS=Psoriatic Arthritis Disease Activity Score. PASI=Psoriasis Area and Severity Index. SPARCC=Spondyloarthritis Research Consortium of Canada. TNF=tumour necrosis factor. *Full analysis set with baseline body surface area of at least 3%. †Full analysis set with enthesitis at baseline (SPARCC Enthesitis Index >0). ‡Full analysis set with enthesitis at baseline (Leeds Enthesitis Index >0). §Patients might have stopped treatment with anti-TNF medication because of an insufficient response, adverse events, or financial constraints.

Table 1: **Baseline patient and disease characteristics (full analysis set)**

	Filgotinib (n = 65)	Placebo (n = 66)
Female	36 (55.4)	30 (45.5)
Age, years, mean	49	50
BMI, kg/m², mean	28.6	30.1
Duration of PsA, mean years since diagnosis	7	7
Prior TNFi use	11 (16.9)	9 (13.6)
Concurrent csDMARD use	47 (72.3)	50 (75.8
Concurrent steroid use	17 (26.2)	16 (24.2)

	Filgotinib (n = 65)	Placebo (n = 66)
TJC68, mean	18.3	21.6
SJC66, mean	11.6	12.7
HAQ-DI, mean	1.43	1.36
DAS28 (CRP), mean	4.9	5.1
hsCRP, mg/L, mean	13.9	10.9
Enthesitis	38 (58.5)	49 (74.2)
≥ 3% BSA of psoriasis	42 (64.6)	40 (60.6)
Pruritus, mean*	5.4	6.0

Résultats ACR 20 à 16 semaines

	Filgotinib (n=65)		Placebo (n=66)		Treatment difference		
	Response rate	95% CI	Response rate	95% CI	Response rate (%)	95% CI	p value*
Non-responder imputation	52 (80%) of 65	68·7–87·9	22 (33%) of 66	23·2–45·3	47%	30·2–59·6	p<0·0001
Last observation carried forward	54 (83%) of 65	72·2–90·3	22 (33%) of 66	23·2–45·3	50%	33·5–62·2	p<0·0001
Observed cases	52 (87%) of 60	75·8–93·1	22 (34%) of 64	23·9–46·6	52%	36·0–64·6	p<0·0001

Data are n (%) unless otherwise stated. ACR20=20% improvement in the American College of Rheumatology response criteria. *Calculated with the Cochran-Mantel-Haenszel test for general association, controlling for randomisation stratification factors.

Table 2: **Primary and sensitivity analyses of ACR20 response at week 16, by imputation method (full analysis set)**

www.thelancet.com Published online October 22, 2018

Résultats ACR à 16 semaines

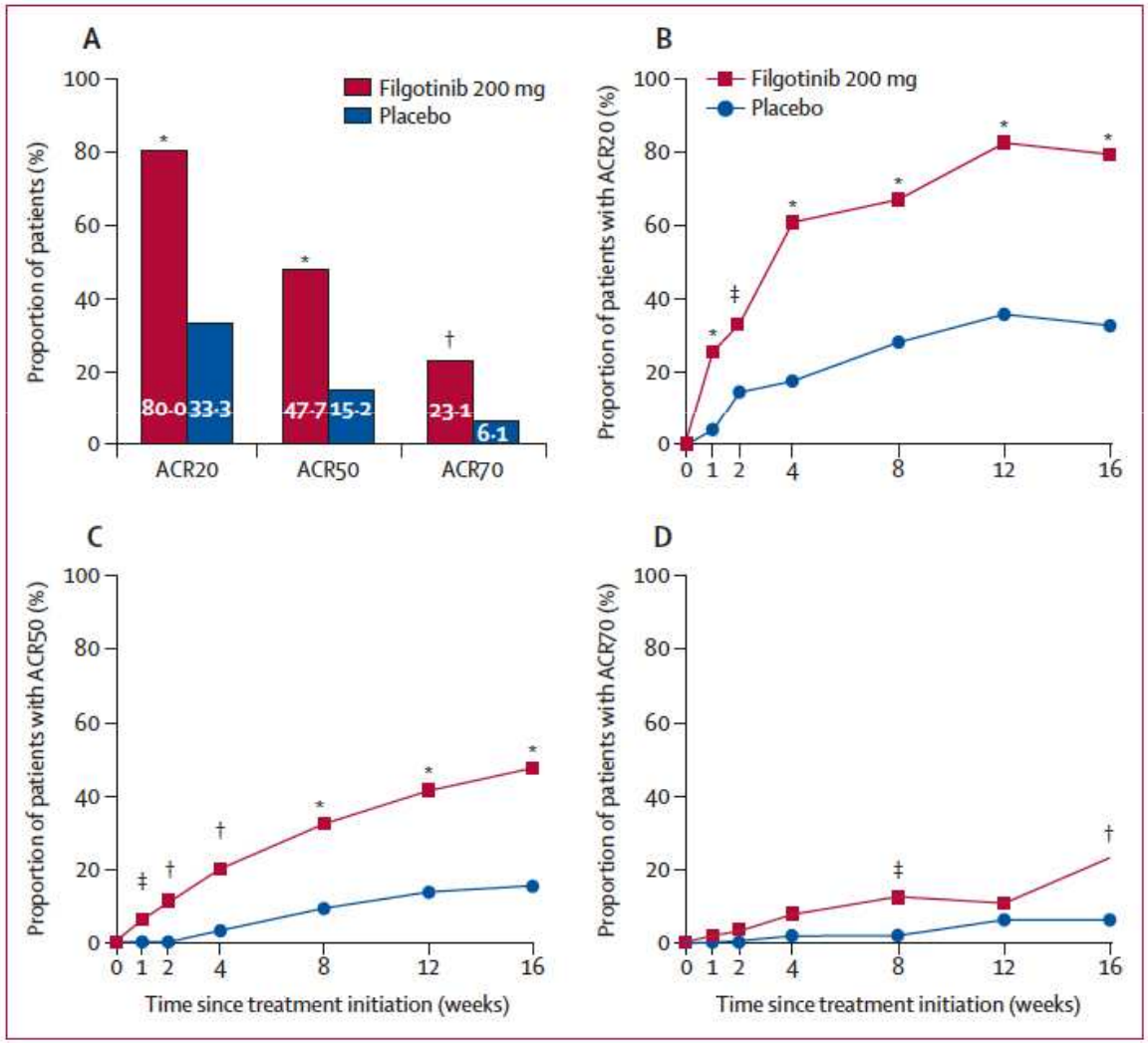
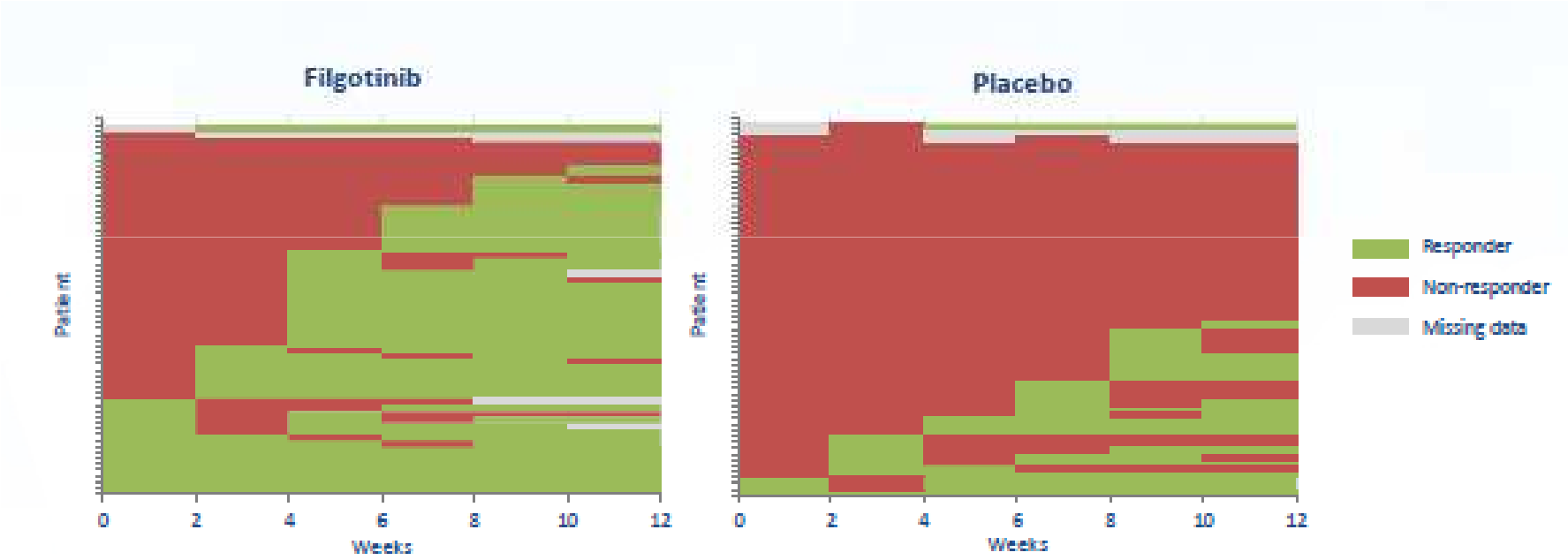


Figure 2: ACR responses (non-responder imputation; full analysis set)

www.thelancet.com Published online October 22, 2018

Résultats au cours du temps



Résultats DAPSA MDA PASI

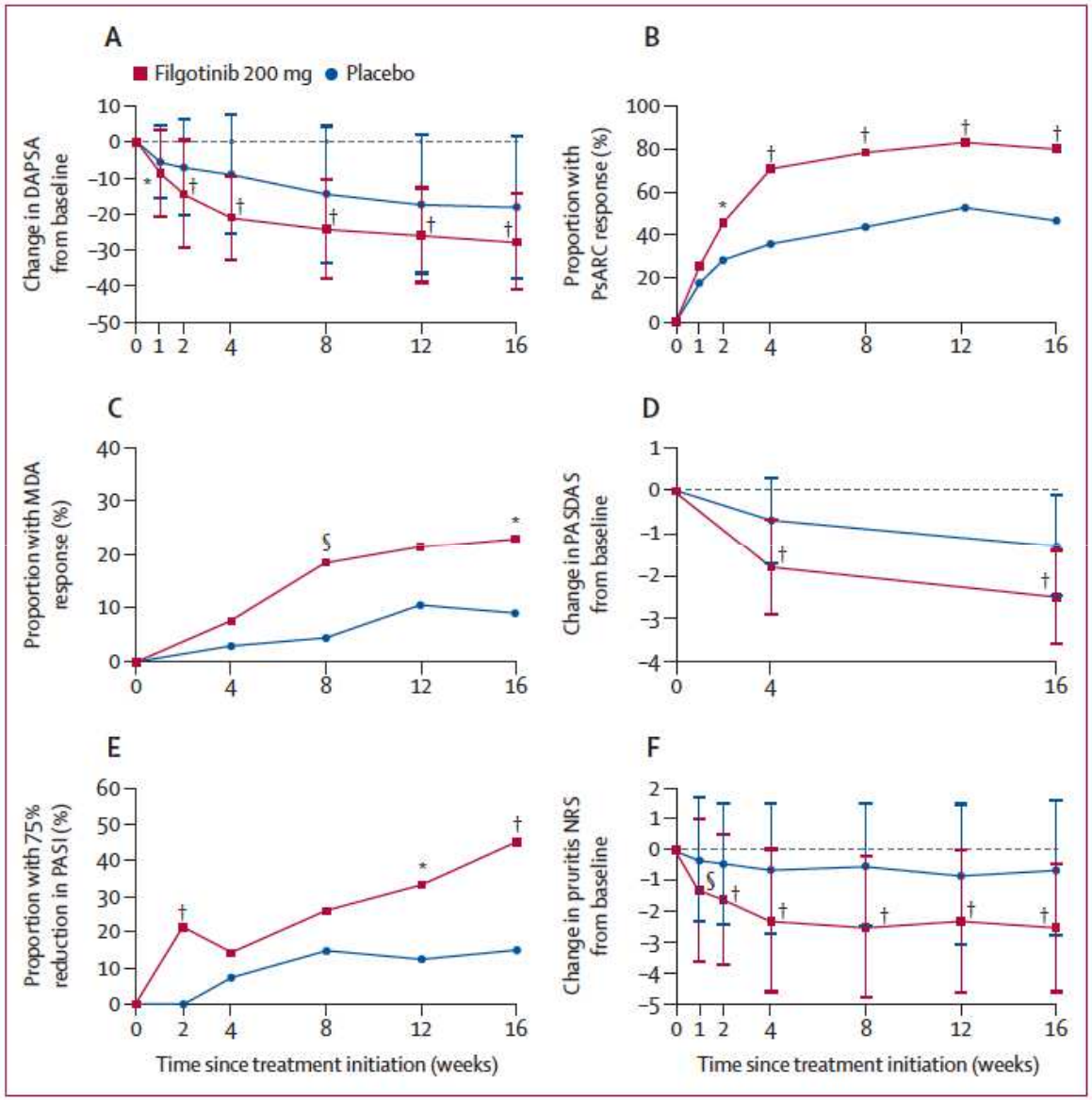


Figure 3: Secondary outcomes up to week 16 (full analysis set)

