“Νεότερες θεραπείες στην ψωρίαση- ψωριασική αρθρίτιδα”

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Επιμελητής Α΄ Ρευματολογίας

Ρευματολογική Κλινική Π.Ν.Ιωαννίνων

Καμία σύγκρουση συμφερόντων

Θεραπεία ψωρίασης – ψωριασικής αρθρίτιδας

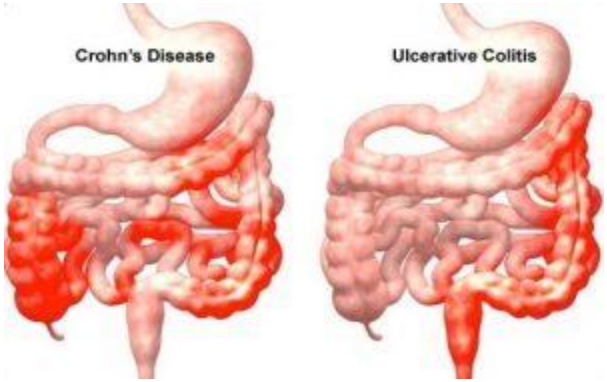
- Θεωρείται γενικά δύσκολη
- Ετερογένεια
- Ποικίλοι κλινικοί φαινότυποι
- Πέρα από τη νόσο του δέρματος και των αρθρώσεων, η ενεργή νόσος επηρεάζει αρνητικά:

✓ Το μεταβολικό προφίλ
✓ Την υγεία των οστών
✓ Τον καρδιαγγειακό κίνδυνο

Σημαντική επιβάρυνση στην ποιότητας ζωής (QoL), και στην παραγωγικότητα εργασίας

Πέρα από το δέρμα και τις αρθρώσεις

- Κατηγοριοποιείται ως «σπονδυλαρθροπάθεια»
- Συχνά συνυπάρχουν η ραγοειδίτιδα και η φλεγμονώδης νόσος του εντέρου



Αυξανόμενη πολυπλοκότητα και διλήμματα θεραπείας

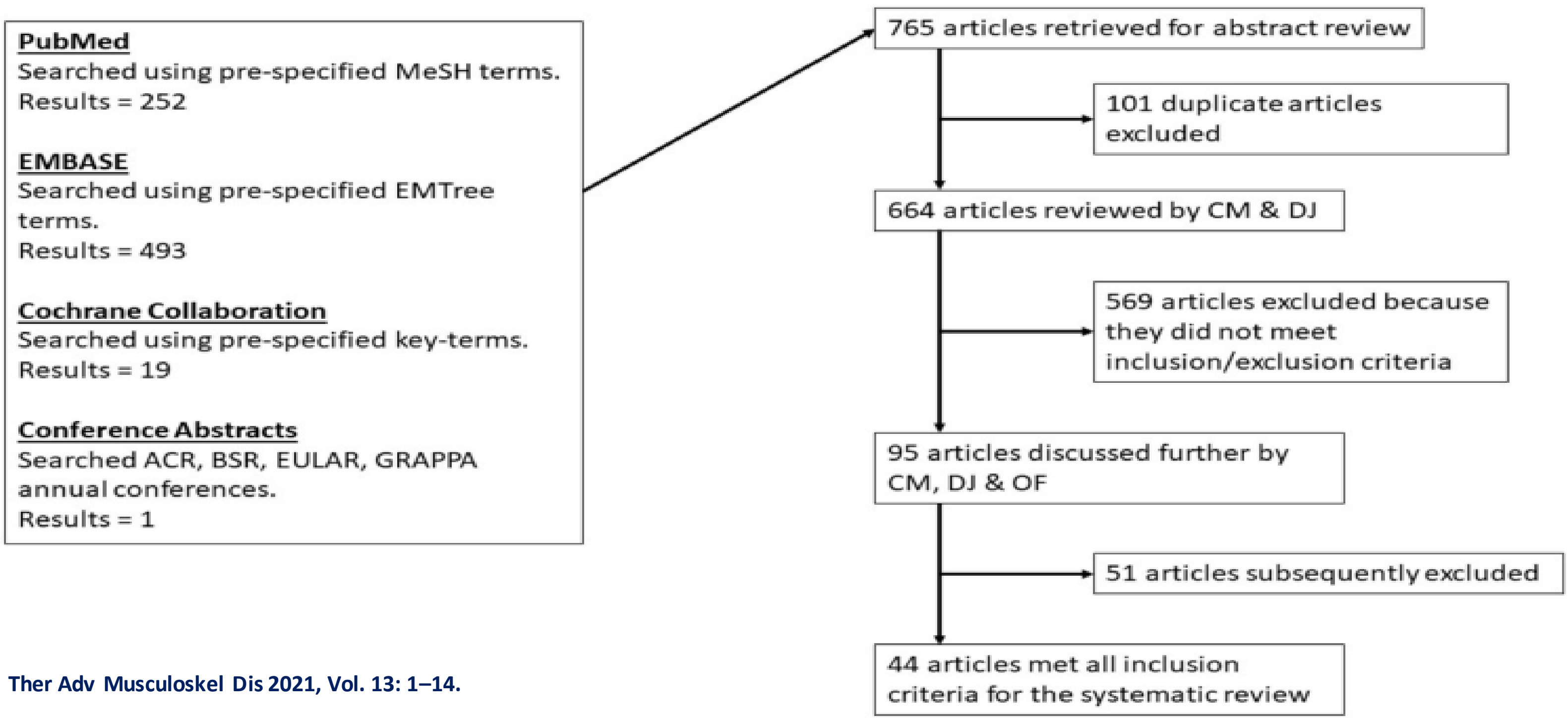
Biomarkers predictive of treatment response in psoriasis and psoriatic arthritis: a systematic review

Ther Adv Musculoskel Dis

2021, Vol. 13: 1–14

DOI: 10.1177/1759720X211014010

Conor Magee, Hannah Jethwa, Oliver M. FitzGerald and Deepak R. Jadon



Therapeutic Advances in Musculoskeletal Disease Review Article

Biomarkers predictive of treatment response in psoriasis and psoriatic arthritis: a systematic review

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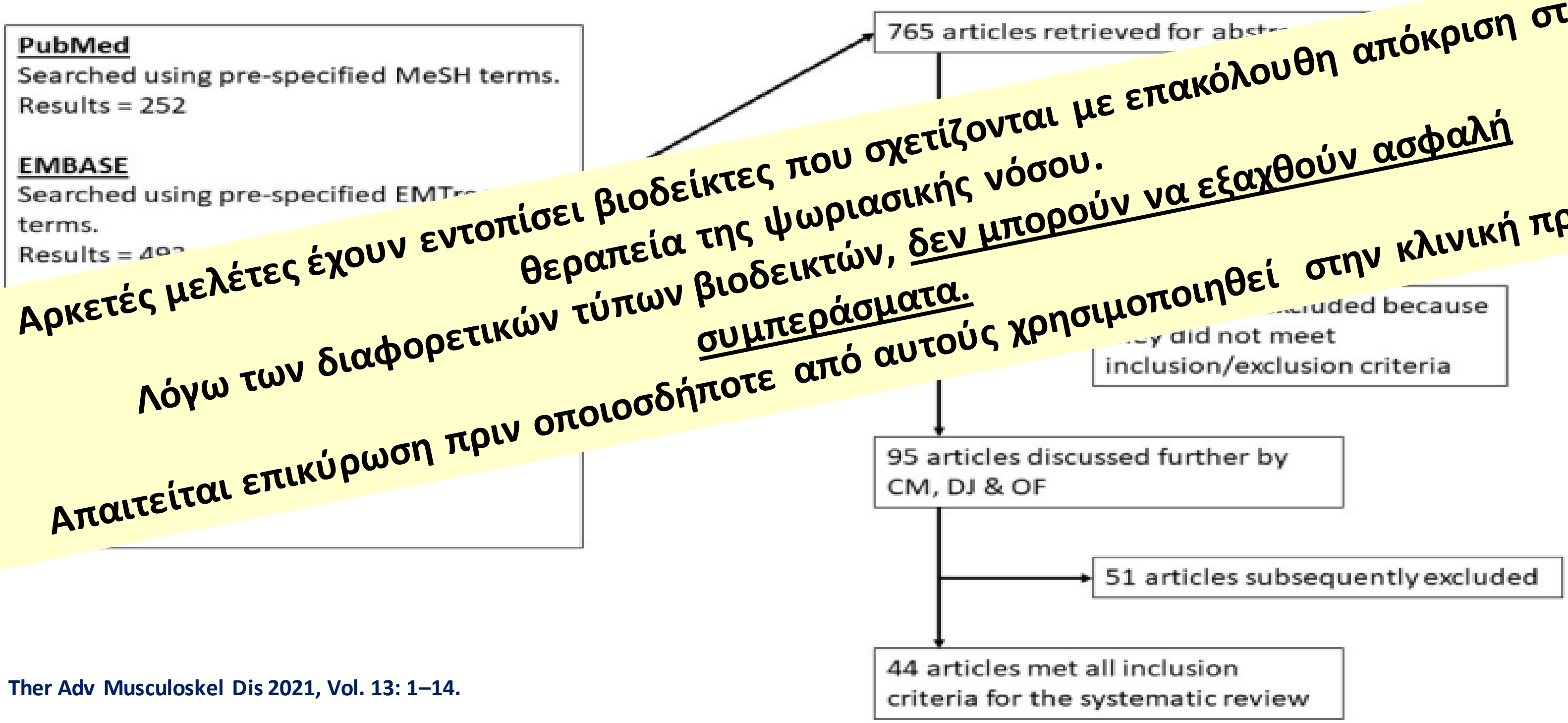


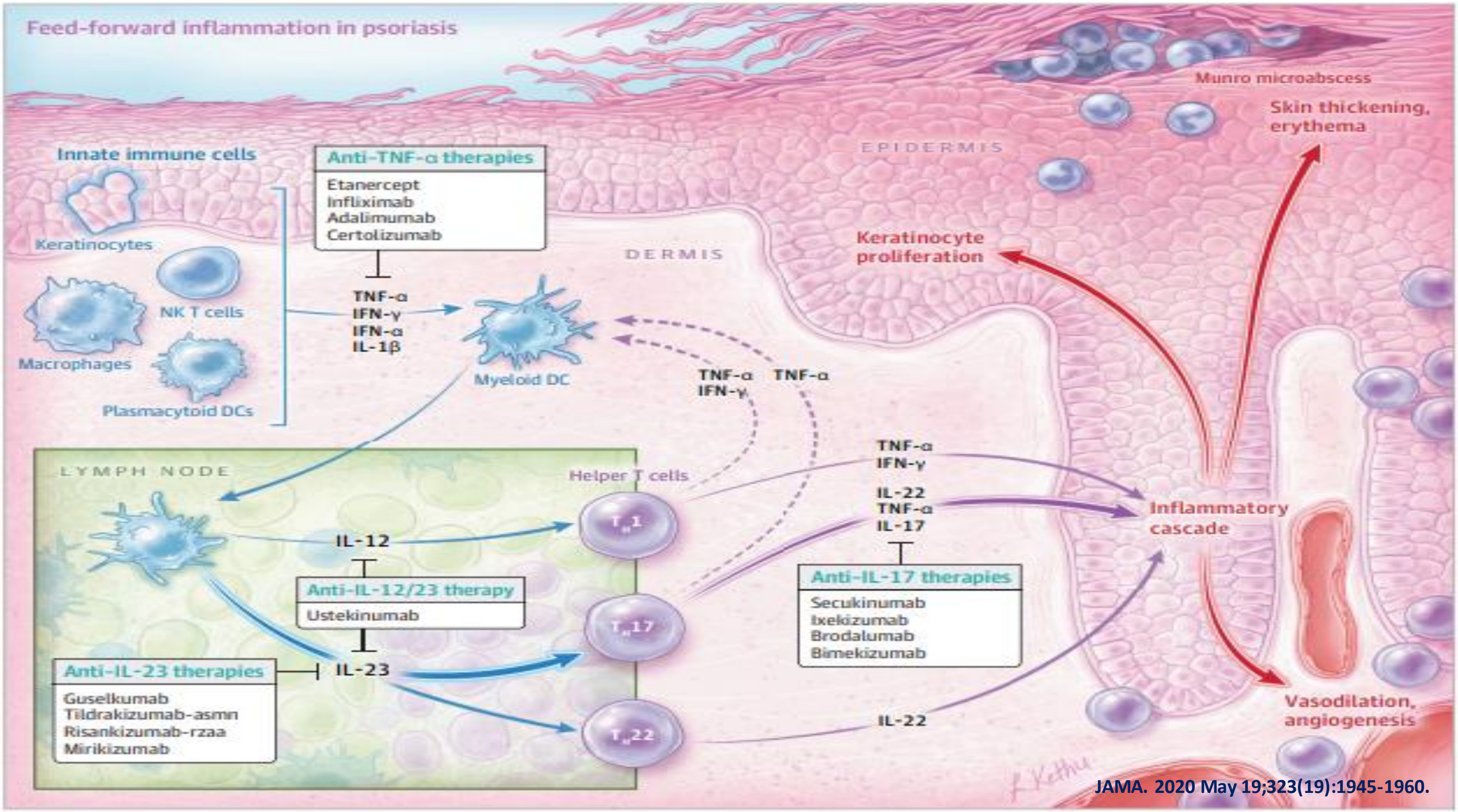
Αρκετές μελέτες έχουν εντοπίσει βιοδείκτες που σχετίζονται με επακόλουθη απόκριση στη θεραπεία της ψωριασικής νόσου.

Λόγω των διαφορετικών τύπων βιοδεικτών, <u>δεν μπορούν να εξαχθούν ασφαλή συμπεράσματα.</u>

Απαιτείται επικύρωση πριν οποιοσδήποτε από αυτούς χρησιμοποιηθεί στην κλινική πράξη

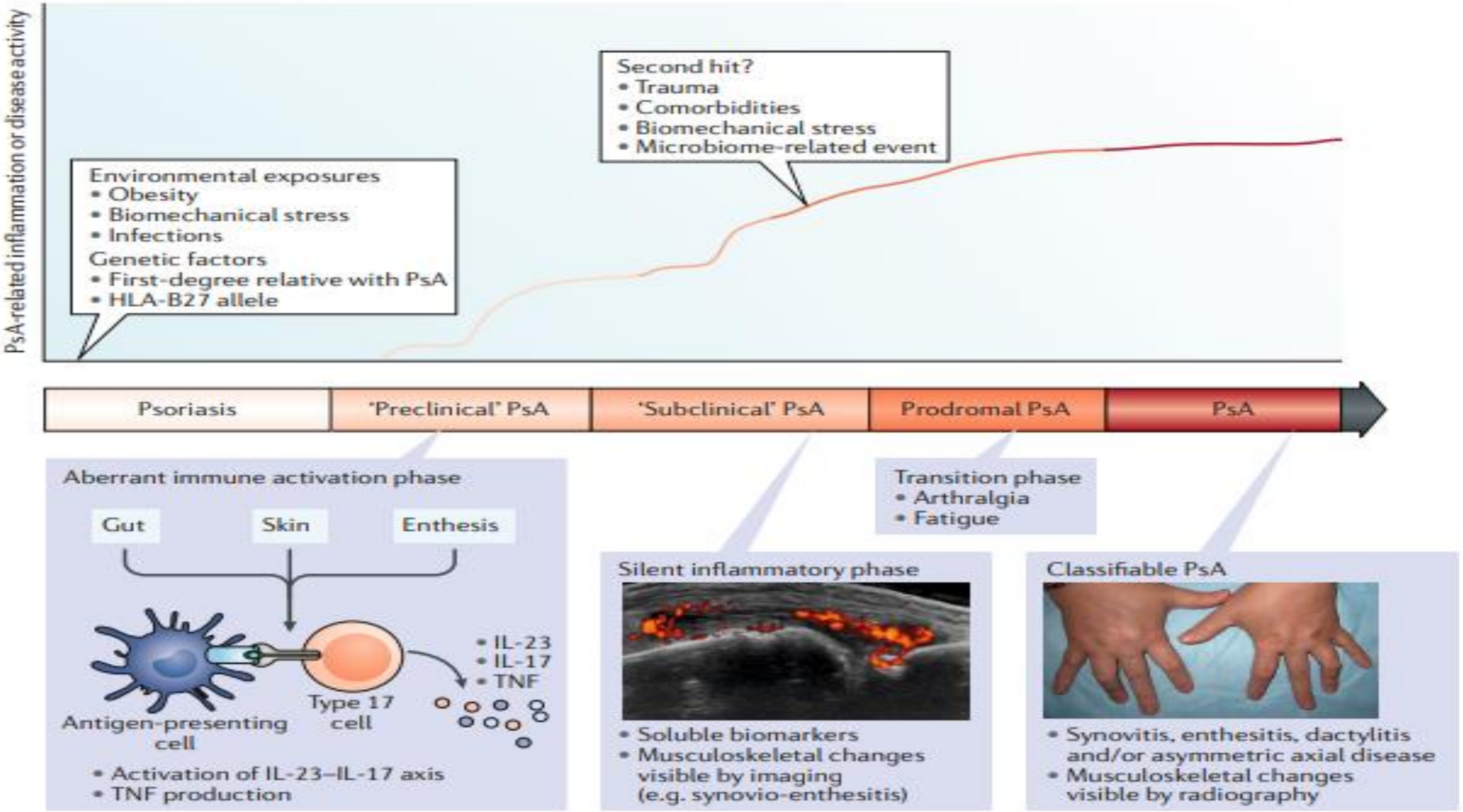
Ther Adv Musculoskel Dis 2021, Vol. 13: 1–14.

Παθοφυσιολογία της ψωρίασης



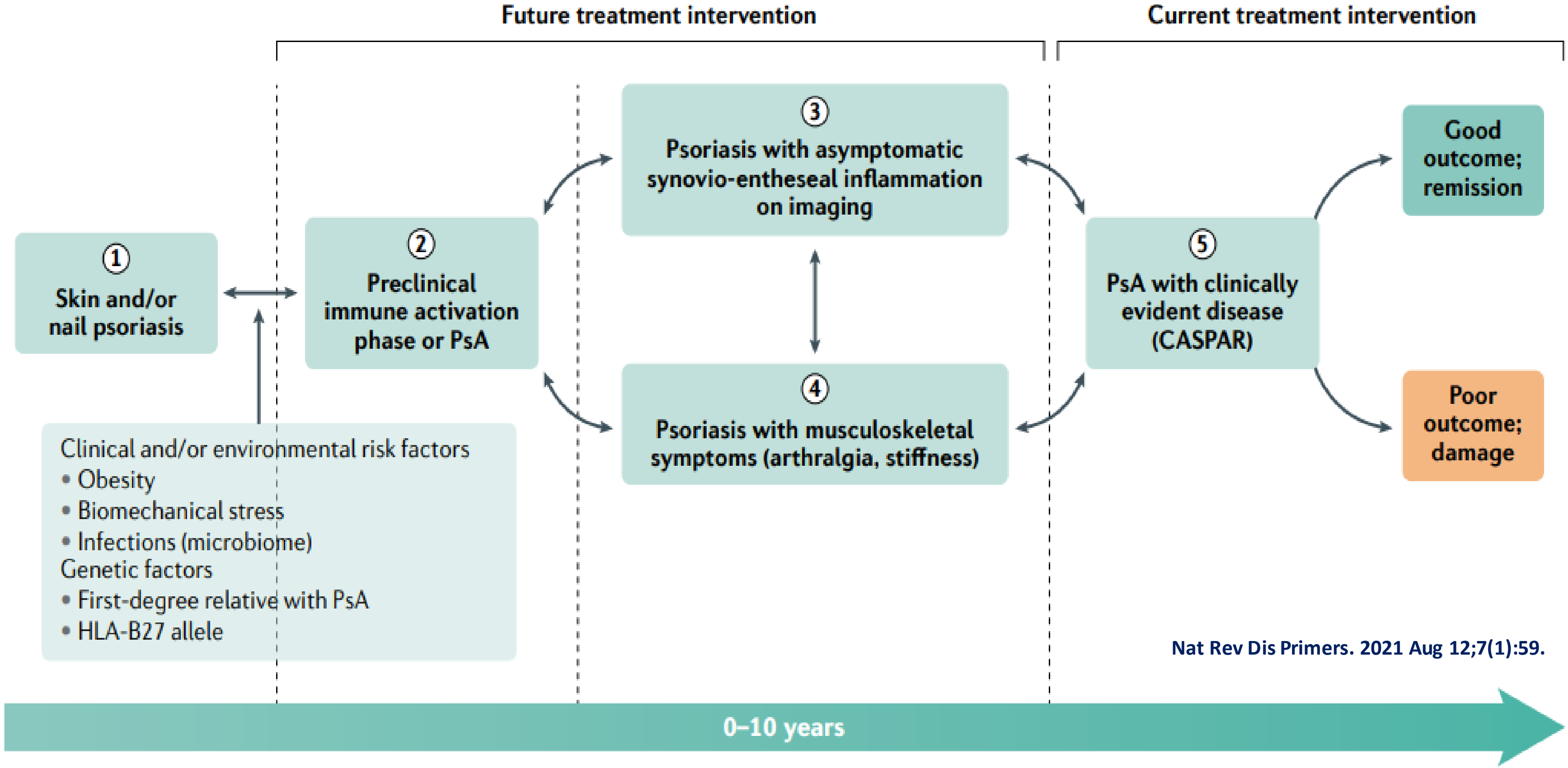
JAMA. 2020 May 19;323(19):1945-1960.

Μετάβαση από την ψωρίαση στην PsA



Nat Rev Rheumatol. 2019 Mar;15(3):153-166.

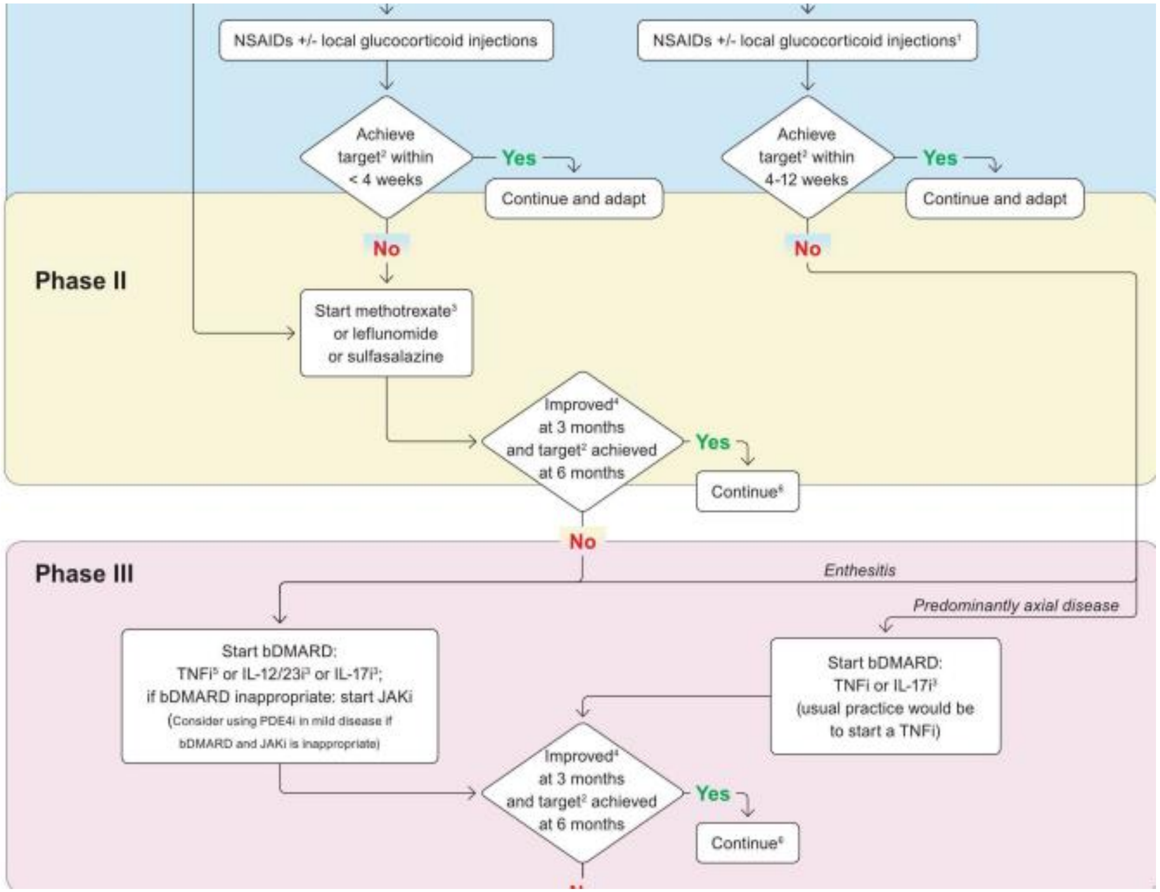
Στάδια στην εξέλιξη της ψωρίασης σε ψωριασική αρθρίτιδα



Nat Rev Dis Primers. 2021 Aug 12;7(1):59.

‘one size fits all’

- Απίθανο να είναι επιτυχής
- Αυτό αποδεικνύεται από τον αναστολέα της φωσφοδιεστεράσης 4 απρεμιλάστη
- Έχει σημαντικά δεδομένα για τη χρήση στο δέρμα
- Αλλά μέτρια αποτελέσματα στην πολυαρθρική PsA
- Στην τελευταία ενημέρωση των συστάσεων της EULAR
- Έχει αντικατασταθεί και από τα bDMARD και από τους JAK (Janus kinase)



Gossec L, et al. Ann Rheum Dis 2020;79:700–712.

Τρέχουσες ακάλυπτες ανάγκες

- Αν και υπήρξε πρόοδος στη θεραπεία (στοχευμένες θεραπείες)

Table 1. Current biological and small-molecule therapies available in the UK.

