SOCIÉTÉ DE RHUMATOLOGIE DE L'OUEST

Comment utiliser les résultats des essais cliniques dans ma pratique ?

94ème journées **scientifiques de la SRO**

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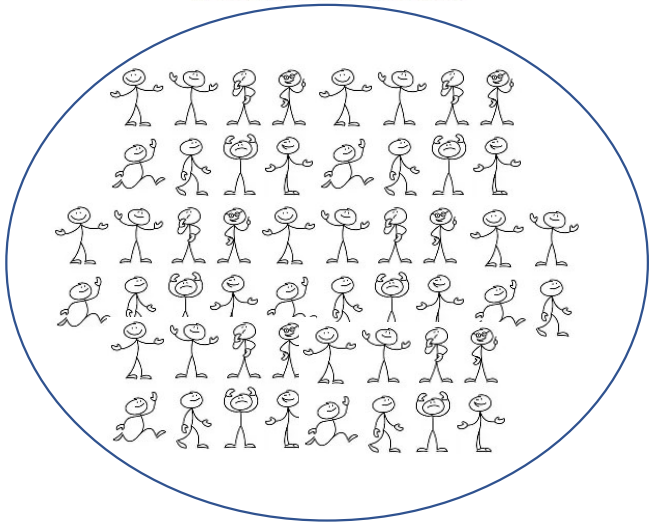
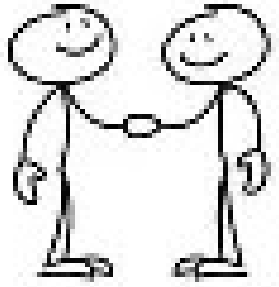
Réalité clinique vs Etude thérapeutique contrôlée : Un point de vue Différent !



Maladie (Classification)

Impact Thérapeutique à l'échelle d'une population « homogène » (%ge répondeur ou moyenne)

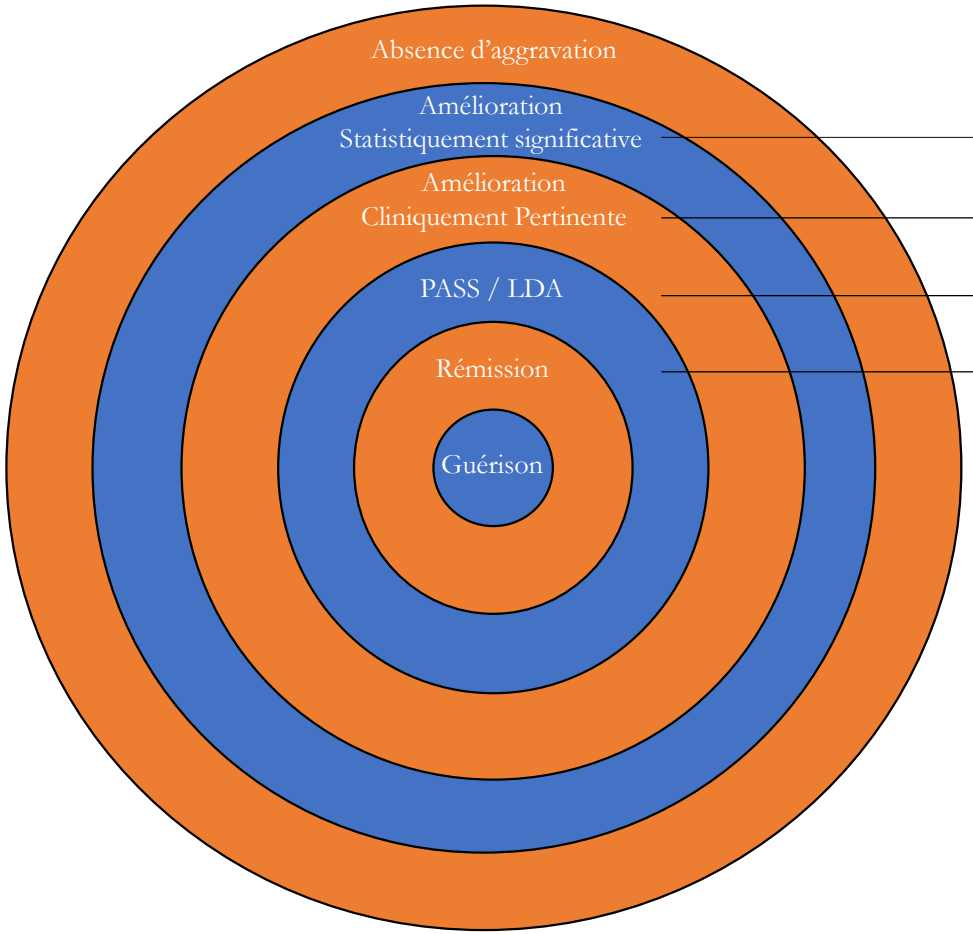


Malade (patient)

Impact Thérapeutique à l'échelle d'une individu (ça marche ou ça marche pas !)

Réalité clinique vs Etude thérapeutique contrôlée : Un point de vue Différent !

Treat to Target : Exemple de la Spondyloarthrite axiale



ASAS 20

ASAS 40 ou BASDAI 50 ou ΔASDAS > 1,1

BASDAI < 32/100 (PASS) ou ASDAS < 2,1

ASDAS < 1,3 (ou BASDAI < 20/100)

PASS : « Etat acceptable jugé par le patient »

Etude Phase 3 SpA

- BASDAI à l'inclusion > 60/100 (malgré AINS > 2 mois)
- Critère de jugement principal de l'étude ASAS 20 (FDA) ou ASAS 40 (EMA)

« vraie vie »

- BASDAI > 40/100 malgré AINS > 2 mois
- Critère de jugement du patient « je vais mieux docteur » (PASS soit BASDAI < 32/100)

Rappel Méthodologique études comparatives

L'étude veut vérifier l'hypothèse (H1) que le traitement est significativement efficace (supérieur) au placebo (ou autre traitement de référence).

H0 est l'hypothèse nulle soit l'absence de différence entre traitement et placebo.

		Décision Test	
		Rejet de H0	Echec du Rejet d'H0
Hypothèse formulée	H0 vraie	Erreur de Type 1 (risque α) Faux positif	**Décision correct** Intervalle de confiance (1-α)
	H1 vraie	**Décision correct** Puissance (1 - β)	Erreur de Type 2 (risque β) Faux Négatif

Risque α (risque de première espèce)

=

garantie une relative solidité à la conclusion sur l'effet du traitement en écartant raisonnablement le risque d'une conclusion erronée

IC95% , risque α = 5%

Risque β (risque de deuxième espèce)

=

Manque de puissance ne permettant pas de voir une réelle différence

Puissance (1- β) (80 à 90%)

Rappel Méthodologique études comparatives

En théorie, une étude ne devrait évaluer qu'une seule question (HO *ou* H1) permettant de calculer le nombre de sujet nécessaire en assumant les risques α et β, selon l'ampleur de la réponse thérapeutique attendue avec le traitement et l'effet placebo

		Décision Test	
		Rejet de H0	Echec du Rejet d'H0
Hypothèse formulée	H0 vraie	Erreur de Type 1 (risque α) Faux positif	**Décision correct** Intervalle de confiance (1-α)
	H1 vraie	**Décision correct** Puissance (1 - β)	Erreur de Type 2 (risque β) Faux Négatif

= Critère de jugement principal

Rappel Méthodologique études comparatives

⚠️ Culte du « *p < 0,05* » *(différence statiquement significative)*

		Décision Test	
		Rejet de H0	Echec du Rejet d'H0
Hypothèse formulée	H0 vraie	Erreur de Type 1 (risque α) Faux positif	**Décision correct** Intervalle de confiance (1-α)
	H1 vraie	**Décision correct** Puissance (1 - β)	Erreur de Type 2 (risque β) Faux Négatif ?

Nombre de sujet nécessaire suffisant (Puissance)

- Rôle de l'effet thérapeutique
- Rôle de l'effet placebo

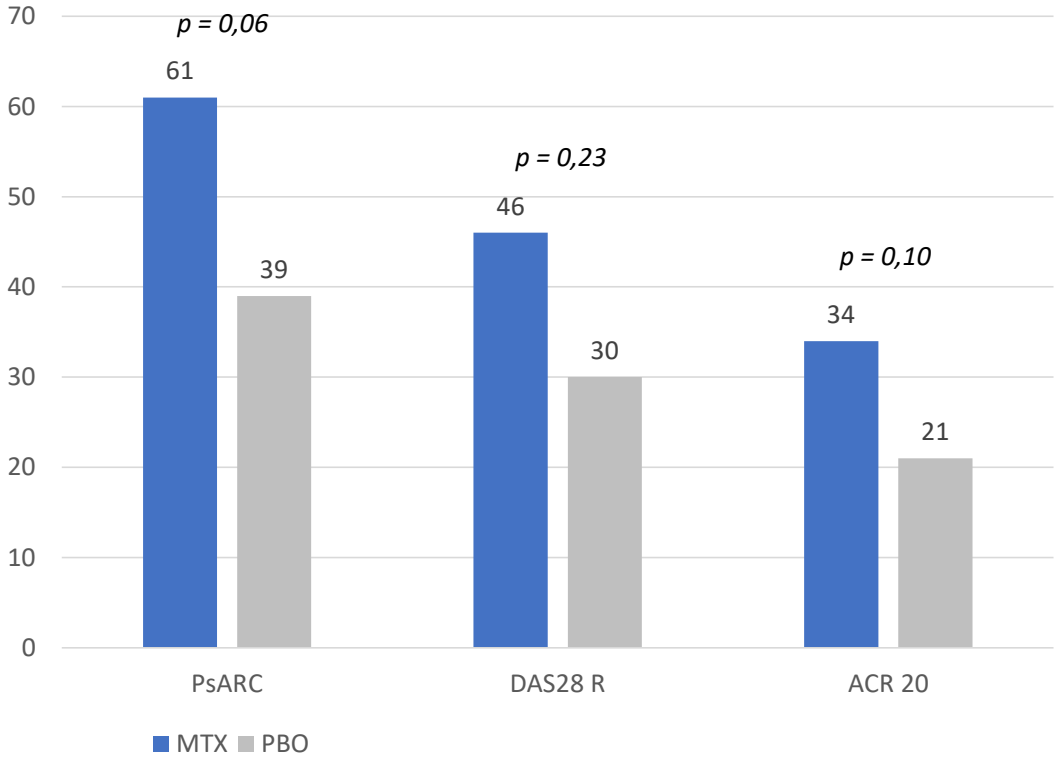
RHEUMATOLOGY

Rheumat
doi:10.1(
Advance Access publ

Original article

A randomized placebo-controlled trial of methotrexate in psoriatic arthritis

...recommended reducing the PsARC response rates for placebo to 35% and reducing the active response rate to 59%



	MTX (*n* = 109)	Placebo (*n* = 112)
Gender, females : males, *n* (%)	53 (49) : 56 (51)	44 (39) : 68 (61)
Ethnicity, white European/other, *n* (%)	105 (96)/4 (4)	109 (97)/3(3)
Age, mean (S.D.), years	46 (13)	51 (11)
Disease duration, years	1 (1–5)	1 (1–6)
Smoking status		
Never, *n* (%)	57 (53)	51 (45)
Previous, *n* (%)	23 (21)	38 (34)
Current, *n* (%)	28 (26)	23 (21)
Height, cm	170 (162–177)	170 (162–178)
Weight, kg	83 (74–96)	86 (74–97)
Pattern of arthritis, oligoarticular/polyarticular disease, *n* (%)	38 (35)/71 (65)	41 (37)/71 (63)
Previous SSZ treatment, *n* (%)	25 (23)	22 (20)
Concomitant analgesics, *n* (%)	10 (9)	13 (12)
Concomitant NSAIDs, *n* (%)	89 (82)	90 (80)
Tender joint count, range 0–68	9 (4–15)	11 (6–18)
Swollen joint count, range 0–66	6 (3–12)	6 (2–11)
ESR, mm/h	15 (7–28)	12 (6–24)
CRP, mg/dl	7 (5–16)	9 (5–19)
HAQ, range 0–3	0.88 (0.38–1.50)	1.13 (0.63–1.63)
Patient's global assessment, 100-mm VAS	47 (30–70)	49 (28–69)
Assessor's global assessment, 100-mm VAS	39 (28–56)	41 (30–57)
Pain, 100-mm VAS	36 (25–59)	42 (27–65)

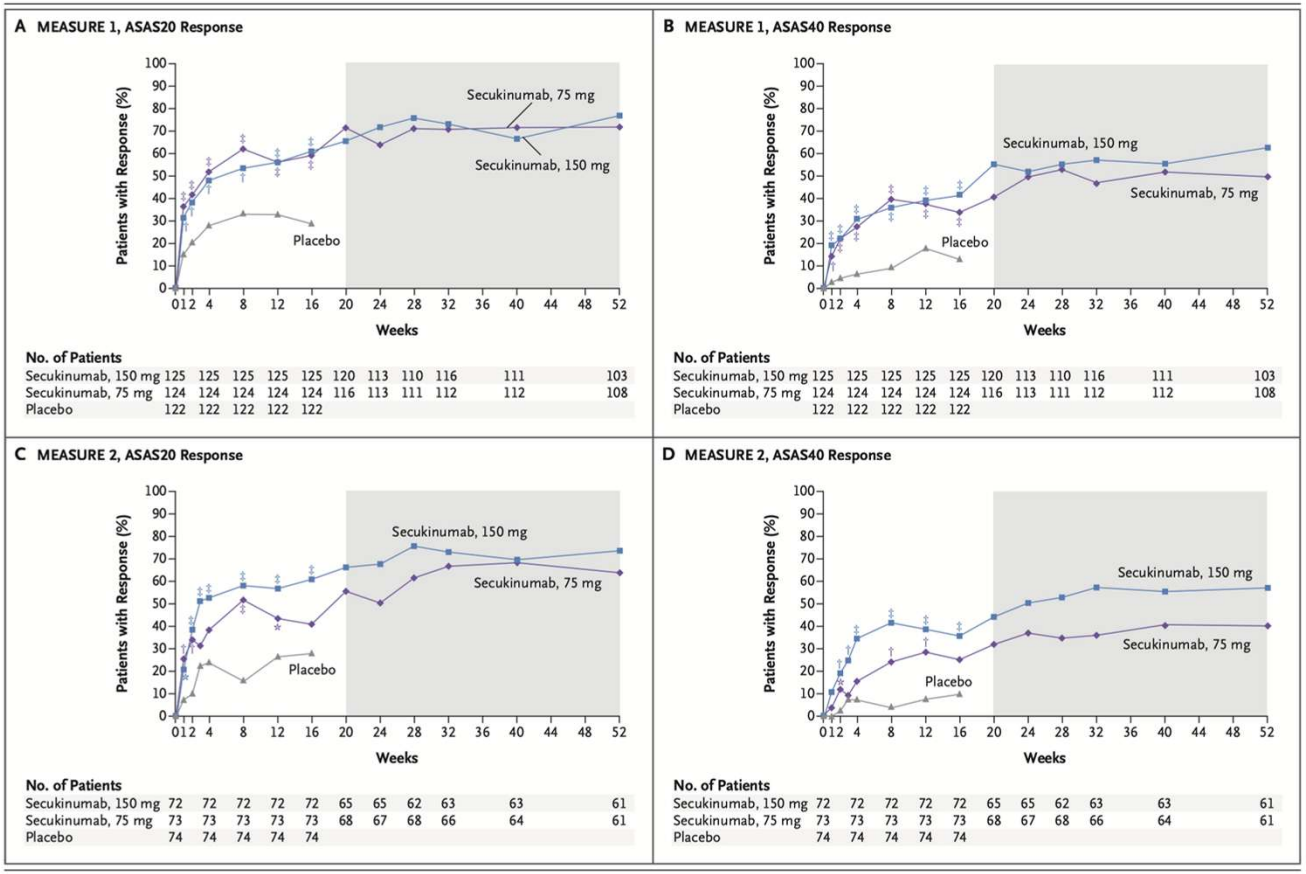
Medians (interquartile range) are shown for clinical variables, unless otherwise mentioned.

Kingsley. Rheumatology 2012;51:1368-1377

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Secukinumab, an Interleukin-17A Inhibitor, in Ankylosing Spondylitis



Baeten D. N Engl J Med. 2015 Dec 24;373(26):2534-48.

Rheumatol Ther (2018) 5:447–462
https://doi.org/10.1007/s40744-018-0123-5

ORIGINAL RESEARCH

Efficacy and Safety of Secukinumab 150 mg with and Without Loading Regimen in Ankylosing Spondylitis: 104-week Results from MEASURE 4 Study

Alan J. Kivitz · Ulf Wagner · Eva Dokoupilova · Jerzy Supronik · Ruvie Martin · Zsolt Talloczy · Hanno B. Richards · Brian Porter

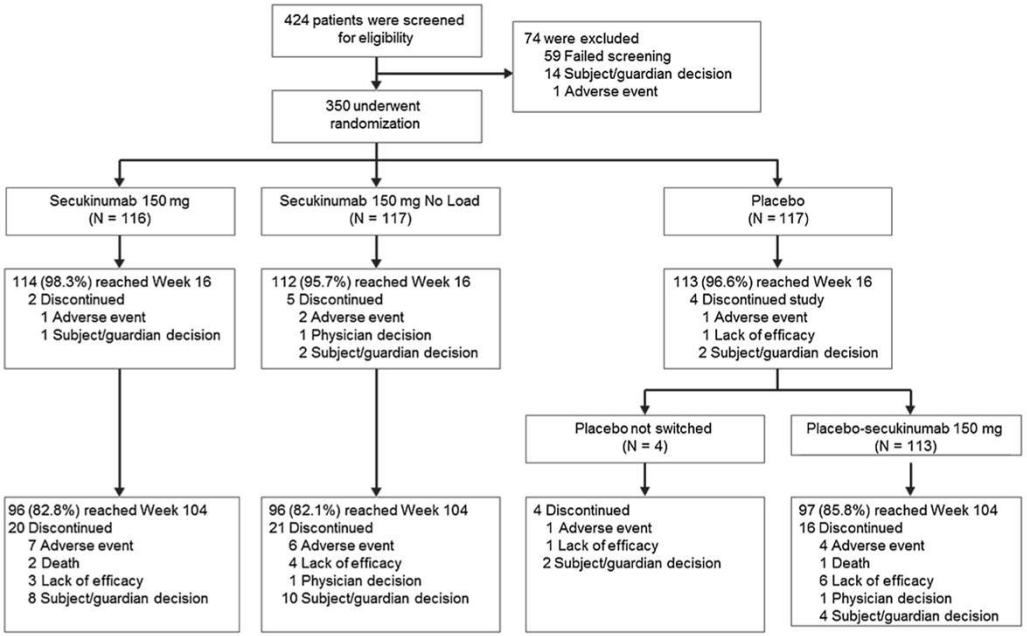


Table 1 Patient demographics and baseline clinical characteristics

Characteristic	Secukinumab 150 mg (*N* = 116)	Secukinumab 150 mg no load (*N* = 117)	Placebo (*N* = 117)
Age (years), mean ± SD	44.5 ± 11.62	41.2 ± 11.07	43.4 ± 12.46
Male, *n* (%)	81 (69.8)	83 (70.9)	76 (65.0)
Caucasian, *n* (%)	113 (97.4)	117 (100)	114 (97.4)
Weight (kg), mean ± SD	83.4 ± 20.35	80.3 ± 18.23	80.6 ± 17.10
Time since AS diagnosis (years), mean ± SD	8.4 ± 10.84	6.5 ± 7.55	7.1 ± 9.23
HLA-B27 positive at baseline, *n* (%)	100 (86.2)	99 (84.6)	93 (79.5)
TNFi-naïve, *n* (%)	85 (73.3)	85 (72.6)	83 (70.9)
Total BASDAI score, mean ± SD	7.0 ± 1.23	6.95 ± 1.31	7.1 ± 1.27
hsCRP (mg/l), median (min–max)	6.25 (0.4–123.0)	6.20 (0.3–120.9)	5.40 (0.3–129.3)
Total back pain score (0–100 mm scale), mean ± SD	74.9 ± 13.07	74.2 ± 14.18	75.0 ± 13.80
Previous systemic treatment, *n* (%)			
Methotrexate use at randomization	11 (9.5)	11 (9.4)	10 (8.5)
Sulfasalazine use at randomization	16 (13.8)	16 (13.7)	27 (23.1)
Corticosteroid use at randomization	11 (9.5)	10 (8.5)	13 (11.1)
Cumulative NSAID score, mean ± SD	64.0 (46.10)	68.3 (46.20)	60.4 (51.25)
Medical history, *n* (%)			
Uveitis	23 (19.8)	21 (17.9)	27 (23.1)
Inflammatory bowel disease	2 (1.7)	4 (3.4)	0

AS ankylosing spondylitis, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *hsCRP* high-sensitivity C-reactive protein, *HLA* human leukocyte antigen, *N* number of patients randomized, *n* number of responders, *NSAID* non-steroidal anti-inflammatory drugs, *s.c.* subcutaneous, *SD* standard deviation, *TNFi* tumor necrosis factor-alpha inhibitors

The ASAS20 response rate (primary endpoint) was assumed to be 61% for the secukinumab 150 mg and 56% for the secukinumab 150 mg no load groups, both compared with placebo (27%) at week 16.