www.thelancet.com Published online October 22, 2018

Résultats enthèses

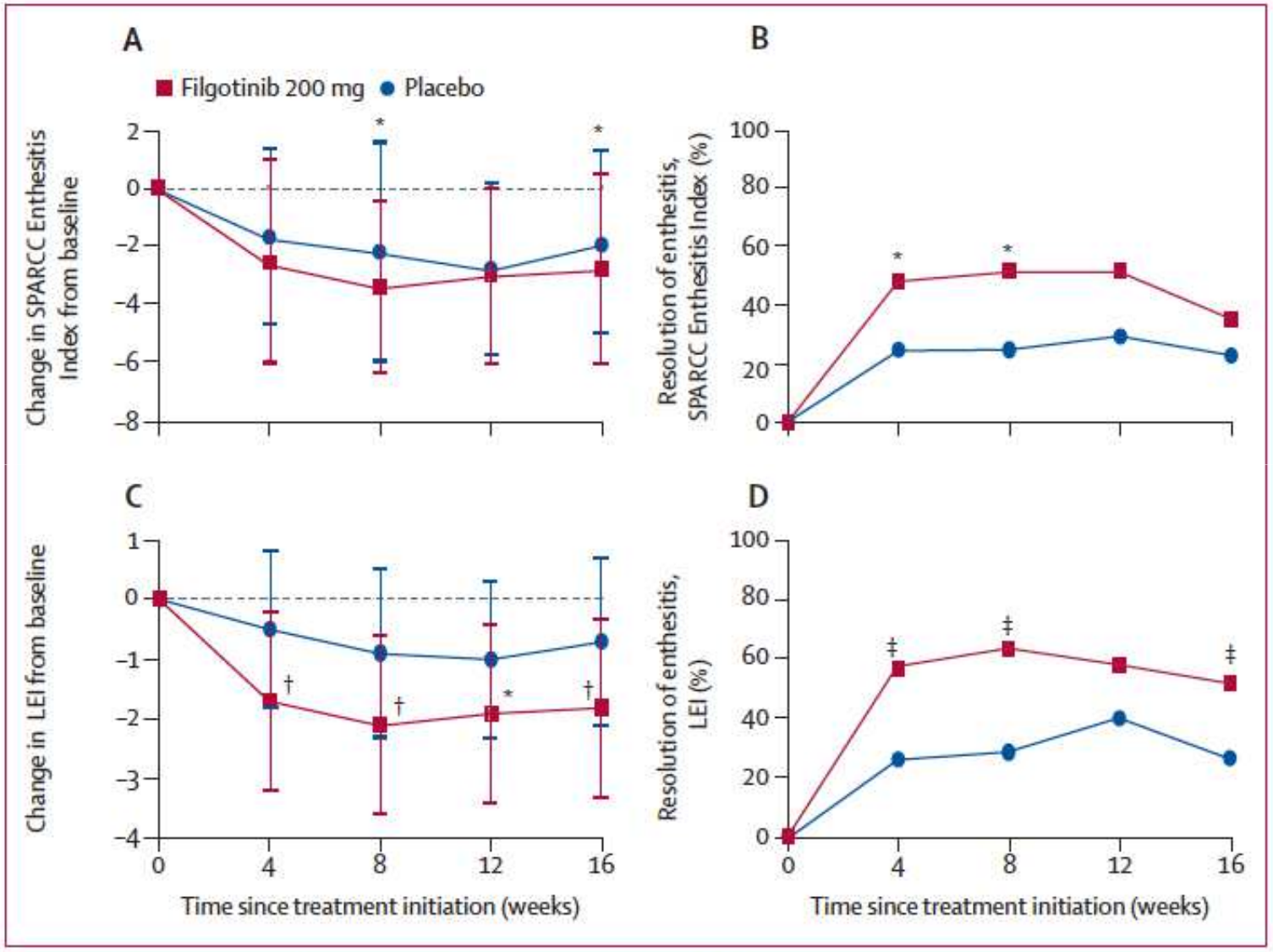


Figure 4: Enthesitis according to SPARCC Enthesitis Index and LEI

www.thelancet.com Published online October 22, 2018

	Filgotinib (n=65)	Placebo (n=66)
Treatment-emergent adverse events		
All	37 (57%)	39 (59%)
Nasopharyngitis	8 (12%)	10 (15%)
Headache	3 (5%)	5 (8%)
Blood cholesterol increased	5 (8%)	0
Diarrhoea	2 (3%)	2 (3%)
Dizziness	2 (3%)	2 (3%)
Drug-related	11 (17%)	9 (14%)
Serious	1 (2%)*	1 (2%)
Drug-related serious	1 (2%)*	0
Serious treatment-emergent infection	1 (2%)*	0
Grade 3 or worse	1 (2%)*	5 (8%)
Led to permanent discontinuation of study drug	1 (2%)†	0
Treatment-emergent adverse events of special interest		
Infections	14 (22%)	14 (21%)
All serious infections	1 (2%)*	0
Opportunistic infections	0	0
Herpes zoster	1 (2%)	0
Active tuberculosis	0	0
Urinary tract infections	1 (2%)	3 (5%)
Respiratory tract infections	10 (15%)*	10 (15%)
Malignancies	0	0
Deep venous thrombosis	0	0
Pulmonary embolism	0	0
Major adverse cardiovascular events	1 (2%)*	0
Deaths due to treatment-emergent adverse event	1 (2%)*	0

Data are n (%). The top five most common treatment-emergent adverse events are shown. *One patient died following onset of pneumonia (the same single case is represented in several categories). †Since treatment in the patient that died was not discontinued before, this patient is not included here.

Table 4: **Safety endpoints (full analysis set)**

Efficacy and safety of guselkumab in patients with active psoriatic arthritis: a randomised, double-blind, placebo-controlled, phase 2 study

Atul Deodhar, Alice B Gottlieb*, Wolf-Henning Boehncke, Bin Dong, Yuhua Wang, Yanli Zhuang, William Barchuk, Xie L Xu, Elizabeth C Hsia, on behalf of the CNTO1959PSA2001 Study Group*

Lancet 2018; 391: 2213–24

Phase 2 Study of ABT-122, a TNF- and IL-17A–Targeted Dual Variable Domain Immunoglobulin, in Psoriatic Arthritis With Inadequate Methotrexate Response

Running Head: ABT-122 efficacy and safety in PsA

Authors: Philip J. Mease, MD[1], Mark C. Genovese, MD[2], Michael E. Weinblatt, MD[3], Paul M. Peloso, MD[4], Kun Chen, PhD[4], Ahmed A. Othman, PhD[4], Yihan Li, PhD[4], Heikki T. Mansikka, MD, PhD[4†], Amit Khatri, PhD[4], Neil Wishart, PhD[4†], John Liu, MD[4]

Secukinumab improves active psoriatic arthritis symptoms and inhibits radiographic progression: primary results from the randomised, double-blind, phase III FUTURE 5 study

Philip Mease,[1] Désirée van der Heijde,[2] Robert Landewé,[3] Shephard Mpofu,[4] Proton Rahman,[5] Hasan Tahir,[6] Atul Singhal,[7] Elke Boettcher,[8] Sandra Navarra,[9] Karin Meiser,[4] Aimee Readie,[10] Luminita Pricop,[10] Ken Abrams[10]

Mease P, *et al*. *Ann Rheum Dis* 2018;**0**:1–8.

Dual IL-17A and IL-17F neutralisation by bimekizumab in psoriatic arthritis: evidence from preclinical experiments and a randomised placebo-controlled clinical trial that IL-17F contributes to human chronic tissue inflammation

Sophie Glatt,[1] Dominique Baeten,[2,3] Terry Baker,[4] Meryn Griffiths,[5] Lucian Ionescu,[3] Alastair D G Lawson,[4] Ash Maroof,[5] Ruth Oliver,[1] Serghei Popa,[6] Foteini Strimenopoulou,[1] Pavan Vajjah,[1] Mark I L Watling,[1] Nataliya Yeremenko,[2] Pierre Miossec,[7] Stevan Shaw[5]

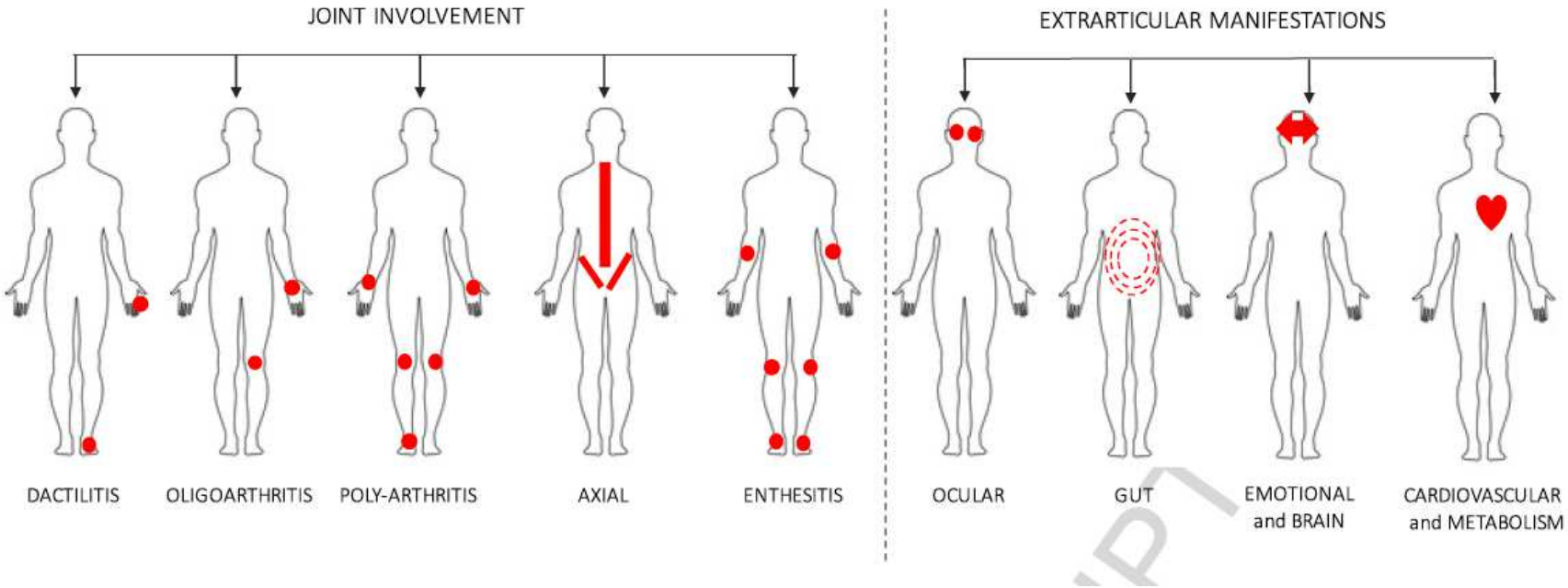
Traitements de fond des RIC

Box 1 | Future directions

- Future clinical trials comparing agents with different mechanisms of action (that is, TNF, IL-12–IL-23 and/or IL-17 inhibition) in head-to-head studies, supplemented with translational research, could provide us with information about which cytokine pathway predominates in the pathophysiology of psoriatic arthritis (PsA).
- Future clinical trials evaluating multidomain measures, such as composite disease activity indices and minimal disease activity criteria, might inform us about which targeted therapy enables better disease control for PsA.
- The microbiome of the gut or skin has been suggested to be relevant to the pathogenesis of PsA and could provide potential therapeutic targets.