Generic name ()	Class	Target	Molecular Structure	Dose Regime
Adalimumab	TNF inhibitor	TNF	Fully human monoclonal Antibody	40 mg s.c fortnightly
Etanercept	TNF inhibitor	TNF	Receptor fusion protein	50 mg s.c weekly
Infliximab	TNF inhibitor	TNF	Chimeric monoclonal Antibody	5 mg/kg i.v every 8 weeks post induction
Golilumab	TNF inhibitor	TNF	Fully human monoclonal Antibody	50 mg s.c monthly
Certolizumab pegol	TNF inhibitor	TNF	Humanized monoclonal Antibody	200 mg s.c fortnightly post induction
Ixekizumab	IL-17 Inhibitor	IL-17a	Fully human monoclonal Antibody	80 mg s.c monthly post induction
Secukinumab	IL-17 Inhibitor	IL-17a	Recombinant human monoclonal Antibody	150 mg s.c monthly post induction
Ustekinumab	Il12-23/12 Inhibitor	P40 subunit	Fully human monoclonal Antibody	45 mg* s.c three monthly post induction *90 mg used in BW >100 kg
Apremilast	PDE4 Inhibitor	PDE4	Small molecule	30 mg oral twice daily after induction
Tofacitinib	JAK Inhibitor	JAK 1&3	Small molecule	5 mg oral twice daily

- Ορισμένοι ασθενείς αποτυγχάνουν ή παρουσιάζουν δυσανεξία στις επί του παρόντος διαθέσιμες θεραπείες

EXPERT OPINION ON PHARMACOTHERAPY 2022, VOL. 23, NO. 4, 417–420.

Τρέχουσες ακάλυπτες ανάγκες

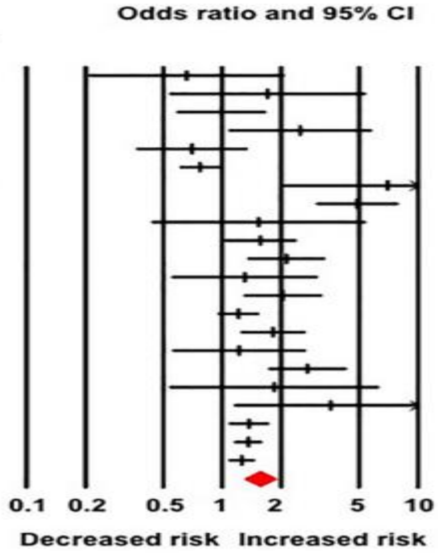
- Κλινικές δοκιμές με bDMARD μας πληροφορούν ότι:

έως και το 40% είναι μη ανταποκρινόμενοι

- 50% στην παχυσαρκία, που είναι πιο συχνή στην PsA

Obesity and Failure of Anti-TNF Therapy - Psoriasis-Psoriatic Arthriti

Study name	Odds ratio	Lower limit	Upper limit	Relative weight
Bagel 2012 - Cohort 1	0.66	0.21	2.07	1.99
Bagel 2012 - Cohort 2	1.71	0.54	5.38	1.99
Cai 2017	0.99	0.59	1.66	4.96
Cassano 2008	2.51	1.09	5.80	3.07
Chiricozzi 2016	0.70	0.37	1.33	4.11
Costa 2014	0.77	0.61	0.97	7.15
Di Lernia 2014	7.02	2.05	24.02	1.79
Di Munno 2012	4.90	3.04	7.90	5.27
Di Renzo 2012	1.53	0.44	5.38	1.73
Gottlieb 2012	1.57	1.03	2.39	5.71
Hojgaard 2016	2.13	1.36	3.35	5.47
Iannone 2013	1.30	0.56	3.06	3.01
Menter 2010	2.04	1.30	3.21	5.46
Menter 2016	1.21	0.96	1.53	7.15
Naldi 2008 - ETN	1.82	1.25	2.64	6.10
Naldi 2008 - IFX	1.22	0.56	2.66	3.35
Paul 2012	2.73	1.73	4.30	5.44
Poulin 2014	1.85	0.54	6.30	1.80
Prussick 2015	3.58	1.16	11.07	2.04
Vilarrasa 2016	1.37	1.09	1.73	7.16
Warren 2015	1.36	1.16	1.59	7.61
Zweegers 2016	1.26	1.08	1.46	7.64
	1.57	**1.30**	**1.89**	

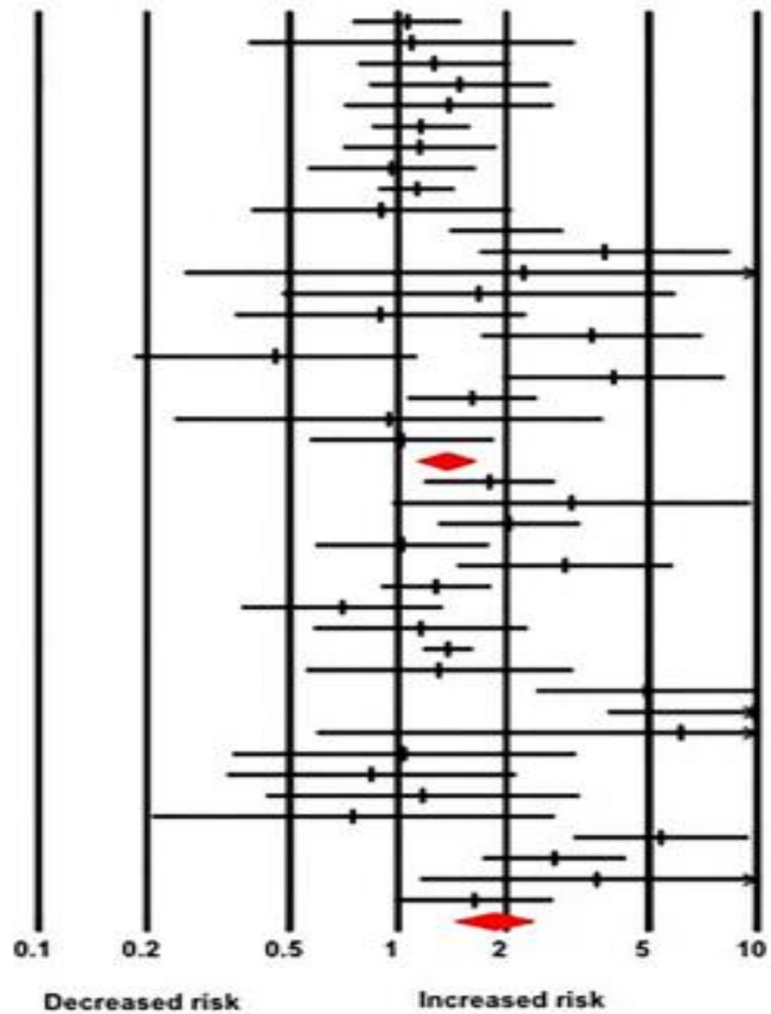


PLoS ONE 13(5): e0195123.

Obesity and Failure of Anti-TNF Therapy - Dose-response Relationsh

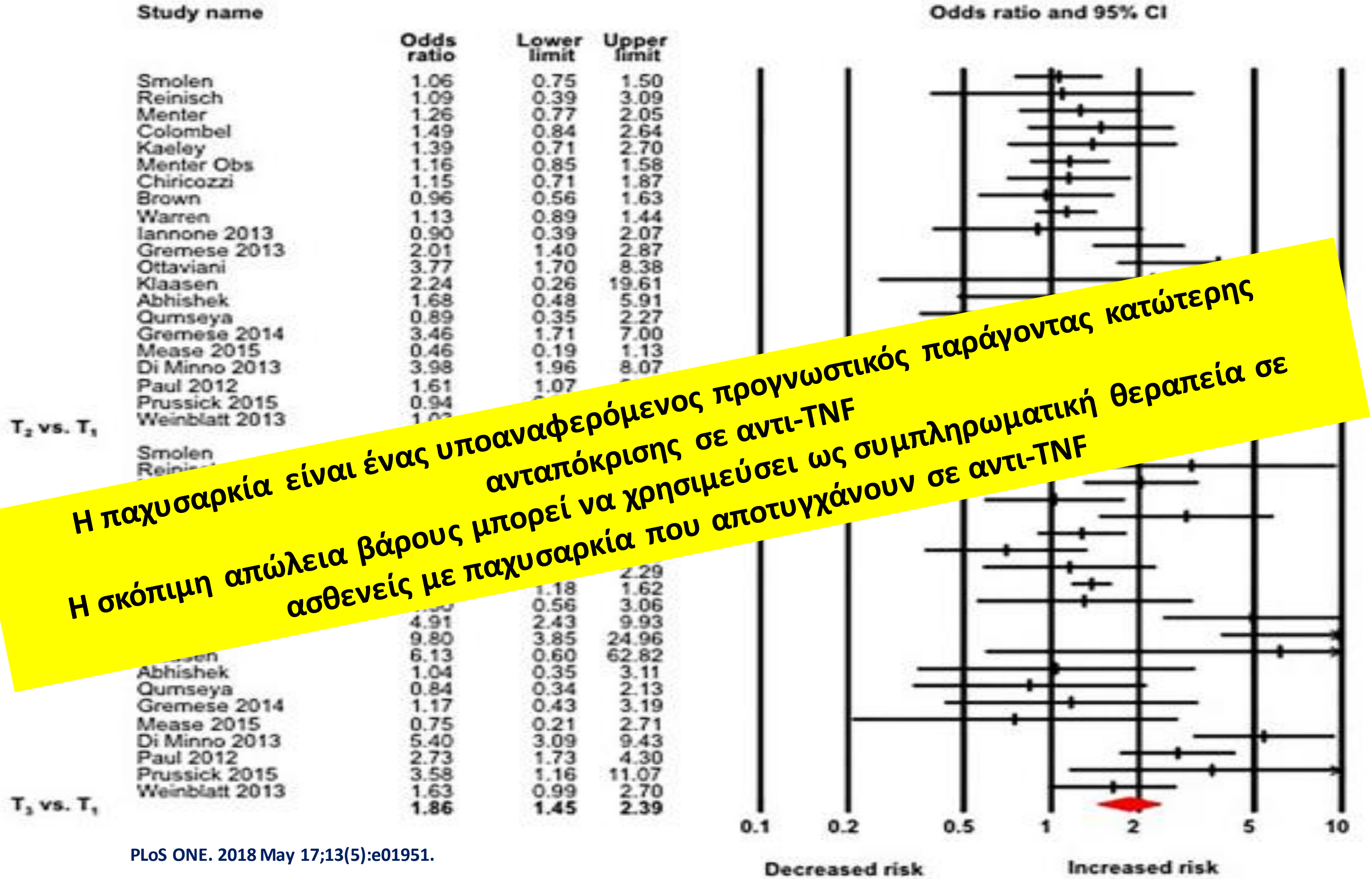
	Study name	Odds ratio	Lower limit	Upper limit
	Smolen	1.06	0.75	1.50
	Reinisch	1.09	0.39	3.09
	Menter	1.26	0.77	2.05
	Colombel	1.49	0.84	2.64
	Kaeley	1.39	0.71	2.70
	Menter Obs	1.16	0.85	1.58
	Chiricozzi	1.15	0.71	1.87
	Brown	0.96	0.56	1.63
	Warren	1.13	0.89	1.44
	Iannone 2013	0.90	0.39	2.07
	Gremese 2013	2.01	1.40	2.87
	Ottaviani	3.77	1.70	8.38
	Klaasen	2.24	0.26	19.61
	Abhishek	1.68	0.48	5.91
	Qumseya	0.89	0.35	2.27
	Gremese 2014	3.46	1.71	7.00
	Mease 2015	0.46	0.19	1.13
	Di Minno 2013	3.98	1.96	8.07
	Paul 2012	1.61	1.07	2.43
	Prussick 2015	0.94	0.24	3.71
	Weinblatt 2013	1.03	0.57	1.84
T_2 vs. T_1		**1.37**	**1.14**	**1.64**
	Smolen	1.80	1.19	2.72
	Reinisch	3.04	0.97	9.56
	Menter	2.04	1.30	3.21
	Colombel	1.03	0.59	1.79
	Kaeley	2.93	1.47	5.83
	Menter Obs	1.28	0.91	1.81
	Chiricozzi	0.70	0.37	1.33
	Brown	1.16	0.59	2.29
	Warren	1.38	1.18	1.62
	Iannone 2013	1.30	0.56	3.06
	Gremese 2013	4.91	2.43	9.93
	Ottaviani	9.80	3.85	24.96
	Klaasen	6.13	0.60	62.82
	Abhishek	1.04	0.35	3.11
	Qumseya	0.84	0.34	2.13
	Gremese 2014	1.17	0.43	3.19
	Mease 2015	0.75	0.21	2.71
	Di Minno 2013	5.40	3.09	9.43
	Paul 2012	2.73	1.73	4.30
	Prussick 2015	3.58	1.16	11.07
	Weinblatt 2013	1.63	0.99	2.70
T_3 vs. T_1		**1.86**	**1.45**	**2.39**

Odds ratio and 95% CI



PLoS ONE. 2018 May 17;13(5):e01951.

Obesity and Failure of Anti-TNF Therapy - Dose-response Relationsh



PLoS ONE. 2018 May 17;13(5):e01951.

Η παχυσαρκία είναι ένας υποαναφερόμενος προγνωστικός παράγοντας κατώτερης ανταπόκρισης σε αντι-TNF

Η σκόπιμη απώλεια βάρους μπορεί να χρησιμεύσει ως συμπληρωματική θεραπεία σε ασθενείς με παχυσαρκία που αποτυγχάνουν σε αντι-TNF

Φαινόμενο δευτερογενούς μη ανταπόκρισης

- Δευτερογενής μη ανταπόκριση είναι επίσης καλά αναγνωρισμένη σε ασθενείς με ΨΑ

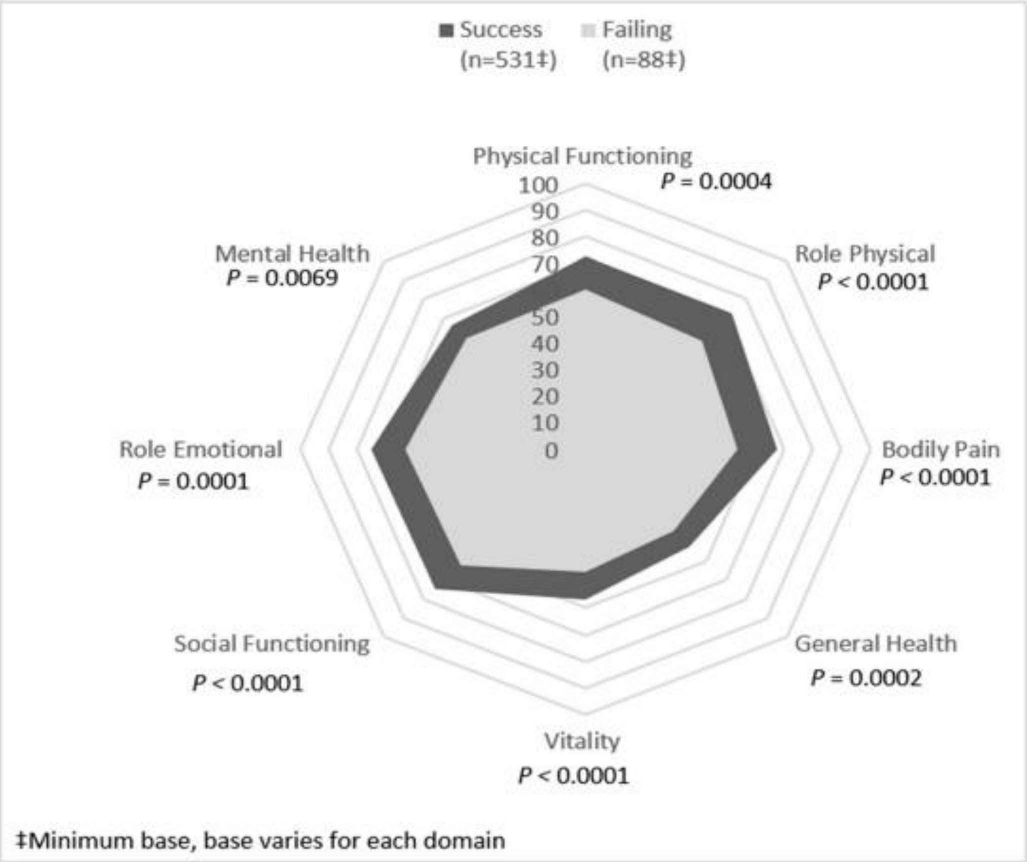
έως το 30% θα διακόψουν τους TNFi στο έτος

Γυναίκες με συννοσηρότητες που σχετίζονται με το μεταβολικό σύνδρομο έχουν χαμηλότερη παραμονή στους TNFi

Characteristic	Complete cohort	Adalimumab	Etanercept	Univariate analysesOR (95% CI)[a]	P-value
Initial TNFi therapy	(n = 188)	(n = 86)	(n = 102)		
Males, n (%)	92 (49)	45 (52)	47 (46)	1.28 (0.72, 2.28)	0.39
At TNFi initiation					
Age, mean (s.d.), years	47.2 (11.4)	47.3 (11.0)	47.2 (11.7)	−0.04 (−3.34, 3.27)[b]	0.98
Disease duration, median (IQR), years	11 (7–16)	12 (7–16)	10 (7–16)	1.00 (0.97, 1.03)[c]	0.92
CRP, median (IQR)	5 (4–10)	5 (3–10)	7 (4–18)	**1.02 (1.00, 1.04)[c]**	**0.02**
ESR, median (IQR)	12 (7–23)	12 (7–23)	13 (7–22)	1.00 (0.99, 1.01)[c]	0.85
Tender joint count, median (IQR)	21 (11–32)	19 (11–30)	22 (10–34)	1.00 (0.99, 1.01)	0.97
Swollen joint count, median (IQR)	8 (5–12)	8 (6–11)	8 (4–13)	0.99 (0.97, 1.03)	0.78
PGA score, median (IQR)	4 (3–4)	4 (3–4)	4 (3–4)	0.86 (0.61, 1.21)	0.39
Smoking ever, n (%)	53/94 (56)[d]	25/40 (63)[d]	28/54 (52)[d]	—	—
Co-morbidities, n (%)					
Any metabolic[e]	101 (54)	50 (58)	51 (50)	1.39 (0.78, 2.48)	0.27
Hypertension	59 (31)	20 (23)	39 (38)	**2.04 (1.08, 3.87)**	**0.03**
Diabetes	21 (11)	10 (12)	11 (11)	0.92 (0.37, 2.28)	0.86
Dyslipidaemia	12 (7)	3 (4)	9 (9)	2.68 (0.70, 10.22)	0.15
BMI, mean (s.d.)	32.6 (7.4)	33.2 (7.4)	31.9 (7.4)	−0.01 (−0.03, 0.01)	0.53
Concomitant DMARD use, n (%)					
Any DMARD	121/186 (65)[d]	63/84 (75)[d]	58 (57)	**0.44 (0.23, 0.83)**	**0.01**
MTX	79/186 (43)[d]	46/84 (55)[d]	33 (32)	**0.40 (0.22, 0.72)**	**0.002**
SSZ	40/186 (22)[d]	20/84 (24)[d]	20 (20)	0.78 (0.39, 1.57)	0.49
LEF	29/186 (16)[d]	12/84 (14)[d]	17 (17)	1.20 (0.54, 2.68)	0.66
TNFi switchers	(n = 32)	(n = 19)	(n = 13)		
Males, n (%)	12 (38)	—	—	—	—
At TNFi initiation					
Age, mean (s.d.), years	50.5 (12.1)	—	—	—	—
Disease duration, median (IQR), years	12 (9–20)	—	—	—	—
CRP, median (IQR)	4 (2–12)	—	—	—	—
ESR, median (IQR)	9 (6–22)	—	—	—	—
Tender joint count, median (IQR)	25 (12–44)	—	—	—	—
Swollen joint count, median (IQR)	6.5 (4–12)	—	—	—	—
PGA score, median (IQR)	4 (3–4)	—	—	—	—
Any metabolic co-morbidity[e], n (%)	20 (63)	15 (79)	5 (39)	**0.17 (0.03, 0.80)**	**0.03**
Concomitant DMARD use, n (%)					
Any DMARD	19 (59)	14 (74)	5 (39)	**0.22 (0.05, 1.01)**	**0.05**
MTX	11 (34)	8 (42)	3 (23)	0.41 (0.09, 2.00)	0.27

Rheumatology (Oxford). 2018;57(1):158–163.

Δεδομένα πραγματικού κόσμου



SF-36 σε αποτυχημένη ανοσοτροποποιητική θεραπεία έναντι επιτυχούς
Τα αποτελέσματα προσαρμόζονται για ηλικία, φύλο, κάπνισμα, ΔΜΣ, χρόνο από την έναρξη των συμπτωμάτων

Η κακή ανταπόκριση στη θεραπεία στην PsA σχετίζεται με ουσιαστικό αρνητικό αντίκτυπο στον ασθενή

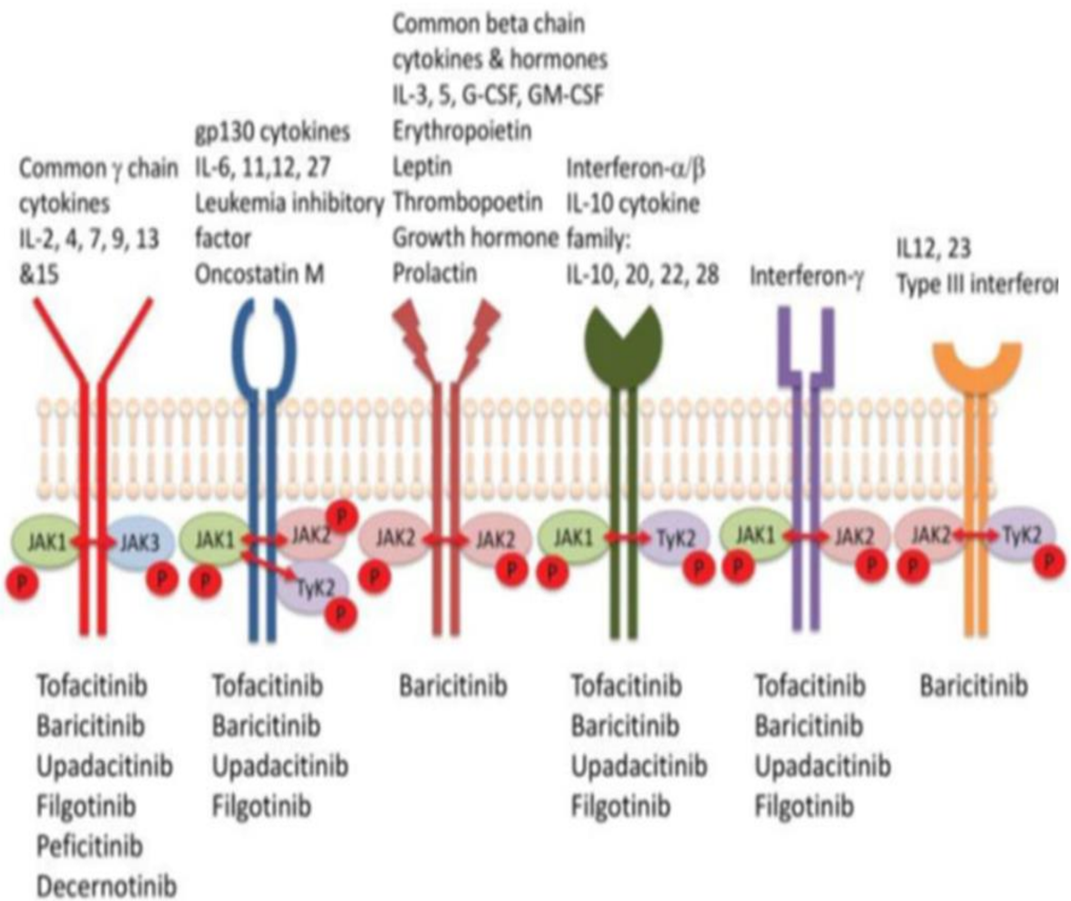
Σε περιπτώσεις πρωτογενούς αποτυχίας, απαιτείται έγκαιρη αλλαγή

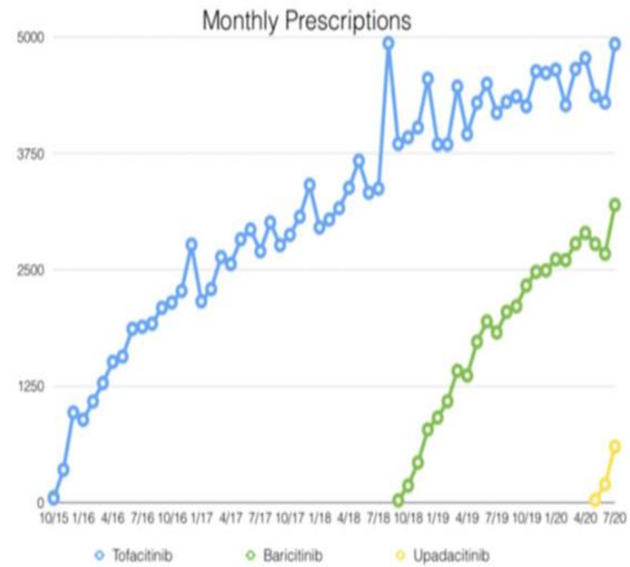
Clin Rheumatol. 2019;38(6):1615–1626.

Νέοι βιολογικοί παράγοντες

- **Αναστολείς JAK1 tofacitinib, upadacitinib και filgotinib**
- **Αναστολέας Tyrosine Kinase 2 (TYK2) deucravacitinib**
- **Αναστολέας IL-17A/ F bimekizumab brodalumab**
- **Αναστολείς IL-23 guselkumab, tildrakizumab και risankizumab**

JAK-inhibitors small molecules, big impact?