Kivitz AJ. Rheumatol Ther. 2018 Dec;5(2):447-462.

Rheumatol Ther (2018) 5:447–462
https://doi.org/10.1007/s40744-018-0123-5

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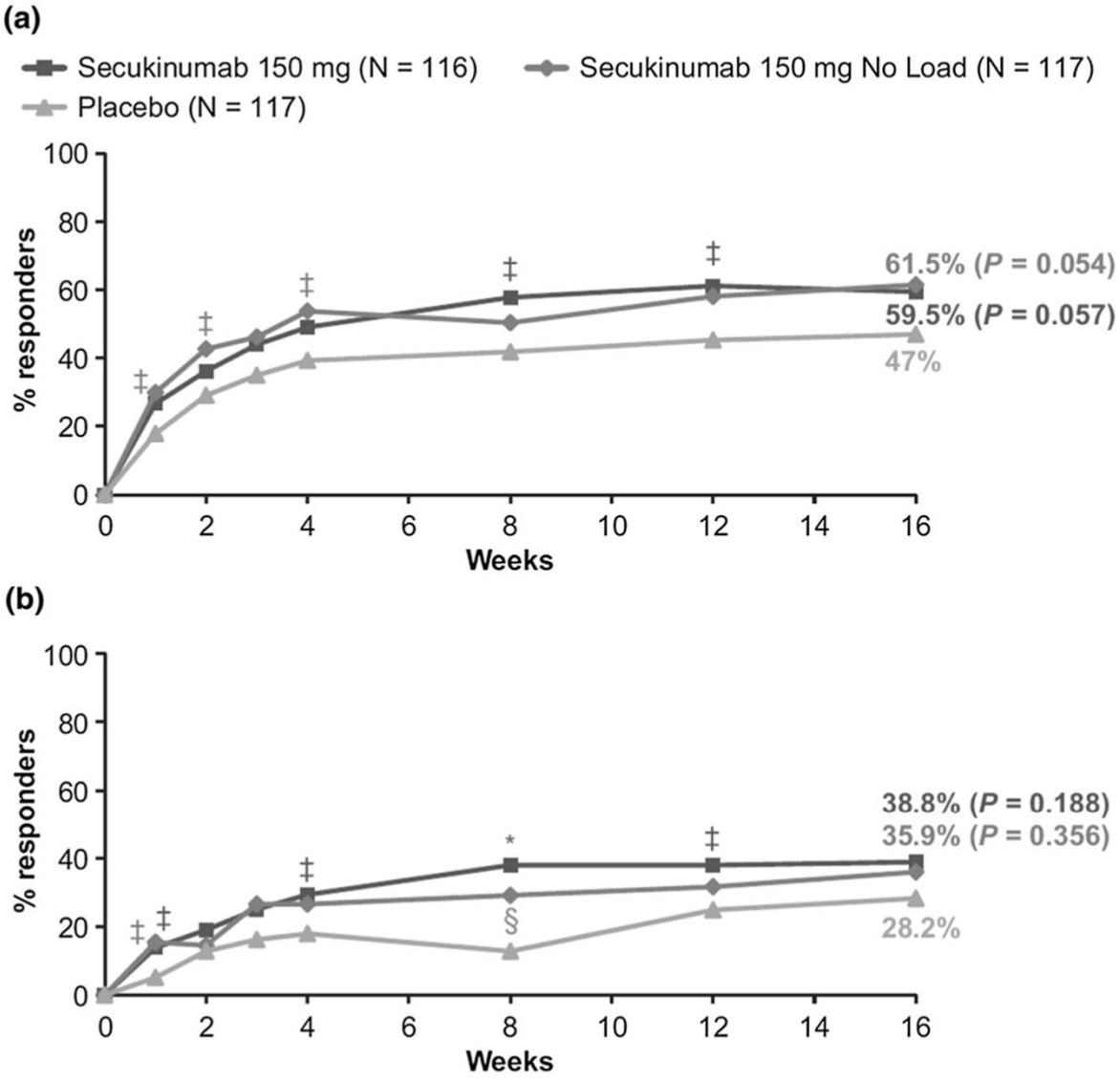
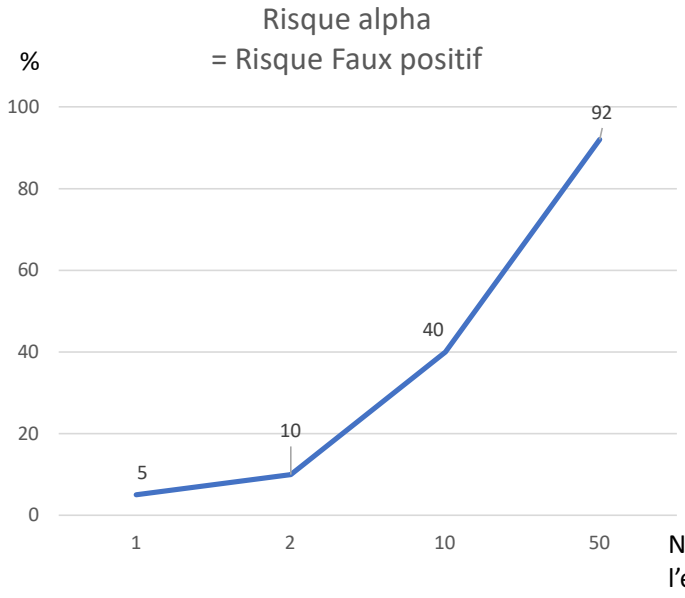


Kivitz AJ. Rheumatol Ther. 2018 Dec;5(2):447-462.

Rappel Méthodologique études comparatives

⚠️ Répondre à plusieurs (« plein ») questions différentes *a posteriori* (non préalablement programmé) = Etude Post-hoc



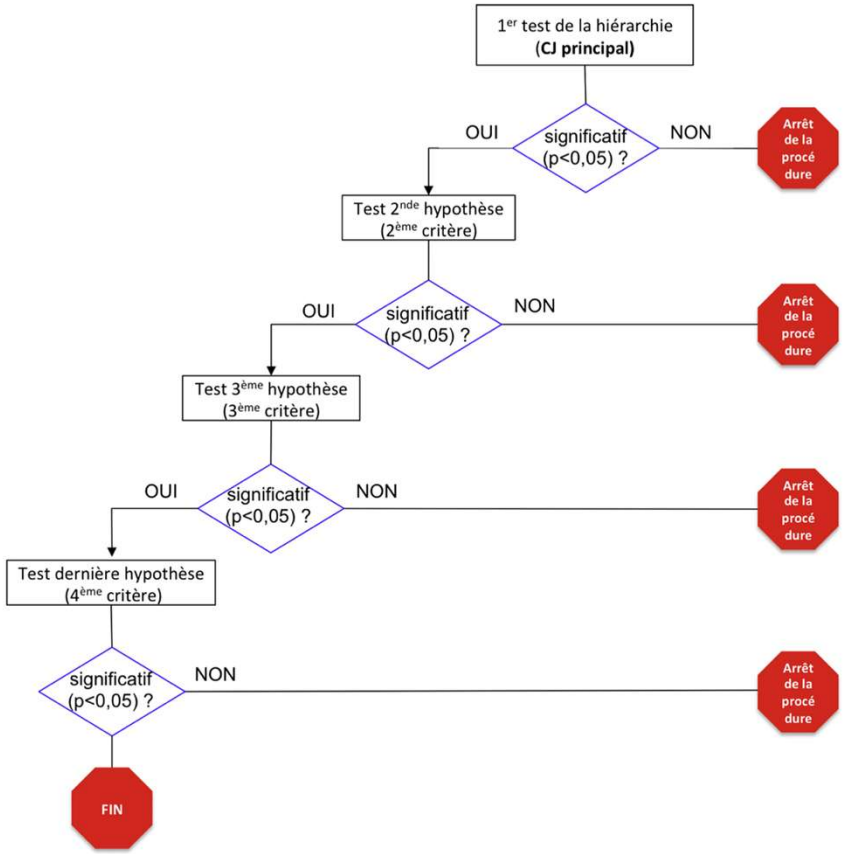
La répétition à chaque test du risque d'obtenir un résultat significatif « par hasard » augmente le risque global de conclure à tort à l'efficacité du traitement.

=

inflation du risque alpha

« les données ont été torturées jusqu'à ce qu'elles avouent ! »

Rappel Méthodologique études comparatives



La méthode séquentielle hiérarchique.

Pour éviter une « pêche à la ligne» sur tous les critères secondaires restants, la **méthode séquentielle hiérarchique** a parfaitement défini le critère unique qui devait être examiné pour chercher ce second avantage supplémentaire et ainsi il n'y a pas d'inflation du risque alpha sur cette recherche.

Comment sélectionner les critères à inclure dans la hiérarchie ?

- Point du vue du clinicien : le plus pertinent pour le patient
- Point de vue de l'industriel : le plus de critère secondaire possible (le plus pertinent pour la molécule)
- Point de vue des autorités : cahier des charges consultatifs

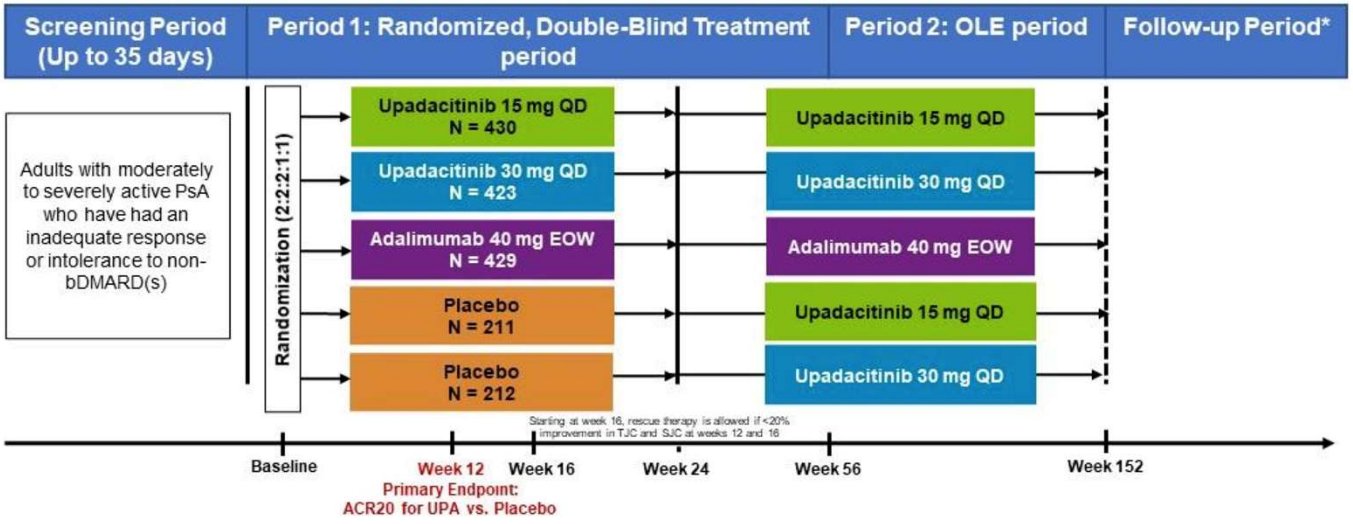
Laporte S. Therapie. 2016 Feb;71(1):27-41.

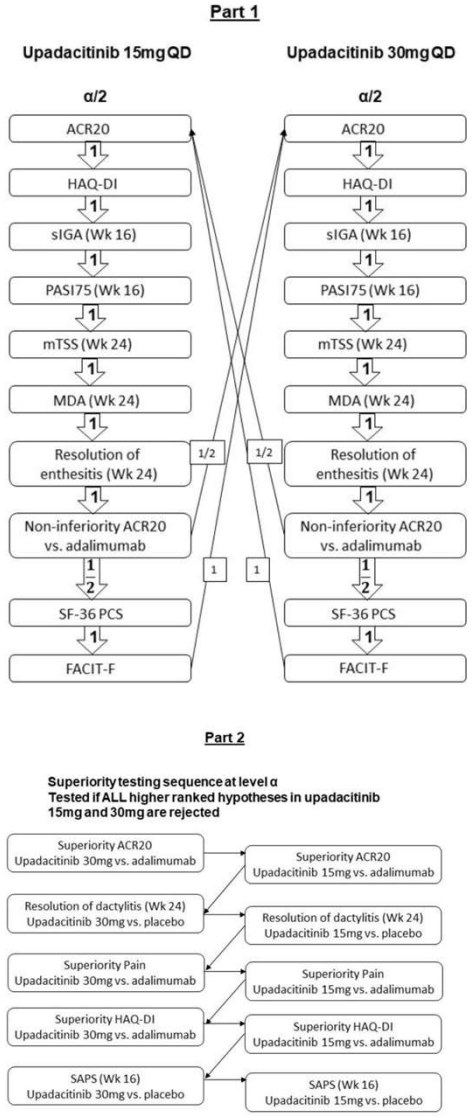
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trial of Upadacitinib and Adalimumab for Psoriatic Arthritis

Iain B. McInnes, F.R.C.P., Jaclyn K. Anderson, D.O., Marina Magrey, M.D., Joseph F. Merola, M.D., Yi Liu, M.D., Mitsumasa Kishimoto, M.D., Slawomir Jeka, M.D., Cesar Pacheco-Tena, M.D., Ph.D., Xin Wang, Ph.D., Liang Chen, M.S., Patrick Zueger, Pharm.D., Ph.D., John Liu, M.D., Aileen L. Pangan, M.D., and Frank Behrens, M.D.





McInnes IB. N Engl J Med. 2021 Apr 1;384(13):1227-1239.

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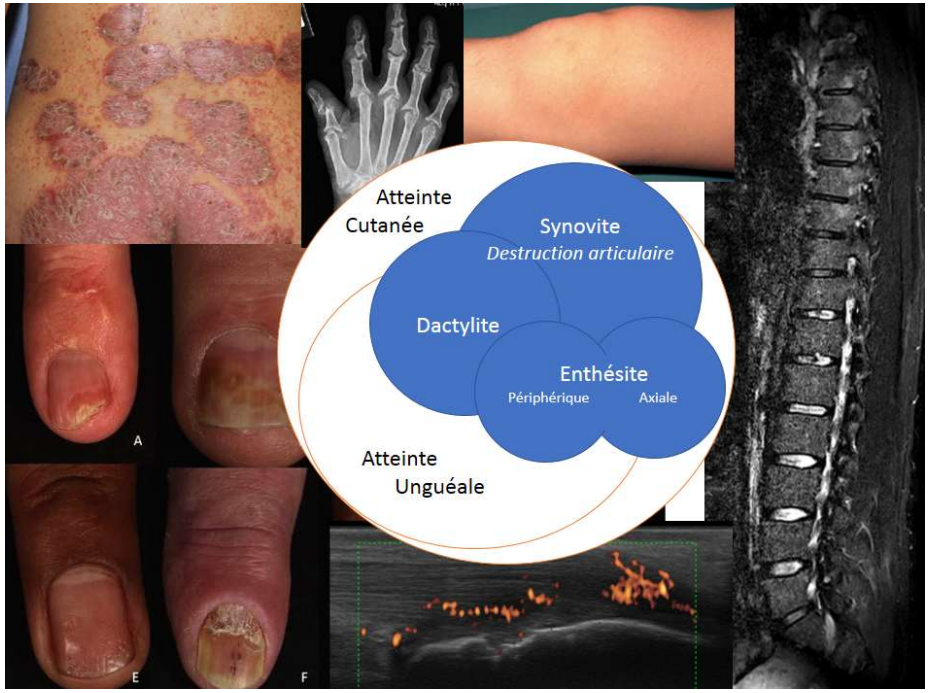
Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Upadacitinib, 15 mg (N=429)	Upadacitinib, 30 mg (N=423)	Placebo (N=423)	Adalimumab (N=429)
Female sex — no. (%)	238 (55.5)	236 (55.8)	211 (49.9)	222 (51.7)
Age — yr	51.6±12.2	49.9±12.4	50.4±12.2	51.4±12.0
White race — no. (%)†	386 (90.0)	377 (89.1)	377 (89.1)	375 (87.4)
Body-mass index ≥25 — no. (%)‡	342 (79.7)	319 (75.4)	329 (77.8)	334 (77.9)
Duration of psoriatic arthritis — yr	6.2±7.4	5.9±6.4	6.2±7.0	5.9±7.1
Any nonbiologic DMARD at baseline — no. (%)§	353 (82.3)	346 (81.8)	347 (82.0)	347 (80.9)
Methotrexate alone	279 (65.0)	268 (63.4)	267 (63.1)	270 (62.9)
Methotrexate + another nonbiologic DMARD	20 (4.7)	27 (6.4)	26 (6.1)	16 (3.7)
Nonbiologic DMARD other than methotrexate	54 (12.6)	51 (12.1)	54 (12.8)	61 (14.2)
Glucocorticoid use at baseline — no. (%)	73 (17.0)	71 (16.8)	70 (16.5)	72 (16.8)
Tender-joint count of 68 joints	20.4±14.7	19.4±13.3	20.0±14.3	20.1±13.8
Swollen-joint count of 66 joints	11.6±9.3	10.6±7.1	11.0±8.2	11.6±8.8
High-sensitivity C-reactive protein >ULN — no. (%)¶	324 (75.5)	324 (76.6)	324 (76.6)	308 (71.8)
HAQ-DI score‖	1.2±0.7	1.1±0.6	1.1±0.6	1.1±0.6
Score for patient's assessment of pain**	6.2±2.1	5.9±2.1	6.1±2.1	6.0±2.1
Affected body-surface area ≥3% — no. (%)	214 (49.9)	210 (49.6)	211 (49.9)	211 (49.2)
PASI score††	9.8±10.0	9.5±8.8	11.2±11.4	9.4±8.5
Score on the sIGA of Psoriasis — no. (%)‡‡				
0	34 (7.9)	21 (5.0)	24 (5.7)	34 (7.9)
1	73 (17.0)	78 (18.4)	86 (20.3)	65 (15.2)
2	170 (39.6)	173 (40.9)	167 (39.5)	181 (42.2)
3	133 (31.0)	128 (30.3)	119 (28.1)	132 (30.8)
4	19 (4.4)	23 (5.4)	27 (6.4)	17 (4.0)
Presence of enthesitis — no. (%)§§	270 (62.9)	267 (63.1)	241 (57.0)	265 (61.8)
Presence of dactylitis — no. (%)¶¶	136 (31.7)	127 (30.0)	126 (29.8)	127 (29.6)

McInnes IB. N Engl J Med. 2021 Apr 1;384(13):1227-1239.