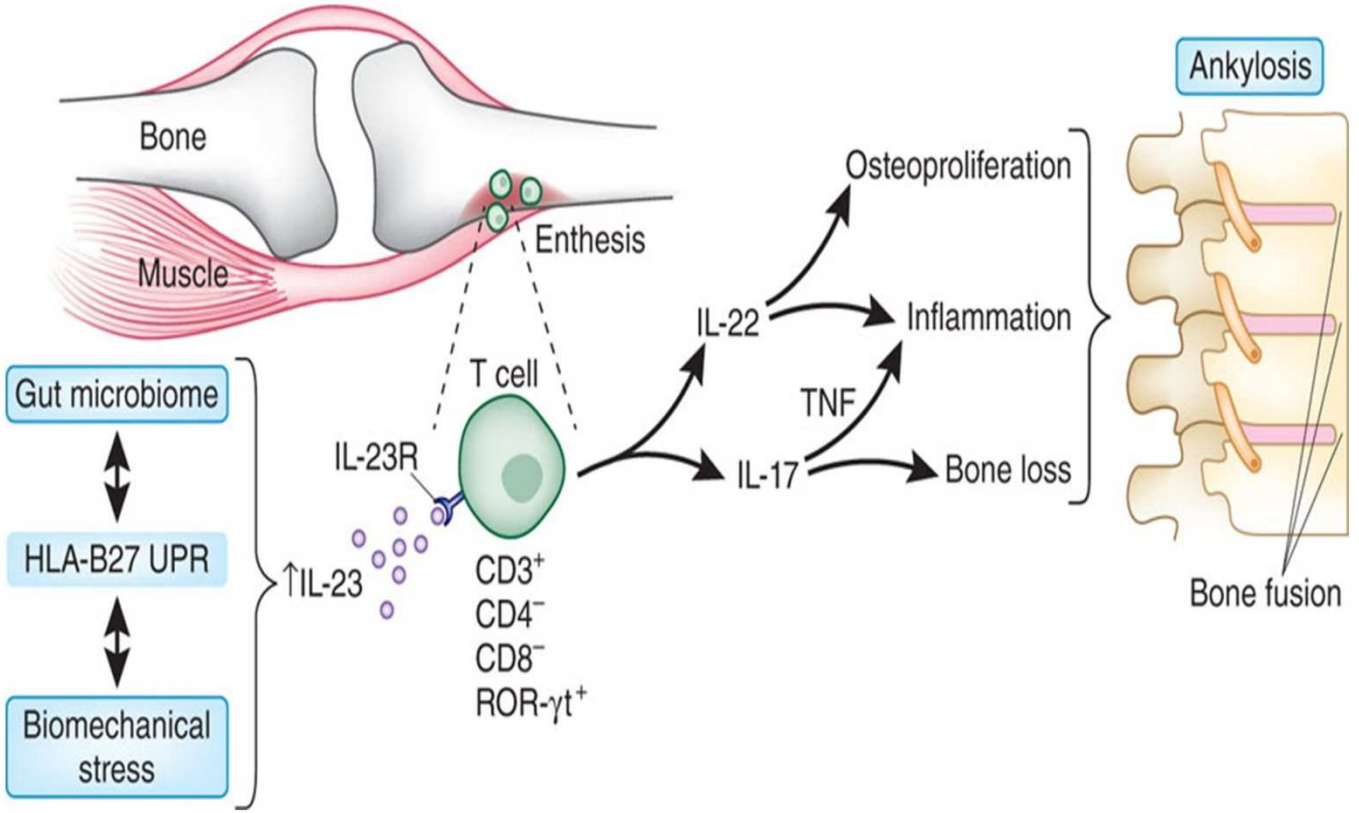
Amplifying the concept of psoriatic arthritis: The role of autoimmunity in systemic psoriatic disease

Maria Sole Chimenti, Francesco Caso, Stefano Alivernini, Erica De Martino, Luisa Costa, Barbara Tolusso, Paola Triggianese, Paola Conigliaro, Elisa Gremese, Raffaele Scarpa, Roberto Perricone



L’enthésite murine

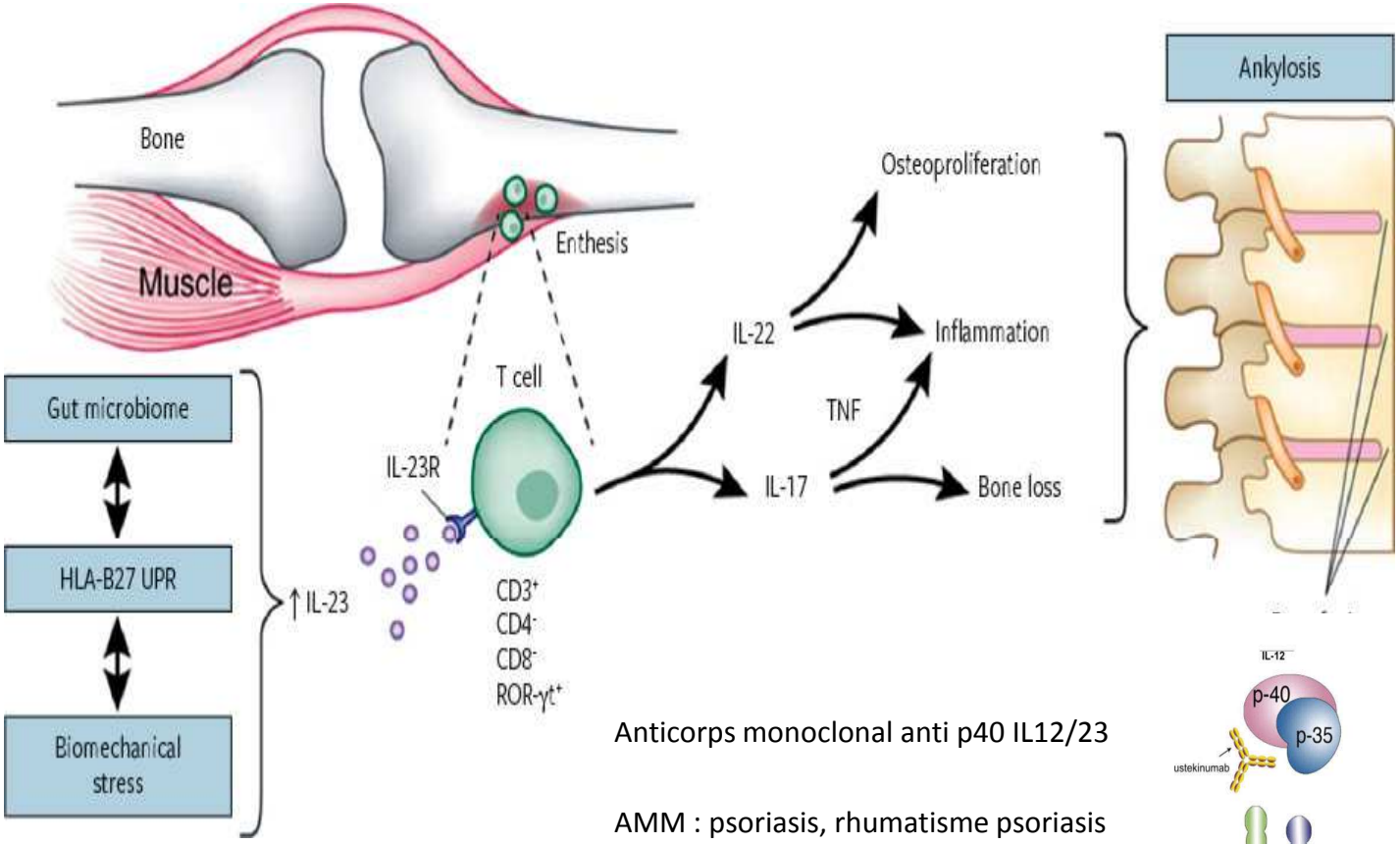
In a recent mouse model of SpA, IL-23 and entheseal-resident T cells were found to promote enthesitis and bone remodeling through IL-17 and IL-22[2,3]



SpA, spondyloarthritis.

1. Daoussis D et al. *Semin Arthritis Rheum.* 2010;39:369-383.
2. Lories RJ et al. *Nat Med*. 2012;18:1018-1019.
3. Sherlock JP et al. *Nat Med.* 2012;18:1069-1076.

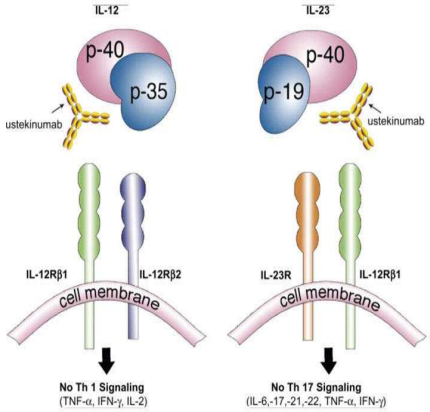
Etude ECLIPSA



Anticorps monoclonal anti p40 IL12/23

AMM : psoriasis, rhumatisme psoriasis et maladie de Crohn

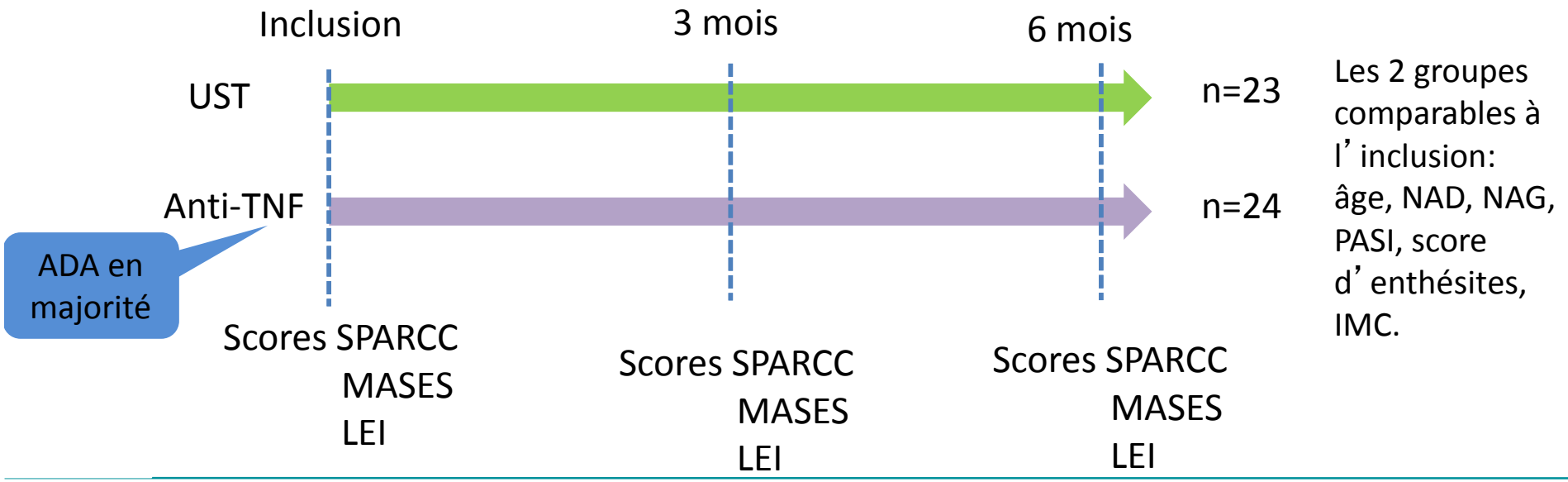
Commercialisé depuis 2009



Etude ECLIPSA

L'IL-23 est connue pour avoir un rôle dans le développement des enthésites. L'ustékinumab (UST), anticorps monoclonal anti-IL-12/IL-23, a démontré un effet important dans le rhumatisme psoriasique, rhumatisme dans lequel l'enthésite semble être la lésion centrale