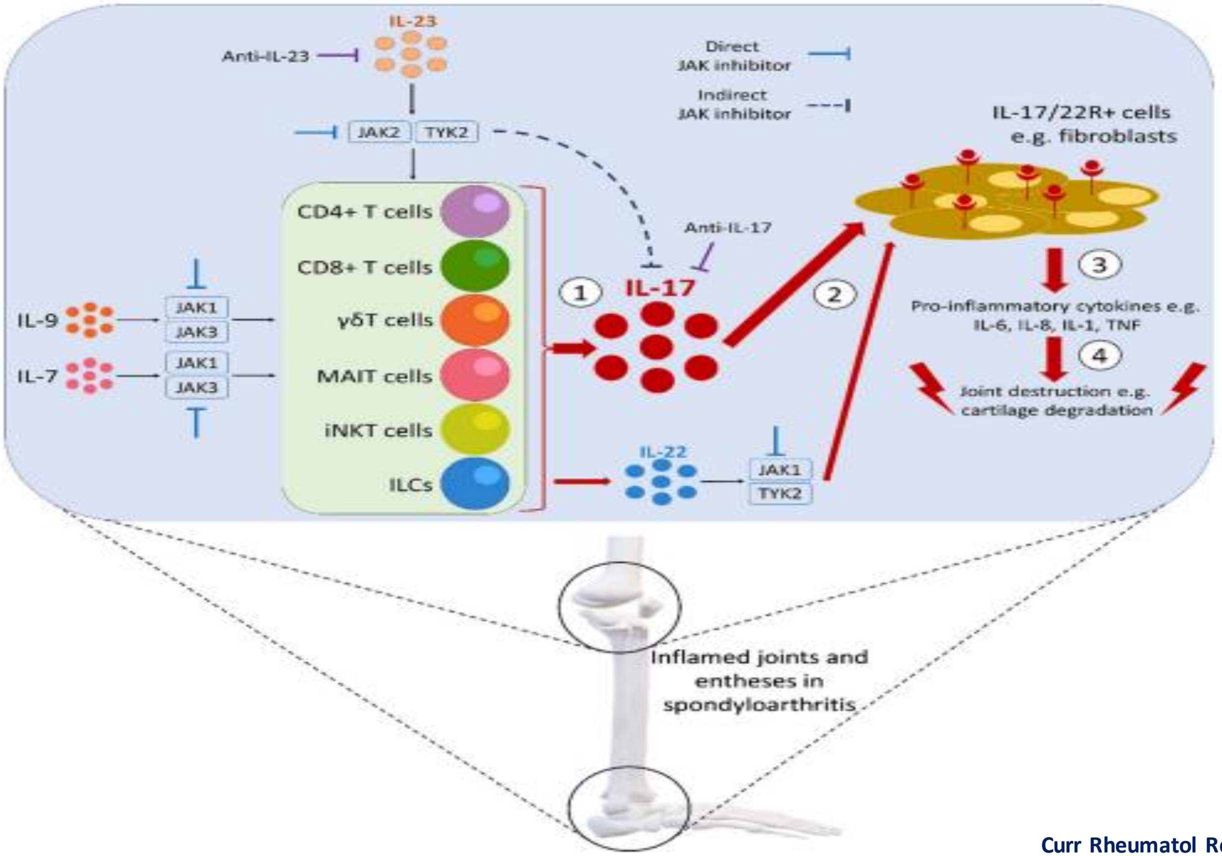




- Tofacitinib
- Filgotinib
- Upadacitinib

Nash P, Rheumatology 2021
Bravo A. Nat Rev Rheumatol 2019
Klein B. et al, JDDG 2021

Οδηγοί της φλεγμονής στην ψωριασική αρθρίτιδα: το παλιό και το νέο



Curr Rheumatol Rep. 2021 Apr 28;23(6):40.

Autoimmunity Reviews

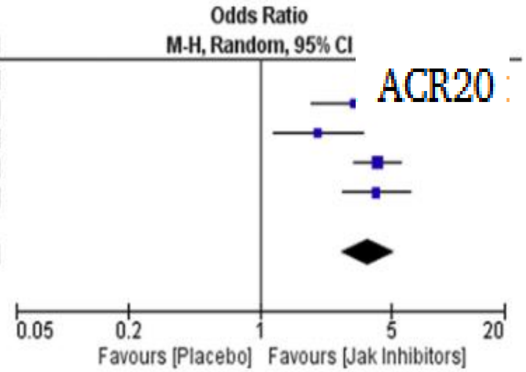
Review

JAK inhibitors and psoriatic arthritis: A systematic review and meta-analysis

Francesco Campanaro [a,1], Alberto Batticciotto [a,1], Andrea Zaffaroni [b], Antonella Cappelli [a], Marco Paolo Donadini [c], Alessandro Squizzato [c,*]

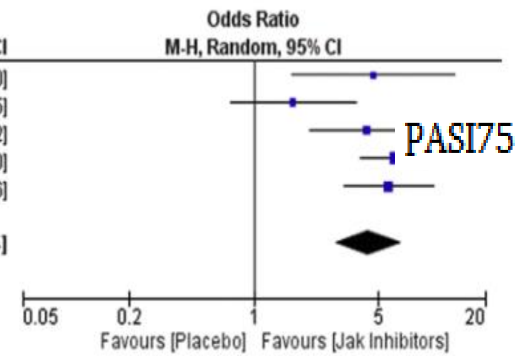
Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
EQUATOR 2018	52	65	22	66	11.6%	8.00 [3.61, 17.71]
OPAL Beyond 2017	65	131	31	131	18.8%	3.18 [1.87, 5.39]
OPAL Broaden 2017	54	107	35	105	17.9%	2.04 [1.17, 3.55]
SELECT-PsA 1 2021	303	429	153	423	28.7%	4.24 [3.18, 5.66]
SELECT-PsA 2 2020	120	211	51	212	23.1%	4.16 [2.75, 6.31]
Total (95% CI)		**943**		**937**	**100.0%**	**3.78 [2.72, 5.24]**
Total events	594		292			

Heterogeneity: Tau² = 0.08; Chi² = 9.38, df = 4 (P = 0.05); I² = 57%
Test for overall effect: Z = 7.95 (P < 0.00001)

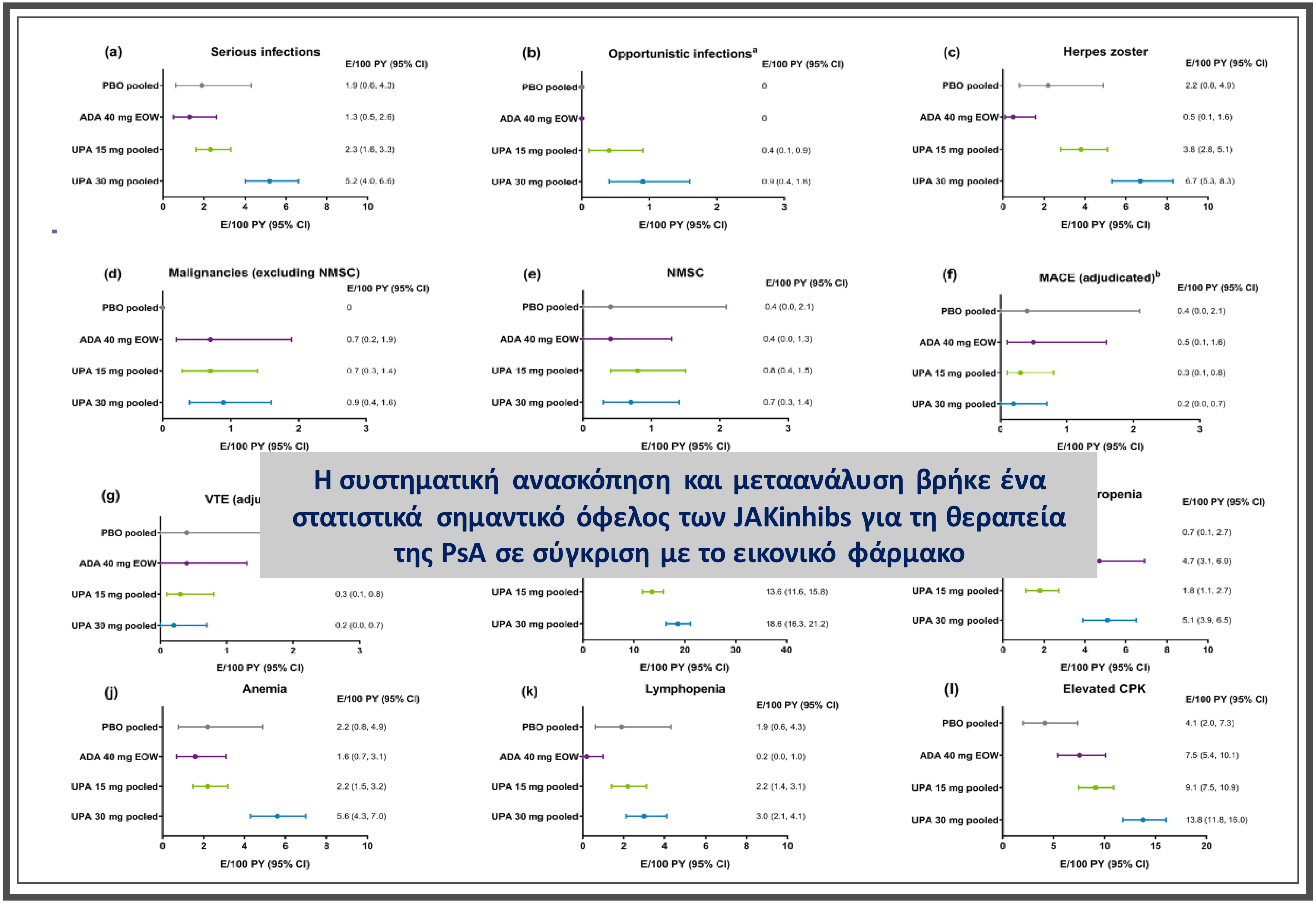


Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
EQUATOR 2018	19	42	6	40	12.0%	4.68 [1.62, 13.50]
OPAL Beyond 2017	17	80	12	86	16.9%	1.66 [0.74, 3.75]
OPAL Broaden 2017	35	82	12	82	18.4%	4.34 [2.05, 9.22]
SELECT-PsA 1 2021	134	214	45	211	29.0%	6.18 [4.02, 9.50]
SELECT-PsA 2 2020	68	130	21	131	23.6%	5.75 [3.22, 10.26]
Total (95% CI)		**548**		**550**	**100.0%**	**4.41 [2.84, 6.84]**
Total events	273		96			

Heterogeneity: Tau² = 0.12; Chi² = 8.30, df = 4 (P = 0.08); I² = 52%
Test for overall effect: Z = 6.63 (P < 0.00001)



Campanaro F. et al, Autoimmun Rev 2021



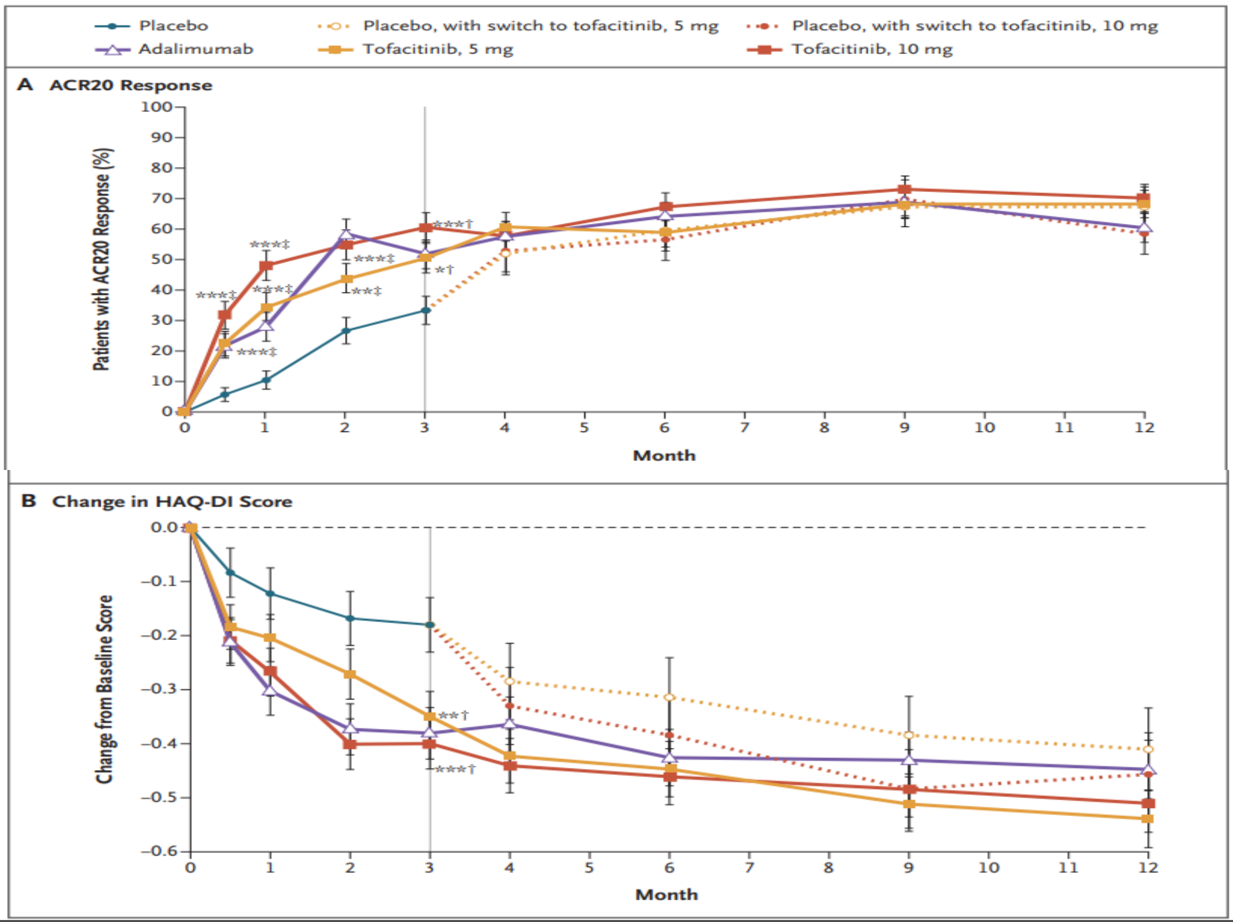
Η συστηματική ανασκόπηση και μεταανάλυση βρήκε ένα στατιστικά σημαντικό όφελος των JAKinhibs για τη θεραπεία της PsA σε σύγκριση με το εικονικό φάρμακο

Burnmester G. et al, Rheumatol Ther 2021

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tofacitinib or Adalimumab versus Placebo for Psoriatic Arthritis



❖ Η αποτελεσματικότητα του Tofacitinib ήταν ανώτερη από το εικονικό φαρμάκου στον 3° μήνα σε ασθενείς που είχαν προηγουμένως ανεπαρκή ανταπόκριση στα συμβατικά συνθετικά DMARDs

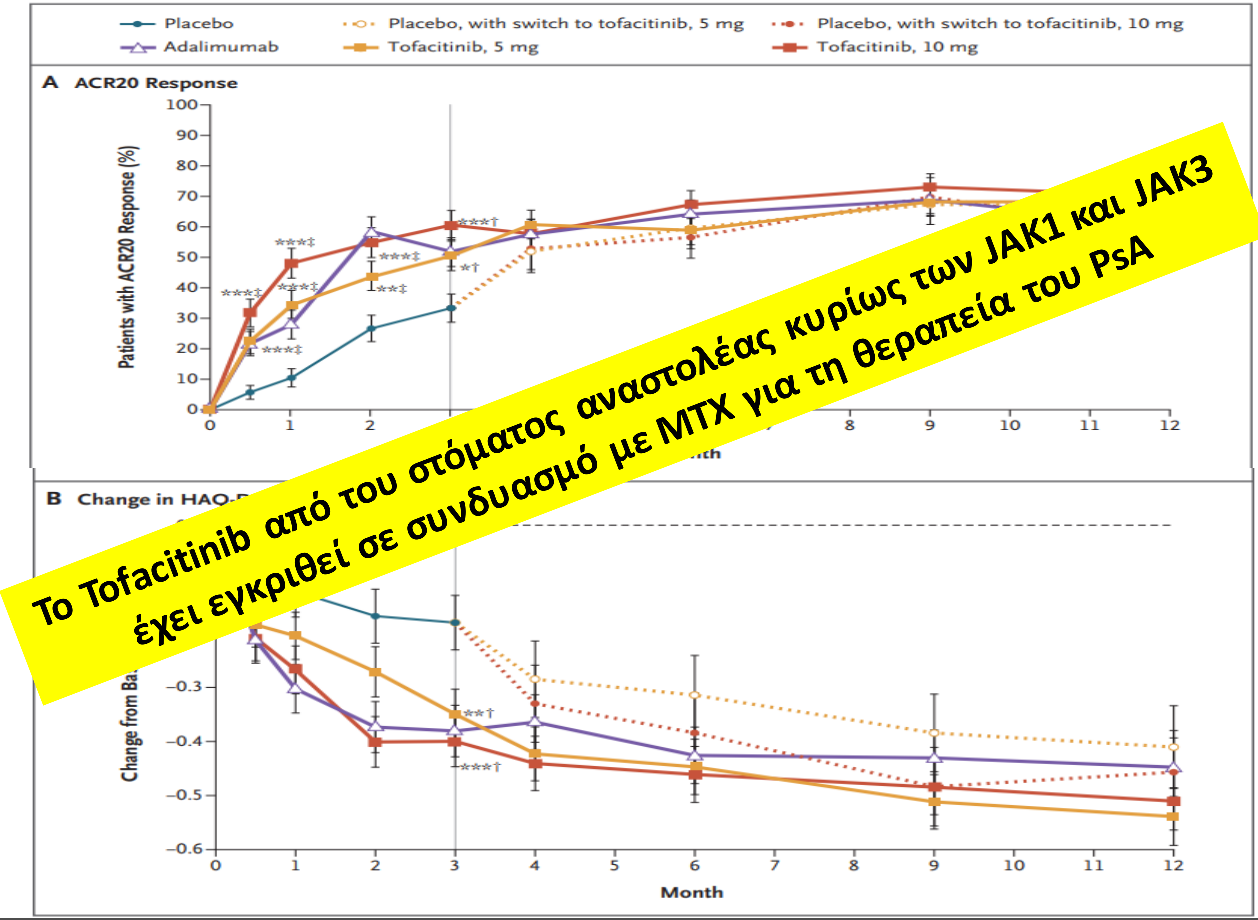
❖ Οι ανεπιθύμητες ενέργειες ήταν πιο συχνές στο Tofacitinib παρά στο εικονικό φάρμακο

N Engl J Med. 2017;377(16):1537–1550.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tofacitinib or Adalimumab versus Placebo for Psoriatic Arthritis



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N Engl J Med. 2017;377(16):1537–1550.

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.

N ENGL J MED 384;13 NEJM.ORG APRIL 1, 2021

SELECT-PsA 1

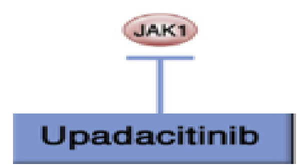
Annals of the Rheumatic Diseases

Psoriatic arthritis

Upadacitinib for psoriatic arthritis refractory to biologics: SELECT-PsA 2

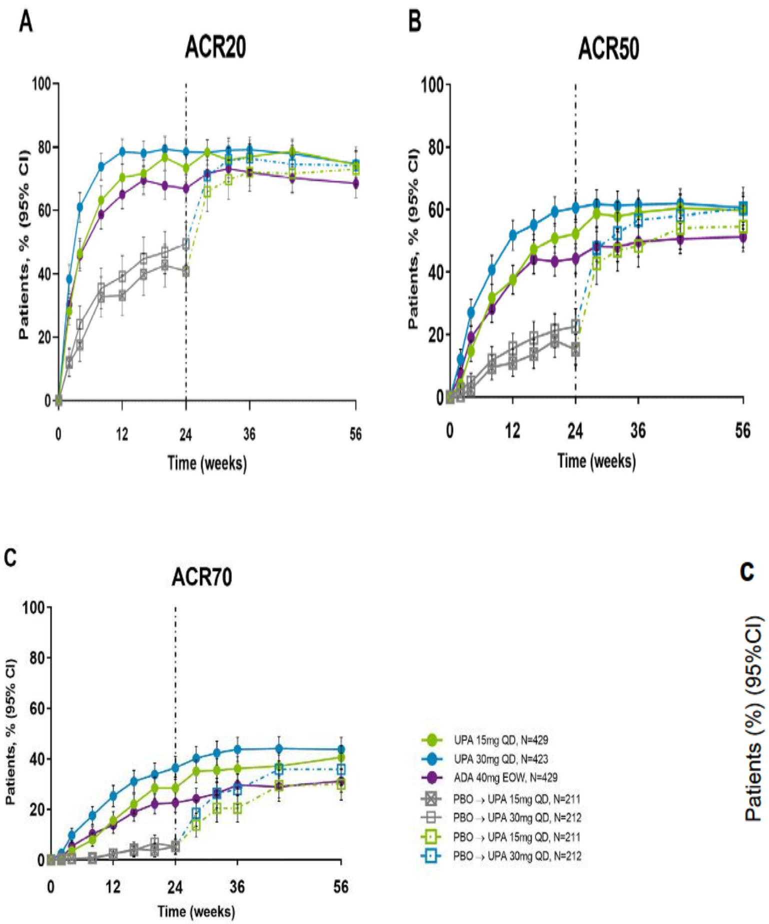
Philip J Mease,[1,2] Apinya Lertratanakul,[3] Jaclyn K Anderson,[3] Kim Papp,[4] Filip Van den Bosch,[5] Shigeyoshi Tsuji,[6] Eva Dokoupilova,[7,8] Mauro Keiserman,[9] Xin Wang,[3] Sheng Zhong,[3] Reva M McCaskill,[3] Patrick Zueger,[3] Aileen L Pangan,[3] William Tillett[10,11]

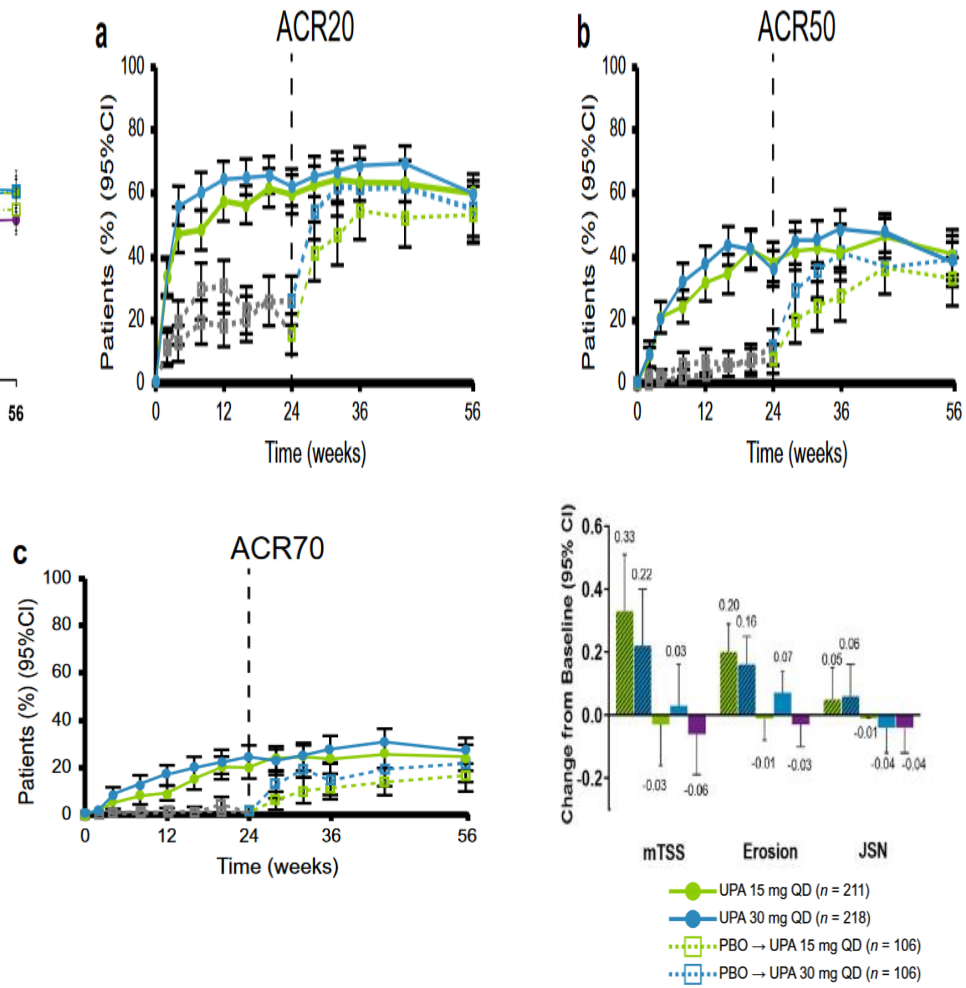
Received 13 August 2020
Revised 22 September 2020
Accepted 12 October 2020



SELECT-PsA 1 56-week

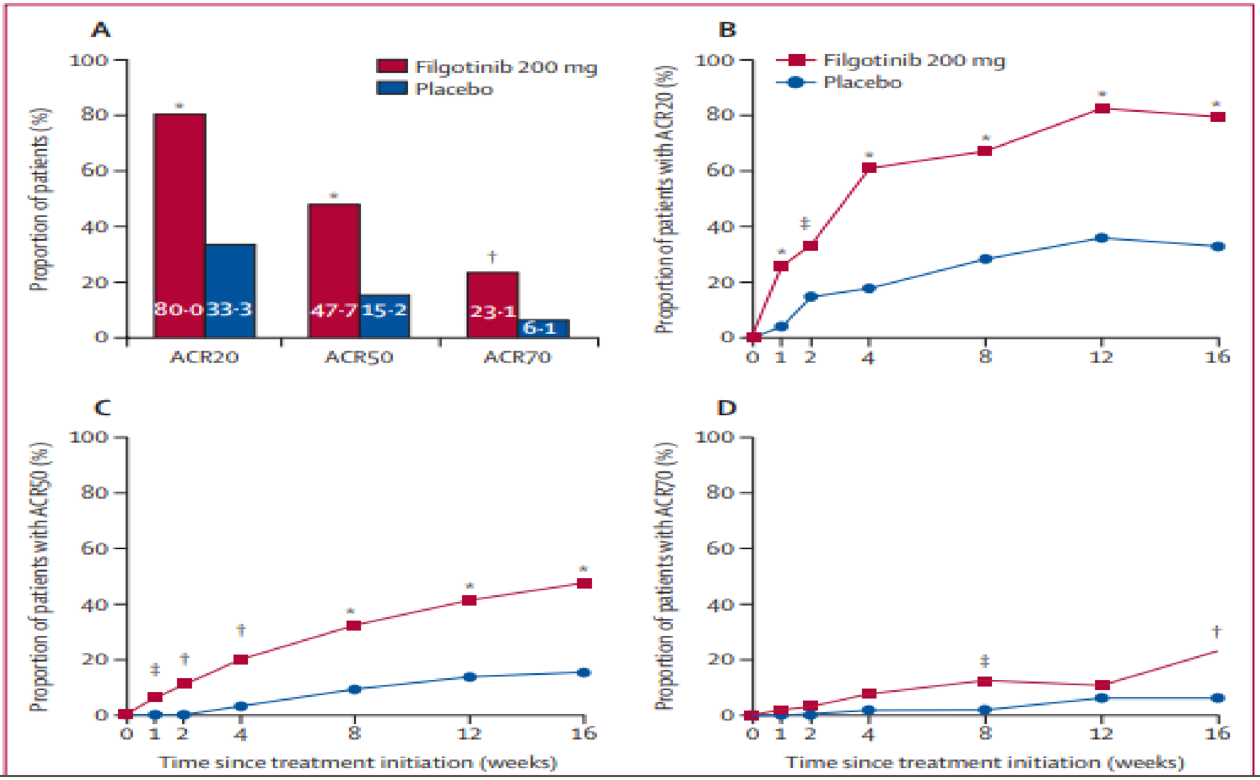
SELECT-PsA 2 56-Week





McInnes I. et al, RMD Open 2021
Mease PJ. et al, Rheumatol Ther 2021

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



Lancet. 2018;392(10162): 2367–2377.