Oligoarthrite asymétrique	50-60%
Polyarthrite (symétrique)	30-40%
Atteinte axiale	< 10% (isolée) 30% (avec arthrite périphérique)

The NEW ENGLAND JOURNAL of MEDICINE

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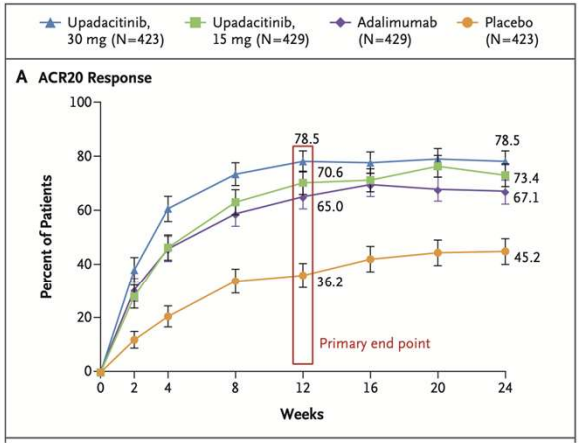
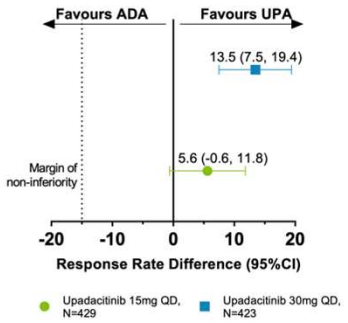


ACR20 at Week 12 (NI Margin = 15%) (NRI)

ADA, adalimumab; CI, confidence interval; NRI, non-responder imputation; QD, once daily; UPA upadacitinib.



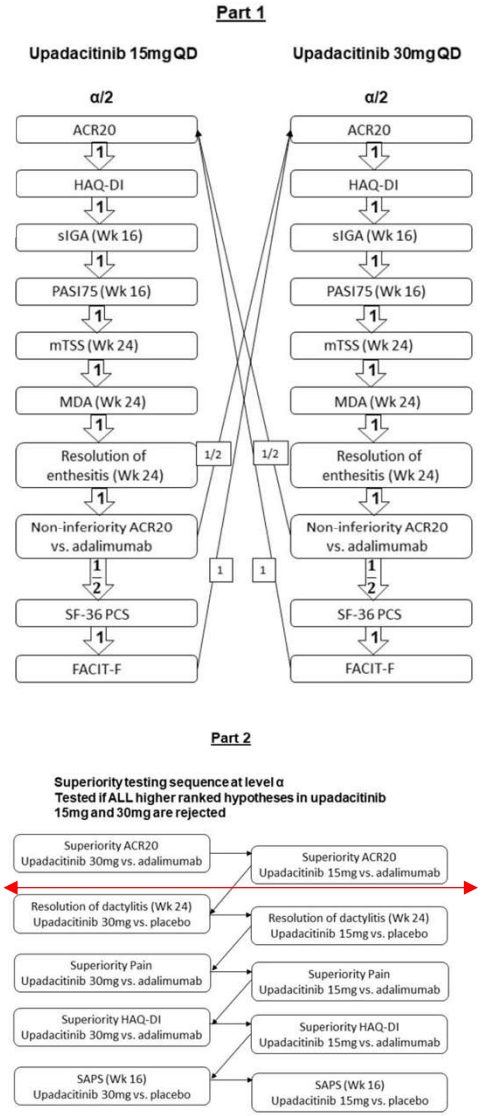


Table 2. Primary and Secondary End Points.*

End Point	Upadacitinib, 15 mg (N=429)	Upadacitinib, 30 mg (N=423)	Placebo (N=423)	Adalimumab (N=429)
Primary				
ACR20 response at wk 12 — no. (%)†	303 (70.6)	332 (78.5)	153 (36.2)	279 (65.0)
Difference vs. placebo — percentage points (95% CI)	34.5 (28.2 to 40.7); P<0.001	42.3 (36.3 to 48.3); P<0.001		
Secondary				
Least-squares mean change in HAQ-DI score at wk 12 (95% CI)	−0.42 (−0.47 to −0.37) [404]	−0.47 (−0.52 to −0.42) [398]	−0.14 (−0.18 to −0.09) [392]	−0.34 (−0.38 to −0.29) [406]
Least-squares mean difference vs. placebo (95% CI)	−0.28 (−0.35 to −0.22); P<0.001	−0.34 (−0.40 to −0.27); P<0.001		
Score on the sIGA of Psoriasis of 0 or 1 and a decrease of ≥2 points from baseline at wk 16 — no./total no. (%) ‡	135/322 (41.9)	175/324 (54.0)	34/313 (10.9)	127/330 (38.5)
Difference vs. placebo — percentage points (95% CI)	31.1 (24.7 to 37.5); P<0.001	43.1 (36.7 to 49.6); P<0.001		
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		
Least-squares mean change in mTSS at wk 24 (95% CI)¶	−0.04 (−0.16 to 0.07) [391]	0.03 (−0.08 to 0.15) [383]	0.25 (0.13 to 0.36) [372]	0.01 (−0.11 to 0.13) [384]
Least-squares mean difference vs. placebo (95% CI)	−0.29 (−0.44 to −0.14); P<0.001	−0.21 (−0.36 to −0.06); P=0.007		
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		
ACR20 response at wk 12: noninferiority of upadacitinib to adalimumab — no. (%)	303 (70.6)	332 (78.5)	153 (36.2)	279 (65.0)
Percentage of adalimumab effect preserved (95% CI)††	119.4 (98.0 to 147.9); P<0.001	146.6 (122.8 to 180.4); P<0.001		
Least-squares mean change in SF-36 PCS score at wk 12 (95% CI)‡‡	7.9 (7.1 to 8.6) [405]	8.9 (8.1 to 9.7) [398]	3.2 (2.4 to 4.0) [394]	6.8 (6.1 to 7.6) [410]
Least-squares mean difference vs. placebo (95% CI)	4.7 (3.7 to 5.7); P<0.001	5.7 (4.7 to 6.7); P<0.001		
Least-squares mean change in FACIT-Fatigue score (95% CI)§§	6.3 (5.4 to 7.2) [404]	7.1 (6.2 to 8.0) [398]	2.8 (1.9 to 3.7) [394]	5.7 (4.8 to 6.6) [410]
Least-squares mean difference vs. placebo (95% CI)	3.5 (2.4 to 4.7); P<0.001	4.3 (3.1 to 5.5); P<0.001		
ACR20 response at wk 12: superiority of upadacitinib to adalimumab — no. (%)	303 (70.6)	332 (78.5)	153 (36.2)	279 (65.0)
Difference vs. adalimumab — percentage points (95% CI)	5.6 (−0.6 to 11.8)¶¶	13.5 (7.5 to 19.4); P<0.001		

McInnes IB. N Engl J Med. 2021 Apr 1;384(13):1227-1239.

Psoriatic arthritis

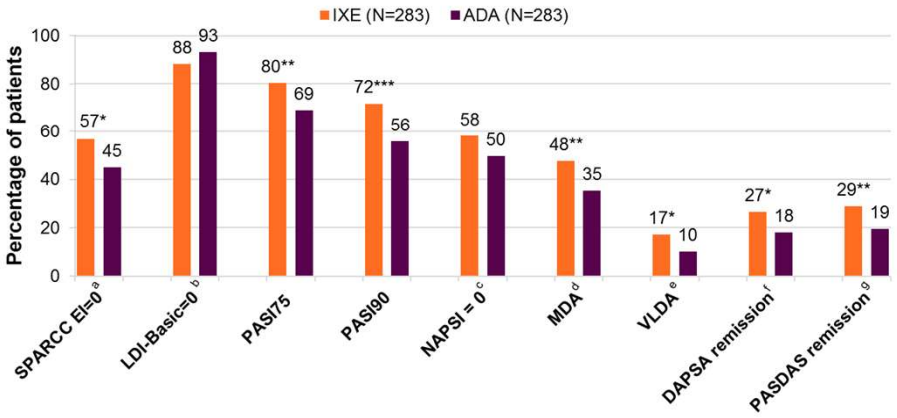
OPEN ACCESS

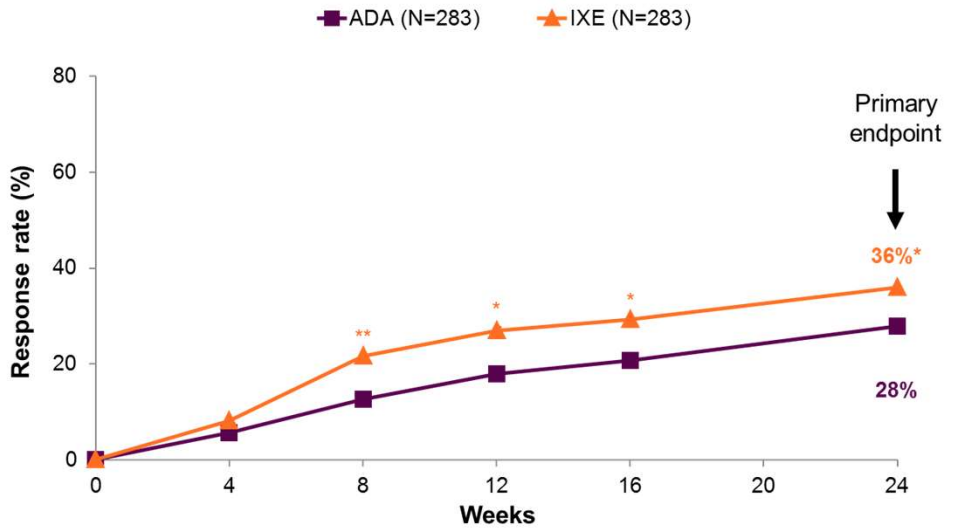
CLINICAL SCIENCE

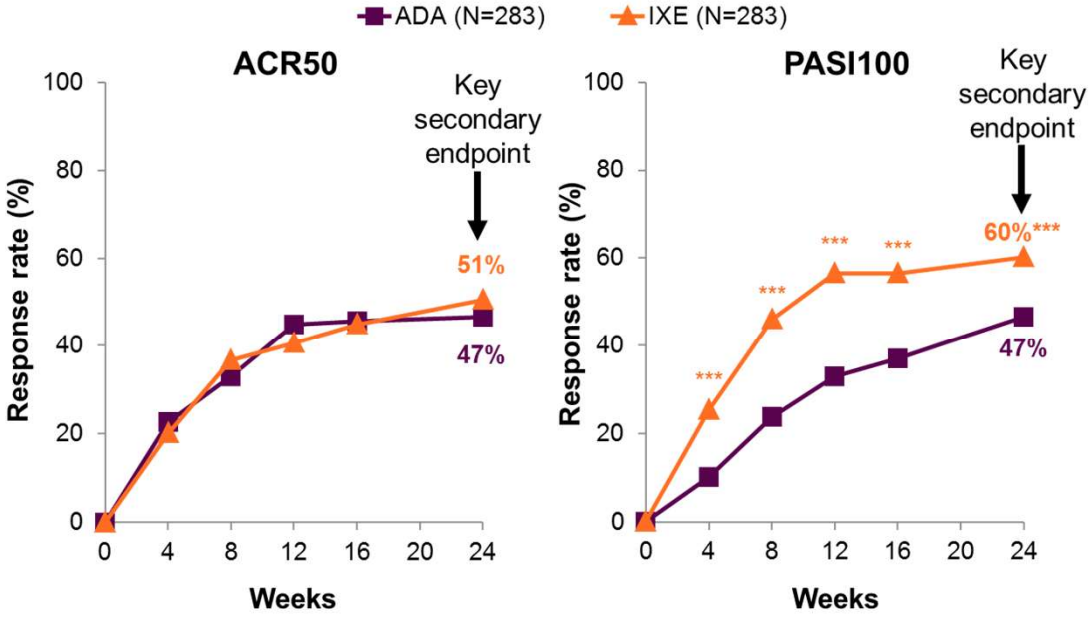
A head-to-head comparison of the efficacy and safety of ixekizumab and adalimumab in biological-naïve patients with active psoriatic arthritis: 24-week results of a randomised, open-label, blinded-assessor trial

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

SPIRIT H2H Ixekizumab (n = 283) vs Adalimumab (n = 283)
PsA naif de biothérapie en échec MTX
Polyarthrite Psoriasique (NAG 7, HAQ 1.2)
100% BSA > 3%, 40 % BSA > 10 %
60 % atteinte unguéal
50 % dactylites



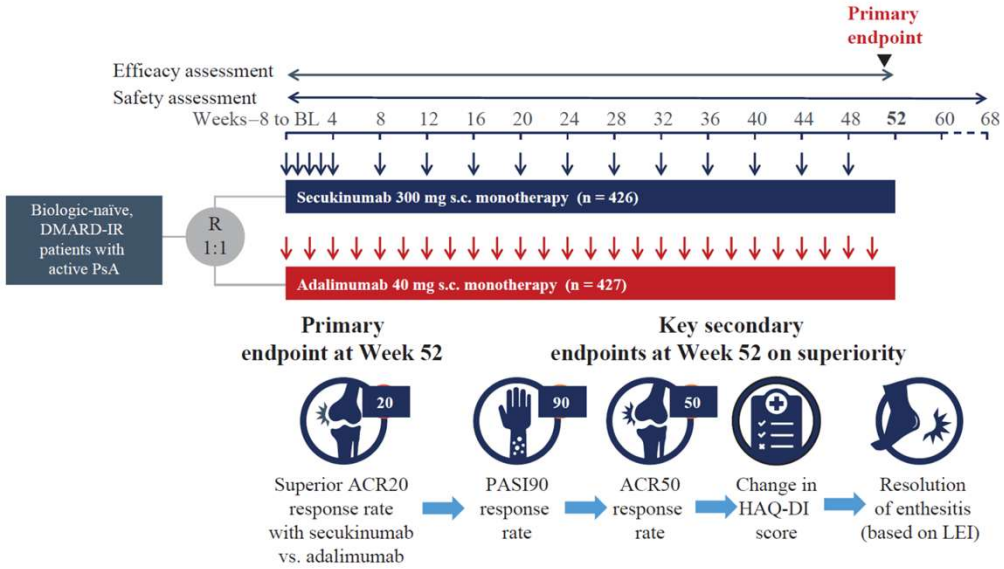




Mease PJ. Ann Rheum Dis. 2020 Jan;79(1):123-131.

Secukinumab versus adalimumab for treatment of active psoriatic arthritis (EXCEED): a double-blind, parallel-group, randomised, active-controlled, phase 3b trial

Iain B McInnes, Frank Behrens, Philip J Mease, Arthur Kavanaugh, Christopher Ritchlin, Peter Nash, Jordi Gratacós Masmitja, Philippe Goupille, Tatiana Korotaeva, Alice B Gottlieb, Ruvie Martin, Kevin Ding, Pascale Pellet, Shephard Mpofu, Luminita Pricop, on behalf of EXCEED Study Group



n, number of patients
ACR, American college of rheumatology; BL, baseline; DMARD-IR, disease modifying anti-rheumatic drugs-inadequate responders; HAQ-DI, health assessment quality-disability index; PASI, psoriasis activity severity index; s.c., subcutaneous; PsA, psoriatic arthritis

	Secukinumab 300 mg (n=426)	Adalimumab 40 mg (n=427)	Total (n=853)
Age (years)	48·5 (12·38)	49·5 (12·44)	49·0 (12·41)
Sex			
Male	208 (49%)	229 (54%)	437 (51%)
Female	218 (51%)	198 (46%)	416 (49%)
Weight (kg)	83·5 (19·12)	84·1 (18·33)	83·8 (18·72)
Body-mass index (kg/m²)	28·8 (6·03)	28·9 (5·55)	28·8 (5·79)
Race			
White	402 (94%)	391 (92%)	793 (93%)
Asian	16 (4%)	20 (5%)	36 (4%)
Other or unknown	8 (2%)	16 (4%)	24 (3%)
No smoking status at baseline	333 (78%)	351 (82%)	684 (80%)
Systemic glucocorticoids use at randomisation	61 (14%)	58 (14%)	119 (14%)
Time since first diagnosis of psoriatic arthritis (years)	5·1 (7·60)	5·7 (7·29)	5·4 (7·45)
Baseline PASI score	10·6 (9·00)	10·0 (8·15)	10·3 (8·60)
Patients with psoriasis (BSA ≥3%)	215 (50%)	202 (47%)	417 (49%)
Patients with psoriasis (BSA >10% or PASI ≥10)	110 (26%)	101 (24%)	211 (25%)
Adjusted tender joint total score for psoriatic arthritis (78 joints)	19·4 (13·86)	20·6 (14·81)	20·0 (14·35)
Adjusted swollen joint total score for psoriatic arthritis (76 joints)	9·7 (7·30)	10·2 (7·86)	10·0 (7·58)
Patient's global assessment (0–100)	64·0 (19·67)	61·9 (20·75)	62·9 (20·23)
Physician's global assessment (0–100)	60·0 (17·12)	61·4 (15·92)	60·7 (16·54)
Psoriatic arthritis pain (0–100)	58·6 (23·49)	57·9 (22·42)	58·3 (22·95)
Health Assessment Questionnaire-Disability Index	1·3 (0·64)	1·2 (0·64)	1·3 (0·64)
CRP ≥10 mg/L	131 (31%)	128 (30%)	259 (30%)
Disease Activity Score 28-CRP	4·7 (1·00)	4·7 (0·94)	4·7 (0·97)
Presence of enthesitis (Leeds Enthesitis Index)	234 (55%)	264 (62%)	498 (58%)
Presence of enthesitis (Spondyloarthritis Research Consortium of Canada)	301 (71%)	330 (77%)	631 (74%)
Presence of dactylitis	130 (31%)	137 (32%)	267 (31%)

Data are mean (SD) or n (%). BSA=body surface area. CRP=C-reactive protein. PASI=Psoriasis Area Severity Index.