Objectif: Comparer l'effet spécifique sur les enthesites du rhumatisme psoriasique, de l'inhibition de l'IL-23 par rapport à celui des anti-TNF avec une étude prospective, observationnelle ouverte

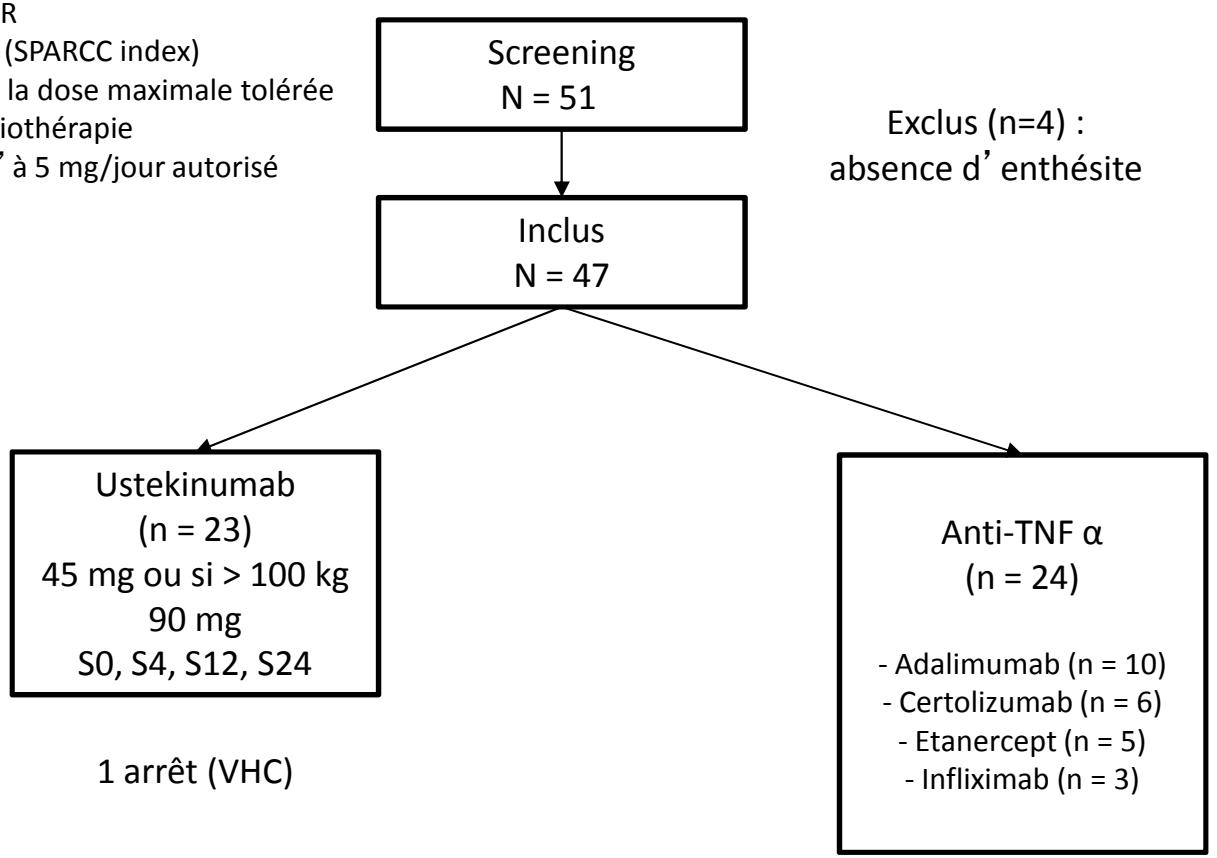


ADA: Adalimumab

ACR 2017 - D'après Araujo EG. et al., abstr. 881

Matériel & Méthodes

Critères d'inclusion :
Patients majeurs avec un diagnostique de rhumatisme psoriasique selon les critères de CASPAR
+ ≥ 1 enthèse douloureuse (SPARCC index)
+ Echec du Methotrexate à la dose maximale tolérée
+ Pas de ttt antérieur par biothérapie
A noter : Prednisone jusqu'à 5 mg/jour autorisé

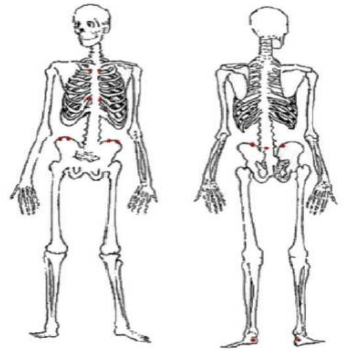


Mesure du CJP (SPARCC = 0) à M6
Visites à S0, M3, M6

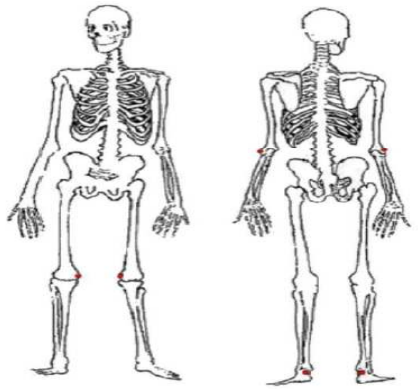
L’enthésite : indice métrologique

	MASES	SPARCC	LEI (Leeds)
First costochondral	R, L		
Seventh costochondral	R, L		
Supraspinatus insertion		R, L	
Lateral epicondyle humerus		R, L	R, L
Medial epicondyle humerus		R, L	
Posterior superior iliac spine	R, L		
Anterior superior iliac spine	R, L		
Iliac crest	R, L		
Fifth lumbar spinous process	X		
Achilles tendon	R, L	R, L	R, L
Greater trochanter		R, L	
Medial condyle femur			R, L
Insertion plantar fascia		R, L	
Quadriceps insertion patella		R, L	
Inferior pole patella (Tibial turbercle)		R, L (R,L)	

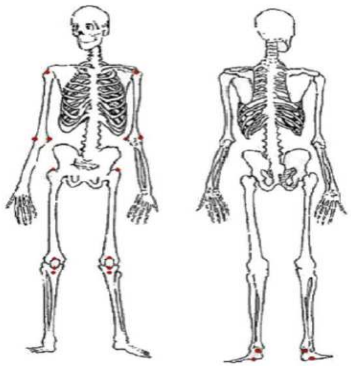
MASES: Maastricht Ankylosing Spondylitis Enthesis Score; SPARCC: Spondyloarthritis Research Consortium of Canada; LEI: Leeds Enthesitis Index; X: single site present, not bilateral; R: right; L: left.



MASES



LEI



SPARCC

Résultats

Table 1
Baseline characteristics

	UST (N = 23)	TNFi (N = 24)	p-value
Demographic characteristics			
Age (years)	62 (18)	58 (21)	0.31
Male/Female (%)	44/56	75/25	0.03*
BMI (units)	26 (4.0)	25 (4.8)	0.43
Duration of PsA (years)	2 (6.0)	3 (4.8)	0.38
Enthesitis Measures			
SPARCC (units)	4 (4.0)	3.5 (4.0)	0.16
MASES (units)	2 (2.0)	2 (2.8)	0.29
LEI (units)	1 (1.0)	1 (1.0)	0.79
Arthritis Measures			
TJC 68 (N)	4 (7)	5.5 (8)	0.30
SJC 66 (N)	4 (6)	5 (5)	0.80
DAS 28 (units)	4.0 (1.09)	4.4 (1.24)	0.14
DAPSA (units)	20.5 (13.37)	23.6 (14.50)	0.39
Skin and Nail Measures			
PASI (units)	3 (6.6)	2.8 (3.6)	0.99
NAPSI (units)	0 (5.0)	0 (15.3)	0.83
Other Measures			
BASDAI (units)	3.45 (2.55)	3.2 (1.6)	0.49
BASFI (units)	2.3 (2.30)	3.45 (2.10)	0.03*
LDI (units)	0 (4)	0 (12)	0.87
Pain, Function and Life Quality			
VAS pain (mm)	55 (35)	67 (28)	0.25
VAS global (mm)	55 (36)	62 (15)	0.50
HAQ-DI (units)	0.87 (0.63)	1.17 (0.62)	0.21
SF36- physical (units)	29.1 (9.6)	29.5 (9.5)	0.44
SF36- mental (units)	44.9 (12.3)	39.2 (10.4)	0.05*
FACIT (units)	32 (14)	33.5 (9)	0.39
Laboratory parameters			
CRP (mg/l)	3.5(3.8)	2.7(2.9)	0.26
ESR (mm/h)	14(16)	14.5(13)	0.69
Concomitant treatment			
Methotrexate (%)	82.6%	100%	0.05*
Glucocorticoids (%)	0%	4.2%	1.00

Values indicate medians and interquartile ranges in brackets. UST, ustekinumab (IL-12/23 inhibitor); TNFi, tumor necrosis factor inhibitors, SPARCC, Spondyloarthritis Research Consortium of Canada enthesitis index; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; LEI, Leeds enthesitis index; TJC, tender joint count, SJC, swollen joint count; DAS28, disease activity score 28; DAPSA, Disease Activity in PSA score; PASI, Psoriasis Area Severity Index; NAPSI, Nail Psoriasis Severity Index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Function Index; VAS, visual analogue scale; HAQ-DI, Health Assessment Questionnaire-Disability Index, SF-36, Short Form Health Survey; FACIT-F, Functional Assessment of Chronic Illness Therapy Fatigue; ESR, Erythrocyte sedimentation rate; CRP, C-reactive protein.

Bounds for significant results after Bonferroni-Holm adjustment are as follows: $p_6 = 0.0083$, $p_5 = 0.01$, $p_4 = 0.0125$, $p_3 = 0.0167$, $p_2 = 0.025$, $p_1 = 0.05$ (index numbers refer to the numbers of remaining inferential tests below the corresponding subheading).