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

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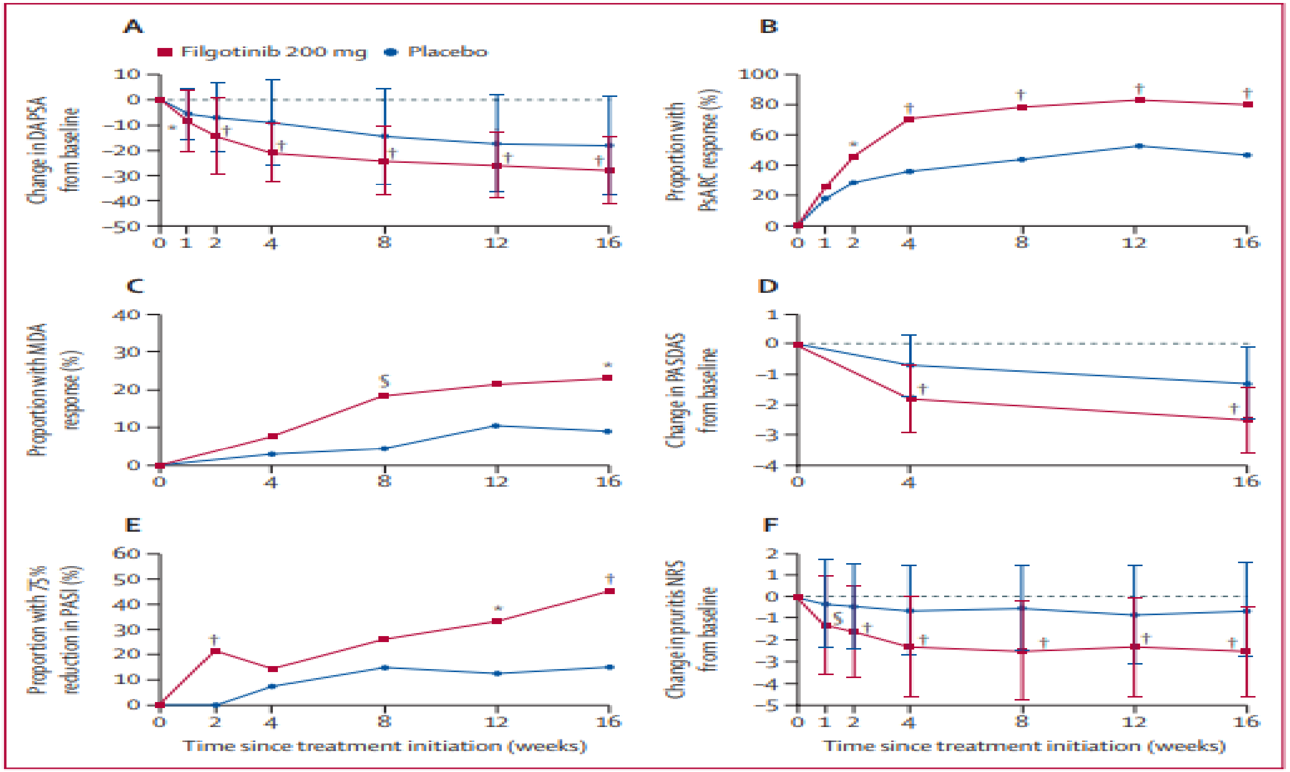

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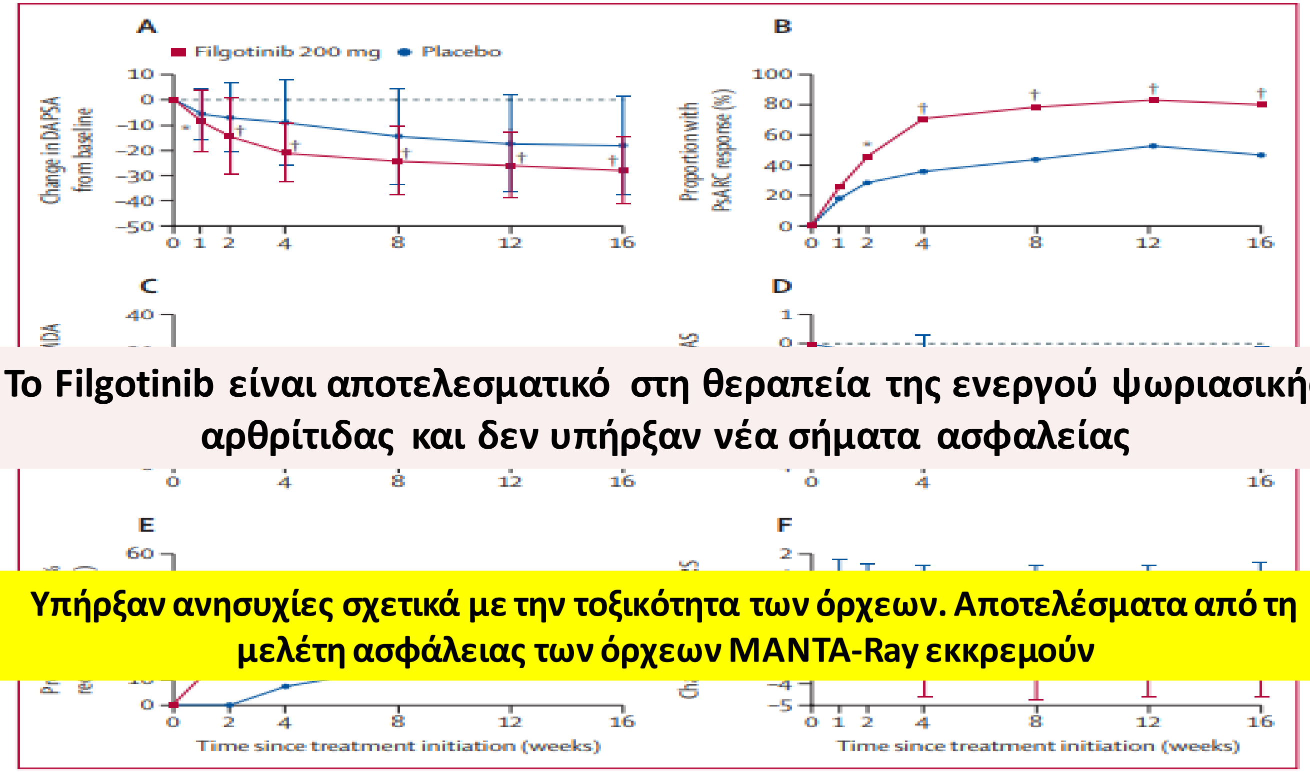


Το Filgotinib είναι αποτελεσματικό στη θεραπεία της ενεργού ψωριασικής αρθρίτιδας και δεν υπήρξαν νέα σήματα ασφαλείας

Υπήρξαν ανησυχίες σχετικά με την τοξικότητα των όρχεων. Αποτελέσματα από τη μελέτη ασφάλειας των όρχεων MANTA-Ray εκκρεμούν

Αναστολείς TYK 2- Deucravacitinib

- Ενδοκυτταρική κινάση που μεσολαβεί στις IL-23, IL-12 και ιντερφερόνη α/β
- Το Deucravacitinib αναστέλλει επιλεκτικά αυτή την κινάση
- Προκαταρκτικά δεδομένα φάσης II (15% ασθενών είχαν προηγούμενη θεραπεία με TNFi)
- 6 mg και 12 mg deucravacitinib: σημαντική ACR20 απόκριση την 16^{η} εβδομάδα v.s PBO

(52,9%, 62,7%και 31,8% αντίστοιχα)

- Αποτελεσματικό σε πολλά δευτερεύοντα τελικά σημεία, ACR50/70 και στην ενθεσίτιδα
- Χωρίς σήματα ασφαλείας σχετικά με τη φλεβική θρομβοεμβολή ή αλλαγές στις αιματολογικές παραμέτρους

Ann Rheum Dis. 2021;80(Suppl 1):314–315.

Αναστολείς JAK και RORγt υπό κλινική αξιολόγηση για τη θεραπεία της ψωρίασης

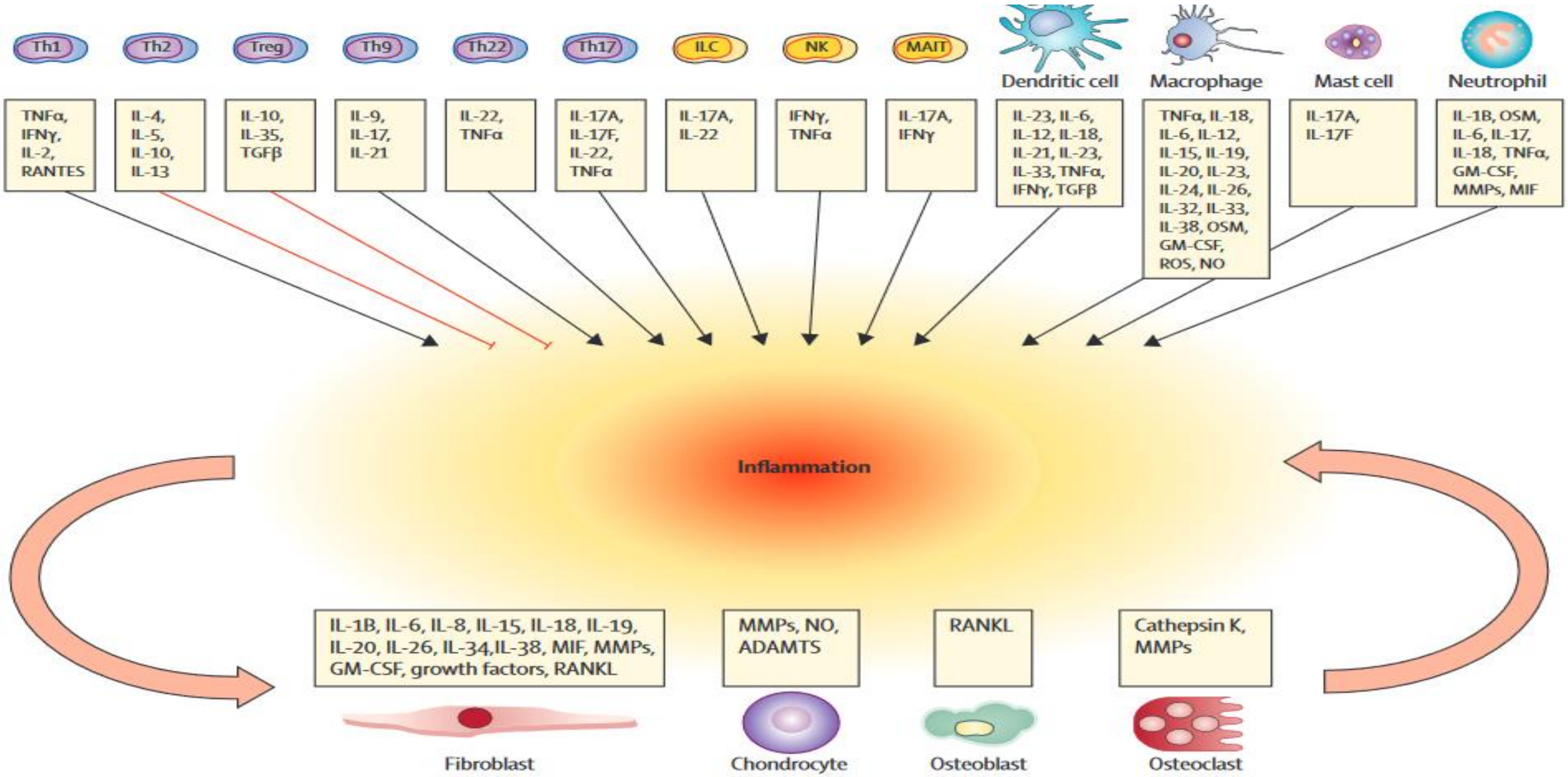
	Target	Phase of trial (ClinicalTrial.org identifier)	Trial dates, start to finish*	Trial phase of published data	PASI-75† (drug dose)	PASI-90† (drug dose)
Baricitinib[135]	JAK1 and JAK2	Phase 2 (NCT01490632)	December, 2011, to August, 2014	2	54% at week 12 (10 mg daily)	35% at week 12 (10 mg daily)
Tofacitinib[136]	JAK1 and JAK3	Phase 3 (NCT01241591)	November, 2010, to January, 2013	3	64% at week 12 (10 mg twice a day)	36% at week 12 (10 mg twice a day)
Itacitinib (INCB039110)[137]	JAK1	Phase 2 (NCT01634087)	June, 2012, to February, 2013	2	..	..
Solcitinib (GSK2586184)[138]	JAK1	Phase 2 (NCT01782664)	March, 2013, to March, 2014	2	57% at week 12 (400 mg twice a day)	36% at week 12 (400 mg twice a day)
Deucravacitinib (BMS-986165)[139]	TYK2	Phase 3 (NCT03924427)	April, 2019, to November, 2020	2	75% at week 12 (12 mg daily)	43% at week 12 (12 mg daily)
PF-06826647	TYK2	Phase 2 (NCT03895372)	June, 2019, to November, 2020	..	..	..
PF-06700841[140]	JAK1 and TYK2	Phase 2 (NCT02969018)	December, 2016, to March, 2018	2	86% at week 12 (30 mg daily)	52% at week 12 (30 mg daily)
VTP-43742	RORγt	Phase 1, 2 (NCT02555709)	August 2015, to March, 2016	..	..	..
BI 730357	RORγt	Phase 2 (NCT03635099)	September, 2018, to July, 2021 (estimated)	..	..	..
JTE-451	RORγt	Phase 2 (NCT03832738)	January, 2019, to March, 2020	..	..	..
AUR101	RORγt	Phase 2 (NCT04207801)	January, 2020, to March, 2021 (estimated)	..	..	..

JAK=Janus kinase. PASI-75=proportion of patients who had a 75% or greater reduction in Psoriasis Area and Severity Index. PASI-90=proportion of patients who had a 90% or greater reduction in Psoriasis Area and Severity Index. *Start to completion date according to ClinicalTrials.gov. †At highest applied dose.

Table 3: **JAK and RORγt inhibitors under clinical development for psoriasis treatment**

Lancet. 2021 Feb 20;397(10275):754-766.

Παθογένεια ΨΑ



Veale D. et al, Lancet 2018

Εγκεκριμένα μονοκλωνικά αντισώματα έναντι IL-23, IL-17 και IL-17RA για τη θεραπεία της μέτριας έως σοβαρής ψωρίασης κατά πλάκας σε ενήλικες

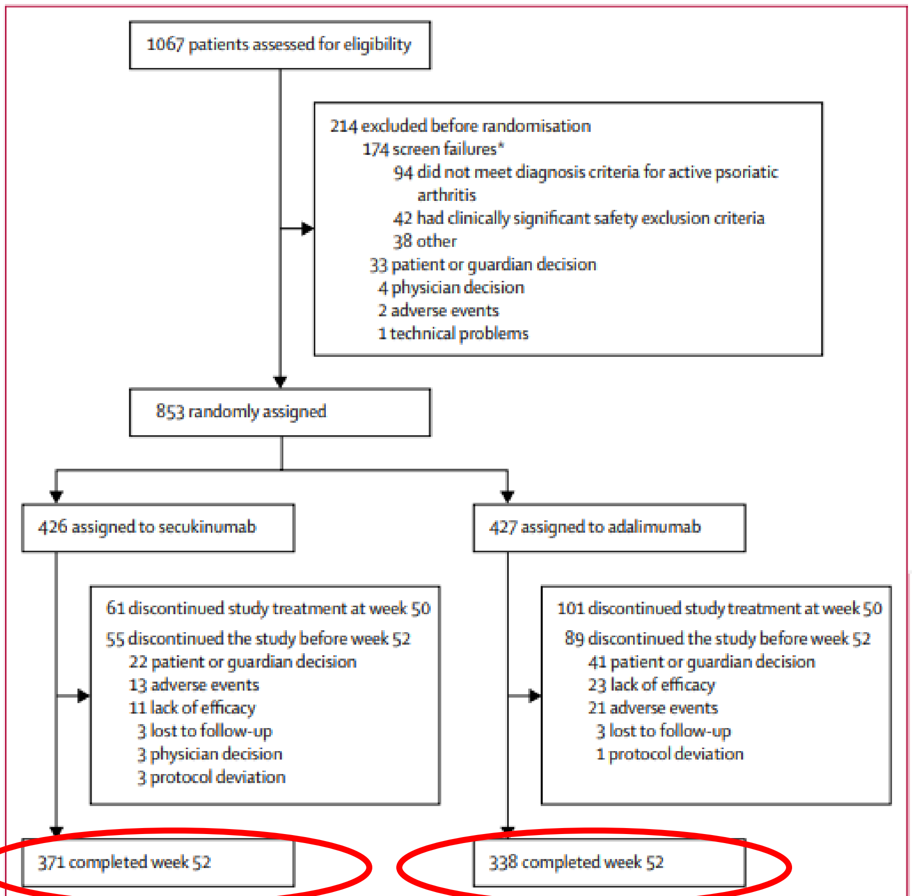
	Target (affected cytokine)	Structure	US FDA approval	EMA approval	Induction dose	Maintenance dose	PASI-75*	PASI-90*
Guselkumab[68,69]	IL-23 p19 (IL-23)	Human IgG1/λ mAb	July, 2017	November, 2017	100 mg at week 0 and week 4	100 mg every 8 weeks	91% at week 16; 86% at week 16	73% at week 16; 70% at week 16
Tildrakizumab[70]	IL-23 p19 (IL-23)	Humanised IgG1/κ mAb	March, 2018	September, 2018	100 mg at week 0 and week 4	100 mg every 12 weeks	64% at week 12; 61% at week 12	35% at week 12; 39% at week 12
Risankizumab[71]	IL-23 p19 (IL-23)	Humanised IgG1/κ mAb	April, 2019	April, 2019	150 mg at week 0 and week 4	150 mg every 12 weeks	89% at week 16; 91% at week 16	75% at week 16; 75% at week 16
Secukinumab[72]	IL-17A (IL-17A/A, IL-17A/F)	Human IgG1/κ mAb	January, 2015	January, 2015	300 mg at weeks 0–5	300 mg every 4 weeks	82% at week 12; 77% at week 12	59% at week 12; 54% at week 12
Ixekizumab[73,74]	IL-17A (IL-17A/A, IL-17A/F)	Humanised IgG4/κ mAb	March, 2016	April, 2016	160 mg at week 0, 80 mg every 2 weeks at weeks 2–12	80 mg every 4 weeks	89% at week 12; 90% at week 12; 87% at week 12	71% at week 12; 71% at week 12; 68% at week 12
Brodalumab[75]	IL-17RA (IL-17A/A, IL-17A/F, IL-17F/F, IL-17C/C, IL-25)	Human IgG2/κ mAb	February, 2017	July, 2017	210 mg at weeks 0–2	210 mg every 2 weeks	86% at week 12; 85% at week 12	70% at week 12; 69% at week 12

Efficacy data summarised is from independent studies and does not represent head-to-head comparison. US FDA=US Food and Drug Administration. EMA=European Medicines Agency. PASI-75=proportion of patients who had a 75% or greater reduction in Psoriasis Area and Severity Index. PASI-90=proportion of patients who had a 90% or greater reduction in Psoriasis Area and Severity Index. mAb=monoclonal antibody. *Multiple results from the same timepoint are shown to give a more accurate description; these results are from two or three different trials (please refer to the referenced trials in column one).

Table 2: **Monoclonal antibodies against IL-23, IL-17, and IL-17RA approved for the treatment of moderate-to-severe plaque psoriasis in adults**

Lancet. 2021 Feb 20;397(10275):754-766.

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



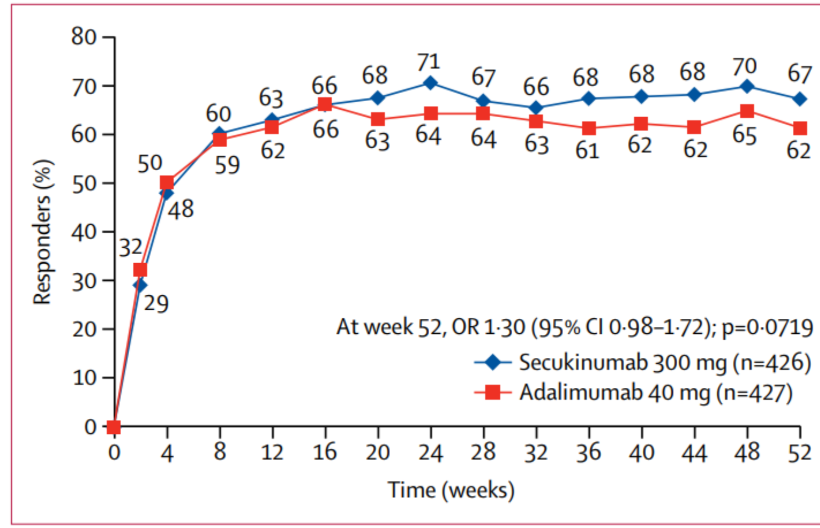
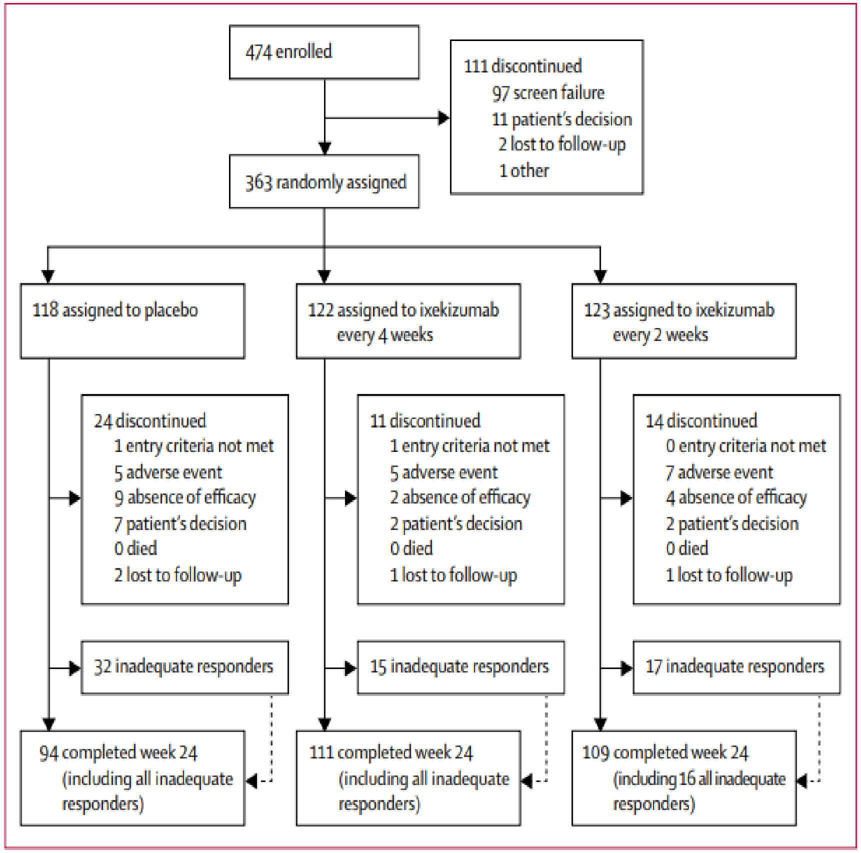


Figure 2: ACR20 response rate through week 52 (multiple imputation)

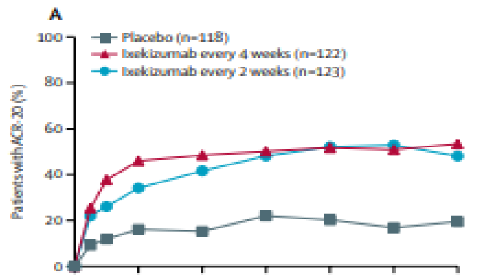
- Υπεροχή χωρίς στατιστική σημασία στο πρωτογενές τελικό σημείο ανταπόκρισης ACR20 την 52η εβδομάδα
- Υψηλότερη διατήρηση στη θεραπεία από το adalimumab

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

Ixekizumab for the treatment of patients with active psoriatic arthritis and an inadequate response to tumour necrosis factor inhibitors: results from the 24-week randomised, double-blind, placebo-controlled period of the SPIRIT-P2 phase 3 trial