Table 1: **Baseline and disease characteristics of patients**

McInnes IB. Lancet. 2020 May 9;395(10235):1496-1505.

Secukinumab versus adalimumab for treatment of active psoriatic arthritis (EXCEED): a double-blind, parallel-group, randomised, active-controlled, phase 3b trial

Iain B McInnes, Frank Behrens, Philip J Mease, Arthur Kavanaugh, Christopher Ritchlin, Peter Nash, Jordi Gratacós Masmitja, Philippe Goupille, Tatiana Korotaeva, Alice B Gottlieb, Ruvie Martin, Kevin Ding, Pascale Pellet, Shephard Mpofu, Luminita Pricop, on behalf of EXCEED Study Group

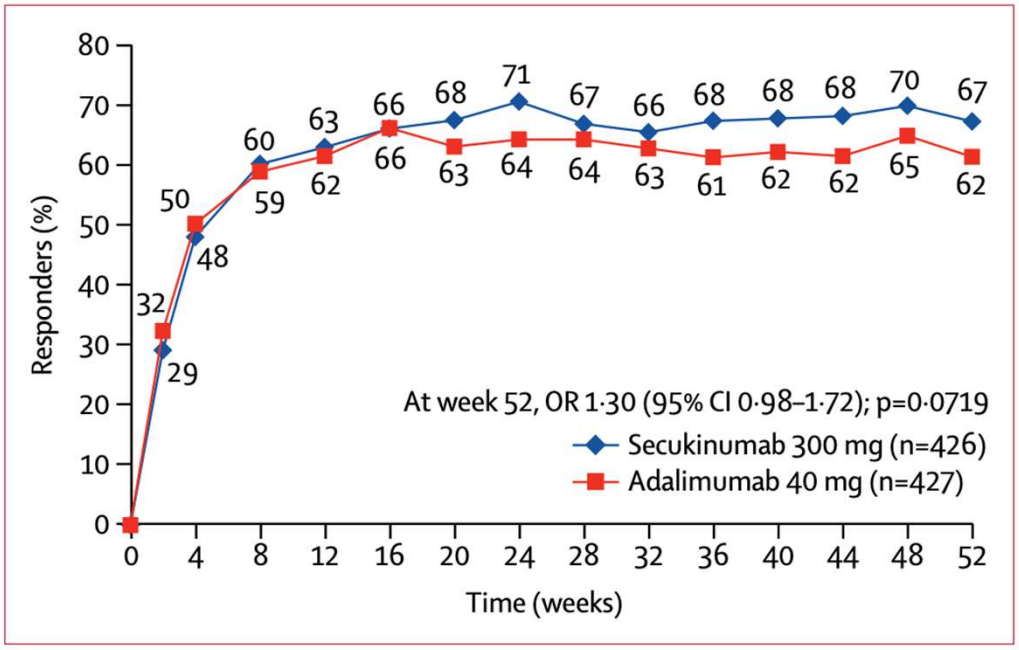


Figure 2: **ACR20 response rate through week 52 (multiple imputation)**

As the superiority of secukinumab versus adalimumab was not established for the primary endpoint, key secondary endpoints in the hierarchy were not formally tested for statistical significance. Therefore, we present unadjusted p values (without adjusting for multiplicity) and ORs with 95% CIs for key secondary endpoints (table 2; figure 3).

McInnes IB. Lancet. 2020 May 9;395(10235):1496-1505.

Secukinumab versus adalimumab for treatment of active psoriatic arthritis (EXCEED): a double-blind, parallel-group, randomised, active-controlled, phase 3b trial

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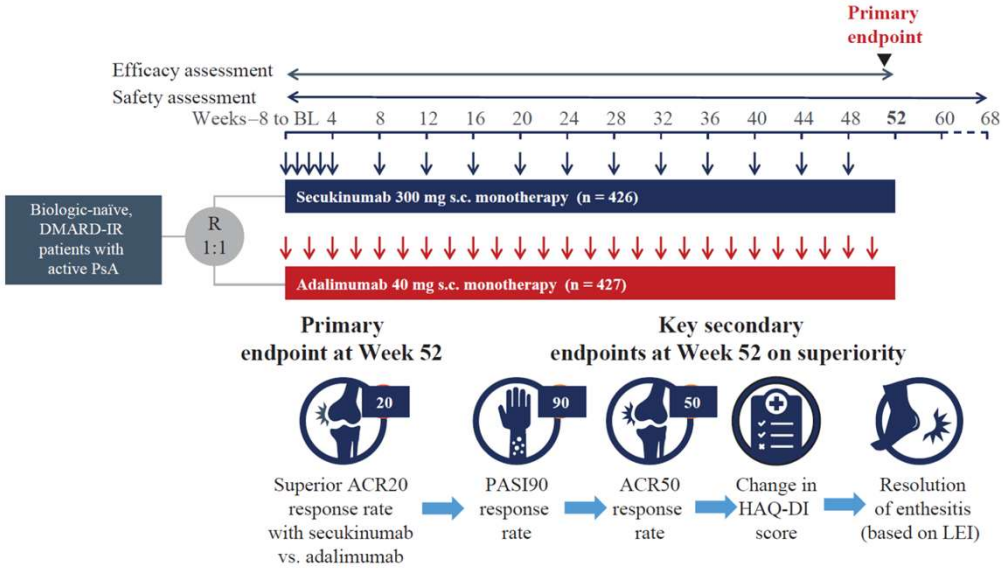
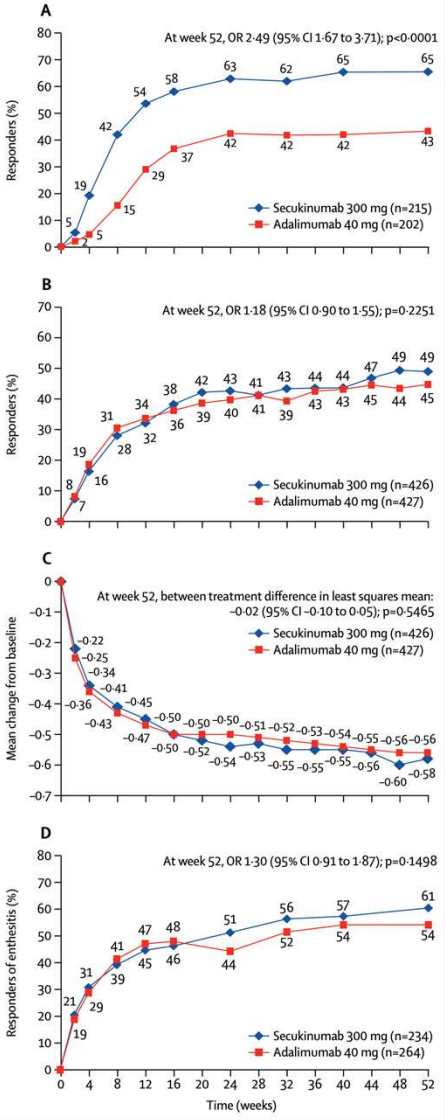
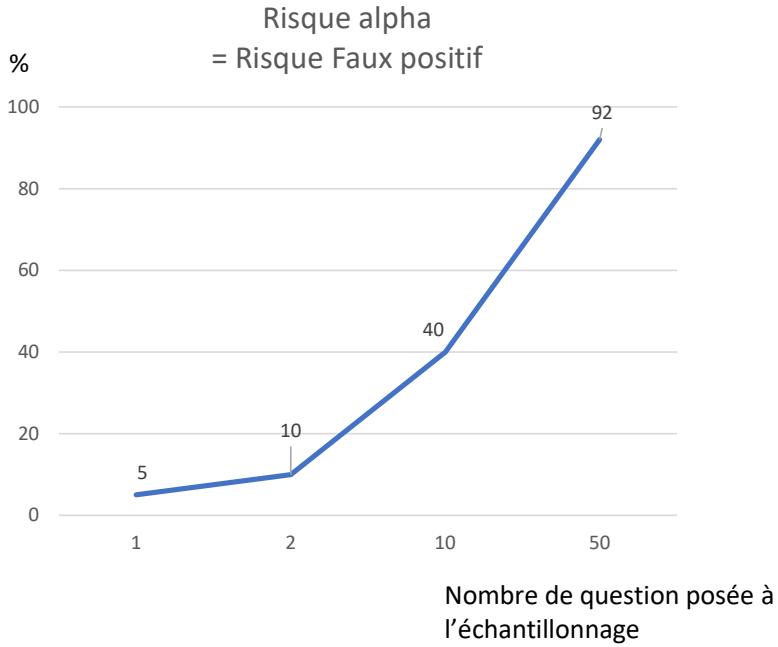


n, number of patients
ACR, American college of rheumatology; BL, baseline; DMARD-IR, disease modifying anti-rheumatic drugs-inadequate responders; HAQ-DI, health assessment quality-disability index; PASI, psoriasis activity severity index; s.c., subcutaneous; PsA, psoriatic arthritis



McInnes IB. Lancet. 2020 May 9;395(10235):1496-1505.

…Se méfier des études post-hoc !
Etudes exploratoires et non vérité clinique !



La répétition à chaque test du risque d'obtenir un résultat significatif par hasard augmente le risque global de conclure à tort à l'efficacité du traitement.

=

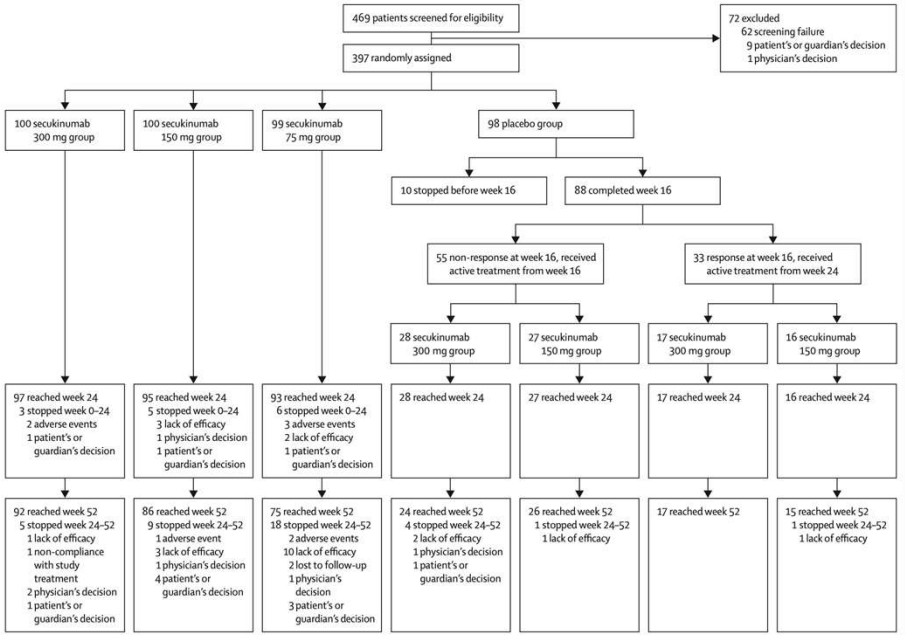
inflation du risque alpha

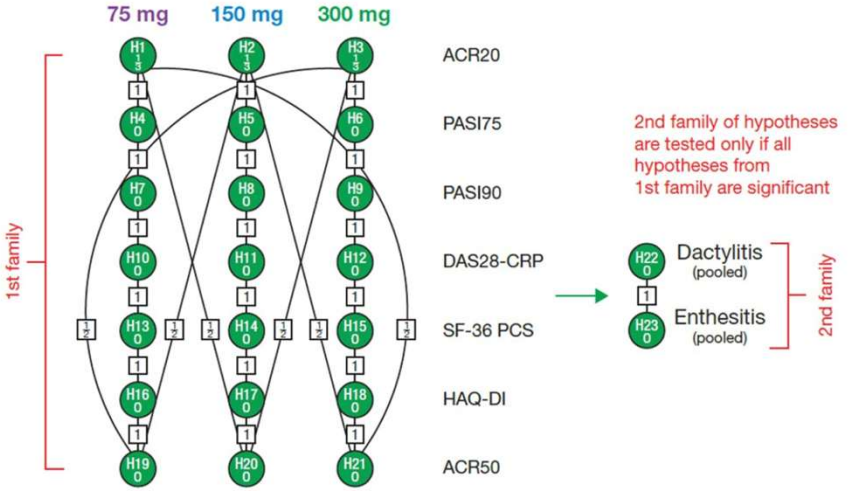
« les données ont été torturées jusqu'à ce qu'elles avouent ! »

Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebo-controlled, phase 3 trial

Iain B McInnes, Philip J Mease, Bruce Kirkham, Arthur Kavanaugh, Christopher T Ritchlin, Proton Rahman, Désirée van der Heijde, Robert Landewé, Philip G Conaghan, Alice B Gottlieb, Hanno Richards, Luminita Pricop, Gregory Ligozio, Manmath Patekar, Shephard Mpofu, on behalf of the FUTURE 2 Study Group

	Secukinumab 300 mg (n=100)	Secukinumab 150 mg (n=100)	Secukinumab 75 mg (n=99)	Placebo (n=98)
Age (years)	46·9 (12·6)	46·5 (11·7)	48·6 (11·4)	49·9 (12·5)
Women	49 (49%)	45 (45%)	52 (53%)	59 (60%)
Ethnic origin				
White	96 (96%)	90 (90%)	90 (91%)	94 (96%)
Black	1 (1%)	0 (0%)	0 (0%)	0 (0%)
Asian	2 (2%)	6 (6%)	5 (5%)	1 (1%)
Unknown	0 (0%)	0 (0%)	1 (1%)	0 (0%)
Other	1 (1%)	4 (4%)	3 (3%)	3 (3%)
Weight (kg)	85·4 (18·4)	91·2 (19·8)	85·6 (20·6)	86·2 (19·8)
Number of previous anti-TNF treatments for psoriatic arthritis				
0	67 (67%)	63 (63%)	65 (66%)	63 (64%)
1	16 (16%)	26 (26%)	21 (21%)	16 (16%)
2 or 3	17 (17%)	11 (11%)	13 (13%)	19 (19%)
Methotrexate use at randomisation	44 (44%)	44 (44%)	47 (47%)	50 (51%)
Systemic glucocorticoid use at randomisation	18 (18%)	23 (23%)	19 (19%)	21 (21%)
Patients with specific disease characteristics				
Psoriasis body surface area ≥3%	41 (41%)	58 (58%)	50 (51%)	43 (44%)
PASI ≤10*	21 (51%)	25 (43%)	28 (56%)	23 (53%)
PASI score >10*	20 (49%)	33 (57%)	22 (44%)	20 (47%)
Dactylitis	46 (46%)	32 (32%)	33 (33%)	27 (28%)
Dactylitis count	3·6 (3·5)	4·5 (5·1)	3·0 (3·6)	2·7 (2·2)
Enthesitis	56 (56%)	64 (64%)	68 (69%)	65 (66%)
Enthesitis count	2·8 (1·7)	3·2 (1·6)	3·2 (1·7)	3·1 (1·7)
Baseline disease and quality-of-life scores				
Tender joint count (78 joints)	20·2 (13·3)	24·1 (19·4)	22·2 (16·3)	23·4 (19·0)
Swollen joint count (76 joints)	11·2 (7·8)	11·9 (10·1)	10·8 (9·2)	12·1 (10·7)
DAS28-CRP	4·8 (1·0)	4·9 (1·1)	4·7 (1·0)	4·7 (1·0)
PASI*	11·9 (8·4)	16·2 (14·3)	12·1 (10·2)	11·6 (8·3)
Physician's global assessment (VAS)	55·0 (14·7)	56·7 (16·6)	59·0 (17·9)	55·0 (16·0)
HAQ-DI	1·3 (0·6)	1·2 (0·6)	1·2 (0·6)	1·2 (0·7)
Pain (VAS)	57·7 (19·0)	58·9 (19·8)	56·7 (21·1)	55·4 (22·1)
Patient's global assessment (VAS)	60·7 (18·9)	62·0 (19·5)	59·0 (19·1)	57·6 (19·8)
SF36-PCS	36·9 (8·0)	36·2 (8·1)	36·2 (8·1)	37·4 (8·8)





McInnes IB. Lancet. 2015 Sep 19;386(9999):1137-46.

Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebo-controlled, phase 3 trial

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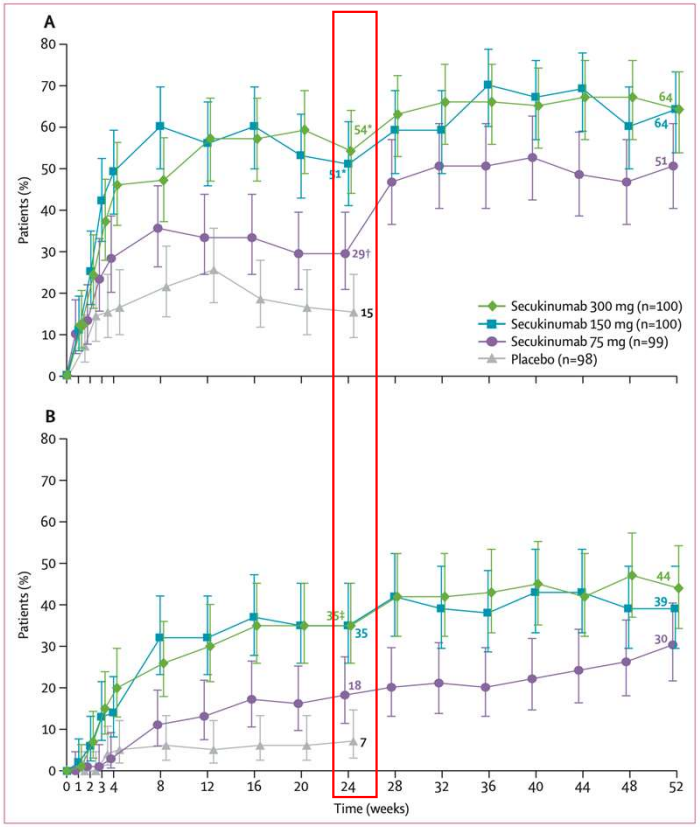


Figure 2: ACR20 (A) and ACR50 (B) response rates from baseline to week 52

	Secukinumab 300 mg			Secukinumab 150 mg			Secukinumab 75 mg			Placebo
	Value*	Odds ratio versus placebo (95% CI)	p value versus placebo	Value*	Odds ratio versus placebo (95% CI)	p value versus placebo	Value*	Odds ratio versus placebo (95% CI)	p value versus placebo	
Anti-TNF-naive patients										
ACR20 response	39/67 (58%)	7·77 (3·36–17·98)	<0·0001	40/63 (63%)	9·99 (4·22–23·66)	<0·0001	24/65 (37%)	3·17 (1·36–7·40)	0·0075	10/63 (16%)
ACR50 response	26/67 (39%)	9·72 (3·14–30·09)	<0·0001	28/63 (44%)	12·54 (4·03–39·05)	<0·0001	16/65 (25%)	4·90 (1·53–15·64)	0·0074	4/63 (6%)
ACR70 response	15/67 (22%)	NE	0·0003	17/63 (27%)	NE	<0·0001	4/65 (6%)	NE	0·3654	1/63 (2%)
PASI75 response†	19/30 (63%)	7·96 (2·42–26·16)	0·0006	20/36 (56%)	6·33 (1·99–20·15)	0·0018	10/33 (30%)	1·94 (0·59–6·34)	0·2729	6/31 (19%)
PASI90 response†	16/30 (53%)	13·11 (3·09–55·59)	0·0005	14/36 (39%)	8·09 (1·92–34·09)	0·0044	4/33 (12%)	1·40 (0·28–7·02)	0·6825	3/31 (10%)
Anti-TNF-IR patients										
ACR20 response	15/33 (45%)	4·97 (1·53–16·15)	0·0077	11/37 (30%)	2·55 (0·78–8·32)	0·1216	5/34 (15%)	1·03 (0·27–3·95)	0·9639	5/35 (14%)
ACR50 response	9/33 (27%)	4·37 (1·05–18·26)	0·0431	7/37 (19%)	2·39 (0·56–10·15)	0·2374	2/34 (6%)	0·69 (0·11–4·42)	0·6941	3/35 (9%)
ACR70 response	5/33 (15%)	NE	0·0228	4/37 (11%)	NE	0·1151	2/34 (6%)	NE	0·2391	0/35 (0%)
PASI75 response†	7/11 (64%)	19·29 (1·77–210·18)	0·0152	8/22 (36%)	6·17 (0·66–57·30)	0·1094	4/17 (24%)	3·46 (0·33–36·06)	0·2986	1/12 (8%)
PASI90 response†	4/11 (36%)	6·43 (0·58–70·74)	0·1282	5/22 (23%)	3·50 (0·35–34·91)	0·2859	2/17 (12%)	1·37 (0·11–17·30)	0·8098	1/12 (8%)

Data are n/N (%), unless otherwise indicated. p values not adjusted for multiplicity of testing. ACR20=at least 20% improvement in the American College of Rheumatology. ACR50=at least 50% improvement in the American College of Rheumatology. ACR70=at least 70% improvement in the American College of Rheumatology. NE=not estimable. PASI=Psoriasis Area and Severity Index. Anti-TNF-IR=inadequate response to a tumour necrosis factor agent or stopped treatment because of safety or tolerability reasons. *Missing data were imputed as non-response. †Assessed in patients with psoriasis on at least 3% of their body surface area at baseline.

Table 3: **Efficacy of secukinumab at week 24 in anti-TNF-naive and anti-TNF-IR patients in a prespecified exploratory analysis**

McInnes IB. Lancet. 2015 Sep 19;386(9999):1137-46.

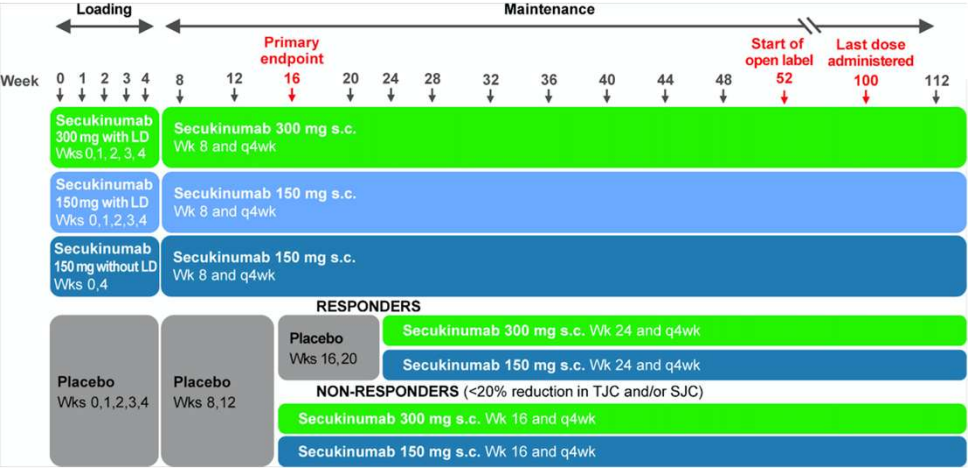
Clinical and epidemiological research

OPEN ACCESS

EXTENDED REPORT

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]



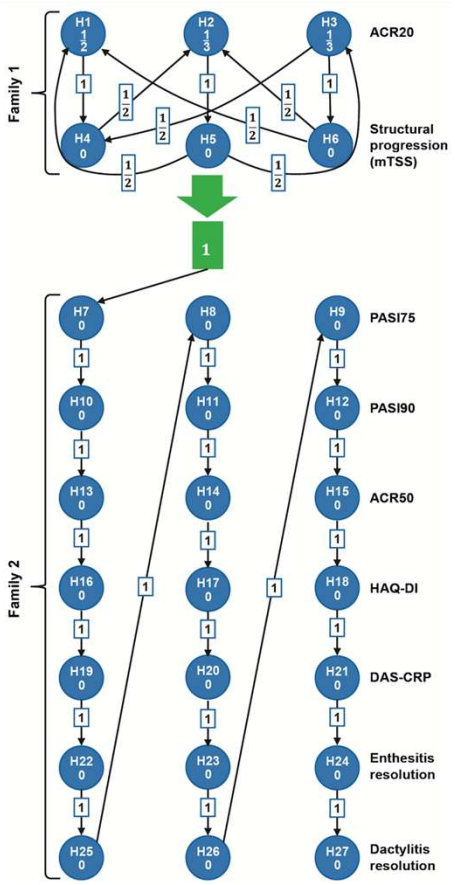


Table 1 Demographics and baseline characteristics for

Characteristic	Total (n=996)
Age (years), mean (SD)	48.8 (12.4)
Female, n (%)	496 (49.8)
Weight (kg)	83.4 (19.2)
Race, n (%)	
White	816 (81.9)
Asian	113 (11.3)
American Indian or Alaska Native	10 (1.0)
Black or African American	6 (0.6)
Unknown	4 (0.4)
Other	47 (4.7)
Time since first diagnosis of psoriatic disease (years), mean (SD)	6.6 (7.3)
Number of prior anti-TNF therapies, n (%)	
0	701 (70.4)
1	197 (19.8)
≥2	98 (9.8)
Methotrexate use at randomisation, n (%)	499 (50.1)
Systemic glucocorticoid at randomisation, n (%)	168 (16.9)
Patients with specific disease characteristics, n (%)	
Psoriasis affecting≥3% of BSA	514 (51.6)
Presence of enthesitis	602 (60.4)
Presence of dactylitis	389 (39.1)
Disease and quality of life scores, mean (SD)	
Tender joint count (78 joints)	21.0 (15.8)
Swollen joint count (76 joints)	11.5 (10.1)
DAS28-CRP score	4.6 (1.1)
HAQ-DI score	1.3 (0.6)
vdH-mTSS	–
PsA pain, VAS 0–100 mm	54.3 (23.9)
Patients' global assessment of disease activity, VAS 0–100 mm	53.9 (22.7)
Physician's global assessment of disease activity, VAS 0–100 mm	55.9 (19.3)

Mease P. Ann Rheum Dis. 2018 Jun;77(6):890-897.

Clinical and epidemiological research

OPEN ACCESS

EXTENDED REPORT

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

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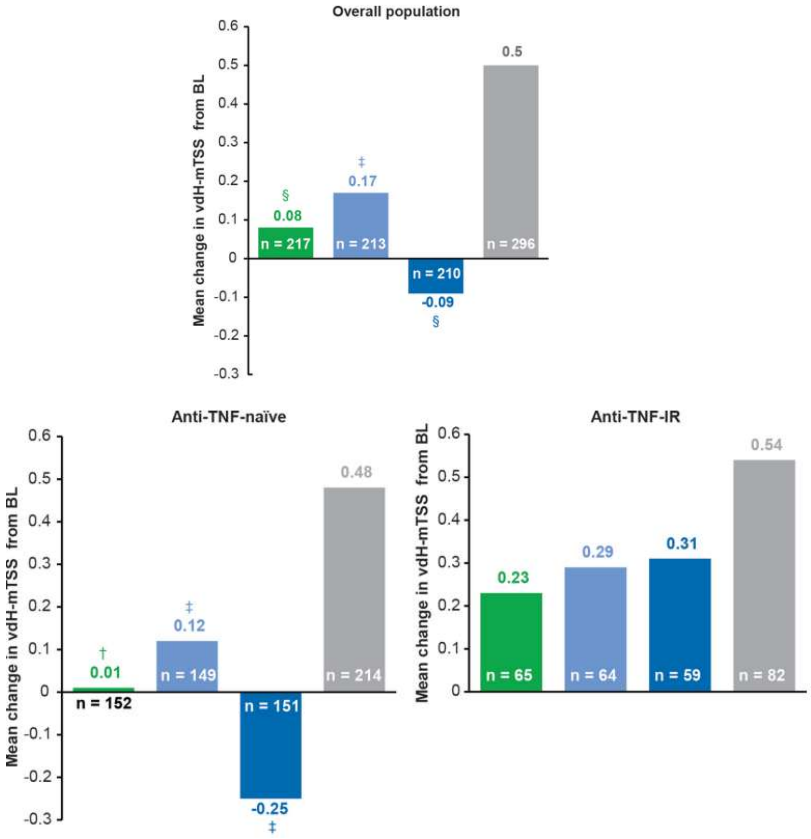

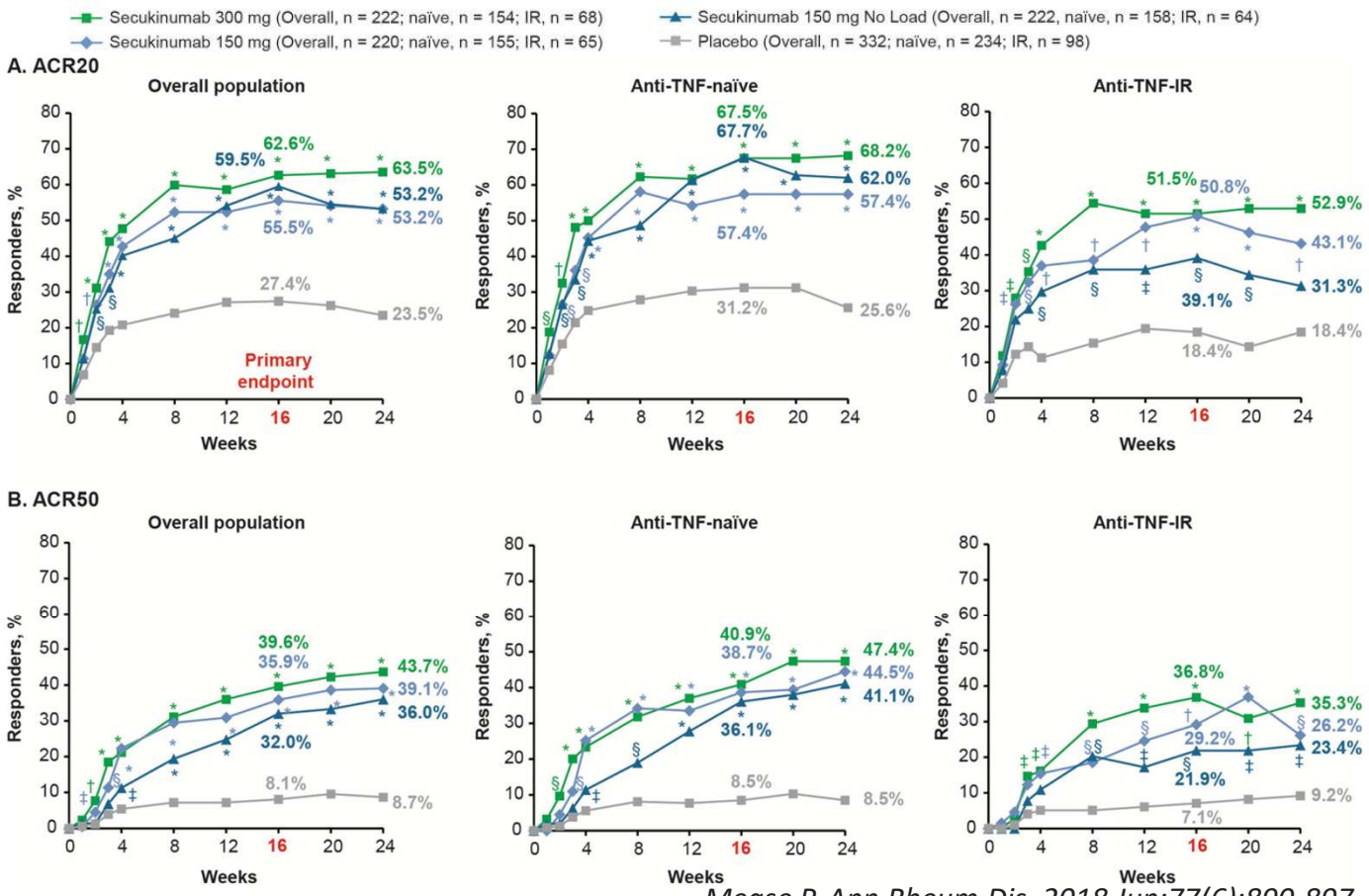

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RHEUMATOLOGY

Rheumatology 2019;58:859-868
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Advance Access publication 19 December 2018

Original article

Secukinumab shows sustained efficacy and low structural progression in ankylosing spondylitis: 4-year results from the MEASURE 1 study

Jürgen Braun[1], Xenofon Baraliakos[1], Atul Deodhar[2], Denis Poddubnyy[3], Paul Emery[4], Eumorphia M. Delicha[5], Zsolt Talloczy[6] and Brian Porter[6]

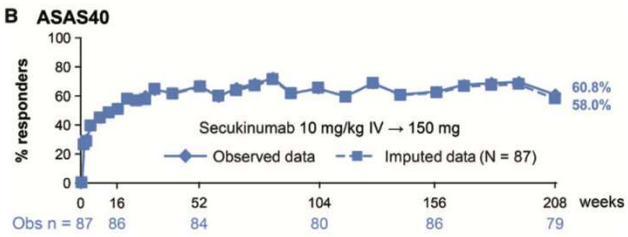


Fig. 2 Cumulative probability plot for change from baseline in the mSASSS through Wk208

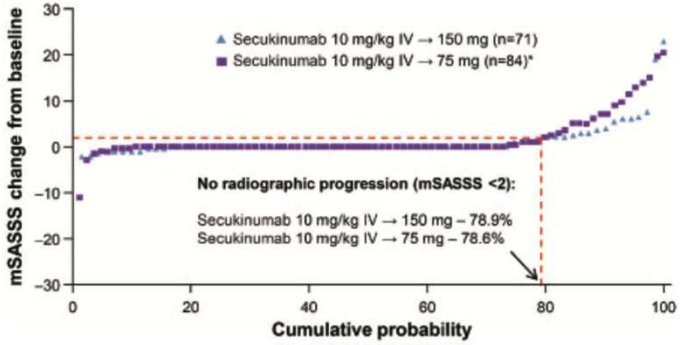
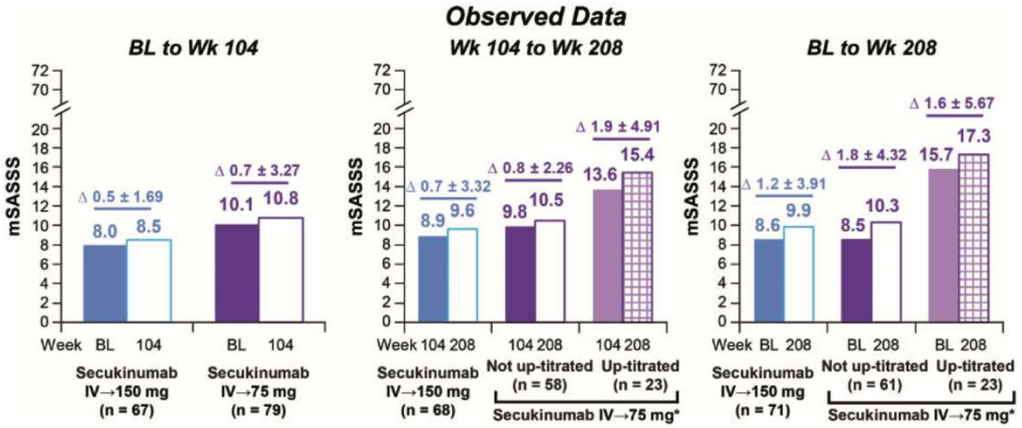
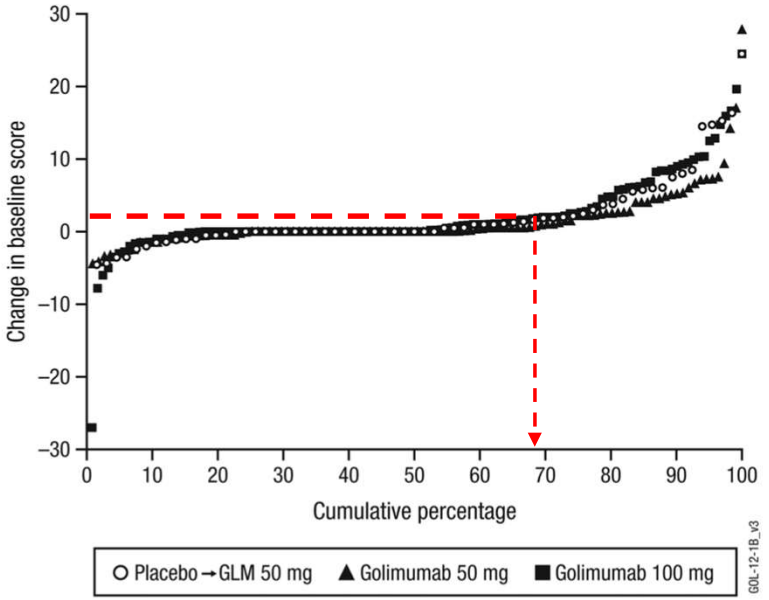


Fig. 3 Change in mSASSS between (**A**) Baseline to Wk104, (**B**) Wk104 to Wk208, (**C**) Baseline to Wk208



Braun J. Rheumatology (Oxford). 2019 May 1;58(5):859-868.



Braun J. Ann Rheum Dis 2014;73:1107-13.