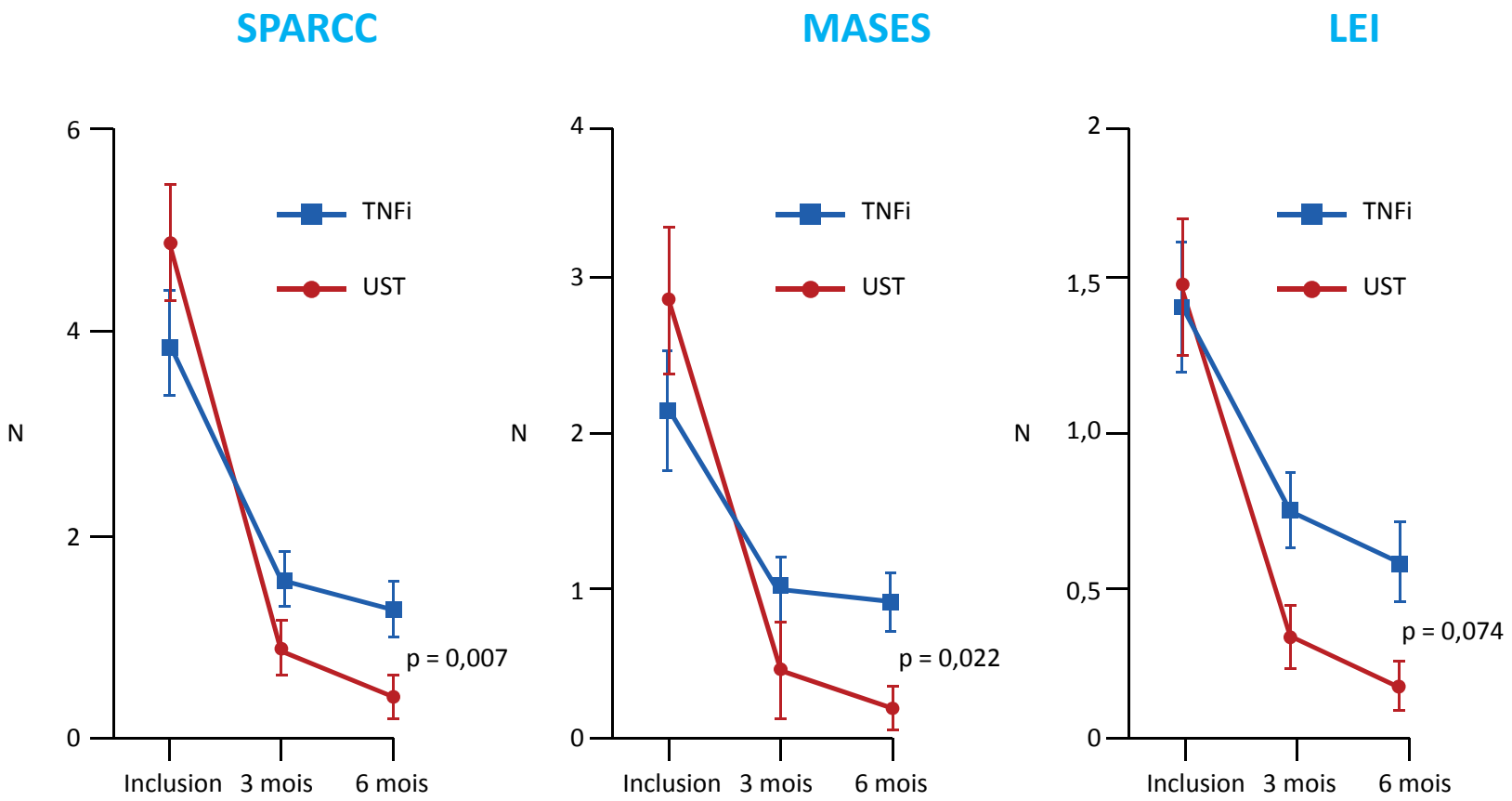
* Results are not significant after Bonferroni-Holm adjustment.

Table 2
Effects of IL-12/23- and TNF inhibition on enthesitis and other disease components of PsA

	UST				TNFi			
	Baseline	12 weeks	24 weeks	P value	Baseline	12 weeks	24 weeks	*p* value
Enthesitis Measures								
SPARCC	4 (4)	0 (2)	0 (0.3)	<0.001	3.5 (4)	1 (1.8)	1 (2)	<0.001
MASES	2 (2)	0 (0)	0 (0)	<0.001	2 (2.8)	1 (2)	1 (1.8)	0.001
LEI	1 (1)	0 (1)	0 (0)	<0.001	1 (1)	1 (1)	0.5 (1)	0.001
Arthritis Measures								
TJC68	4 (7)	0 (2)	0 (2)	<0.001	5.5 (8)	2 (4)	1 (2)	<0.001
SJC66	4 (6)	1 (2)	0 (1)	<0.001	5 (5)	1 (3)	1 (2)	<0.001
DAS28	4.04 (1.09)	2.2 (1.82)	2.7 (1.63)	<0.001	4.43 (1.24)	2.83 (1.73)	2.76 (1.33)	<0.001
DAPSA	20.6 (13.4)	4.7 (9.4)	3.61 (4.54)	<0.001	23.6 (14.5)	11.4 (10.6)	6.88 (6.22)	<0.001
Skin and Nail Measures								
PASI	3 (6.6)	0 (1.1)	0 (0.3)	<0.001	2.8 (3.6)	1.5 (2.9)	1 (2.1)	<0.001
NAPSI	0 (5)	0 (2)	0 (0.5)	0.021	0 (15.3)	0 (12)	0 (10.3)	0.012
Other Measures								
BASDAI	3.45 (2.55)	0.65 (1.03)	0.4 (0.75)	<0.001	3.20 (1.6)	1.50 (0.9)	1.1 (1.55)	<0.001
BASFI	2.3 (2.3)	0.28 (0.52)	0.19 (0.37)	<0.001	3.45 (2.1)	1.9 (1.2)	1.4 (1.28)	<0.001
LDI	0 (4)	0 (0)	0 (0)	0.043	0 (12)	0 (0)	0 (0)	0.028
Pain, Function and Life Quality								
VAS-pain	55 (35)	10 (27)	6 (19)	<0.001	67 (28)	30 (25)	19 (19)	<0.001
VAS-Global	55 (36)	10 (31)	9 (9)	<0.001	62 (15)	33 (20)	23.5 (18)	<0.001
HAQ-DI	0.87 (0.63)	0.25 (0.6)	0 (0.25)	<0.001	1.17 (0.62)	0.5 (0.5)	0.3 (0.35)	<0.001
SF36-physical	29.1 (9.6)	50.1 (13.3)	52.8 (6.1)	<0.001	29.5 (9.5)	40.9 (11.3)	46 (11.6)	<0.001
SF36- mental	44.9 (12.3)	52.9 (4.3)	52.9 (4.9)	0.001	39.2 (10.4)	46.2 (10)	48.15 (11.1)	<0.001
FACIT	32 (14)	48 (6)	49 (2)	<0.001	33.5 (9)	39 (7)	42.5 (7)	<0.001

Values indicate medians and interquartile ranges in brackets. UST, ustekinumab (IL-12/23 inhibitor); TNFi, tumor necrosis factor inhibitors, SPARCC, Spondyloarthritis Research Consortium of Canada enthesitis index; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; LEI, Leeds enthesitis index; TJC, tender joint count, SJC, swollen joint count; DAS28, disease activity score 28; DAPSA, Disease Activity in PSA score; PASI, Psoriasis Area Severity Index; NAPSI, Nail Psoriasis Severity Index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Function Index; VAS, visual analogue scale; HAQ-DI, Health Assessment Questionnaire- Disability Index, SF-36, Short Form Health Survey; FACIT-F, Functional Assessment of Chronic Illness Therapy Fatigue; ESR, Erythrocyte sedimentation rate; CRP, C-reactive protein. Bounds for significant results after Bonferroni-Holm adjustment are as follows: $p_6 = 0.0083$, $p_5 = 0.01$, $p_4 = 0.0125$, $p_3 = 0.0167$, $p_2 = 0.025$, $p_1 = 0.05$ (index numbers refer to the numbers of remaining inferential tests below the corresponding subheading in each treatment group). * All results remained significant after Bonferroni-Holm adjustment.

Effets sur les scores d'enthésites



ACR 2017 - D'après Araujo EG. et al., abstr. 881

Effets sur les scores cliniques

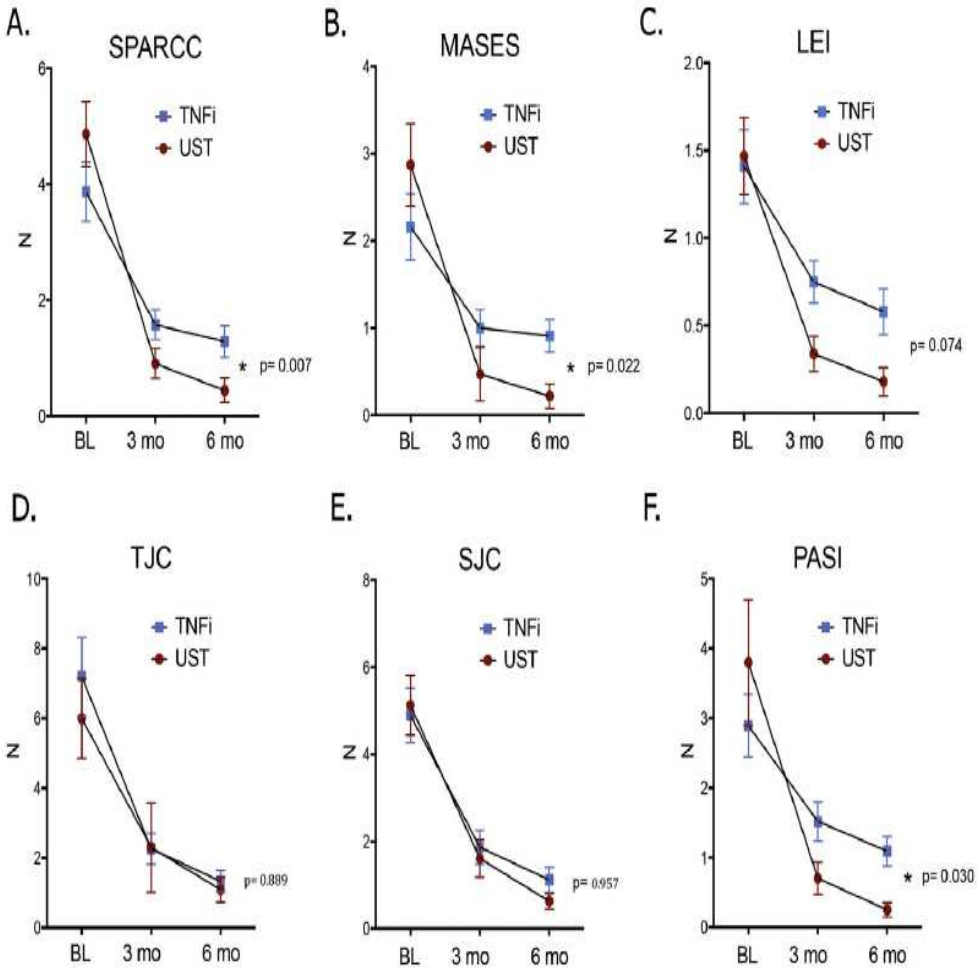


Fig. 1. Comparison of the effects of p40-IL-12/23- and TNF- inhibition on enthesitis, arthritis and skin disease in patients with psoriatic arthritis

Graphs show the effects of the p40-IL-12/23 inhibitor ustekinumab (UST) and of tumor necrosis factor inhibitors (TNFi) on measures of enthesitis (A-C), arthritis (D,E) and psoriatic skin disease (F); SPARCC, Spondyloarthritis Research Consortium of Canada enthesitis index; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; LEI, Leeds enthesitis index; TJC, tender joint count, SJC, swollen joint count; PASI, Psoriasis Area Severity Index; Values indicate means SEM. Statistics are based on ANOVA.