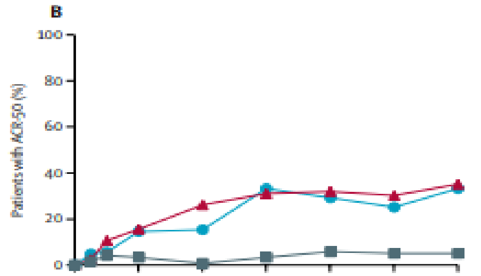


A



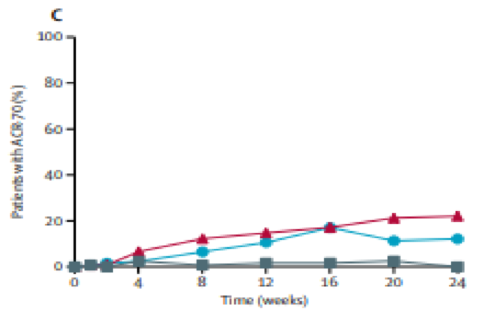
Weeks	Ixekizumab every 4 weeks	Ixekizumab every 2 weeks
1	0·0012	0·0057
2	<0·0001	0·0055
4	<0·0001	0·0017
8	<0·0001	<0·0001
12	<0·0001	<0·0001
16	<0·0001	<0·0001
20	<0·0001	<0·0001
24	<0·0001	<0·0001

B



Weeks	Ixekizumab every 4 weeks	Ixekizumab every 2 weeks
1	>0·99	0·28
2	0·06	0·77
4	0·0031	0·0030
8	0·0003	<0·0001
12	<0·0001	<0·0001
16	<0·0001	<0·0001
20	<0·0001	0·0001
24	<0·0001	<0·0001

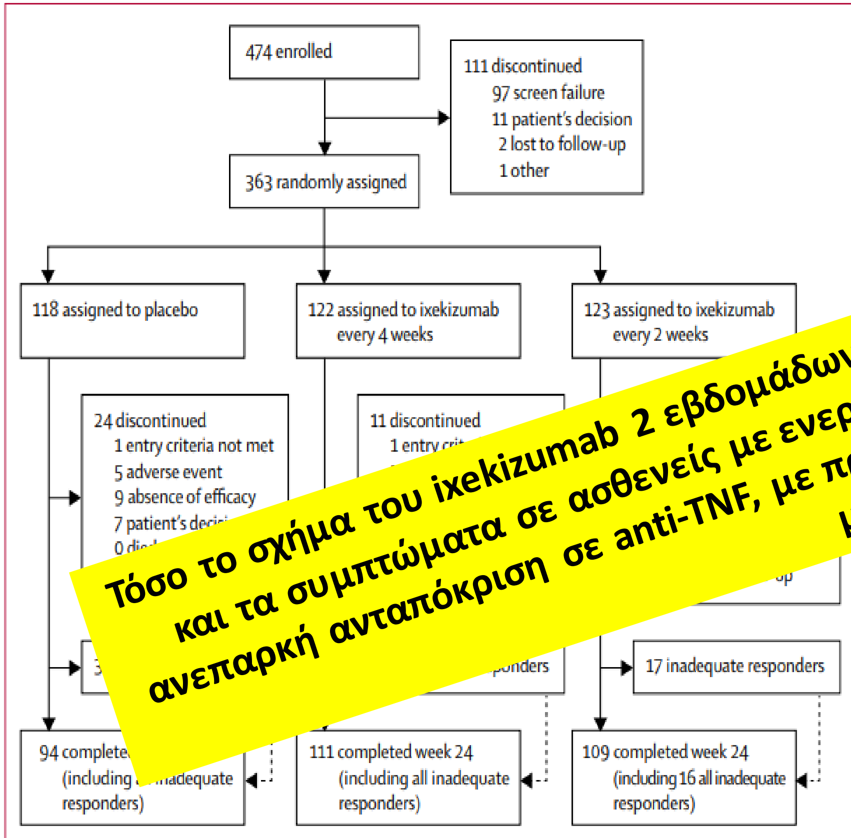
C

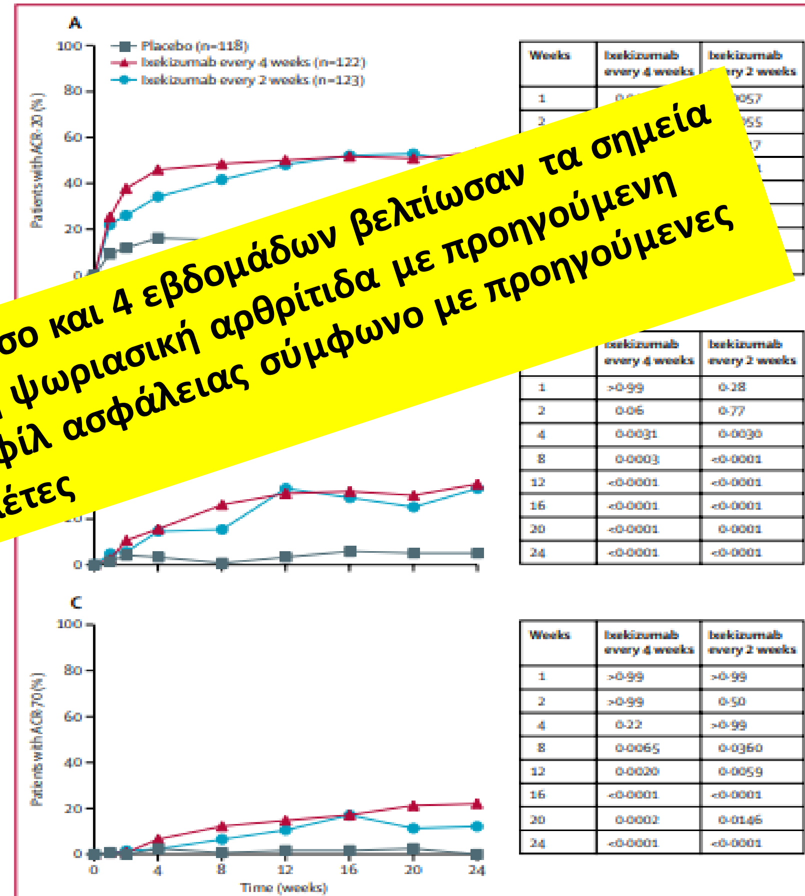


Weeks	Ixekizumab every 4 weeks	Ixekizumab every 2 weeks
1	>0·99	>0·99
2	>0·99	0·50
4	0·22	>0·99
8	0·0065	0·0360
12	0·0020	0·0059
16	<0·0001	<0·0001
20	0·0002	0·0146
24	<0·0001	<0·0001

Lancet. 2017 Jun 10;389(10086):2317-2327.

Ixekizumab for the treatment of patients with active psoriatic arthritis and an inadequate response to tumour necrosis factor inhibitors: results from the 24-week randomised, double-blind, placebo-controlled period of the SPIRIT-P2 phase 3 trial





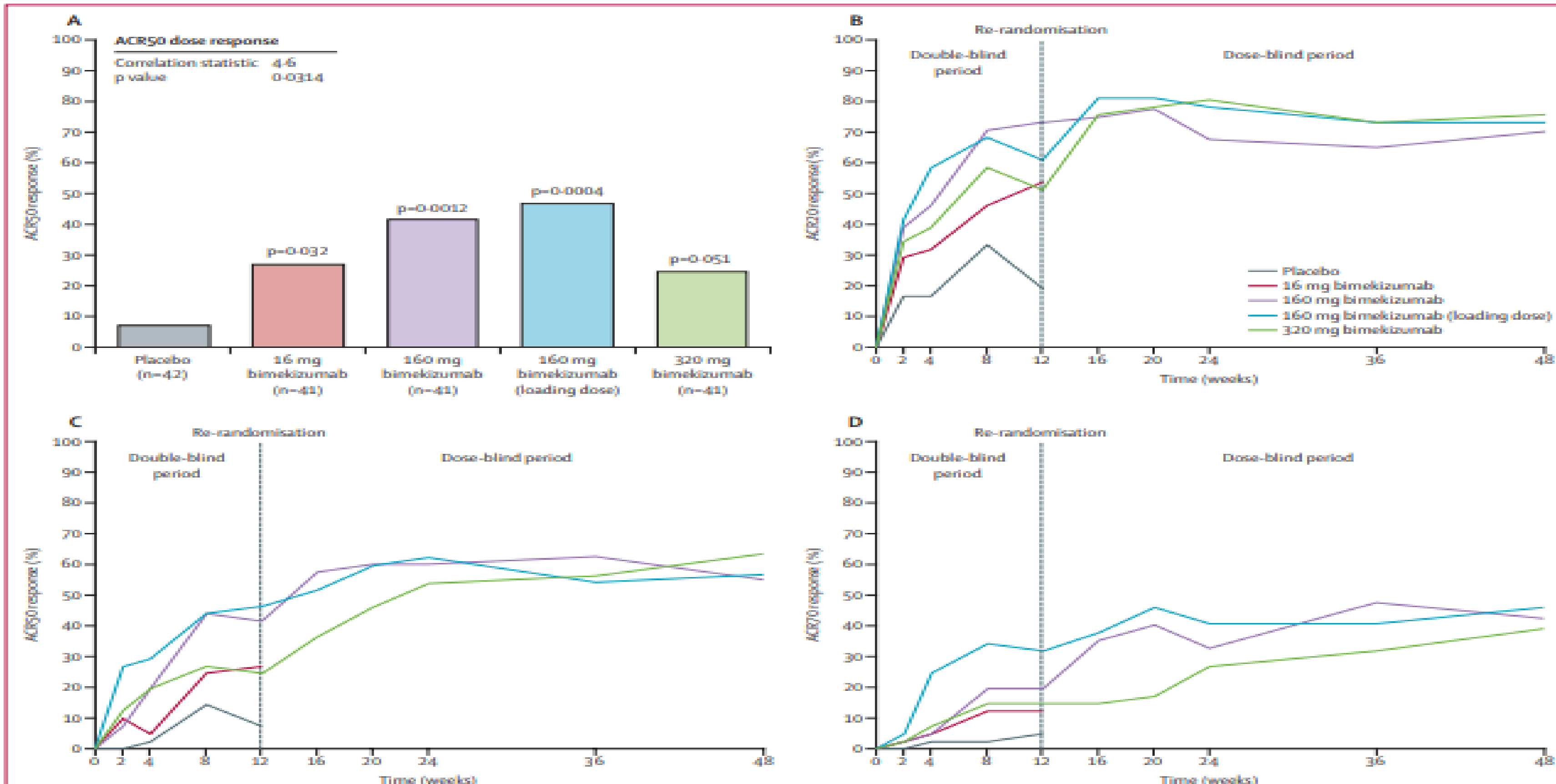
Τόσο το σχήμα του ixekizumab 2 εβδομάδων όσο και 4 εβδομάδων βελτίωσαν τα σημεία και τα συμπτώματα σε ασθενείς με ενεργή ψωριασική αρθρίτιδα με προηγούμενη ανεπαρκή ανταπόκριση σε anti-TNF, με προφίλ ασφάλειας σύμφωνο με προηγούμενες μελέτες

Lancet. 2017 Jun 10;389(10086):2317-2327.

Bimekizumab in patients with active psoriatic arthritis: results from a 48-week, randomised, double-blind, placebo-controlled, dose-ranging phase 2b trial

Lancet. 2020 Feb 8;395(10222):427-440.

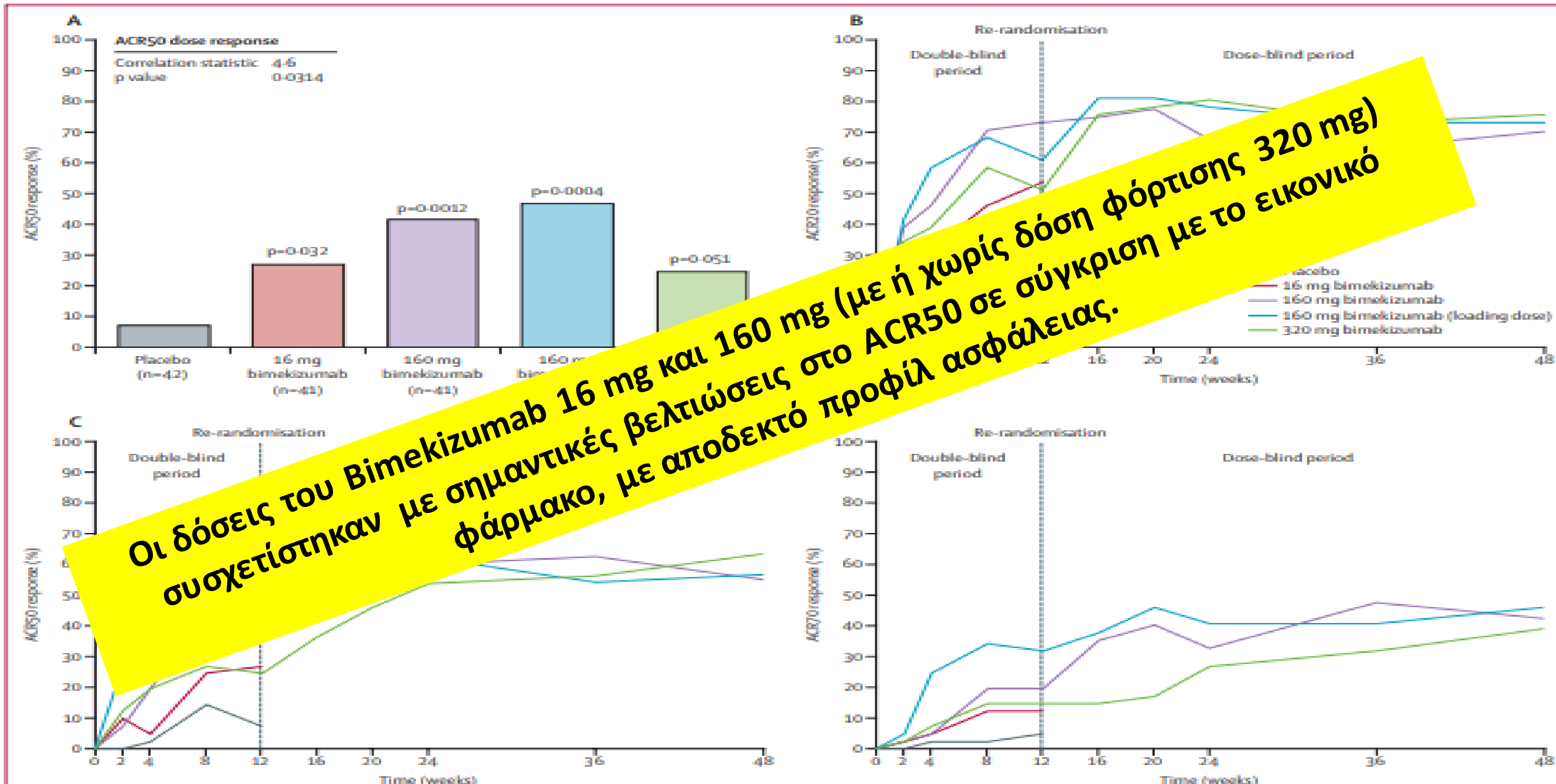
interleukin 17A (IL17A) and interleukin 17F (IL17F)



Bimekizumab in patients with active psoriatic arthritis: results from a 48-week, randomised, double-blind, placebo-controlled, dose-ranging phase 2b trial

Lancet. 2020 Feb 8;395(10222):427-440.

interleukin 17A (IL17A) and interleukin 17F (IL17F)



Οι δόσεις του Bimekizumab 16 mg και 160 mg (με ή χωρίς δόση φόρτισης 320 mg) συσχετίστηκαν με σημαντικές βελτιώσεις στο ACR50 σε σύγκριση με το εικονικό φάρμακο, με αποδεκτό προφίλ ασφάλειας.

Drugs
https://doi.org/10.1007/s40265-018-0888-4

CrossMark

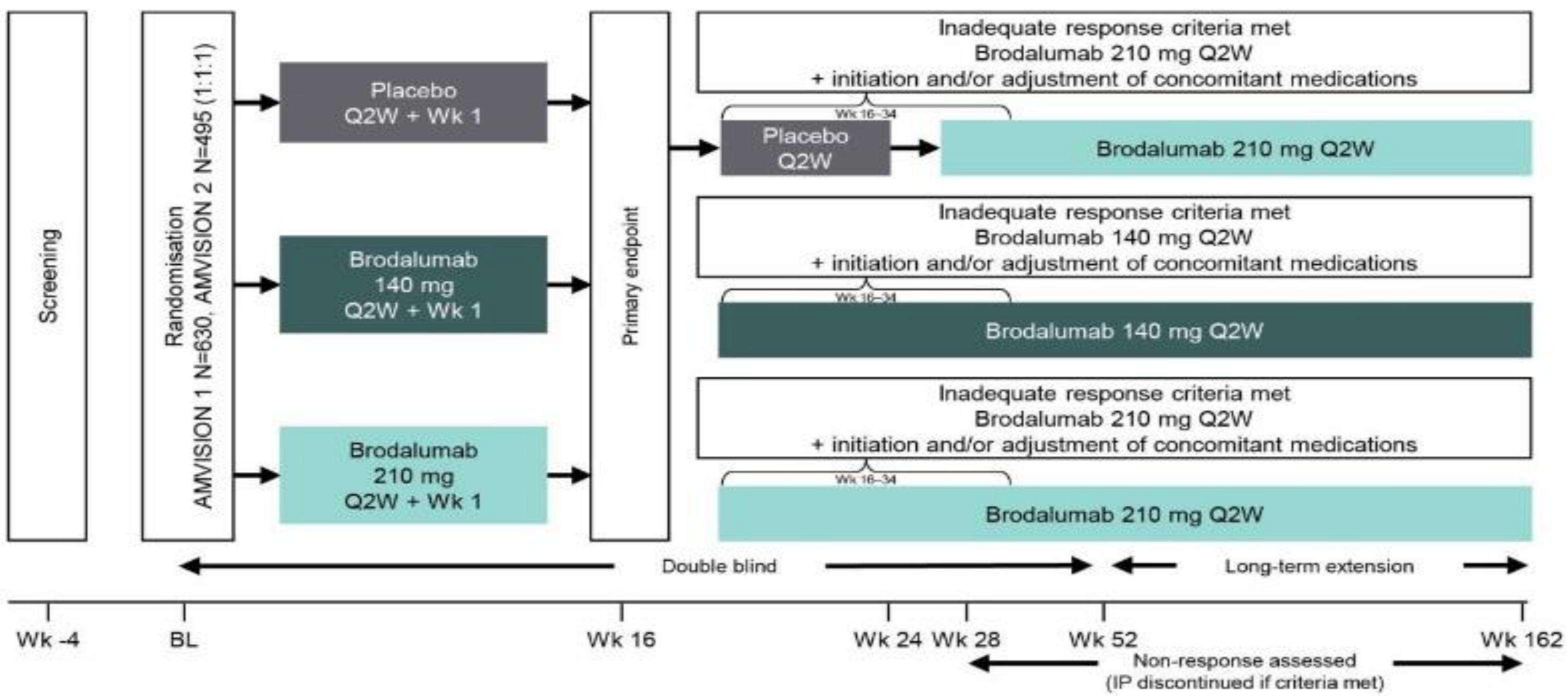
ADIS DRUG EVALUATION

Brodalumab: A Review in Moderate to Severe Plaque Psoriasis

Table 2 Efficacy of brodalumab at week 52 in adults with moderate to severe plaque psoriasis in the phase III AMAGINE trials

Study	Re-randomized treatment groups (mg)	No. of pts	PASI (% pts)		sPGA success (% pts)
			90	100	
AMAGINE-1 [10]	BRO 140 q2w → BRO 140 q2w	59	67*	44*	70*
	BRO 210 q2w → BRO 210 q2w	83	78*	68*	83*
	BRO 140 q2w → PL	59	3	2	5
	BRO 210 q2w → PL	84	0	0	0
AMAGINE-2 [11]	BRO → BRO 140 q2w	337			43†
	BRO → BRO 140 q4w	335			9
	BRO → BRO 140 q8w	168			5
	BRO → BRO 210 q2w	334	75	56	63†,‡
	PL → BRO 210 q2w	297		62	62
AMAGINE-3 [11]	BRO → BRO 140 q2w	343			45†
	BRO → BRO 140 q4w	341			16
	BRO → BRO 140 q8w	174			6
	BRO → BRO 210 q2w	342	73	53	61†,‡
	PL → BRO 210 q2w	298		68	68

Brodalumab in psoriatic arthritis: results from the randomised phase III AMVISION-1 and AMVISION-2 trials



Mease PJ, et al..Ann Rheum Dis. 2021 Feb;80(2):185-193.

Brodalumab in psoriatic arthritis: results from the randomised phase III AMVISION-1 and AMVISION-2 trials

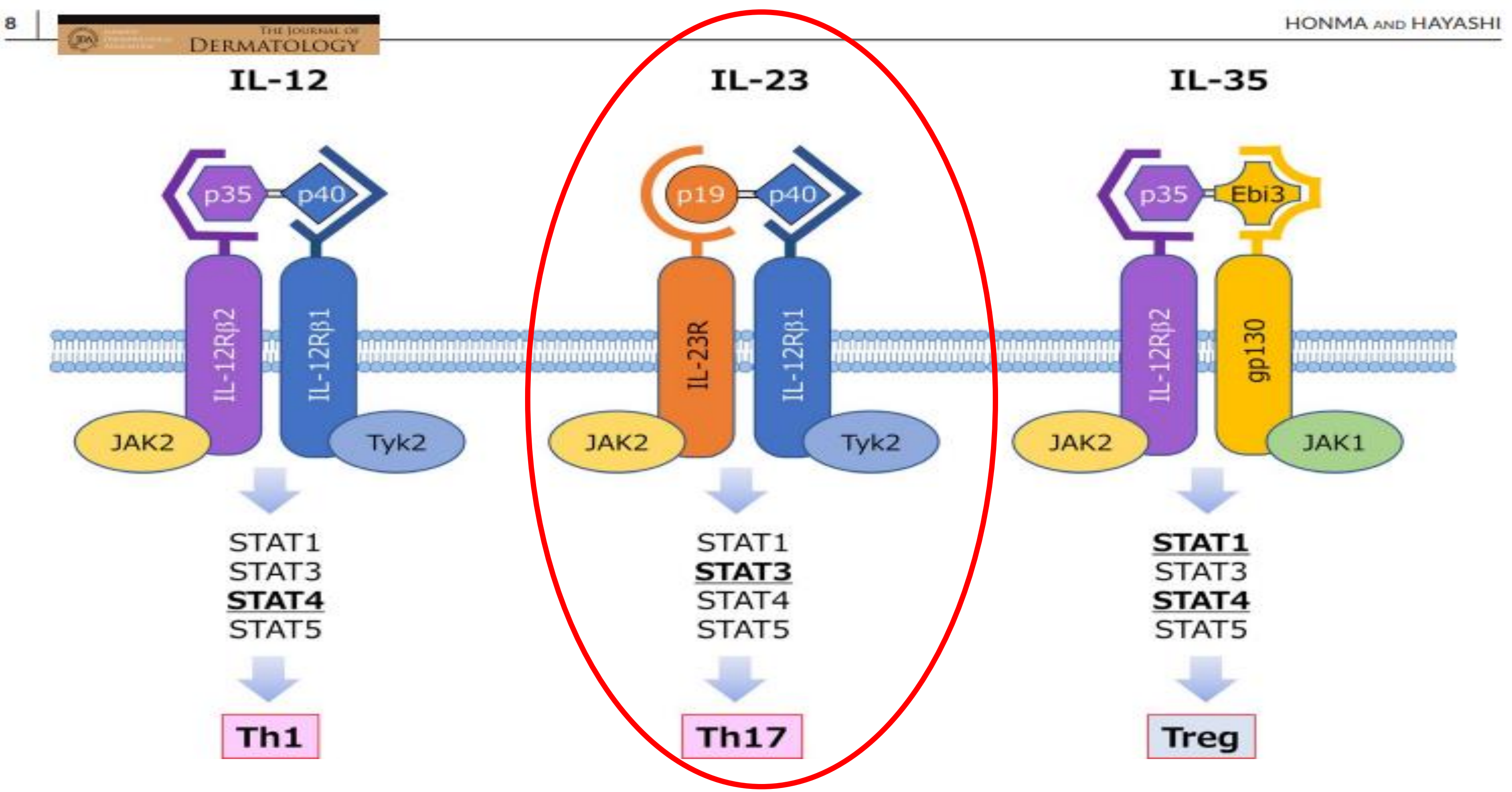
Mease PJ, et al..Ann Rheum Dis. 2021 Feb;80(2):185-193.