Facteurs de risques de progression radiographique mSASS selon données observationnelles *ou post-hoc*

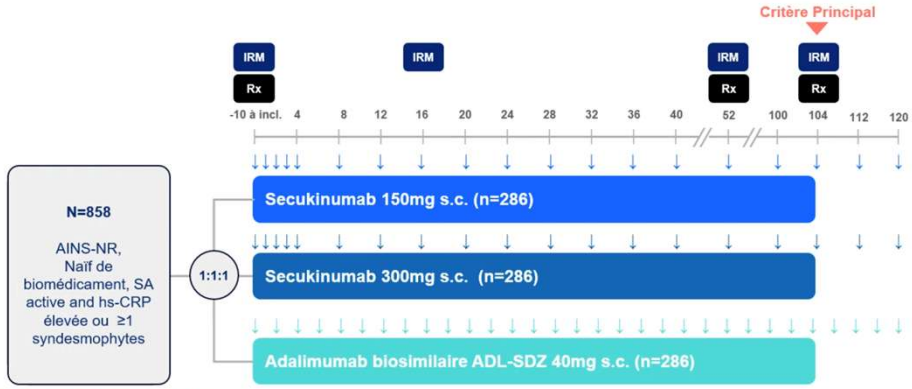
- . Homme
- . Tabac
- . Profession manuelle ?
- . CRP élevée
- . Présence d'un syndesmophyte radiographique
- . mSASSS > 10

Arthritis & Rheumatology
Vol. 76, No. 8, August 2024, pp 1278–1287
DOI 10.1002/art.42852

American College of Rheumatology
Empowering Rheumatology Professionals

Effect of Secukinumab Versus Adalimumab Biosimilar on Radiographic Progression in Patients With Radiographic Axial Spondyloarthritis: Results From a Head-to-Head Randomized Phase IIIb Study

Xenofon Baraliakos,[1] Mikkel Østergaard,[2] Denis Poddubnyy,[3] Désirée van der Heijde,[4] Atul Deodhar,[5] Pedro M. Machado,[6] Victoria Navarro-Compán,[7] Kay Geert A. Hermann,[8] Mitsumasa Kishimoto,[9] Eun Young Lee,[10] Lianne S. Gensler,[11] Uta Kiltz,[1] Marco F. Eigenmann,[12] Patricia Pertel,[12] Aimee Readie,[13] Hanno B. Richards,[12] Brian Porter,[13] and Juergen Braun[14]



SURPASS est une étude en aveugle partiel :
- Les patients avaient connaissance du traitement reçu (secukinumab ou biosimilaire d'adalimumab), mais pas du dosage du secukinumab (150 ou 300mg) ;
- Les données d'imagerie étaient analysées de manière centralisée par 3 relecteurs indépendants, en aveugle sur la chronologie des images, les données patients incluant le traitement reçu et les résultats d'efficacité et de tolérance.

Démontrer l'impact du traitement par secukinumab sur l'évolution structurale* mesurée par le score mSASSS à 104 semaines chez les patients atteints de SA

Critère principal

Supériorité du secukinumab 150mg ou 300mg *versus* adalimumab bs (ADA-SDZ) sur l'évolution structurale* à 104 semaines

Critères secondaires principaux

- Variation du mSASSS par rapport à l'inclusion
- Absence de nouveaux syndesmophytes chez les patients avec ≥1 syndesmophyte à l'inclusion
- Score de Berlin sur l'œdème des articulations SI *(chez un sous-groupe de patients)*
- Score modifié de Berlin ASspiMRI-a *(chez un sous-groupe de patients)*

Supériorité du secukinumab versus adalimumab bs à 104 semaines

Critères exploratoires

Réponses ASAS20, ASAS40, BASDAI50, ASAS rémission partielle, ASDAS maladie inactive & qualité de vie du secukinumab 150mg *versus* secukinumab 300mg à 104 semaines

Tolérance

Tolérance générale du secukinumab *versus* adalimumab bs à 104 semaines

Calcul d'effectif nécessaire pour supériorité prévu pour 63% patients non-progresseur groupe secukinumab et 51% patients non progresseurs SDZ-ADA

***Variation du mSASSS≤0.5 par rapport à l'inclusion**

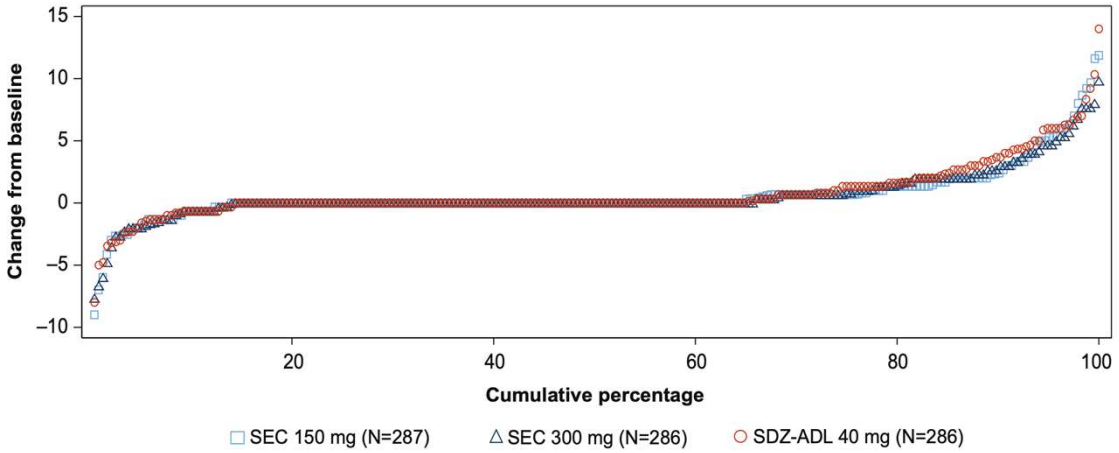
mSA, spondylarthrite ankylosante ; SASSS, modified Stoke Ankylosing Spondylitis Spinal Score ; ADA-SDZ, adalimumab Sandoz ; ASAS: Assessment of SpondyloArthritis international Society ; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index ; ASDAS: Ankylosing Spondylitis Disease Activity Score.
Baraliakos X, *et al.* Clinical Drug Investigation (2020);40:269–278.

Baraliakos X. Arthritis Rheumatol. 2024 Aug;76(8):1278-1287.

Critère principal : absence de progression radiographique rachidienne (mSASS) sous secukinumab et adalimumab biosimilaire à 2ans

Table 1. Demographic and baseline disease characteristics of the participants

Patient characteristics	SEC 150 mg, n = 287	SEC 300 mg, n = 286	SDZ-ADL 40 mg, n = 286
Age, mean ± SD, y	42.1 ± 12.0	42.2 ± 12.5	41.9 ± 12.7
Male, n (%)	230 (80.1)	223 (78.0)	221 (77.3)
HLA-B27 positive, n (%)	235 (81.9)	227 (79.4)	236 (82.5)
BMI, mean ± SD, kg/m^2	27.7 ± 5.7	26.9 ± 5.5	27.2 ± 5.4
Smoking status, n (%)			
Former	58 (20.2)	54 (18.9)	45 (15.7)
Current	85 (29.6)	82 (28.7)	80 (28.0)
Time since diagnosis of AS/radiographic axial SpA, mean ± SD, y	6.4 ± 9.0	6.6 ± 8.4	7.1 ± 10.1
mSASSS (0–72), mean ± SD	17.6 ± 21.3	16.5 ± 20.8	15.7 ± 19.5
Patients with syndesmophyte(s), n (%)	211 (73.5)	204 (71.3)	212 (74.1)
Number of syndesmophytes, mean ± SD	7.3 ± 7.8	7.0 ± 7.6	6.7 ± 7.3
Total back pain (0–100 mm), mean ± SD	72.6 ± 15.9	73.0 ± 16.0	72.7 ± 16.8
BASFI (0–10), mean ± SD	6.7 ± 1.9	6.7 ± 2.0	6.5 ± 2.1
BASDAI (0–10), mean ± SD	7.1 ± 1.4	7.2 ± 1.4	7.2 ± 1.5
Patients with hsCRP ≥5, n (%), mg/L	220 (76.7)	217 (75.9)	216 (75.5)
hsCRP, mean ± SD, mg/L	20.8 ± 28.6	20.7 ± 26.5	19.8 ± 22.6
Medication use at randomization, n (%)			
NSAIDs	244 (85.3)	237 (83.2)	229 (80.4)
Methotrexate	28 (9.8)	35 (12.2)	26 (9.1)
Sulfasalazine	57 (19.9)	65 (22.7)	57 (19.9)
Corticosteroids	38 (13.2)	33 (11.5)	28 (9.8)



Proportion of patients with no radiographic progression

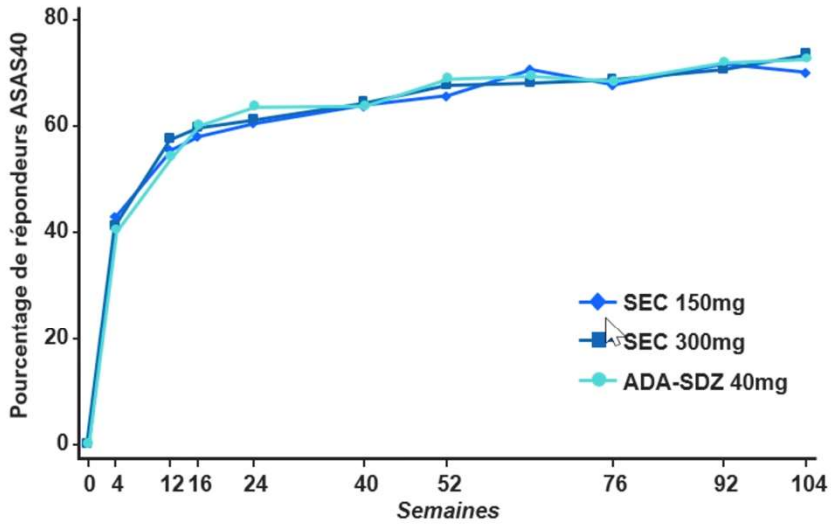
Treatment group	n	No progression rate, %	Estimated mean (95% CI)	Marginal difference (95% CI) vs SDZ-ADL 40 mg	Nominal *P* value
SEC 150 mg (n = 287)	283	66.1	66.6 (60.7–72.5)	1.51 (−6.63 to 9.64)	0.716
SEC 300 mg (n = 286)	280	66.9	66.8 (60.5–73.1)	1.67 (−6.61 to 9.95)	0.693
SDZ-ADL 40 mg (n = 286)	283	65.6	65.1 (58.8–71.5)	–	–

Baraliakos X. Arthritis Rheumatol. 2024 Aug;76(8):1278-1287.

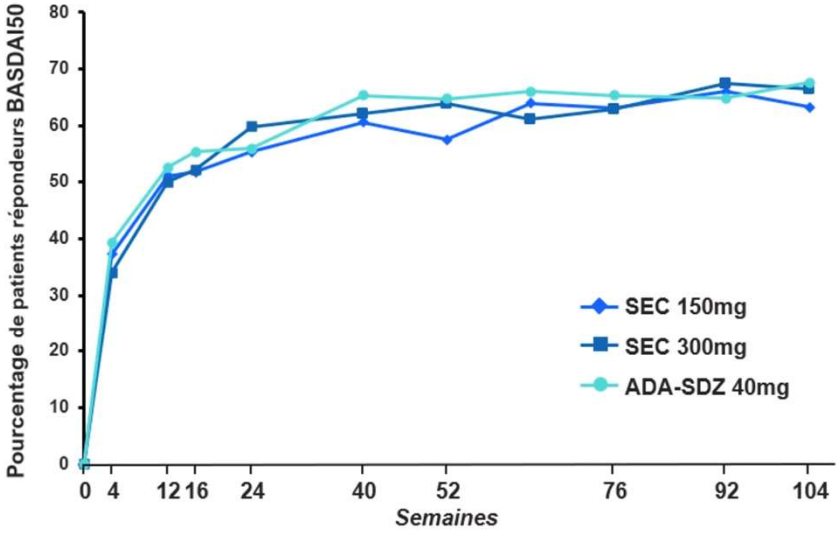
Critères exploratoires : quelle évolution clinique chez les patients traités par secukinumab et adalimumab biosimilaire à 2 ans ?

SURPASS

Réponse ASAS40 sur 104 semaines



Réponse BASDAI50 sur 104 semaines

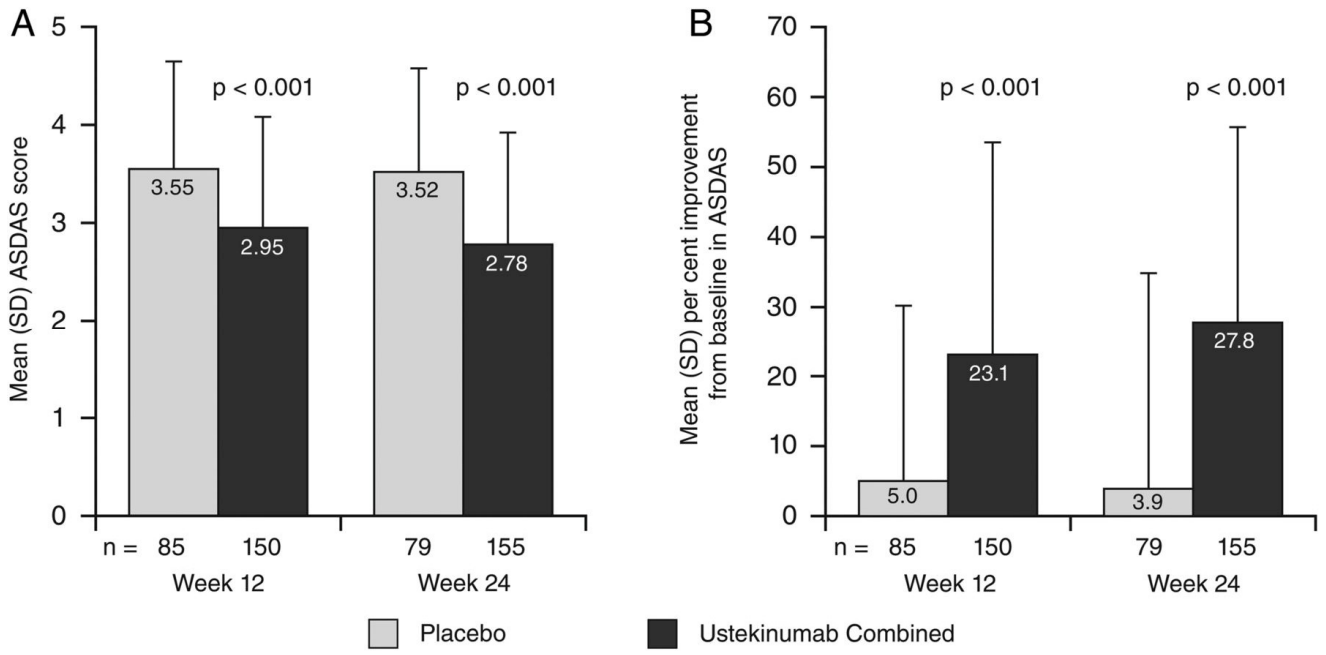


Étude en ouvert sur le type de traitement (SEC ou ADA-SDZ).

Données observées.
ASAS, Assessment of Spondyloarthritis International Society ; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index ; ADA-SDZ, adalimumab biosimilaire ; SEC, secukinumab.
1. Baraliakos *et al.* Arthritis Rheum. (2024);doi:10.1002/Art.42852.

Baraliakos X. Arthritis Rheumatol. 2024 Aug;76(8):1278-1287.

Efficacy and safety of ustekinumab in psoriatic arthritis patients with peripheral arthritis and physician-reported spondylitis: post-hoc analyses from two phase III, multicentre, double-blind, placebo-controlled studies (PSUMMIT-1/PSUMMIT-2)

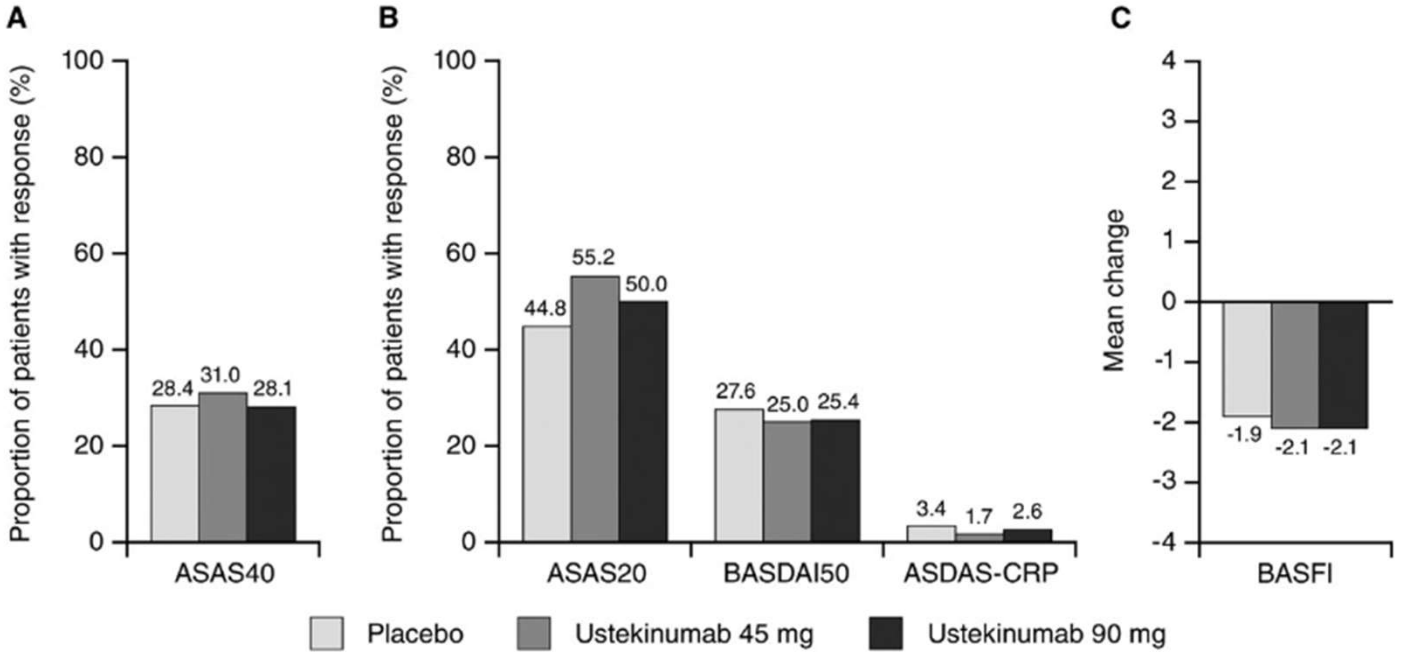


Kavanaugh A. Ann Rheum Dis. 2016 Nov;75(11):1984-1988.

AMERICAN COLLEGE OF RHEUMATOLOGY
EDUCATION • TREATMENT • RESEARCH

Arthritis & Rheumatology
Vol. 71, No. 2, February 2019, pp 258–270
DOI 10.1002/art.40728

Three Multicenter, Randomized, Double-Blind, Placebo-Controlled Studies Evaluating the Efficacy and Safety of Ustekinumab in Axial Spondyloarthritis



Deodhar A. Arthritis Rheumatol. 2019 Feb;71(2):258-270.