Résultat principal : CJP atteinte pour 73,9% des patients dans le groupe UST vs 41,7% dans le groupe anti-TNF α (p = 0,018)

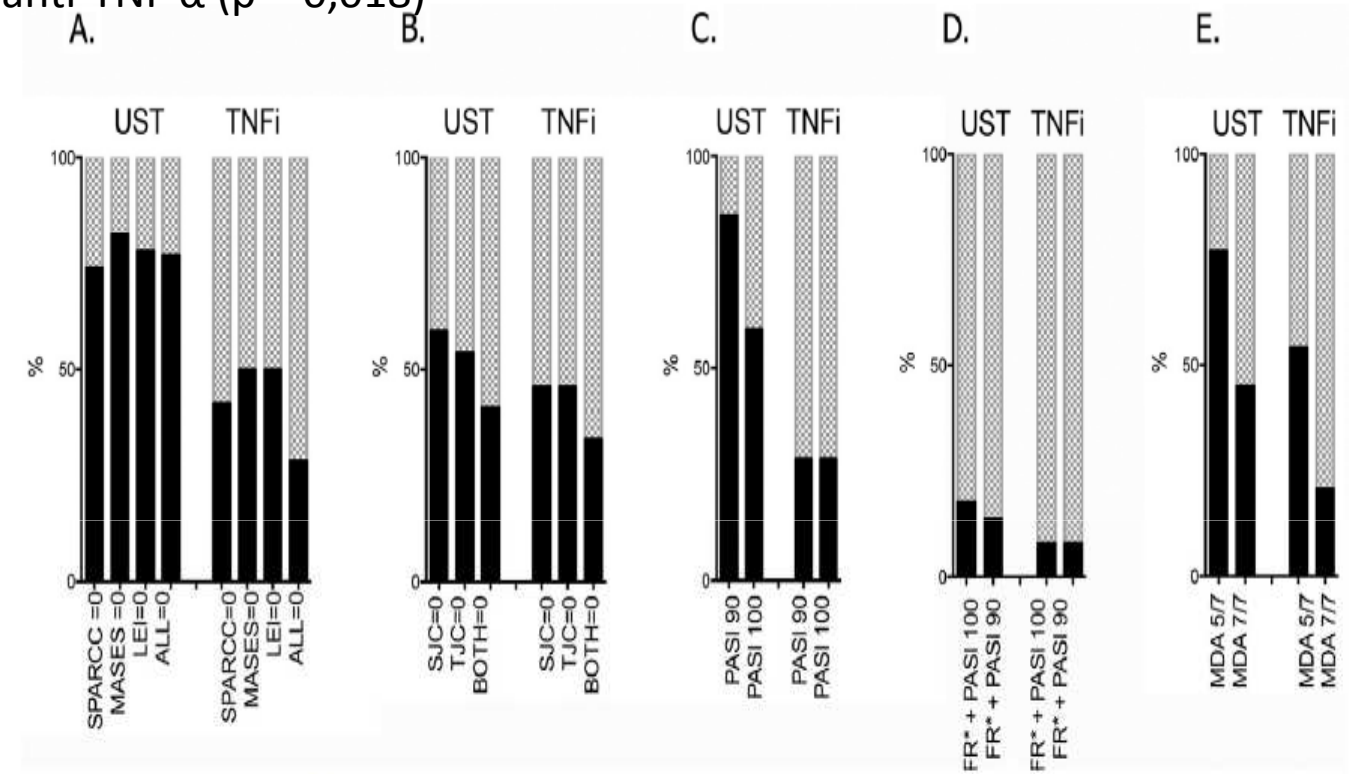


Fig. 2. Frequencies of complete clearance from enthesitis, arthritis and psoriatic skin disease

Graphs show the frequency of complete clearance of enthesitis (A), arthritis (B), psoriatic skin disease (C) and all three disease manifestations (D) in psoriatic arthritis patients treated with the p40-IL-12/23 inhibitor ustekinumab (UST) or tumor necrosis factor inhibitors (TNFi). In addition, the frequency of minimal disease activity (MDA) is shown (E). MDA5/7 indicates that 5 out of 7 components of MDA are fulfilled, 7/7 indicated that all 7 components are fulfilled. SPARCC, Spondyloarthritis Research Consortium of Canada enthesitis index; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; LEI, Leeds enthesitis index; TJC, tender joint count, SJC, swollen joint count; PASI, Psoriasis Area Severity Index; FR, full remission indicating that SPARCC, MASES, LEI, TJC, SJC are all equal to zero.

Conclusion

Etude non controlée observationnelle comparant deux stratégies thérapeutiques chez les patients présentant une atteinte enthésitique de rhumatisme psoriasique

Etude positive : meilleure efficacité de l'Ustekinumab vs anti-TNF-α sur l'atteinte enthésitique à 6 mois de traitement

Mais :

-Population non comparable

-Population faible et absence d'aveugle

Traitements de fond des RIC

Box 1 | Future directions

- Future clinical trials comparing agents with different mechanisms of action (that is, TNF, IL-12–IL-23 and/or IL-17 inhibition) in head-to-head studies, supplemented with translational research, could provide us with information about which cytokine pathway predominates in the pathophysiology of psoriatic arthritis (PsA).
- Future clinical trials evaluating multidomain measures, such as composite disease activity indices and minimal disease activity criteria, might inform us about which targeted therapy enables better disease control for PsA.
- The microbiome of the gut or skin has been suggested to be relevant to the pathogenesis of PsA and could provide potential therapeutic targets.

A head-to-head comparison of the efficacy and safety of ixekizumab and adalimumab in biological-naïve patients with active psoriatic arthritis: 24-week results of a randomised, open-label, blinded-assessor trial

Philip J Mease ,[1] Josef S Smolen,[2] Frank Behrens,[3] Peter Nash,[4] Soyi Liu Leage,[5] Lingnan Li,[5] Hasan Tahir,[6] Melinda Gooderham,[7] Eswar Krishnan,[5] Hong Liu-Seifert,[5] Paul Emery ,[8,9] Sreekumar G Pillai,[5] Philip S Helliwell,[10] The SPIRIT H2H study group

Author affiliations
[1]Swedish Medical Center/Providence St. Joseph Health and University of Washingtc Seattle, Washington, USA
[2]Department of Medicine 3, Medical University of Vienna, Vienna, Austria
[3]Rheumatology and Fraunhofer IME - Translational Medicine and Pharmacology, Goethe University, Frankfurt, Germany
[4]University of Queensland, Brisbane, Queensland, Australia
[5]Eli Lilly and Company, Indianapolis, Indiana, USA
[6]Barts Health, London, UK
[7]Skin Centre for Dermatology, Peterborough, Ontario, Canada
[8]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK
[9]Leeds Teaching Hospitals NHS Trust, Leeds, UK
[10]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK

Funding This study was funded by Eli Lilly and Company, which contributed to study design, data collection, data analysis, data interpretation, manuscript preparation and publication decisions.

Data availability statement Lilly provides access to all individual participant data collected during the trial, after anonymization, with the exception of pharmacokinetic or genetic data. Data are available to request 6 months after the indication studied has been approved in the US and EU and after primary publication acceptance, whichever is later. No expiration date of data requests is currently set once data are made available. Access is provided after a proposal has been approved by an independent review committee identified for this purpose and after receipt of a signed data sharing agreement. Data and documents, including the study protocol, statistical analysis plan, clinical study report, blank or annotated case report forms, will be provided in a secure data sharing environment. For details on submitting a request, see the instructions provided at www.vivli.org.

Received 14 March 2019
Revised 23 July 2019
Accepted 29 August 2019

Ixekizumab vs Adalimumab

IXEKIZUMAB (TALZ)

AC monoclonal humanisé
Anti IL17A

AMM dans le psoriasis modéré à sévère
depuis avril 2016
AMM dans le rhumatisme psoriasique
depuis avril 2018

ADALIMUMAB

AC monoclonal humain
Anti TNF α

AMM dans le rhumatisme psoriasique
depuis 2005
AMM dans le psoriasis modéré à sévère
depuis 2007

Matériel & Méthodes

Etude prospective randomisée multicentrique, en ouvert (évaluateurs en aveugle)

Critères d'inclusion :

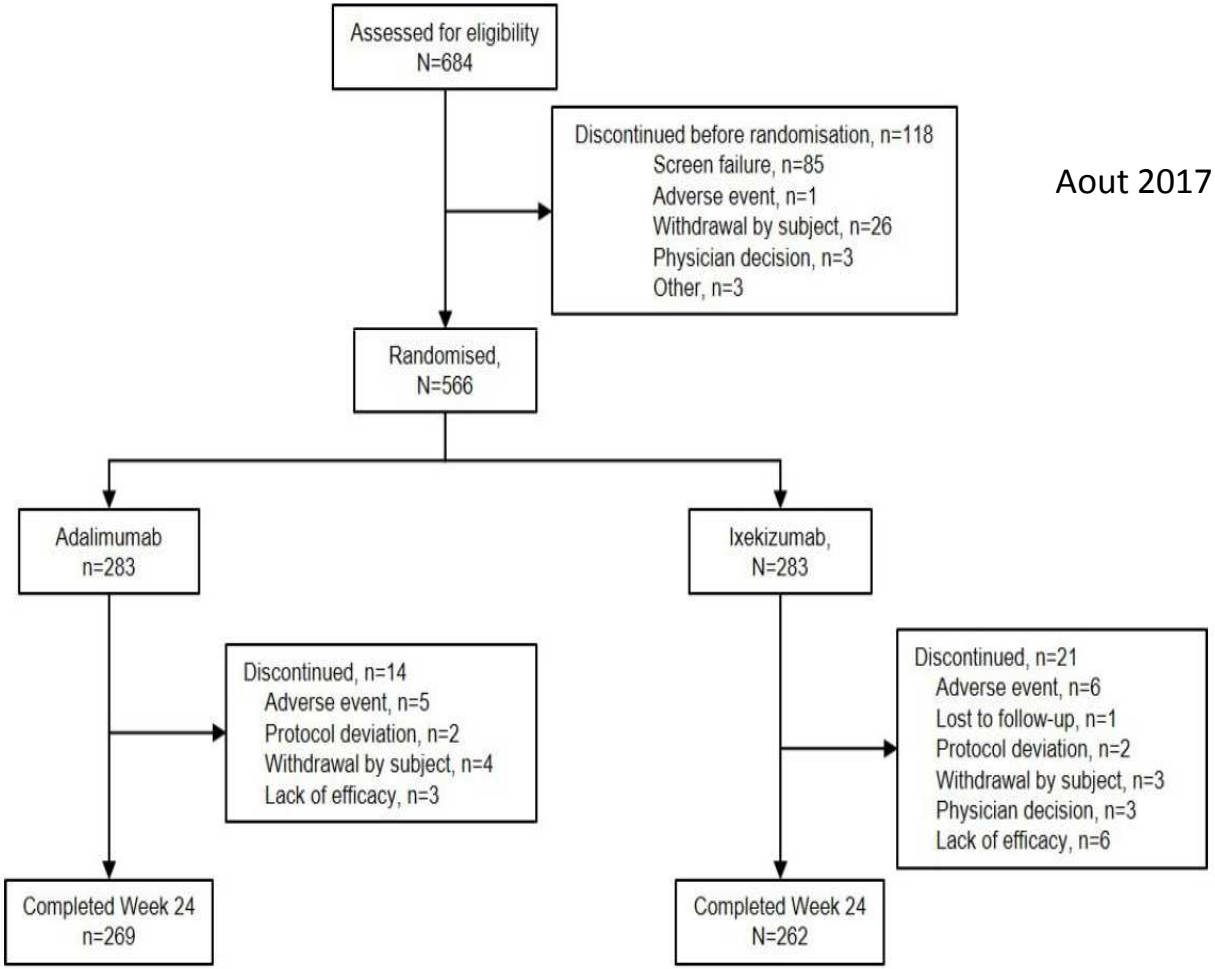
Patients avec un diagnostic de rhumatisme psoriasique selon les critères CASPAR établi depuis ≥ 6 mois

+ ≥ 3/66 NAG et ≥ 3/68 NAD
+ Psoriasis actif avec BSA ≥ 3%
+ Echec des csDMARD
+ Naïf de biothérapie

A noter : Poursuite des csDMARD autorisée

Critères	Points
1. Psoriasis (un des items) • Actuel • Antécédent personnel • Antécédent familial	 2 2 2
2. Onychose psoriasique	1
3. Absence de facteurs rhumatoïdes	1
4. Dactylite (un des items) • Actuel • Antécédent	 1 1
5. Image d'ossification juxta-articulaire à la main ou au pied (en dehors de l'arthrose)	1
→ Rhumatisme psoriasique si ≥ 3 points chez un patient ayant une maladie articulaire inflammatoire. Sensibilité : 91,4 % Spécificité : 98,7 %	