Response, %	AMVISION-1 PBO	AMVISION-1 BRO 140 mg Q2W	AMVISION-1 BRO 210 mg Q2W	AMVISION-2 PBO	AMVISION-2 BRO 140 mg Q2W	AMVISION-2 BRO 210 mg Q2W	Pooled PBO	Pooled BRO 140 mg Q2W	Pooled BRO 210 mg Q2W
Week 16									
ACR20	16.0	39.5***	51.8***	24.8	50.9***	44.3**	20.9	[illegible]	[illegible]
ACR50	4.6	18.3**	28.8***	9.1	29.3***	23.2*	[illegible]	[illegible]	[illegible]
ACR70	2.7	7.8	12.5*	3.6	13.3*	10.2‡	[illegible]	[illegible]	[illegible]
PASI75	10.9	55.0***	81.1***	9.3	51.5***	[illegible]	[illegible]	[illegible]	[illegible]
PASI90	7.3	44.0***	69.0***	5.1	35.0***	[illegible]	[illegible]	[illegible]	[illegible]
PASI100	4.3	21.2**	49.6***	3.0	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Dactylitis resolution	17.3	31.3	48.8**	29.7	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Enthesitis resolution	16.0	34.2‡	37.8*	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	39.1*
HAQ-DI LS mean change from baseline†	−0.136	−0.346**	−0.439***	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	−0.385***
Achievement of HAQ-DI MID§	25.0	42.6*	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	47.5**	56.1***
DAS28 CRP LS mean change from baseline†	−0.203	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	−0.269	−1.115***	−1.189***
CDAI LS mean change from baseline†	−1.981	[illegible]	[illegible]	[illegible]	[illegible]	−11.53***	−3.325	−12.01***	−12.04***
DAPSA LS mean change from baseline†	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	−16.22**	−3.152	−17.51**	−17.61**
PASDAS LS m[illegible] baselin[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	−1.474**	−1.725**	−0.325	−1.526**	−1.913**
[illegible]									
[illegible]	[illegible]	[illegible]	59.7***	27.8	49.5**	48.8**	23.8	51.0***	53.6***
[illegible]	[illegible]	[illegible]	37.5***	11.9	31.2**	35.4***	10.4	29.8***	36.4***
[illegible]	[illegible]	11.2*	20.0***	6.1	15.7‡	19.2*	4.7	14.4**	20.9***
P[illegible]	[illegible]	51.4***	80.7***	8.9	49.0***	62.3***	9.6	50.5***	70.5***
PA[illegible]	3.8	42.2***	61.8***	3.8	32.3***	52.0***	3.8	36.6***	57.1***
PAS[illegible]	3.5	26.8**	52.0***	0.7	23.5*	45.5**	1.9	26.0***	48.6***
Dac[illegible]ion	14.0	26.4	59.4***	22.9	59.5**	60.0**	19.8	43.0**	60.1***
Enthe[illegible]s resolution	15.7	33.8‡	54.8***	27.3	47.2‡	37.8	22.7	41.6*	43.8**
HAQ-DI LS mean change from baseline†	−0.192	−0.411*	−0.526***	−0.226	−0.332	−0.398*	−0.216	−0.371*	−0.467***
Achievement of HAQ-DI MID‡	23.5	44.4*	60.9***	28.9	47.5*	49.6*	26.3	46.1***	54.3***
DAS28 CRP LS mean change from baseline†	−0.682	−1.348*	−1.734***	−0.714	−1.233*	−1.276*	−0.698	−1.275***	−1.495***

Το brodalumab συσχετίστηκε με γρήγορες και σημαντικές βελτιώσεις στα σημεία και τα συμπτώματα της PsA έναντι του εικονικού φαρμάκου.

Το brodalumab ήταν καλά ανεκτό με προφίλ ασφαλείας σύμφωνο με άλλους αναστολείς ιντερλευκίνης-17

Αναστολείς IL-12,-23 -35



Αναστολείς IL-23

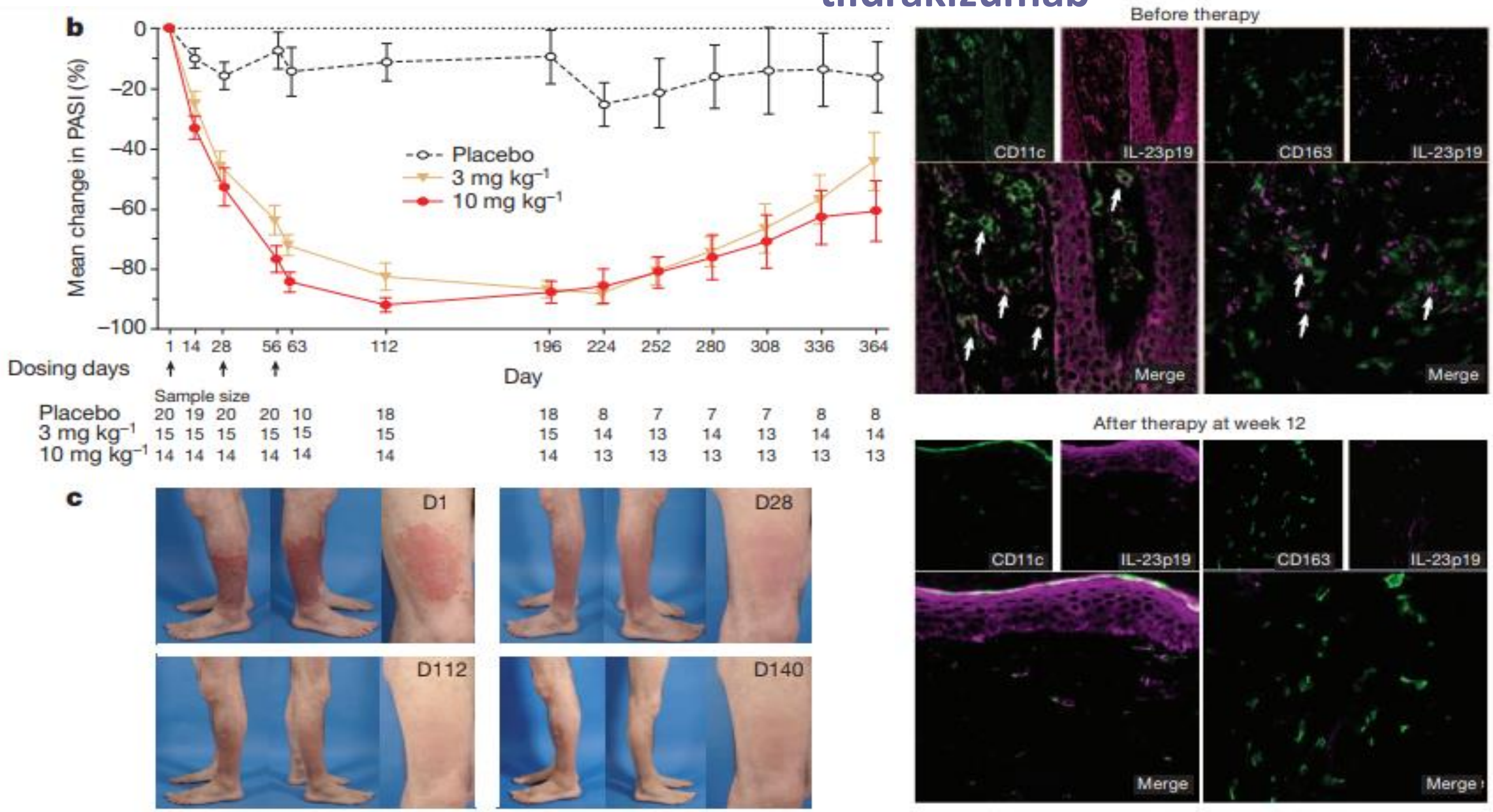
- **Guselkumab** συνδέεται με την υπομονάδα πρωτεΐνης p19 της IL-23
- **Tildrakizumab** μονοκλωνικό αντίσωμα κατά της ιντερλευκίνης-23p19
- **Risankizumab** αντι-ιντερλευκίνη-23p19 μονοκλωνικό αντίσωμα

Εγκεκριμένα για τη θεραπεία μέτριας έως σοβαρής κατά πλάκας ψωρίαση

Clinical improvement in psoriasis with specific targeting of interleukin-23

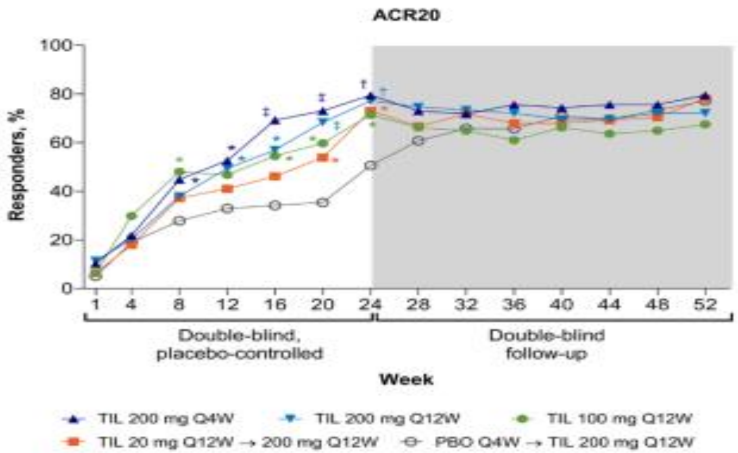
Nature 2015; 521: 222–26.

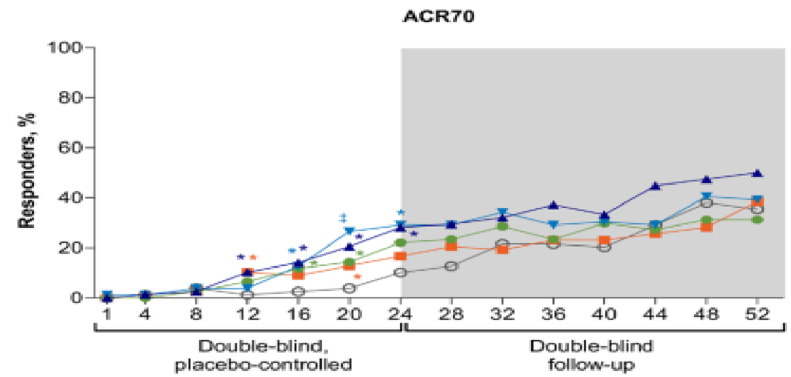
tildrakizumab

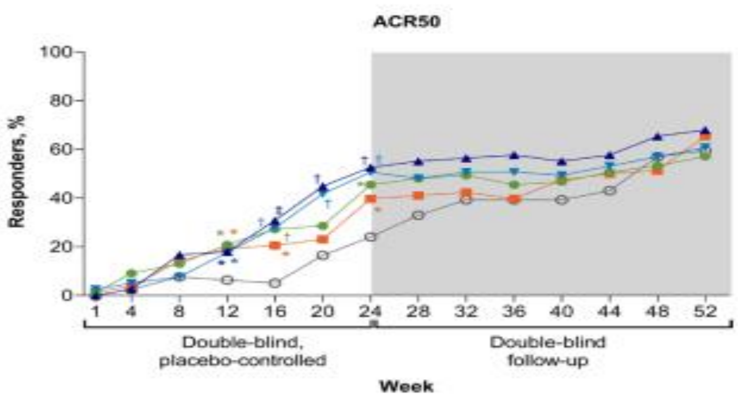


CLINICAL SCIENCE

Efficacy and safety of tildrakizumab in patients with active psoriatic arthritis: results of a randomised, double-blind, placebo-controlled, multiple-dose, 52-week phase IIb study





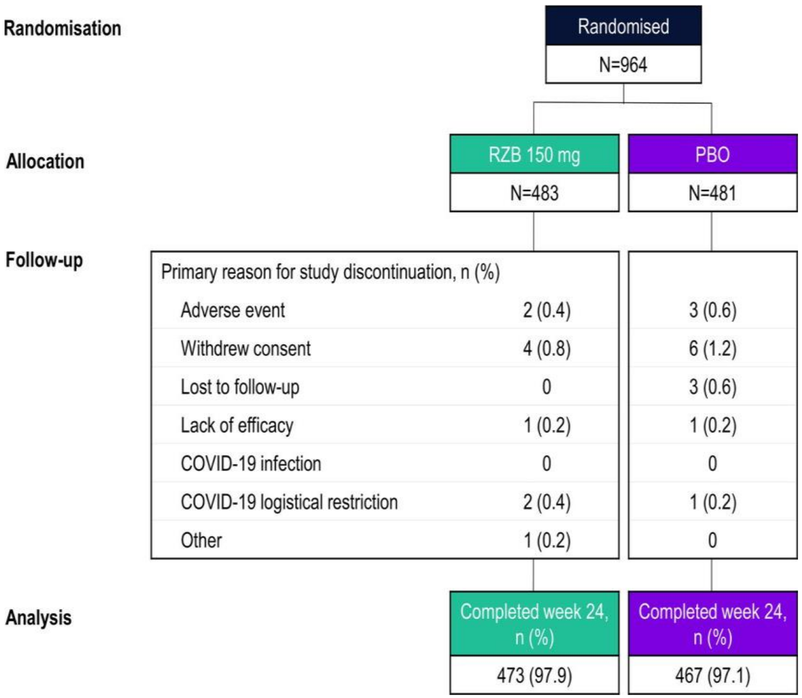


Το Tildrakizumab σημαντικά βελτίωνε τις εκδηλώσεις της PsA (αρθρώσεις, δέρμα, δακτυλίτιδα και ενθεσίτιδα) Ήταν γενικά καλά ανεκτό μέχρι την W52

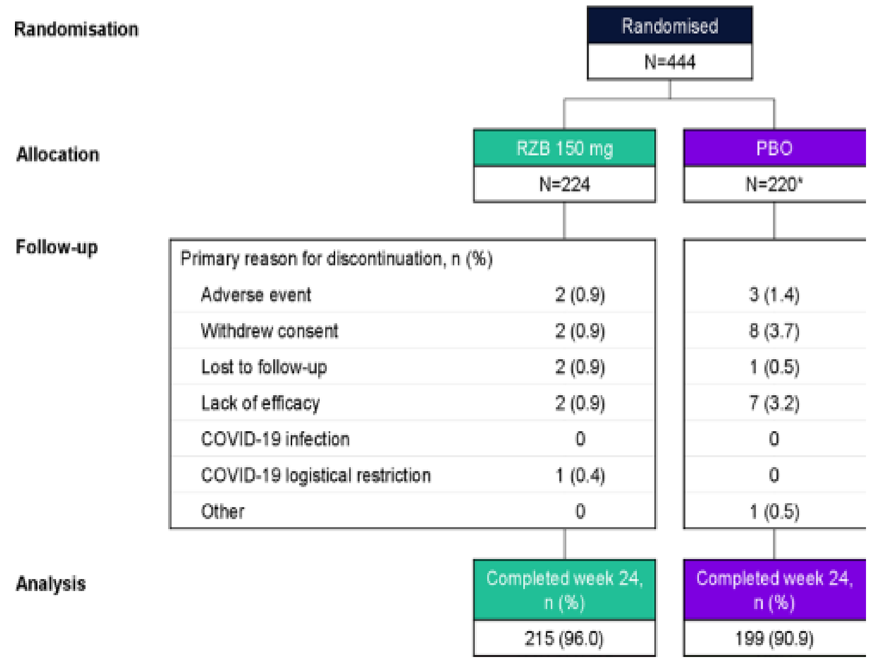
Ann Rheum Dis. 2021;80(9) :2020–219014.

Efficacy and safety of risankizumab for active psoriatic arthritis: 24-week results from the randomised, double-blind, phase 3 KEEPsAKE 2 trial

KEEPsAKE 1 trial

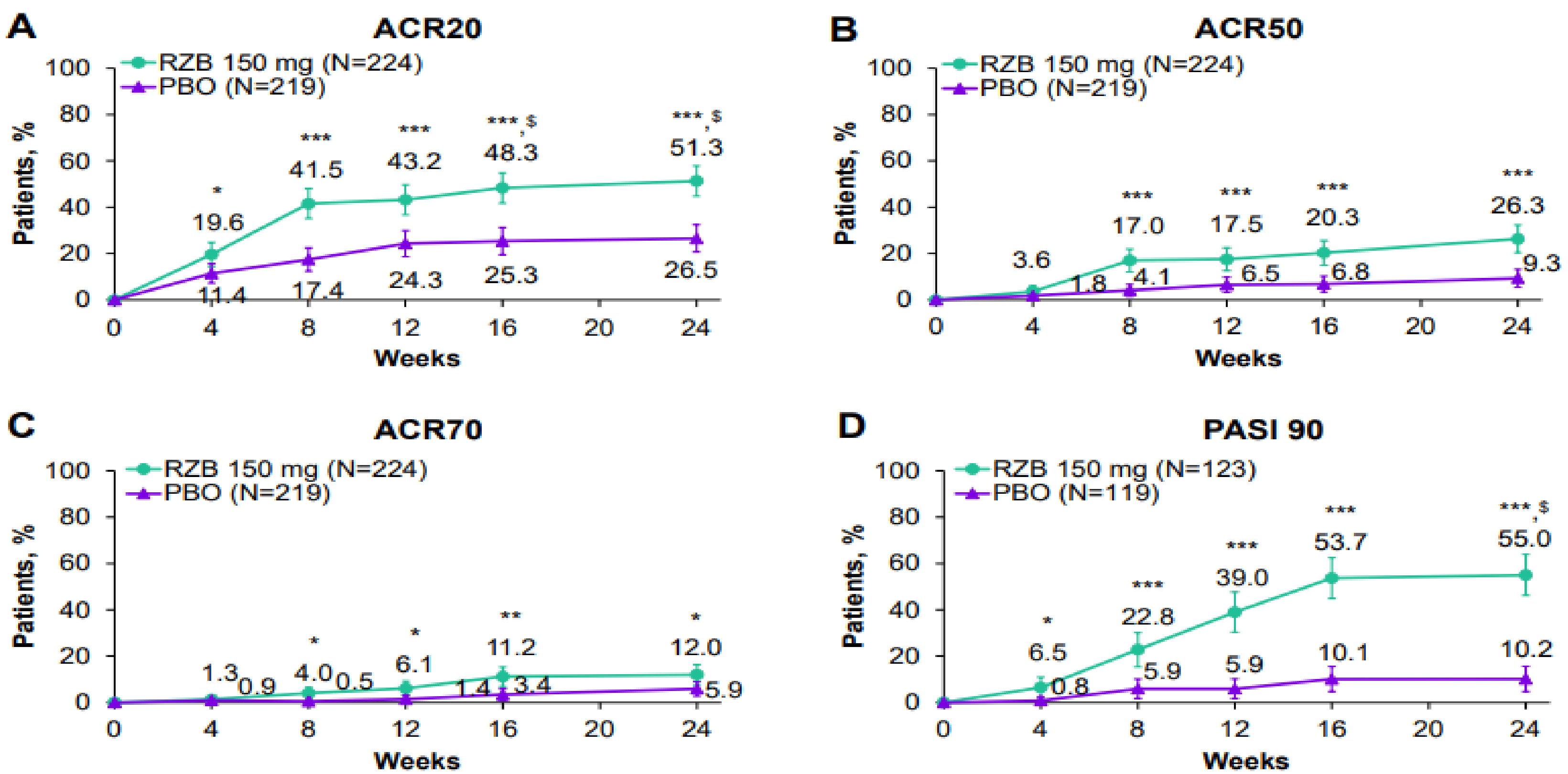


KEEPsAKE 2 trial



Östör A, et al. Ann Rheum Dis 2022;81:351–358.

Efficacy and safety of risankizumab for active psoriatic arthritis: 24-week results from the randomised, double-blind, phase 3 KEEPsAKE 2 trial



Östör A, et al. Ann Rheum Dis 2022;81:351–358.

Efficacy and safety of risankizumab for active psoriatic arthritis: 24-week results from the randomised, double-blind, phase 3 KEEPsAKE 2 trial

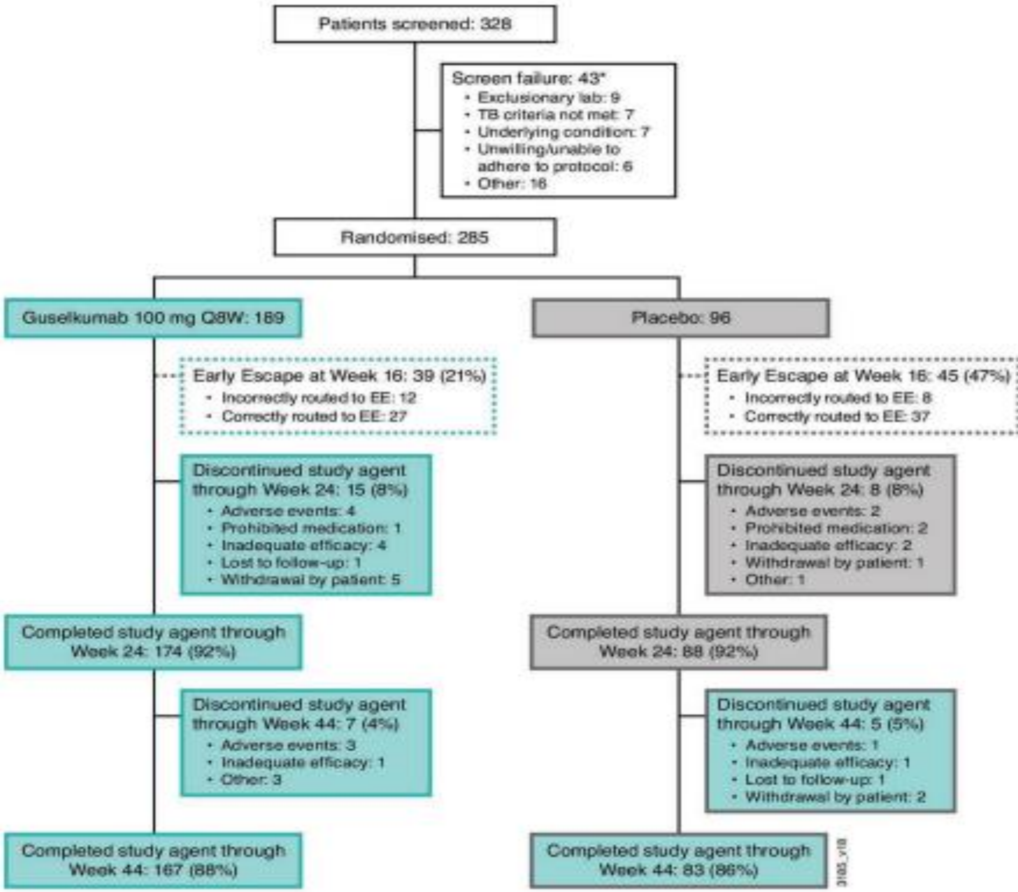
Table 3 Safety summary

Patients, n (%)	RZB 150 mg N=224	PBO N=219
TEAE	124 (55.4)	120 (54.8)
COVID-19-related TEAE	1 (0.4)	0
Serious AE	9 (4.0)	12 (5.5)
Severe TEAE	6 (2.7)	7 (3.2)
TEAE leading to discontinuation of study drug	2 (0.9)	5 (2.3)
Death	0	0
Serious infections*	2 (0.9)	5 (2.3)
Active tuberculosis	0	0
Herpes zoster	0	1 (0.5)
Any other opportunistic infections	0	0
Malignancy†	1 (0.4)	1 (0.5)
Anaphylactic reactions	0	0
Injection site reactions	3 (1.3)‡	1 (0.5)
MACE	1 (0.4)	0

Η θεραπεία με risankizumab είχε ως αποτέλεσμα σημαντικές βελτιώσεις έναντι του εικονικού φαρμάκου σε βασικές εκβάσεις και ήταν καλά ανεκτή σε ασθενείς με ΨΑ σε Bio-IR και/ή csDMARD-IR

Östör A, et al. Ann Rheum Dis 2022;81:351–358.

Efficacy and safety of guselkumab in patients with active psoriatic arthritis who are inadequate responders to tumour necrosis factor inhibitors: results through one year of a phase IIIb, randomised, controlled study (COSMOS)

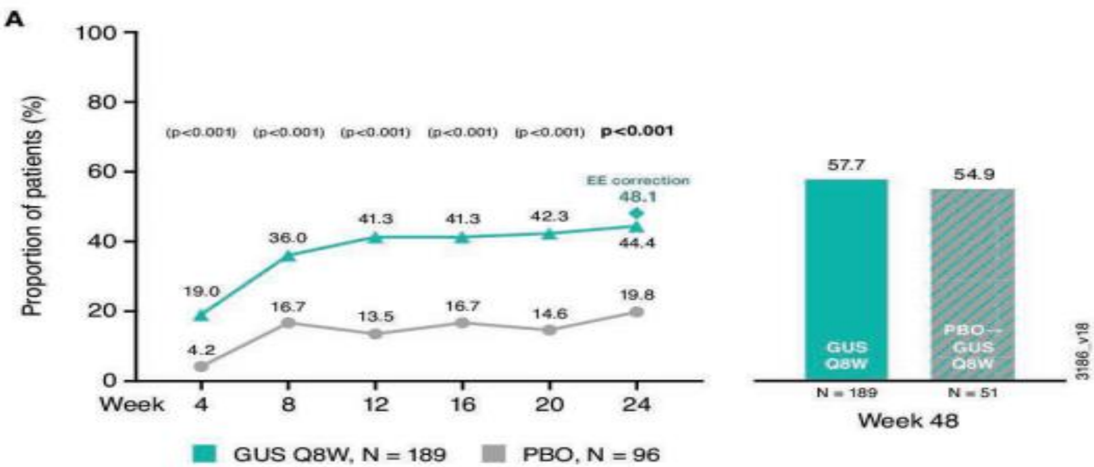


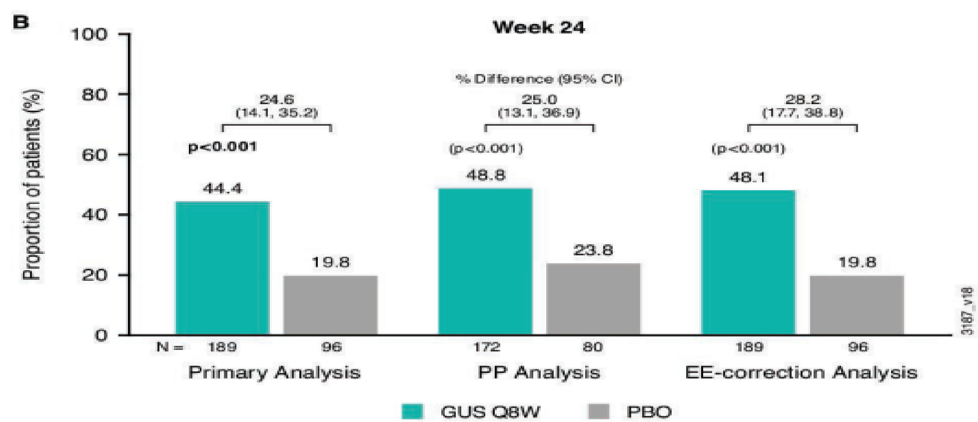
anti-interleukin-23p19-

Οι ασθενείς που έλαβαν εικονικό φάρμακο πέρασαν σε Guselkumab την 24η εβδομάδα

Coates LC, et al. Ann Rheum Dis 2022;81:359–369.