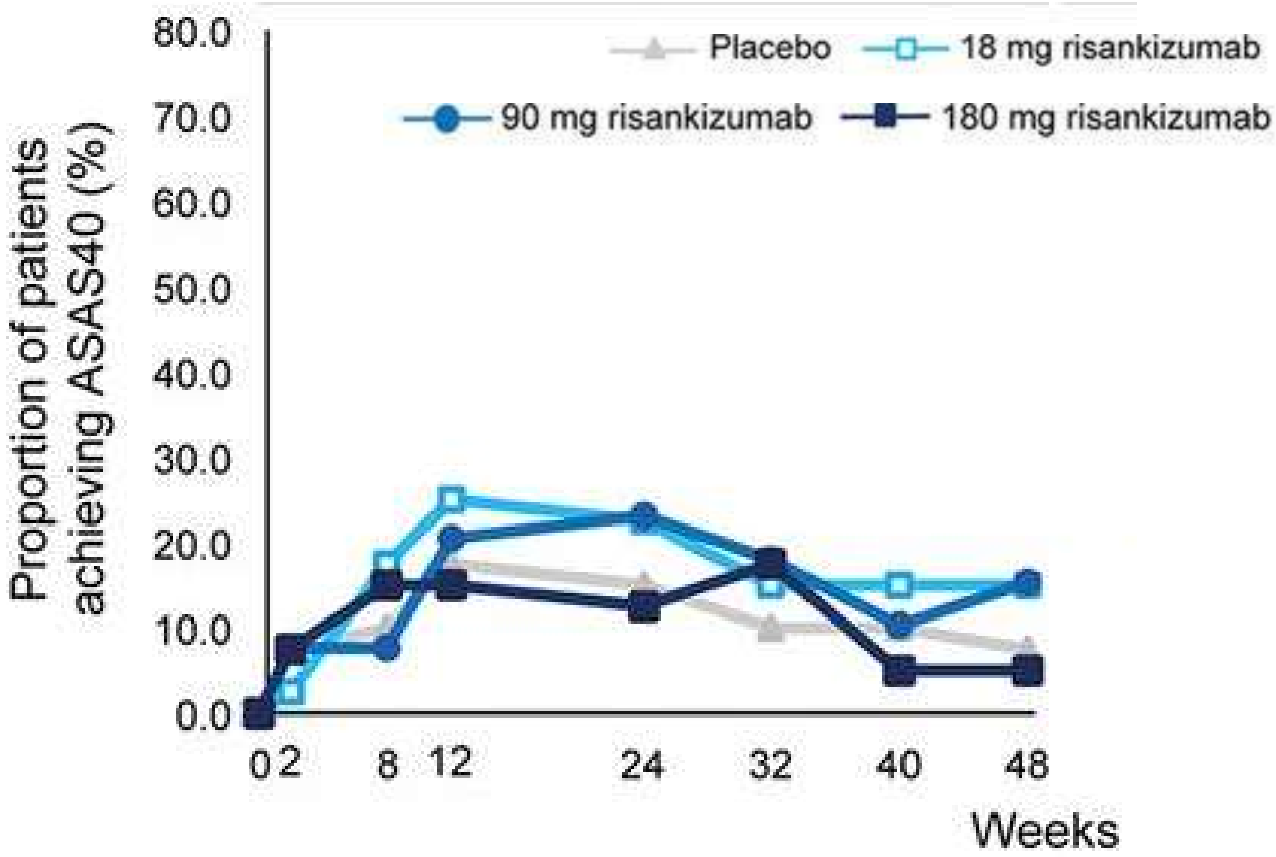
Clinical and epidemiological research

OPEN ACCESS

EXTENDED REPORT

Risankizumab, an IL-23 inhibitor, for ankylosing spondylitis: results of a randomised, double-blind, placebo-controlled, proof-of-concept, dose-finding phase 2 study

Axial SpA mNY (radiographic)
Age moyen < 40 ans
HLA B27+ 75%
Durée moy maladie 8 ans
EVA rachis 65/100
BASDAI 65/100
ASDAS 3.5
CRP > 8 mg/L 40%



Baeten D. Ann Rheum Dis. 2018 Sep;77(9):1295-1302.

Ixekizumab, an interleukin-17A antagonist in the treatment of ankylosing spondylitis or radiographic axial spondyloarthritis in patients previously untreated with biological disease-modifying anti-rheumatic drugs (COAST-V): 16 week results of a phase 3 randomised, double-blind, active-controlled and placebo-controlled trial

*Désirée van der Heijde, James Cheng-Chung Wei, Maxime Dougados, Philip Mease, Atul Deodhar, Walter P Maksymowych, Filip Van den Bosch, Joachim Sieper, Tetsuya Tomita, Robert Landewé, Fangyi Zhao, Eswar Krishnan, David H. Adams, Beth Pangallo, Hilde Carlier on behalf of the COAST-V study group**

Lancet 2018; 392: 2441–51
Published Online
October 22, 2018

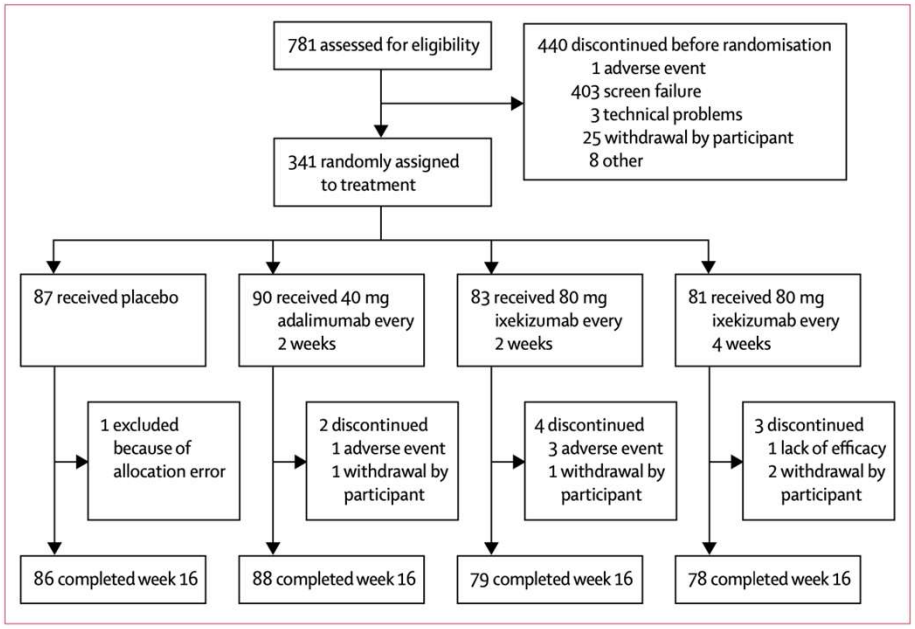
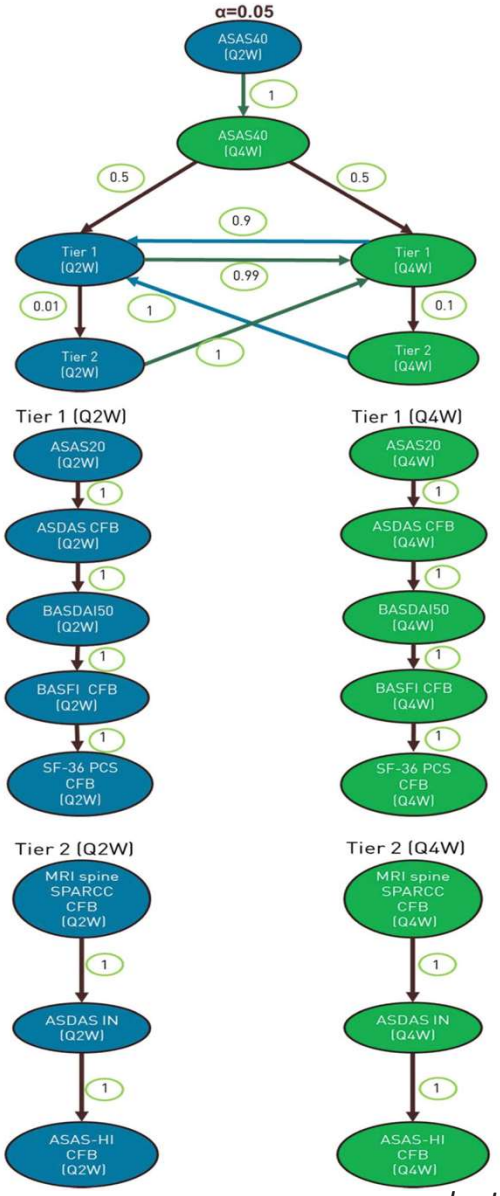


Figure 1: **Trial profile**



	Placebo (n=87*)	Adalimumab Q2W (n=90)	Ixekizumab Q2W (n=83)	Ixekizumab Q4W (n=81)
Age, years	42·7 (12·0)	41·8 (11·4)	41·3 (11·2)	41·0 (12·1)
Sex				
Men	71 (83%)	73 (81%)	64 (77%)	68 (84%)
Women	15 (17%)	17 (19%)	19 (23%)	13 (16%)
Race				
White	52 (60%)	57 (63%)	52 (63%)	52 (64%)
Asian	28 (33%)	29 (32%)	25 (30%)	25 (31%)
Other	6 (7%)	4 (4%)	6 (7%)	4 (5%)
Mean weight, kg	79·9 (17·1)	78·2 (17·2)	76·6 (13·8)	77·6 (14·7)
<70	25 (29%)	29 (32%)	29 (35%)	24 (30%)
≥70	61 (71%)	61 (68%)	54 (65%)	57 (70%)
Mean age of onset of axial spondyloarthritis, years	26·4 (8·4)	26·5 (8·6)	25·8 (8·2)	25·4 (7·7)
Mean duration of symptoms since axial spondyloarthritis onset, years	16·6 (10·1)	15·6 (9·3)	15·8 (10·6)	15·8 (11·2)
Mean duration of disease since axial spondyloarthritis diagnosis, years	6·8 (7·6)	7·5 (7·5)	8·2 (9·0)	8·3 (9·6)
Number of patients positive for HLA-B27	76 (89%)	82 (91%)	75 (90%)	75 (93%)
Number of patients using NSAIDs at baseline	78 (91%)	83 (92%)	79 (95%)	72 (89%)
Use of conventional synthetic DMARDs at baseline	31 (36%)	32 (36%)	29 (35%)	33 (41%)
Sulfasalazine	23 (27%)	25 (28%)	25 (30%)	24 (30%)
Methotrexate	8 (9%)	8 (9%)	4 (5%)	9 (11%)
Mean patient global assessment of disease activity numeric rating score	7·1 (1·7)	7·1 (1·7)	7·1 (1·6)	6·9 (1·5)
Mean CRP concentration, mg/L	16·0 (21·0)	12·5 (17·6)	13·4 (15·3)	12·2 (13·3)
Number of patients with CRP concentration >5 mg/L	60 (70%)	52 (58%)	55 (66%)	52 (64%)
Mean disease-related scores				
ASDAS	3·9 (0·7)	3·7 (0·8)	3·8 (0·8)	3·7 (0·7)
BASDAI	6·8 (1·2)	6·7 (1·5)	6·7 (1·6)	6·8 (1·3)
BASFI	6·4 (1·9)	6·1 (2·1)	6·3 (2·1)	6·1 (1·8)
ASAS Health Index	8·1 (3·5)	8·2 (3·7)	8·4 (3·6)	7·5 (3·3)
SF-36 PCS	32·0 (8·3)	33·5 (8·3)	34·1 (7·6)	34·0 (7·5)
MRI SPARCC spine	15·8 (21·2)	20·0 (28·4)	16·6 (23·8)	14·5 (20·6)
MRI SPARCC sacroiliac joint	5·0 (9·6)	4·7 (11·2)	6·4 (10·9)	4·5 (9·1)

Data are n (%) or mean (SD). Data are presented for patients with non-missing values. Q2W=every two weeks. Q4W=every four weeks. HLA=human leukocyte antigen. NSAID=non-steroidal anti-inflammatory drug. DMARD=disease-modifying anti-rheumatic drug. CRP=C-reactive protein. ASDAS=Ankylosing Spondylitis Disease Activity Score. BASDAI=Bath Ankylosing Spondylitis Disease Activity Index. BASFI=Bath Ankylosing Spondylitis Functional Index. ASAS=Assessment of SpondyloArthritis international Society. SF-36 PCS=Medical Outcomes Study 36-item Short-Form Health Survey Physical Component Score. SPARCC=Spondyloarthritis Research Consortium of Canada. *The placebo population excludes one patient who was excluded during screening and accidentally assigned to the placebo group. This patient discontinued before receiving study drug.

Table 1: **Baseline demographics and disease characteristics according to assigned treatment**

van der Heijde D. Lancet. 2018 Dec 8;392(10163):2441-2451.

Ixekizumab, an interleukin-17A antagonist in the treatment of ankylosing spondylitis or radiographic axial spondyloarthritis in patients previously untreated with biological disease-modifying anti-rheumatic drugs (COAST-V): 16 week results of a phase 3 randomised, double-blind, active-controlled and placebo-controlled trial

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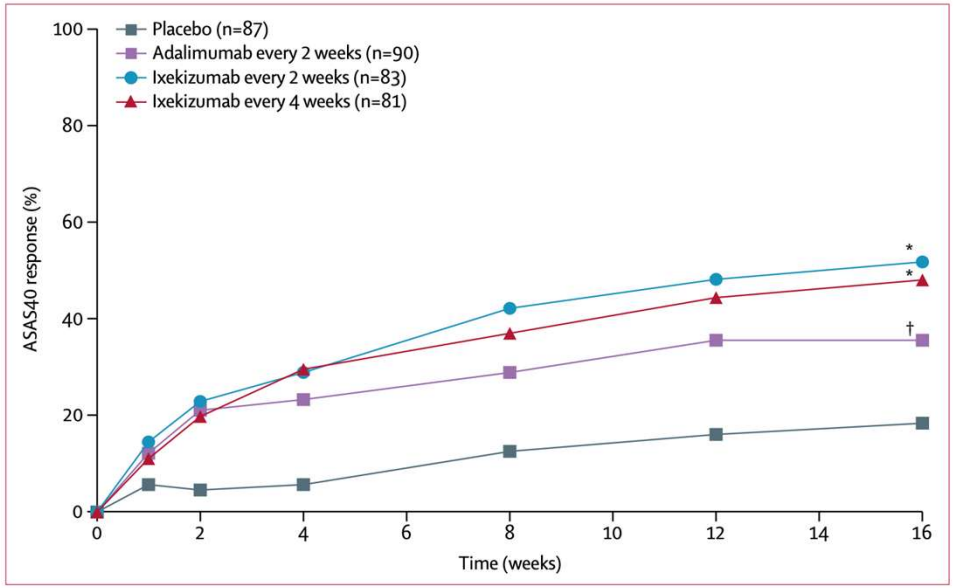


***Figure 2*: Proportion of patients achieving ASAS40 response through Week 16**

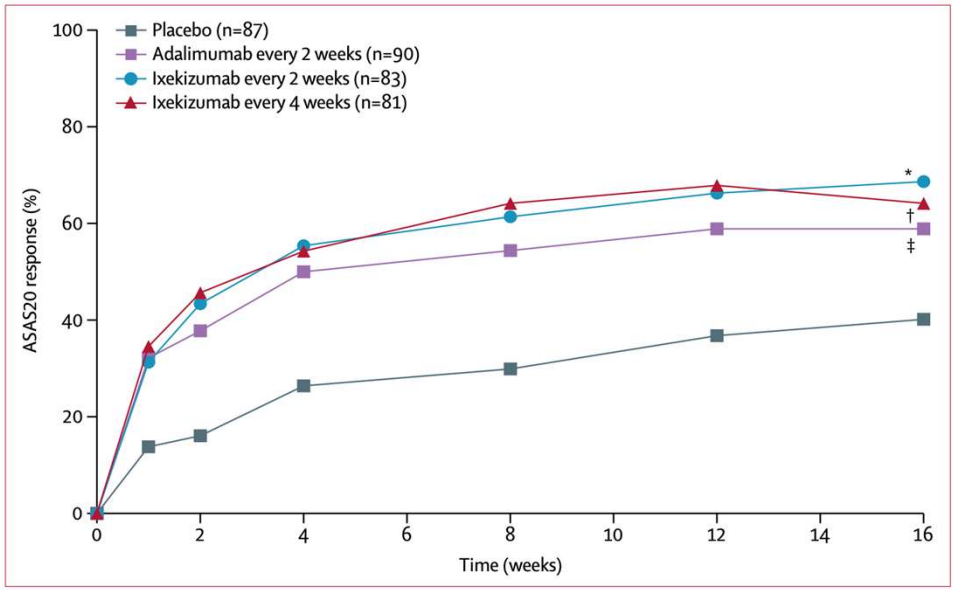


***Figure 3*: Proportion of patients achieving ASAS20 response through Week 16**

van der Heijde D. Lancet. 2018 Dec 8;392(10163):2441-2451.