Matériel & Méthodes



Aout 2017 – Mai 2018

Résultats

Table 1 Baseline demographics and disease characteristics

	IXE (n=283)	ADA (n=283)
Baseline demographics		
Age, years	47.5 (12.0)	48.3 (12.3)
Sex, n (%)		
Male	162 (57)	150 (53)
Female	121 (43)	133 (47)
Race, n (%)		
White	222 (78)	211 (75)
Asian	29 (10)	33 (12)
Weight, kg	85.3 (19.8)	81.9 (18.3)
Body mass index, kg/m^2	30.0 (6.9)	29.7 (8.3)
Duration of symptoms since PsA diagnosis, years	6.6 (7.4)	5.9 (6.4)
Duration of symptoms since psoriasis diagnosis, years	16.1 (13.1)	14.7 (12.6)
Concomitant csDMARD use, n (%)	193 (68)	199 (70)
Concomitant methotrexate use, n (%)	167 (59)	169 (60)
Baseline disease scores		
Tender joint count	19.1 (12.7)	21.3 (15.4)
Swollen joint count	10.1 (7.5)	10.7 (8.1)
Patient pain VAS	59.7 (21.9)	62.4 (21.1)
Patient's global assessment of disease activity VAS, mm	62.4 (20.3)	65.2 (20.7)
Physician's global assessment of disease activity VAS, mm	58.9 (17.5)	59.4 (18.2)
HAQ-DI	1.2 (0.6)	1.3 (0.7)
C-reactive protein, mg/L	9.8 (13.7)	10.5 (19.3)
SPARCC Enthesitis Index >0, n (%)	189 (67)	171 (60)
SPARCC Enthesitis Index*	4.9 (3.5)	5.7 (3.8)
LEI >0, n (%)	159 (56)	147 (52)
LEI†	2.5 (1.4)	2.7 (1.5)
LDI-B >0, n (%)	42 (15)	58 (21)
LDI-B‡	40.1 (42.4)	55.8 (128.4)
PASDAS	5.8 (0.9)	5.8 (1.0)
DAPSA	42.7 (20.6)	45.8 (23.5)
Moderate-to-severe psoriasis, n (%)	49 (17)	51 (18)
PASI ≥12, n (%)	55 (19)	57 (20)
sPGA ≥3, n (%)	173 (61)	181 (64)
BSA ≥3%, n (%)	283 (100)	283 (100)
BSA ≥10%, n (%)	113 (40)	104 (37)
PASI	7.9 (8.7)	7.7 (7.3)
Percentage BSA	14.8 (18.4)	12.9 (15.6)
DLQI	9.8 (7.6)	9.8 (7.6)
NAPSI fingernails >0, n (%)	191 (68)	177 (63)
NAPSI fingernails§	19.7 (18.5)	19.1 (16.3)

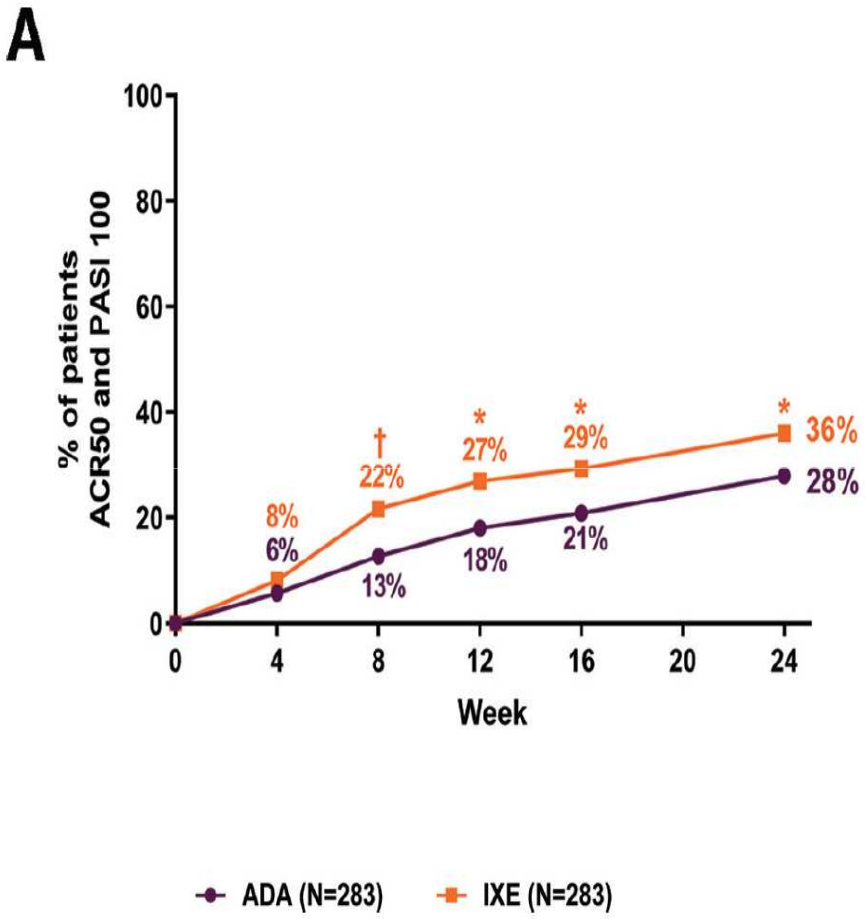
Table 2 Efficacy and health outcomes at week 24

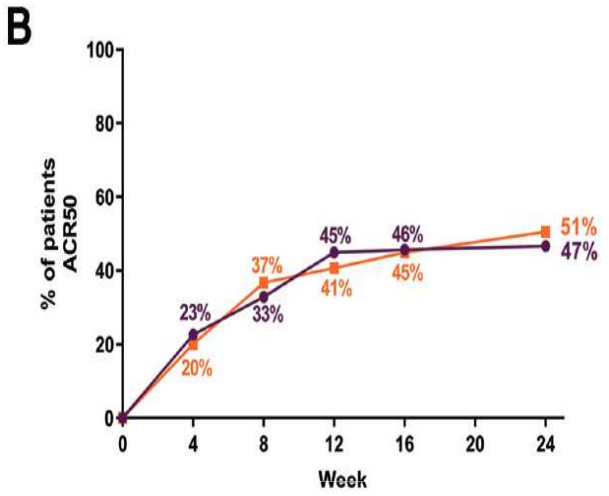
	IXE (n=283)	ADA (n=283)	Treatment difference IXE versus ADA (95% CI)	IXE versus ADA P value
Primary endpoint				
ACR50+PASI100	102/283 (36.0) 30.4% to 41.6%	79/283 (27.9) 22.7% to 33.1%	8.1% (0.5% to 15.8%)	0.036
Major secondary endpoints				
ACR50*	143/283 (50.5) 44.7% to 56.4%	132/283 (46.6) 40.8% to 52.5%	3.9% (-4.3% to 12.1%)	0.338
PASI100	170/283 (60.1) 54.4% to 65.8%	132/283 (46.6) 40.8% to 52.5%	13.4% (5.3% to 21.6%)	0.001
PsA endpoints				
MDA	135/283 (47.7) 41.9% to 53.5%	100/283 (35.3) 29.8% to 40.9%	12.4% (4.3% to 20.4%)	0.003
VLDA†	49/283 (17.3) 12.9% to 21.7%	29/283 (10.2) 6.7% to 13.8%	7.1% (1.4% to 12.7%)	0.015
DAPSA remission (≤4)†	75/283 (26.5) 21.4% to 31.6%	51/283 (18.0) 13.5% to 22.5%	8.5% (1.7% to 15.3%)	0.016
DAPSA low disease activity or remission (≤14)†	174/283 (61.5) 55.8% to 67.2%	171/283 (60.4) 54.7% to 66.1%	1.1% (-7.0% to 9.1%)	0.737
DAPSA, LSM change from baseline (SE)†	−31.74 (0.94)	−30.10 (0.94)	−1.64 (-3.94 to 0.66)	0.161

Table 2 Efficacy and health outcomes at week 24

	IXE (n=283)	ADA (n=283)	Treatment difference IXE versus ADA (95% CI)	IXE versus ADA P value
Primary endpoint				
ACR50+PASI100	102/283 (36.0) 30.4% to 41.6%	79/283 (27.9) 22.7% to 33.1%	8.1% (0.5% to 15.8%)	0.036
Major secondary endpoints				
ACR50*	143/283 (50.5) 44.7% to 56.4%	132/283 (46.6) 40.8% to 52.5%	3.9% (-4.3% to 12.1%)	0.338
PASI100	170/283 (60.1) 54.4% to 65.8%	132/283 (46.6) 40.8% to 52.5%	13.4% (5.3% to 21.6%)	0.001
PsA endpoints				
MDA	135/283 (47.7) 41.9% to 53.5%	100/283 (35.3) 29.8% to 40.9%	12.4% (4.3% to 20.4%)	0.003
VLDA†	49/283 (17.3) 12.9% to 21.7%	29/283 (10.2) 6.7% to 13.8%	7.1% (1.4% to 12.7%)	0.015
DAPSA remission (≤4)†	75/283 (26.5) 21.4% to 31.6%	51/283 (18.0) 13.5% to 22.5%	8.5% (1.7% to 15.3%)	0.016
DAPSA low disease activity or remission (≤14)†	174/283 (61.5) 55.8% to 67.2%	171/283 (60.4) 54.7% to 66.1%	1.1% (-7.0% to 9.1%)	0.737
DAPSA, LSM change from baseline (SE)†	−31.74 (0.94)	−30.10 (0.94)	−1.64 (-3.94 to 0.66)	0.161

Résultat principal :





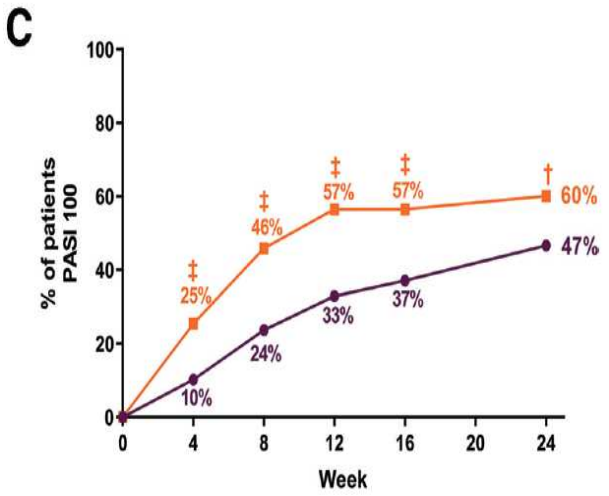


Table 2 Efficacy and health outcomes at week 24

	IXE (n=283)	ADA (n=283)	Treatment difference IXE versus ADA (95% CI)	IXE versus ADA P value
Primary endpoint				
ACR50+PASI100	102/283 (36.0) 30.4% to 41.6%	79/283 (27.9) 22.7% to 33.1%	8.1% (0.5% to 15.8%)	0.036
Major secondary endpoints				
ACR50*	143/283 (50.5) 44.7% to 56.4%	132/283 (46.6) 40.8% to 52.5%	3.9% (-4.3% to 12.1%)	0.338
PASI100	170/283 (60.1) 54.4% to 65.8%	132/283 (46.6) 40.8% to 52.5%	13.4% (5.3% to 21.6%)	0.001
PsA endpoints				
MDA	135/283 (47.7) 41.9% to 53.5%	100/283 (35.3) 29.8% to 40.9%	12.4% (4.3% to 20.4%)	0.003
VLDA†	49/283 (17.3) 12.9% to 21.7%	29/283 (10.2) 6.7% to 13.8%	7.1% (1.4% to 12.7%)	0.015
DAPSA remission (≤4)†	75/283 (26.5) 21.4% to 31.6%	51/283 (18.0) 13.5% to 22.5%	8.5% (1.7% to 15.3%)	0.016
DAPSA low disease activity or remission (≤14)†	174/283 (61.5) 55.8% to 67.2%	171/283 (60.4) 54.7% to 66.1%	1.1% (-7.0% to 9.1%)	0.737
DAPSA, LSM change from baseline (SE)†	−31.74 (0.94)	−30.10 (0.94)	−1.64 (-3.94 to 0.66)	0.161