Efficacy and safety of guselkumab in patients with active psoriatic arthritis who are inadequate responders to tumour necrosis factor inhibitors: results through one year of a phase IIIb, randomised, controlled study (COSMOS)





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Efficacy and safety of guselkumab in patients with active psoriatic arthritis who are inadequate responders to tumour necrosis factor inhibitors: results through one year of a phase IIIb, randomised, controlled study (COSMOS)

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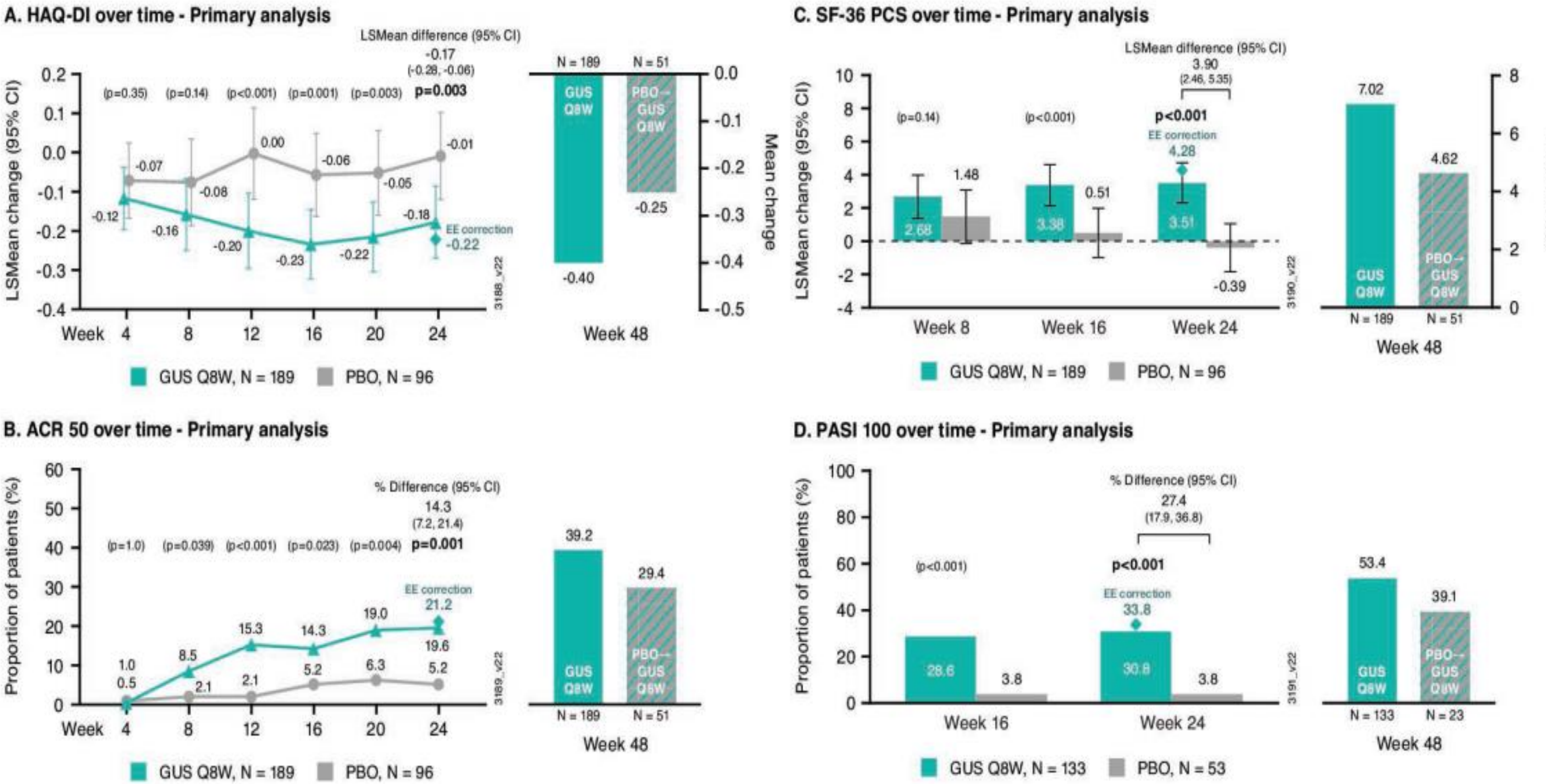

Efficacy and safety of guselkumab in patients with active psoriatic arthritis who are inadequate responders to tumour necrosis factor inhibitors: results through one year of a phase IIIb, randomised, controlled study (COSMOS)

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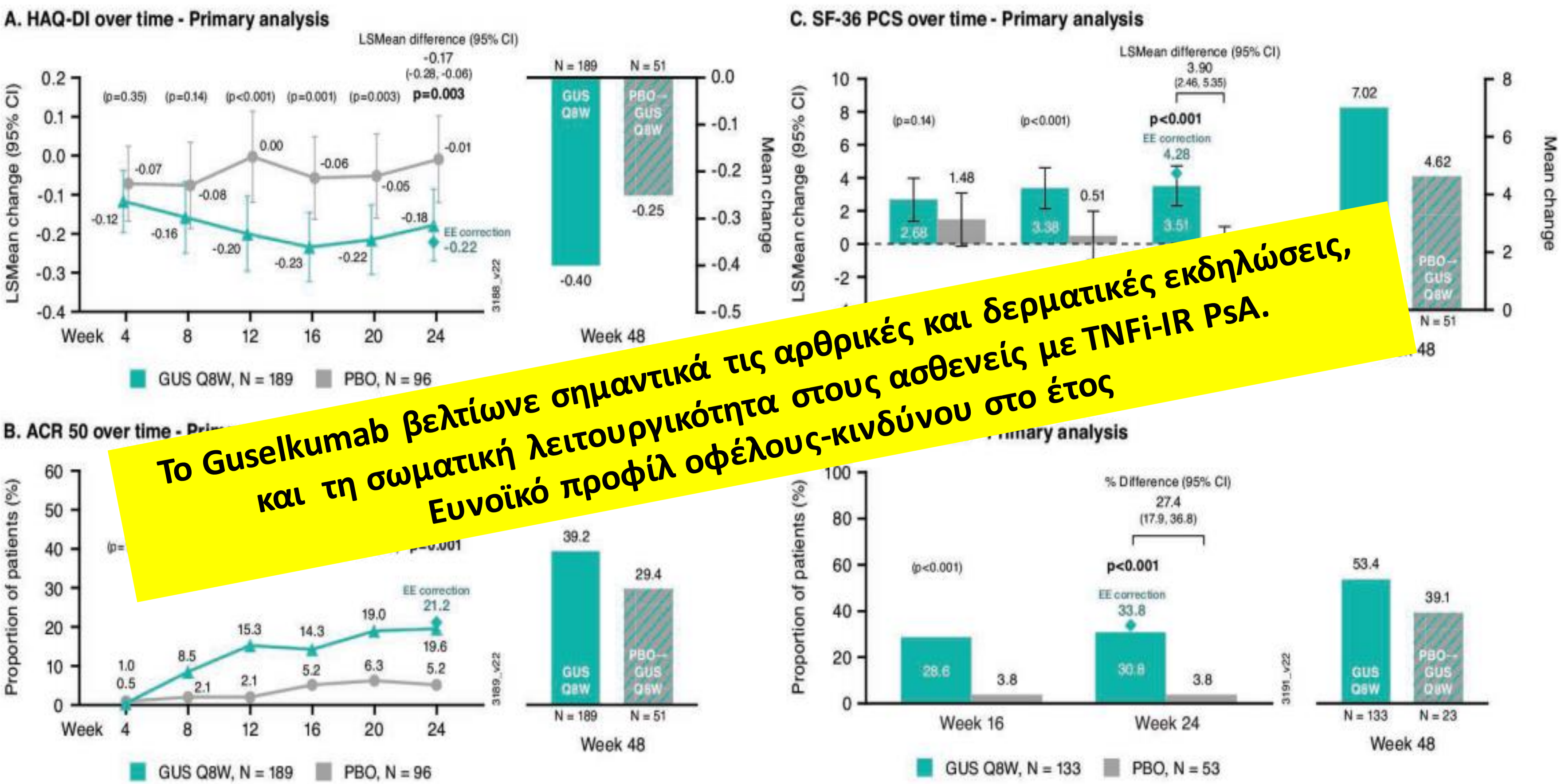


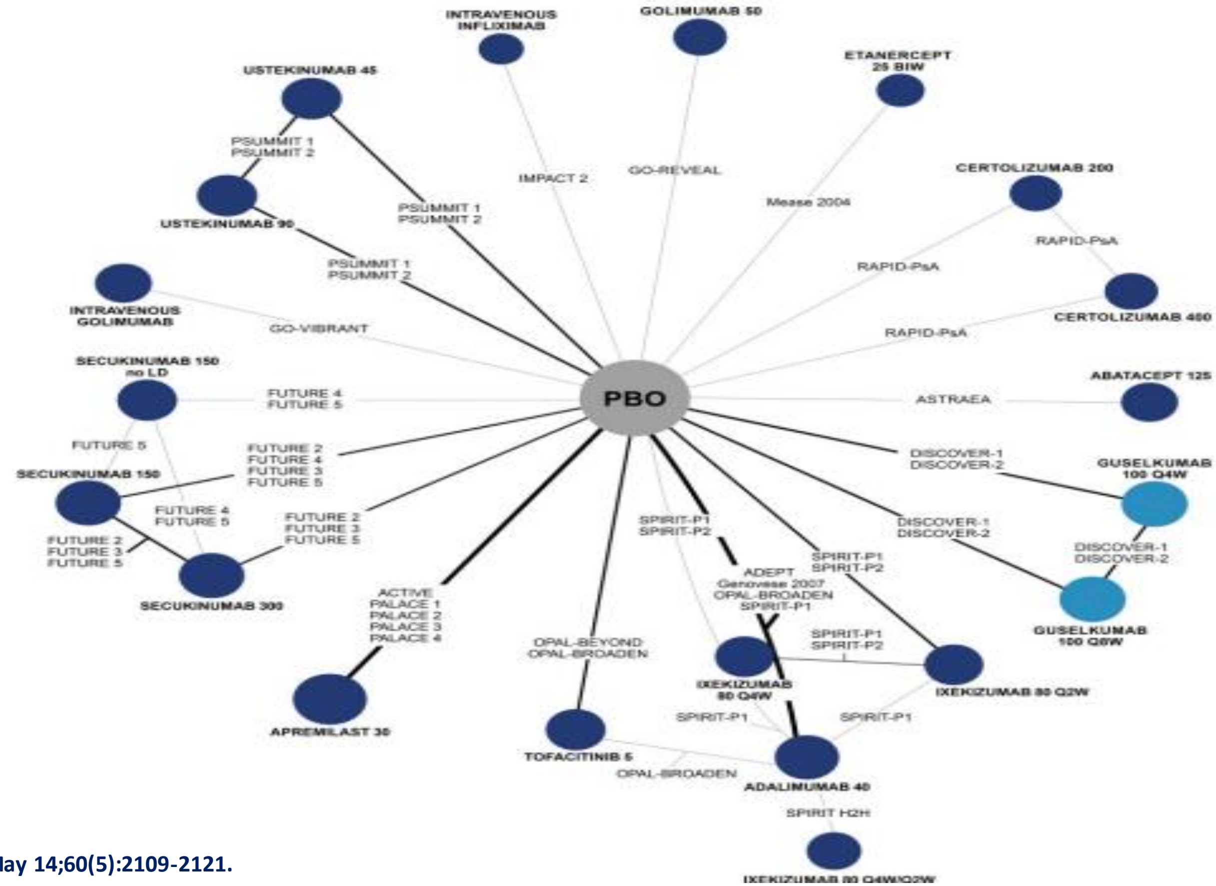
Το Guselkumab βελτίωνε σημαντικά τις αρθρικές και δερματικές εκδηλώσεις, και τη σωματική λειτουργικότητα στους ασθενείς με TNFi-IR PsA. Ευνοϊκό προφίλ οφέλους-κινδύνου στο έτος

RHEUMATOLOGY

Rheumatology 2021;60:2109–2121
doi:10.1093/rheumatology/keab119

Systematic review and meta analysis

Comparative effectiveness of guselkumab in psoriatic arthritis: results from systematic literature review and network meta-analysis



Rheumatology (Oxford). 2021 May 14;60(5):2109-2121.

RHEUMATOLOGY

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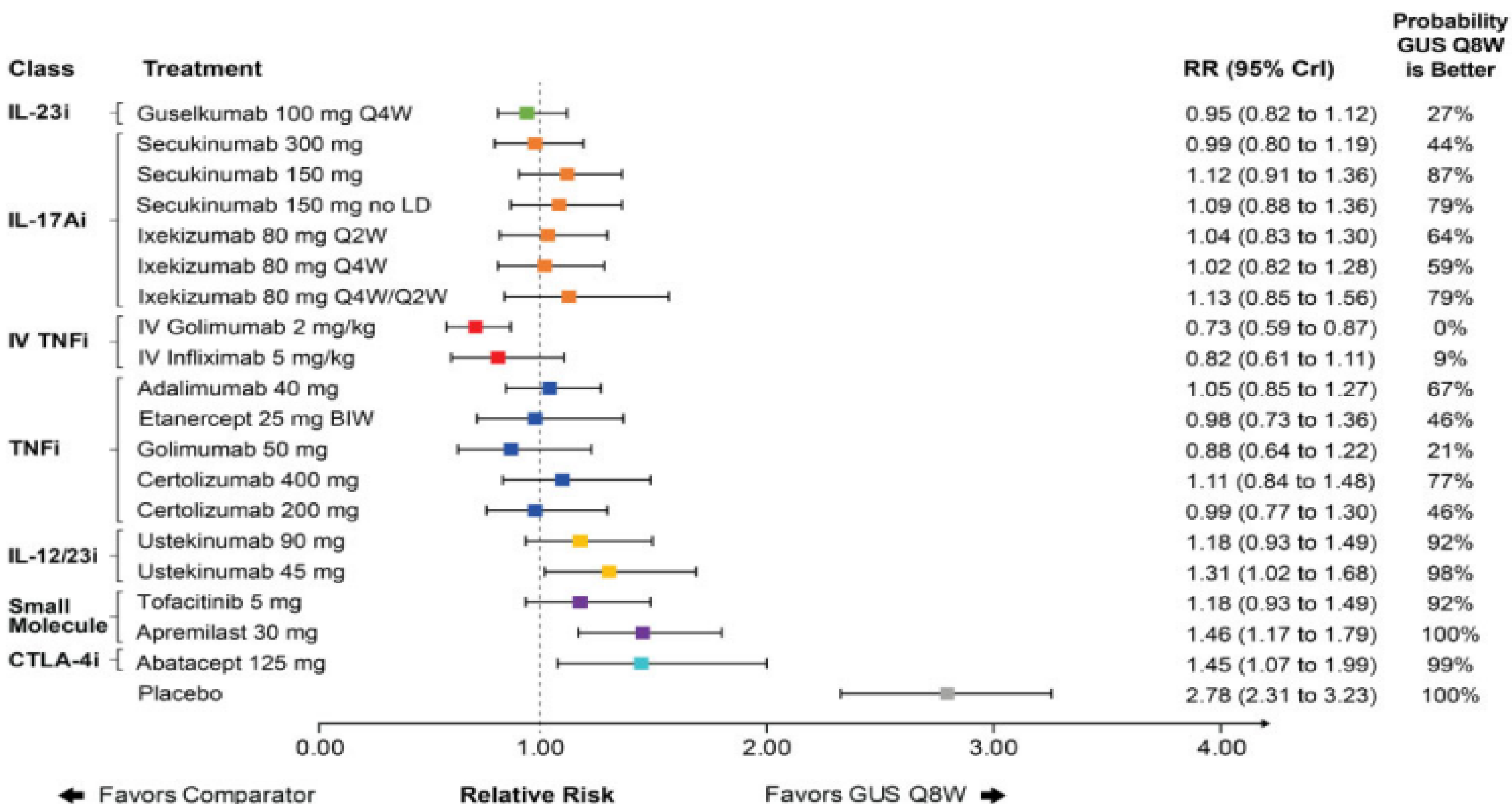

Rheumatology (Oxford). 2021 May 14;60(5):2109-2121.

RHEUMATOLOGY

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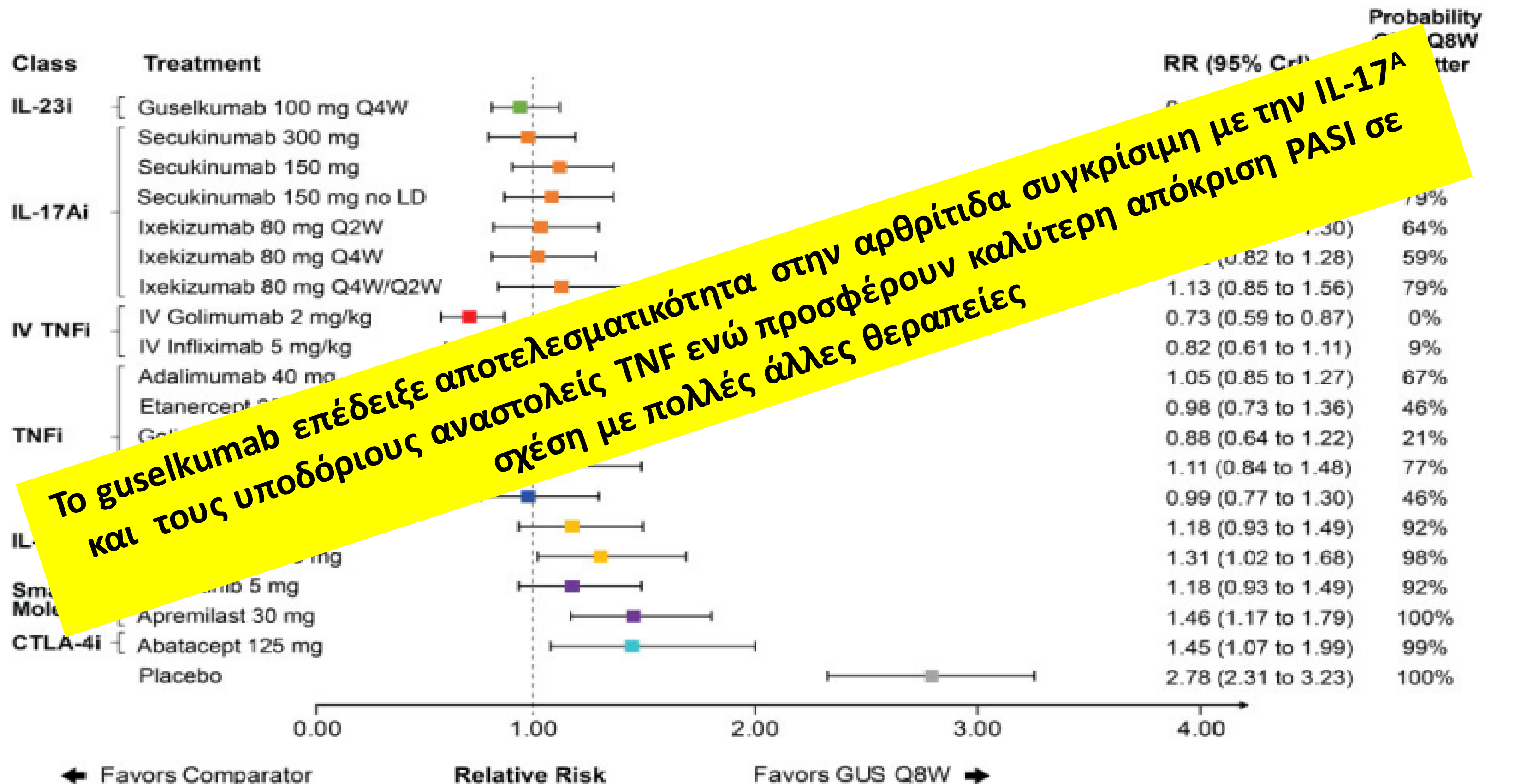
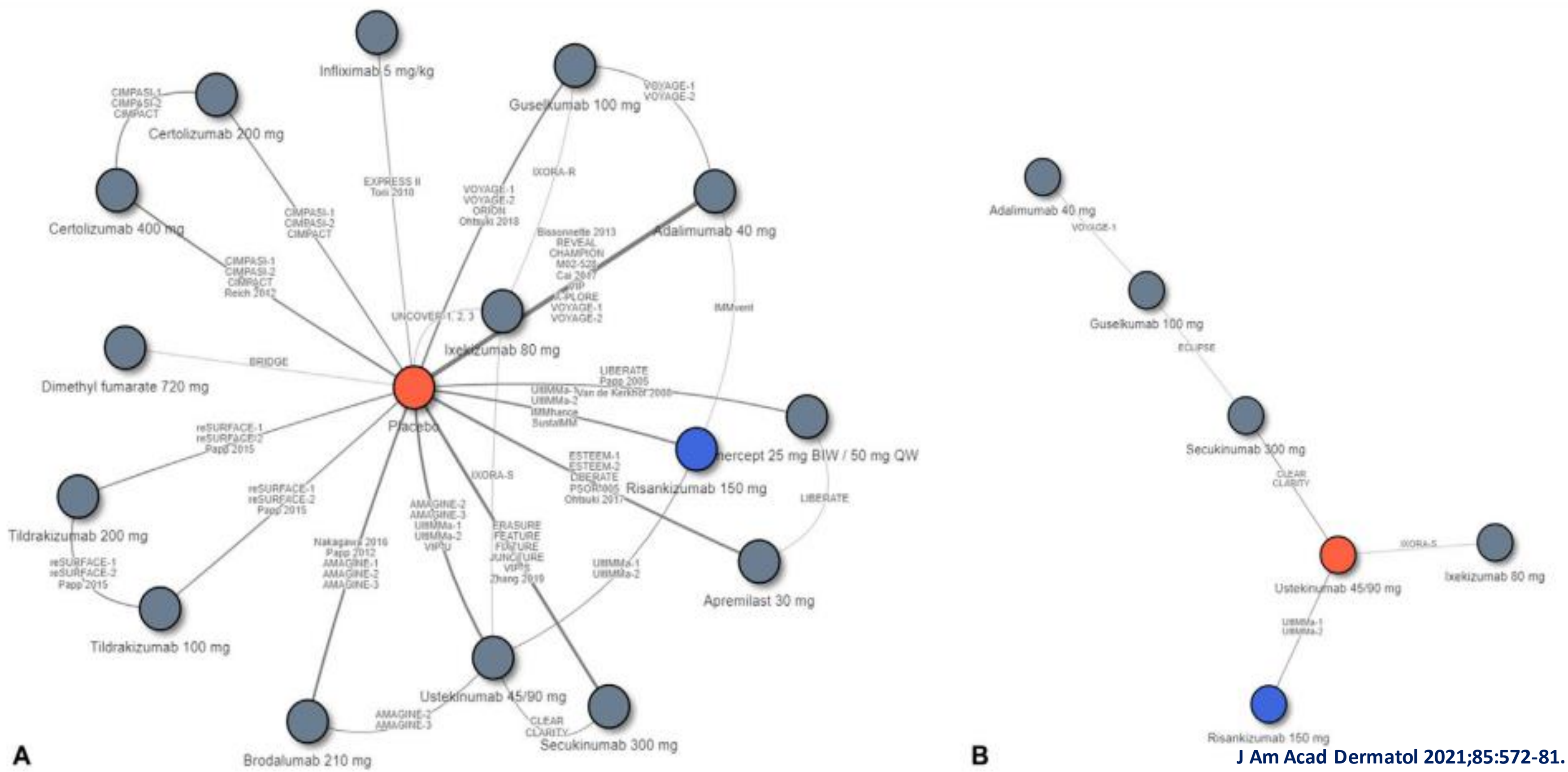


Το guselkumab επέδειξε αποτελεσματικότητα στην αρθρίτιδα συγκρίσιμη με την IL-17A και τους υποδόριους αναστολείς TNF ενώ προσφέρουν καλύτερη απόκριση PASI σε σχέση με πολλές άλλες θεραπείες

Rheumatology (Oxford). 2021 May 14;60(5):2109-2121.

Comparative safety and benefit-risk profile of biologics and oral treatment for moderate-to-severe plaque psoriasis: A network meta-analysis of clinical



J Am Acad Dermatol 2021;85:572-81.