RHEUMATOLOGY

Rheumatology 2022;61:4324–4334
https://doi.org/10.1093/rheumatology/keac104
Advance access publication 21 February 2022

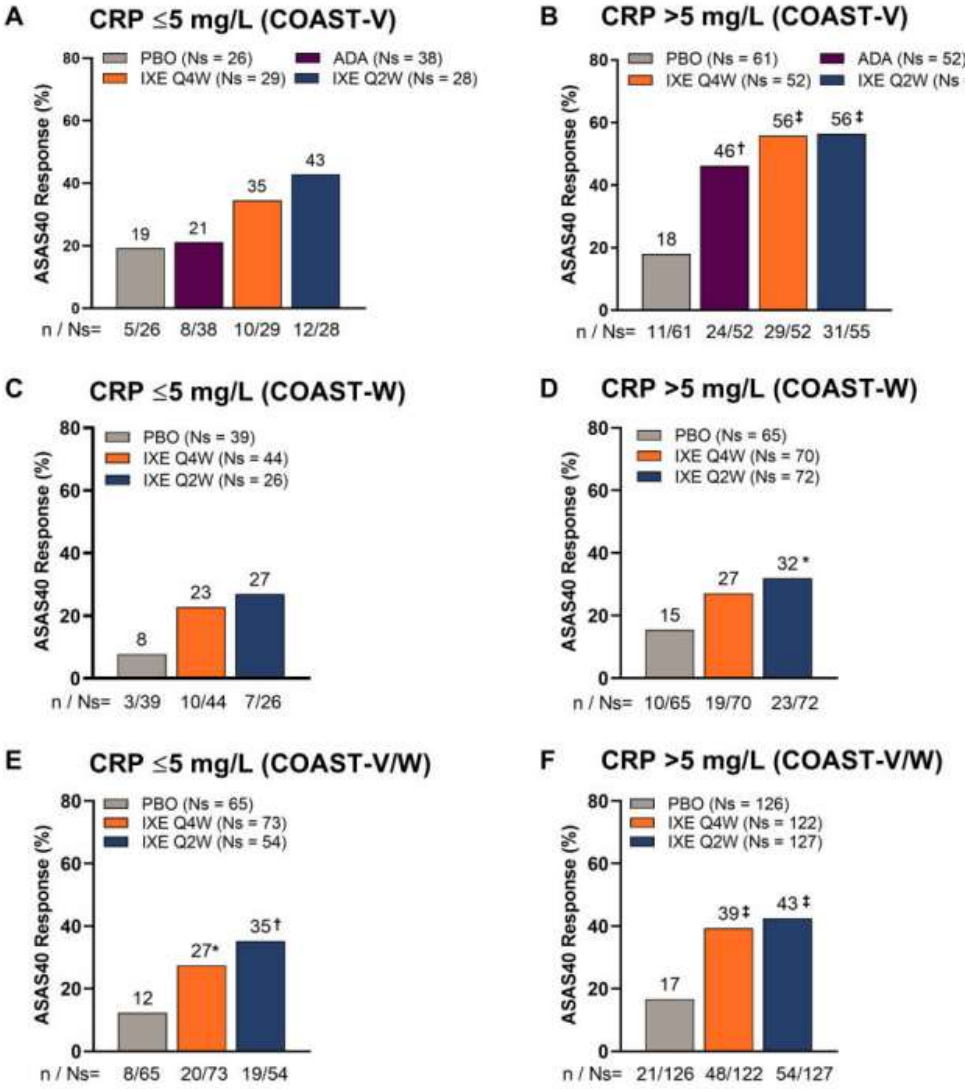
Original article

Ixekizumab in radiographic axial spondyloarthritis with and without elevated C-reactive protein or positive magnetic resonance imaging

Walter P. Maksymowych [1], Rebecca Bolce[2], Gaia Gallo[2], Emily Seem[2], Vladimir J. Geneus[2], David M. Sandoval[2], Mikkel Østergaard [3,4], Kurisu Tada[5], Xenofon Baraliakos [6,7], Atul Deodhar[8] and Lianne S. Gensler[9]

TABLE 1 Baseline demographics and clinical characteristics

Characteristics	COAST-V (biologic naïve)			
	PBO (n = 87)	ADA[a] (n = 90)	IXEQ4W (n = 81)	IXEQ2W (n = 83)
Age, years	42.7 (12.0)	41.8 (11.4)	41.0 (12.1)	41.3 (11.2)
Male, n (%)	71 (82.6)	73 (81.1)	68 (84.0)	64 (77.1)
Weight, kg	79.9 (17.1)	78.2 (17.2)	77.6 (14.7)	76.6 (13.8)
Duration of axSpA symptoms, years	16.6 (10.1)	15.6 (9.3)	15.8 (11.2)	15.8 (10.6)
Time since axSpA diagnosis, years	6.8 (7.6)	7.5 (7.5)	8.3 (9.6)	8.2 (9.0)
Therapy, n (%)				
Current cDMARD use	31 (36.0)	32 (35.6)	33 (40.7)	29 (34.9)
Current MTX use	8 (9.3)	8 (8.9)	9 (11.1)	4 (4.8)
IR to 1 TNFi	–	–	–	–
IR to 2 TNFi	–	–	–	–
Intolerance to TNFi	–	–	–	–
CRP, mg/L	16.0 (21.0)	12.5 (17.6)	12.2 (13.3)	13.4 (15.3)
≤5 mg/L, n (%)	26 (30.2)	38 (42.2)	29 (35.8)	28 (33.7)
>5 mg/L, n (%)	60 (69.8)	52 (57.8)	52 (64.2)	55 (66.3)
SPARCC MRI spine score	15.8 (21.2)	20.0 (28.4)	14.5 (20.6)	16.6 (23.8)
Patients, n	82	85	81	78
<2, n (%)	32 (39.0)	31 (36.5)	33 (40.7)	29 (37.2)
≥2, n (%)	50 (61.0)	54 (63.5)	48 (59.3)	49 (62.8)
SPARCC MRI SI joint score	5.0 (9.6)	4.7 (11.2)	4.5 (9.1)	6.4 (10.9)
Patients, n	82	85	81	79
<2, n (%)	49 (59.8)	55 (64.7)	54 (66.7)	45 (57.0)
≥2, n (%)	33 (40.2)	30 (35.3)	27 (33.3)	34 (43.0)



Maksymowych WP. Rheumatology (Oxford). 2022 Nov 2;61(11):4324-4334.

RHEUMATOLOGY

Rheumatology 2022;61:4324–4334
https://doi.org/10.1093/rheumatology/keac104
Advance access publication 21 February 2022

Original article

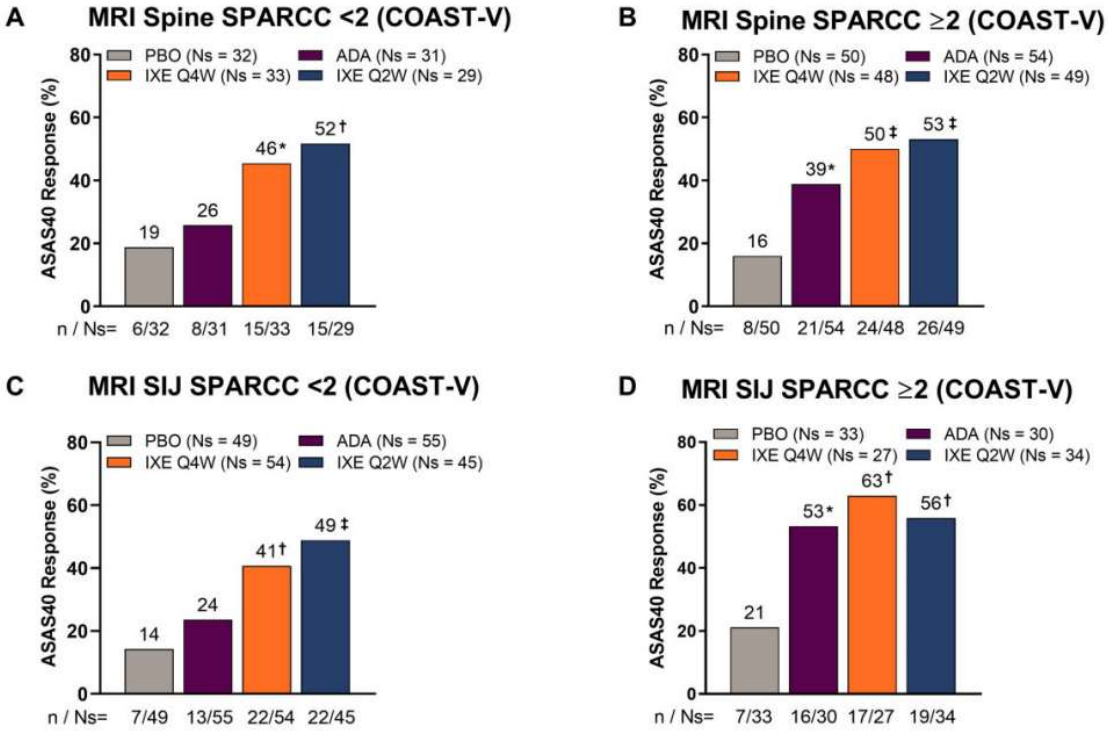
Ixekizumab in radiographic axial spondyloarthritis with and without elevated C-reactive protein or positive magnetic resonance imaging

Walter P. Maksymowych [1], Rebecca Bolce[2], Gaia Gallo[2], Emily Seem[2], Vladimir J. Geneus[2], David M. Sandoval[2], Mikkel Østergaard [3,4], Kurisu Tada[5], Xenofon Baraliakos [6,7], Atul Deodhar[8] and Lianne S. Gensler[9]

TABLE 1 Baseline demographics and clinical characteristics

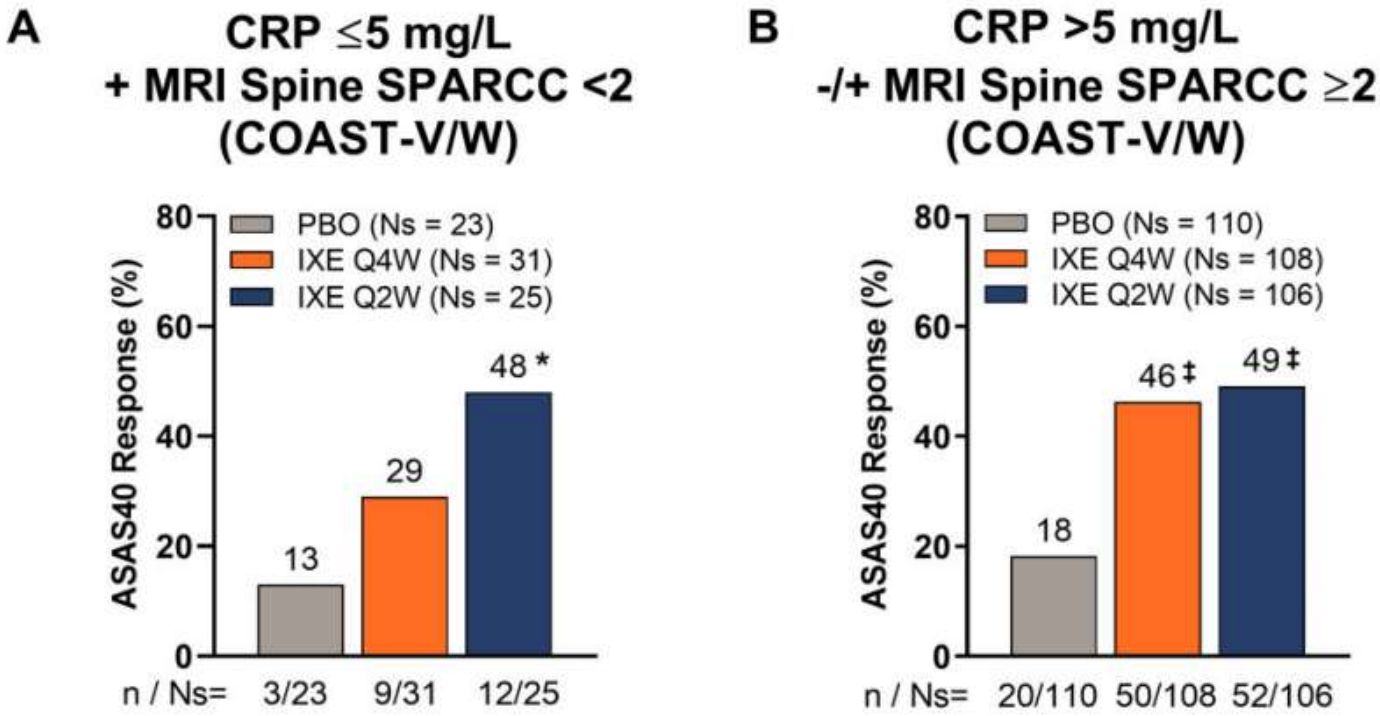
Characteristics	COAST-V (biologic naïve)			
	PBO (n = 87)	ADA[a] (n = 90)	IXEQ4W (n = 81)	IXEQ2W (n = 83)
Age, years	42.7 (12.0)	41.8 (11.4)	41.0 (12.1)	41.3 (11.2)
Male, n (%)	71 (82.6)	73 (81.1)	68 (84.0)	64 (77.1)
Weight, kg	79.9 (17.1)	78.2 (17.2)	77.6 (14.7)	76.6 (13.8)
Duration of axSpA symptoms, years	16.6 (10.1)	15.6 (9.3)	15.8 (11.2)	15.8 (10.6)
Time since axSpA diagnosis, years	6.8 (7.6)	7.5 (7.5)	8.3 (9.6)	8.2 (9.0)
Therapy, n (%)				
Current cDMARD use	31 (36.0)	32 (35.6)	33 (40.7)	29 (34.9)
Current MTX use	8 (9.3)	8 (8.9)	9 (11.1)	4 (4.8)
IR to 1 TNFi	–	–	–	–
IR to 2 TNFi	–	–	–	–
Intolerance to TNFi	–	–	–	–
CRP, mg/L	16.0 (21.0)	12.5 (17.6)	12.2 (13.3)	13.4 (15.3)
≤5 mg/L, n (%)	26 (30.2)	38 (42.2)	29 (35.8)	28 (33.7)
>5 mg/L, n (%)	60 (69.8)	52 (57.8)	52 (64.2)	55 (66.3)
SPARCC MRI spine score	15.8 (21.2)	20.0 (28.4)	14.5 (20.6)	16.6 (23.8)
Patients, n	82	85	81	78
<2, n (%)	32 (39.0)	31 (36.5)	33 (40.7)	29 (37.2)
≥2, n (%)	50 (61.0)	54 (63.5)	48 (59.3)	49 (62.8)
SPARCC MRI SI joint score	5.0 (9.6)	4.7 (11.2)	4.5 (9.1)	6.4 (10.9)
Patients, n	82	85	81	79
<2, n (%)	49 (59.8)	55 (64.7)	54 (66.7)	45 (57.0)
≥2, n (%)	33 (40.2)	30 (35.3)	27 (33.3)	34 (43.0)

FIG. 2 ASAS40 response by baseline MRI inflammation



Maksymowych WP. Rheumatology (Oxford). 2022 Nov 2;61(11):4324-4334.

ASAS40 response by baseline CRP and MRI spine inflammation



Rheumatology key messages

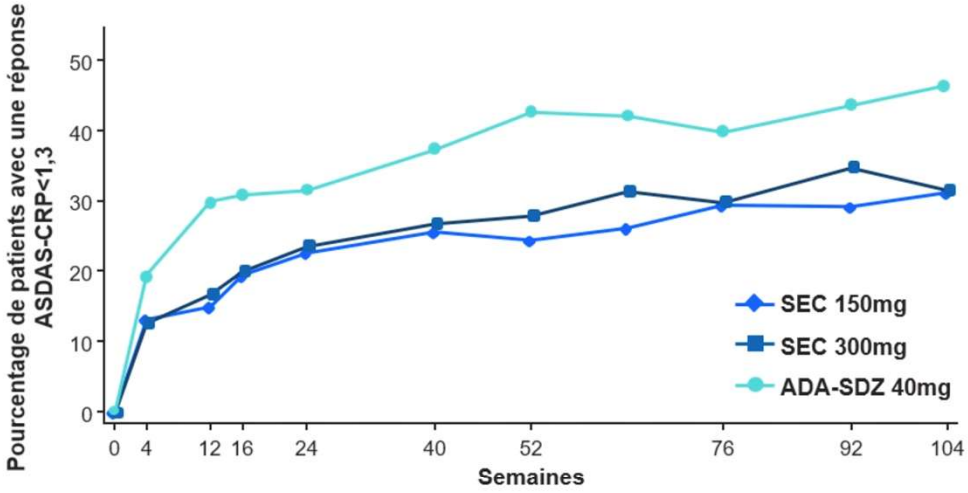
- « Rhumatologues peuvent être réticents à traiter par biothérapies des patients atteints de Spondyloarthrite axiale sans preuve objective inflammatoire »
- Dans les essais, l'ixekizumab démontrent une efficacité en l'absence d'une CRP augmentée ou l'absence d'inflammation en IRM au rachis.

Maksymowych WP. Rheumatology (Oxford). 2022 Nov 2;61(11):4324-4334.

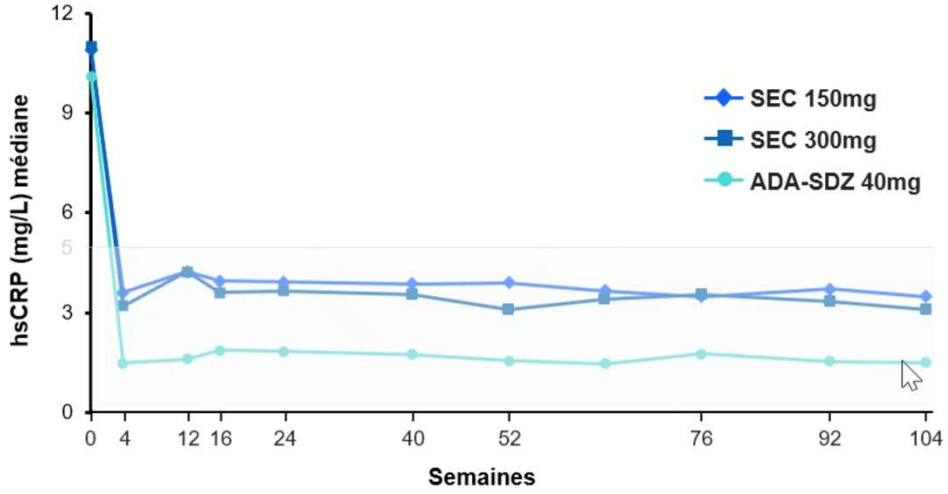
Critères exploratoires : quelle évolution clinique chez les patients traités par secukinumab et adalimumab biosimilaire à 2 ans ?

SURPASS

Réponse ADSAS-CRP maladie inactive sur 104 semaines



Taux médian de CRP ultra-sensible sur 104 semaines

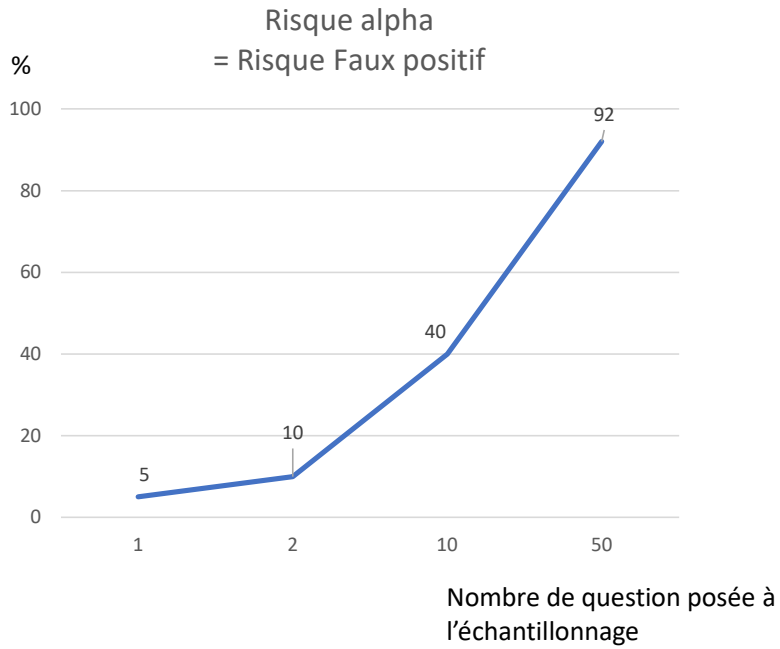


Étude en ouvert sur le type de traitement (SEC ou ADA-SDZ).

Données observes.
ASDAS, Ankylosing Spondylitis Disease Activity Score; hsCRP, Protéine C-reactive ultra-sensible; ADA-SDZ, adalimumab biosimilaire; SEC, secukinumab.
1. Baraliakos *et al.* Arthritis Rheum. (2024);doi:10.1002/Art.42852.

Baraliakos X. Arthritis Rheumatol. 2024 Aug;76(8):1278-1287.

CONCLUSION
...Se méfier des études post-hoc !
Etudes exploratoires et non vérité clinique !



La répétition à chaque test du risque d'obtenir un résultat significatif par hasard augmente le risque global de conclure à tort à l'efficacité du traitement.

=

inflation du risque alpha

« les données ont été torturées jusqu'à ce qu'elles avouent ! »