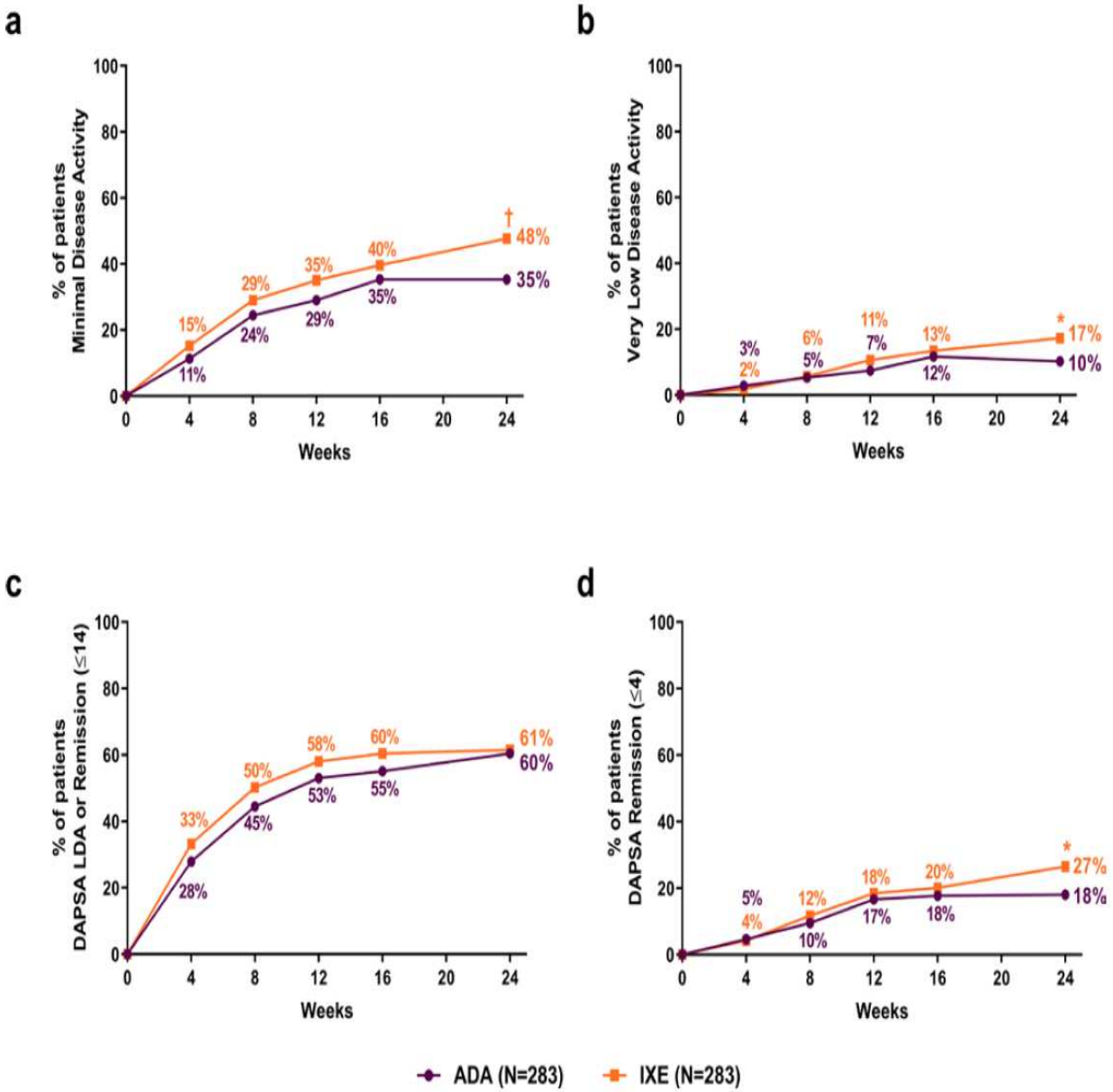


Figure 3 Clinical response rates for treat-to-target outcomes through week 24. (A) Percentage of patients achieving minimal disease activity. (B) Percentage of patients achieving very low disease activity. (C) Percentage of patients achieving a DAPSA score of ≤14 (LDA or remission). (D) Percentage of patients achieving a DAPSA score ≤4 (remission). IXE versus ADA: *P<0.05, †p<0.01, ‡p<0.001. ADA, adalimumab; DAPSA, Disease Activity in Psoriatic Arthritis; IXE, ixekizumab; LDA, low disease activity.

PASDAS low disease activity (≤3.2)†	164/283 (58.0) 52.2% to 63.7%	147/283 (51.9) 46.1% to 57.8%	6.0% (-2.2% to 14.2%)	0.153
PASDAS near remission (≤1.9)†	82/283 (29.0) 23.7% to 34.3%	55/283 (19.4) 14.8% to 24.0%	9.5% (2.5% to 16.6%)	0.009
PASDAS, LSM change from baseline (SE)†	−3.08 (0.10)	−2.94 (0.10)	−0.14 (-0.38 to 0.10)	0.260
mCPDAI, LSM change from baseline (SE)	−3.98 (0.14)	−3.46 (0.13)	−0.53 (-0.85 to −0.20)	0.002
ACR20	195/283 (68.9) 63.5% to 74.3%	204/283 (72.1) 66.9% to 77.3%	−3.2% (-10.7% to 4.3%)	0.403
ACR70	90/283 (31.8) 26.4% to 37.2%	73/283 (25.8) 20.7% to 30.9%	6.0% (-1.4% to 13.5%)	0.111
SPARCC Enthesitis Index=0‡	107/189 (56.6) 49.5% to 63.7%	77/171 (45.0) 37.6% to 52.5%	11.6% (1.3% to 21.9%)	0.019
LEI=0§	95/159 (59.7) 52.1% to 67.4%	81/147 (55.1) 47.1% to 63.1%	4.6% (-6.4% to 15.7%)	0.432
LDI-B=0¶	37/42 (88.1) 78.3% to 97.9%	54/58 (93.1) 86.6% to 99.6%	−5.0% (-16.8% to 6.8%)	0.658
Skin and nail psoriasis endpoints				
PASI75	227/283 (80.2) 75.6% to 84.9%	195/283 (68.9) 63.5% to 74.3%	11.3% (4.2% to 18.4%)	0.002
PASI90	203/283 (71.7) 66.5% to 77.0%	158/283 (55.8) 50.0% to 61.6%	15.9% (8.1% to 23.7%)	<0.001
NAPSI fingernails=0**	111/191 (58.1) 51.1% to 65.1%	88/177 (49.7) 42.4% to 57.1%	8.4% (-1.8% to 18.6%)	0.082
NAPSI, LSM change from baseline (SE)	−15.89 (0.82)	−12.53 (0.82)	−3.37 (-5.40 to −1.33)	0.001
Quality of life endpoints				
HAQ-DI ≥0.35††	168/252 (66.7) 60.8% to 72.5%	166/254 (65.4) 59.5% to 71.2%	1.3% (-6.9% to 9.6%)	0.741
DLQI (0, 1)	174/283 (61.5) 55.8% to 67.2%	147/283 (51.9) 46.1% to 57.8%	9.5% (1.4% to 17.7%)	0.020

Conclusion

Etude positive : meilleure efficacité simultanée sur l'atteinte articulaire et cutanée de Ixekizumab VS Adalimumab dans le rhumatisme psoriasique

Points forts :

- Etude innovante en « head to head ».
- Efficacité dans l'atteinte cutanée.

Points faibles :

- Critère composite.
- Efficacité cutanée attendue pouvant compromettre l'aveugle des évaluateurs.

Traitements de fond des RIC

Box 1 | Future directions

- Future clinical trials comparing agents with different mechanisms of action (that is, TNF, IL-12–IL-23 and/or IL-17 inhibition) in head-to-head studies, supplemented with translational research, could provide us with information about which cytokine pathway predominates in the pathophysiology of psoriatic arthritis (PsA).
- Future clinical trials evaluating multidomain measures, such as composite disease activity indices and minimal disease activity criteria, might inform us about which targeted therapy enables better disease control for PsA.
- The microbiome of the gut or skin has been suggested to be relevant to the pathogenesis of PsA and could provide potential therapeutic targets.

Traitements de fond des RIC

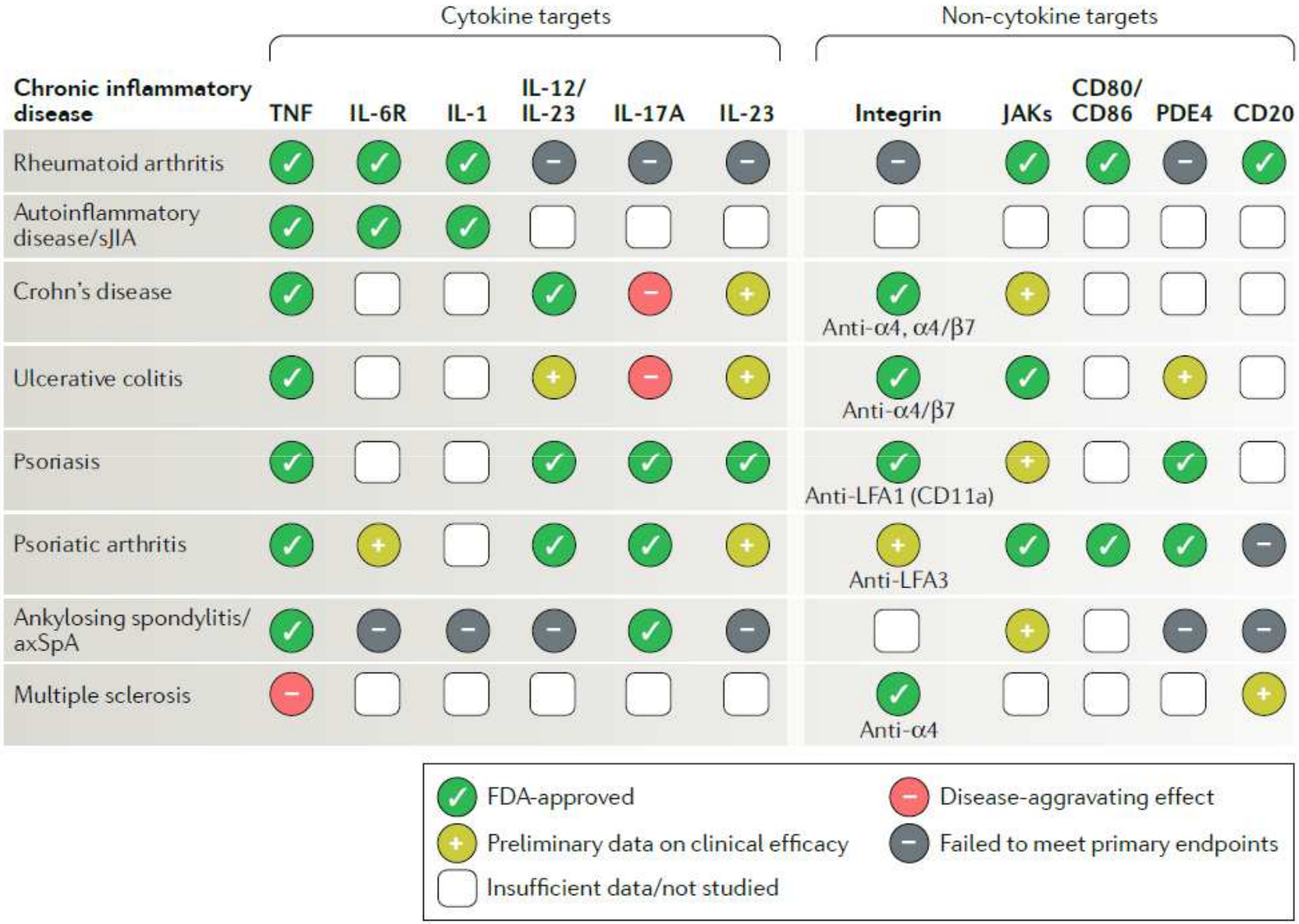


Fig. 3 | **Summary of cytokine and non-cytokine targets in various chronic inflammatory diseases.** This figure

2019