Comparative safety and benefit-risk profile of biologics and oral treatment for moderate-to-severe plaque psoriasis: A network meta-analysis of clinical

Treatment	Short-term			Long-term		
	Any AE, posterior median (95% CrI)	Any SAE, posterior median (95% CrI)	AEs leading to treatment discontinuation, posterior median (95% CrI)	Any AE, posterior median (95% CrI)	Any SAE, posterior median (95% CrI)	AEs leading to treatme discontinuation, posteri median (95% CrI)
Certolizumab at 400 mg at weeks 0, 2, and 4, then 200 mg Q2W	46.2% (37.0%, 55.5%)	0.8% (0.2%, 3.0%)	4.1% (0.7%, 24.9%)	-	-	-
Risankizumab at 150 mg at weeks 0 and 4, then Q12W	52.4% (47.3%, 57.4%)	1.2% (0.6%, 2.4%)	0.5% (0.2%, 1.3%)	67.5% (57.8%, 75.6%)	4.4% (2.4%, 8.1%)	1.0% (0.2%, 4.1%)
Etanercept at 25 mg BIW or 50 mg QW	49.1% (35.5%, 62.9%)	1.6% (0.3%, 7.5%)	1.7% (0.6%, 4.8%)	-	-	-
Dimethyl fumarate uptitrated to a maximum daily dose of 720 mg	79.2% (69.7%, 86.1%)	1.8% (0.5%, 7.0%)	12.1% (4.8%, 30.2%)	-	-	-
Placebo	52.0% (50.7%, 53.3%)	1.9% (1.6%, 2.3%)	2.0% (1.6%, 2.4%)	-	-	-
Brodalumab at 210 mg at weeks 0, 1, and 2, then Q2W	59.9% (55.5%, 64.2%)	1.9% (0.9%, 4.1%)	2.2% (1.0%, 5.1%)	-	-	-
Apremilast at 30 mg BID after initial titration schedule	65.3% (60.2%, 70.2%)	2.0% (0.9%, 4.5%)	2.8% (1.5%, 5.2%)	-	-	-
Adalimumab at 80 mg at week 0, then 40 mg Q2W	55.8% (51.8%, 59.7%)	2.0% (1.1%, 3.7%)	1.7% (0.8%, 3.6%)	72.9% (61.4%, 82.0%)	5.4% (2.1%, 13.5%)	3.4% (0.8%, 12.7%)
Tildrakizumab at 100 mg at weeks 0, and 4, then Q12W	46.3% (39.5%, 53.2%)	2.1% (0.7%, 7.4%)	1.0% (0.2%, 4.4%)	-	-	-
Ustekinumab at 45 mg for ≤100 kg, 90 mg for >100 kg at weeks 0, and 4, then Q12W	57.8% (53.7%, 61.9%)	2.1% (1.1%, 3.9%)	1.6% (0.7%, 3.4%)	76.9% (74.5%, 79.2%)	5.7% (4.5%, 7.1%)	2.2% (1.5%, 3.2%)
Infliximab at 5 mg/kg at weeks 0, 2, and 6, then Q8W	68.3% (59.6%, 76.0%)	2.1% (0.6%, 7.1%)	3.7% (1.3%, 10.8%)	-	-	-
Guselkumab at 100 mg at weeks 0 and 4, then Q8W	55.8% (50.9%, 60.3%)	2.2% (1.1%, 4.6%)	1.5% (0.7%, 3.1%)	72.2% (63.7%, 79.5%)	5.9% (3.1%, 10.9%)	2.5% (0.8%, 7.2%)
Certolizumab at 400 mg Q2W	52.2% (43.3%, 61.1%)	2.6% (1.0%, 7.3%)	3.2% (0.7%, 15.0%)	-	-	-
Ixekizumab at 160 mg at week 0, then 80 mg Q2W	61.1% (56.1%, 65.6%)	2.7% (1.3%, 6.3%)	3.0% (1.4%, 6.5%)	80.9% (68.7%, 89.3%)	10.4% (3.8%, 27.0%)	4.4% (0.7%, 29.0%)
Secukinumab at 300 mg at weeks 0, 1, 2, 3, and 4, then Q4W	60.9% (56.8%, 65.0%)	2.7% (1.4%, 5.2%)	1.9% (0.9%, 4.0%)	76.6% (71.8%, 80.9%)	6.9% (4.4%, 10.6%)	3.2% (1.7%, 6.1%)
Tildrakizumab at 200 mg at weeks 0 and 4, then Q12W	46.0% (39.2%, 52.9%)	3.4% (1.2%, 11.0%)	2.3% (0.7%, 8.8%)	-	-	-

J Am Acad Dermatol 2021;85:572-81.

Comparative safety and benefit-risk profile of biologics and oral treatment for moderate-to-severe plaque psoriasis: A network meta-analysis of clinical

	Short-term			Long-term		
Treatment	Any AE, posterior median (95% CrI)	Any SAE, posterior median (95% CrI)	AEs leading to treatment discontinuation, posterior median (95% CrI)	Any AE, posterior median (95% CrI)	Any SAE, posterior median (95% CrI)	AEs leading to treatment discontinuation, posterior median (95% CrI)
Certolizumab at 400 mg at weeks 0, 2, and 4, then 200 mg Q2W	46.2% (37.0%, 55.5%)	0.8% (0.2%, 3.0%)	4.1% (0.7%, 24.9%)	-	-	-
Risankizumab at 150 mg at weeks 0 and 4, then Q12W	52.4% (47.3%, 57.4%)	1.2% (0.6%, 2.4%)	0.5% (0.2%, 1.3%)	67.5% (57.8%, 75.6%)	4.4% (2.4%, 8.1[illegible]	[illegible]0.2%, 4.1%)
Etanercept at 25 mg BIW or 50 mg QW	49.1% (35.5%, 62.9%)	1.6% (0.3%, 7.5%)	1.7% (0.6%, 4.8%)	-	[illegible]	-
Dimethyl fumarate uptitrated to a maximum daily dose of 720 mg	79.2% (69.7%, 86.1%)	1.8% (0.5%, 7.0%)	12.1% (4.8%, 30.2%)	[illegible]	[illegible]	-
Placebo	52.0% (50.7%, 53.3%)	1.9% (1.6%, 2.3%)	2.0% (1.6[illegible]	[illegible]	[illegible]	-
Brodalumab at 210 mg at weeks 0, 1, and 2, then Q2W	59.9% (55.5%, 64.2%)	1.9% (0.9%, 4.1%)	[illegible]	[illegible]	[illegible]	-
Apremilast at 30 mg BID after initial titration schedule	65.3% (60.2%, 70.2%)	2.0% [illegible]	[illegible]	[illegible]	-	-
Adalimumab at 80 mg at week 0, then 40 mg Q2W	55.8% (51.8[illegible]	[illegible]	[illegible]	[illegible] (61.4%, 82.0%)	5.4% (2.1%, 13.5%)	3.4% (0.8%, 12.7%)
Tildrakizumab at 100 mg at weeks 0[illegible] and 4, then Q12W	[illegible]	[illegible]	[illegible], 4.4%)	-	-	-
Ustekinumab at 45 [illegible] 90 mg fo[illegible] 4, the[illegible]	[illegible]	[illegible]	1.6% (0.7%, 3.4%)	76.9% (74.5%, 79.2%)	5.7% (4.5%, 7.1%)	2.2% (1.5%, 3.2%)
Inflixima[illegible] and 6, [illegible]	[illegible]8.0%)	2.1% (0.6%, 7.1%)	3.7% (1.3%, 10.8%)	-	-	-
Guselkum[illegible] 0 and 4, [illegible]	[illegible]5.8% (50.9%, 60.3%)	2.2% (1.1%, 4.6%)	1.5% (0.7%, 3.1%)	72.2% (63.7%, 79.5%)	5.9% (3.1%, 10.9%)	2.5% (0.8%, 7.2%)
Certolizuma[illegible]ng Q2W	52.2% (43.3%, 61.1%)	2.6% (1.0%, 7.3%)	3.2% (0.7%, 15.0%)	-	-	-
Ixekizumab [illegible] 160 mg at week 0, then 80 mg Q2W	61.1% (56.1%, 65.6%)	2.7% (1.3%, 6.3%)	3.0% (1.4%, 6.5%)	80.9% (68.7%, 89.3%)	10.4% (3.8%, 27.0%)	4.4% (0.7%, 29.0%)
Secukinumab at 300 mg at weeks 0, 1, 2, 3, and 4, then Q4W	60.9% (56.8%, 65.0%)	2.7% (1.4%, 5.2%)	1.9% (0.9%, 4.0%)	76.6% (71.8%, 80.9%)	6.9% (4.4%, 10.6%)	3.2% (1.7%, 6.1%)
Tildrakizumab at 200 mg at weeks 0 and 4, then Q12W	46.0% (39.2%, 52.9%)	3.4% (1.2%, 11.0%)	2.3% (0.7%, 8.8%)	-	[illegible]	[illegible]

Οι παράγοντες κατά της ιντερλευκίνης 23 συσχετίστηκαν με χαμηλά ποσοστά συμβάντων ασφάλειας. Το Risankizumab είχε το πιο ευνοϊκό προφίλ οφέλους-κινδύνου μακροπρόθεσμα

J Am Acad Dermatol 2021;85:572-81.

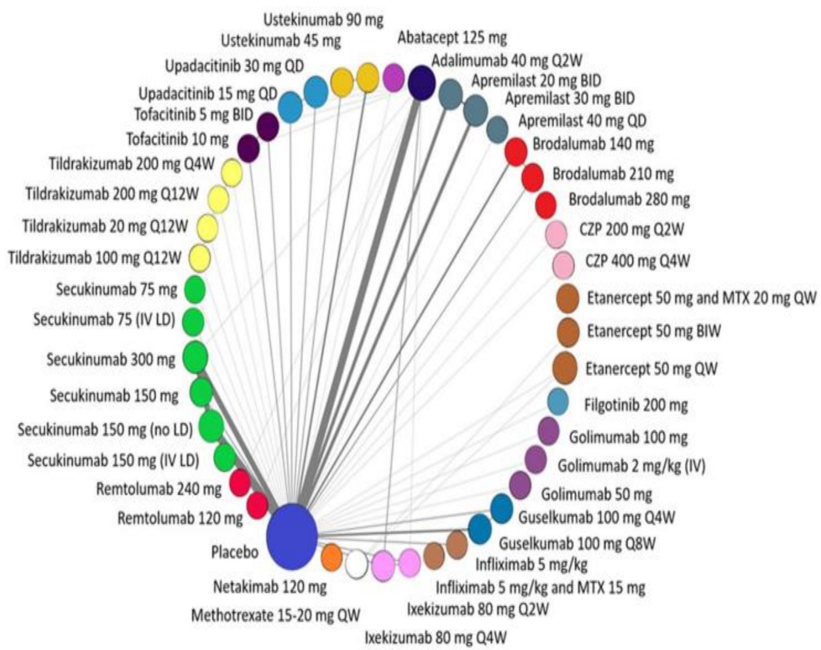
Psoriatic arthritis

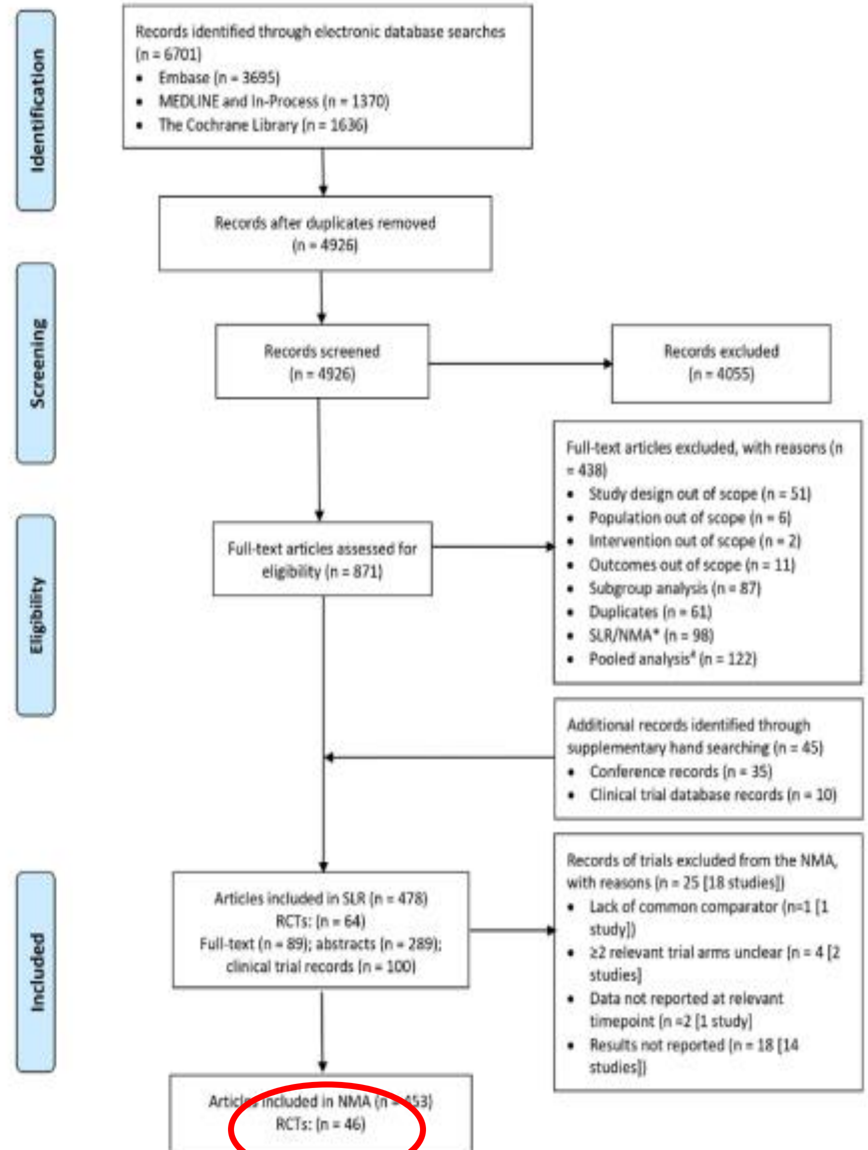
RMD Open

Rheumatic & Musculoskeletal Diseases

ORIGINAL RESEARCH

Targeted systemic therapies for psoriatic arthritis: a systematic review and comparative synthesis of short-term articular, dermatological, enthesitis and dactylitis outcomes





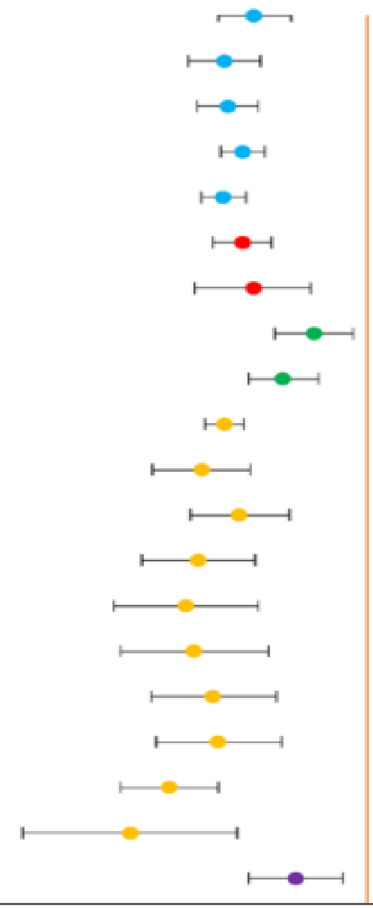
McInnes IB, et al. RMD Open 2022;8:e002074.

RMD Open
Rheumatic & Musculoskeletal Diseases

Συστηματική ανασκόπηση και συγκριτική σύνθεση βραχυπρόθεσμων αρθρικών, δερματολογικών, ενθεσίτιδας και αποτελέσματα δακτυλίτιδας

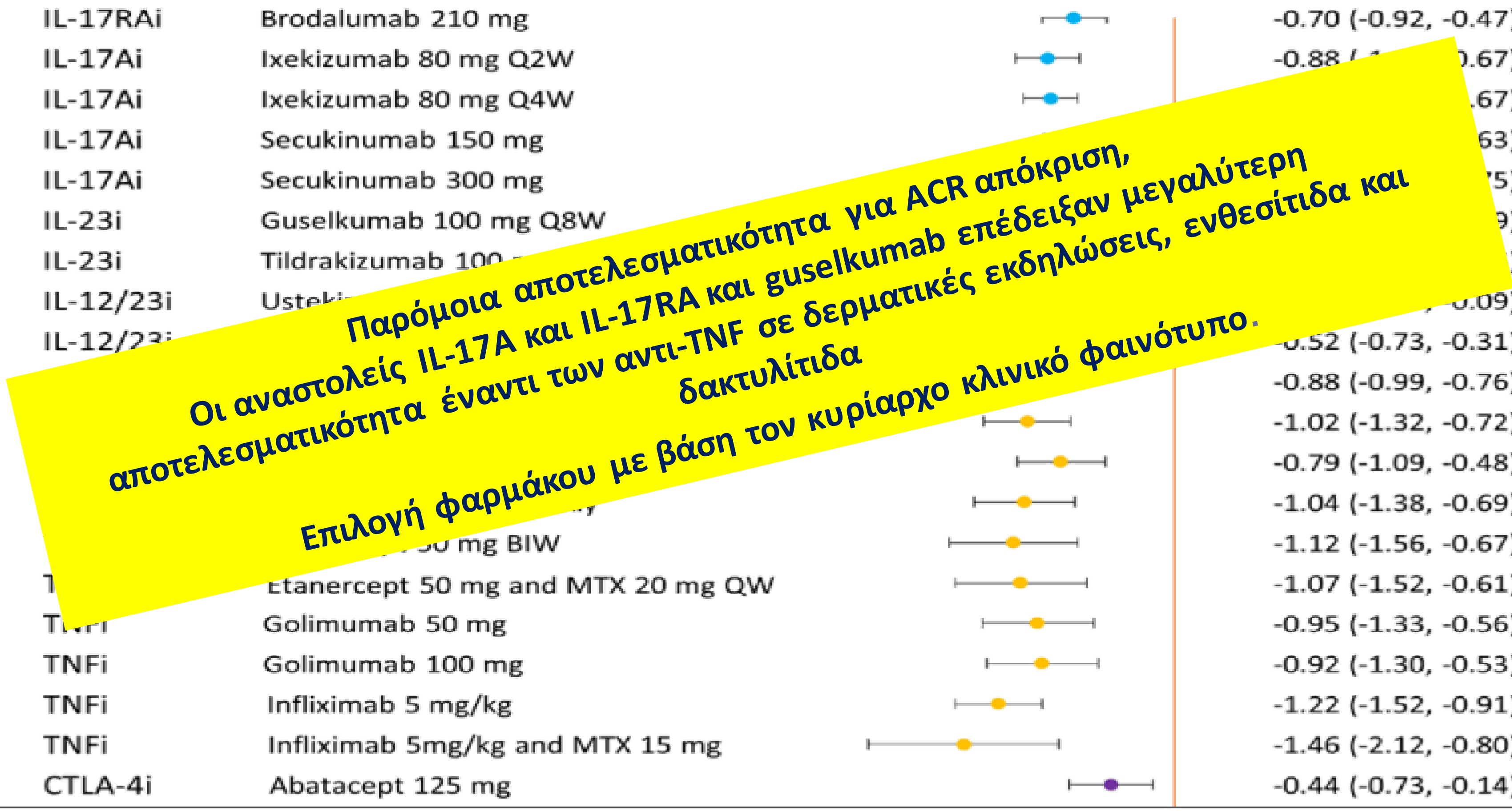
McInnes IB, et al. RMD Open 2022;8:e002074.

IL-17RAi	Brodalumab 210 mg	-0.70 (-0.92, -0.47)
IL-17Ai	Ixekizumab 80 mg Q2W	-0.88 (-1.10, -0.67)
IL-17Ai	Ixekizumab 80 mg Q4W	-0.86 (-1.05, -0.67)
IL-17Ai	Secukinumab 150 mg	-0.77 (-0.91, -0.63)
IL-17Ai	Secukinumab 300 mg	-0.89 (-1.02, -0.75)
IL-23i	Guselkumab 100 mg Q8W	-0.77 (-0.95, -0.59)
IL-23i	Tildrakizumab 100 mg Q12W	-0.70 (-1.06, -0.35)
IL-12/23i	Ustekinumab 45 mg	-0.33 (-0.57, -0.09)
IL-12/23i	Ustekinumab 90 mg	-0.52 (-0.73, -0.31)
TNFi	Adalimumab 40 mg Q2W	-0.88 (-0.99, -0.76)
TNFi	Certolizumab 200 mg Q2W	-1.02 (-1.32, -0.72)
TNFi	Certolizumab 400 mg Q4W	-0.79 (-1.09, -0.48)
TNFi	Etanercept 50 mg weekly	-1.04 (-1.38, -0.69)
TNFi	Etanercept 50 mg BIW	-1.12 (-1.56, -0.67)
TNFi	Etanercept 50 mg and MTX 20 mg QW	-1.07 (-1.52, -0.61)
TNFi	Golimumab 50 mg	-0.95 (-1.33, -0.56)
TNFi	Golimumab 100 mg	-0.92 (-1.30, -0.53)
TNFi	Infliximab 5 mg/kg	-1.22 (-1.52, -0.91)
TNFi	Infliximab 5mg/kg and MTX 15 mg	-1.46 (-2.12, -0.80)
CTLA-4i	Abatacept 125 mg	-0.44 (-0.73, -0.14)



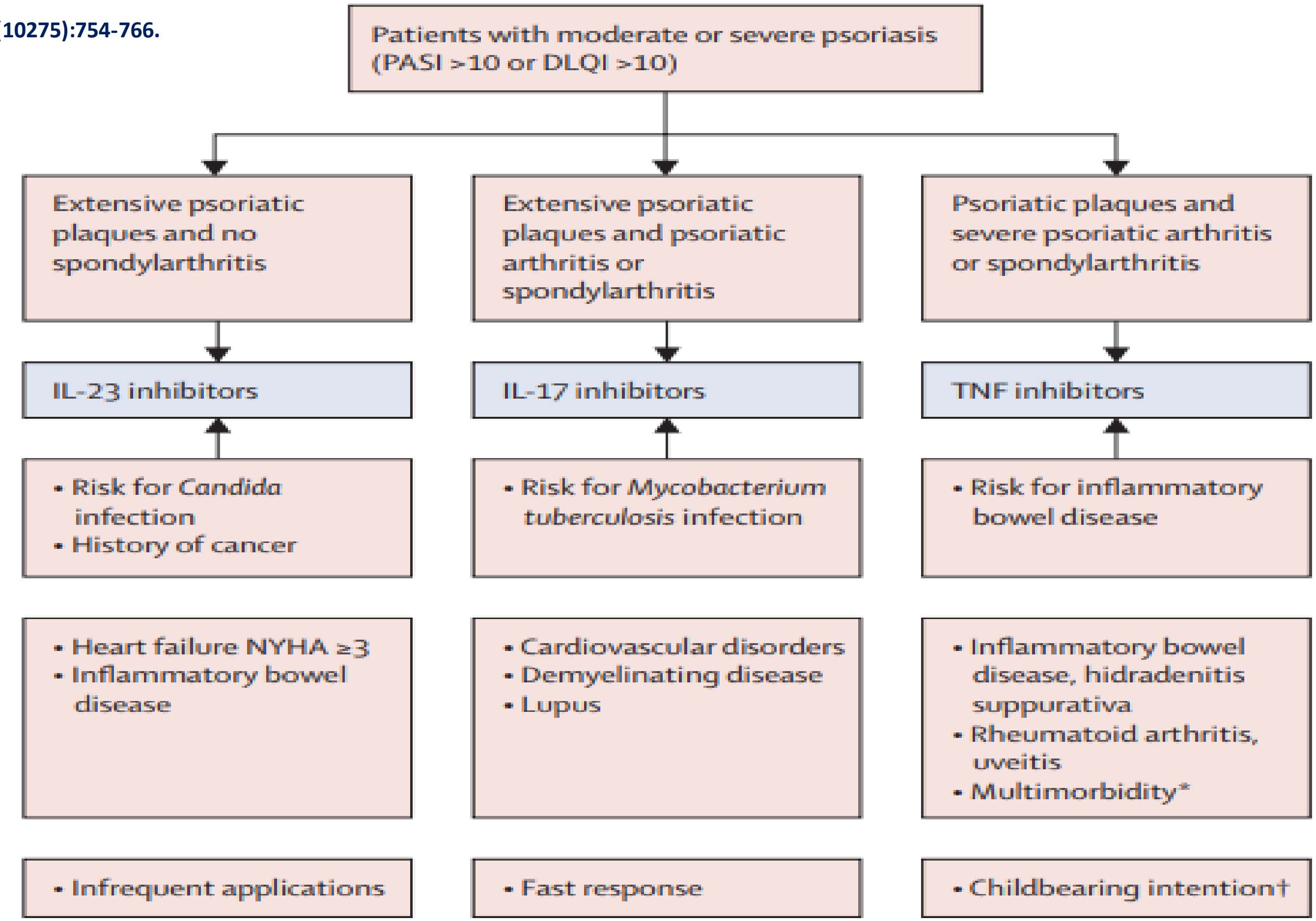
Συστηματική ανασκόπηση και συγκριτική σύνθεση βραχυπρόθεσμων αρθρικών, δερματολογικών, ενθεσίτιδας και αποτελέσματα δακτυλίτιδας

McInnes IB, et al. RMD Open 2022;8:e002074.



Αλγόριθμος για τη θεραπεία της ψωρίασης με διακριτές κατηγορίες βιολογικών φαρμάκων

Lancet. 2021 Feb 20;397(10275):754-766.



Am J Clin Dermatol. 2021 Mar;22(2):173-192.

FDA-approved biologic drugs for plaque psoriasis			
Risankizumab	Humanized IgG1 monoclonal antibody binding p19 subunit of IL-23	Subcutaneous	2019
Certolizumab	Humanized PEGylated Fab fragment binding TNF-α	Subcutaneous	2018
Tildrakizumab	Humanized IgG1κ monoclonal antibody binding p19 subunit of IL-23	Subcutaneous	2018
Guselkumab	Human IgG1λ monoclonal antibody binding p19 subunit of IL-23	Subcutaneous	2017
Brodalumab	Human monoclonal IgG2 antibody binding IL-17RA	Subcutaneous	2017
Ixekizumab	Humanized IgG4 monoclonal antibody binding IL-17A	Subcutaneous	2016
Secukinumab	Human IgG1 monoclonal antibody binding IL-17A	Subcutaneous	2015
Ustekinumab	Human IgG1κ monoclonal antibody binding shared p40 subunit of IL-12 and IL-23	Subcutaneous	2009
Adalimumab	Human IgG1 monoclonal antibody binding TNF-α	Subcutaneous	2008
Infliximab	Chimeric IgG1κ monoclonal antibody binding TNF-α	Intravenous	2006
Etanercept	Decoy TNF receptor	Subcutaneous	2004
FDA-approved biologic drugs for psoriatic arthritis			
Guselkumab	Human IgG1λ monoclonal antibody binding p19 subunit of IL-23	Subcutaneous	2020
Ixekizumab	Humanized IgG4 monoclonal antibody binding IL-17A	Subcutaneous	2017
Abatacept	Binds CD80 and CD86	Intravenous/subcutaneous	2017
Secukinumab	Human IgG1 monoclonal antibody binding IL-17A	Subcutaneous	2016
Certolizumab	Humanized PEGylated Fab fragment binding TNF-α	Subcutaneous	2013
Ustekinumab	Human IgG1κ monoclonal antibody binding shared p40 subunit of IL-12 and IL-23	Subcutaneous	2013
Golimumab	Human IgG1κ monoclonal antibody binding TNF-α	Subcutaneous	2009
Adalimumab	Human IgG1 monoclonal antibody binding TNF-α	Subcutaneous	2005
Infliximab	Chimeric IgG1κ monoclonal antibody binding TNF-α	Intravenous	2005
Etanercept	Decoy TNF receptor	Subcutaneous	2002

Ανησυχίες για τη μακροπρόθεσμη ασφάλεια

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journal homepage: www.elsevierhealth.com/berh

Unmet needs in psoriatic arthritis

Ο φαινοτυπισμός θα ήταν μια σημαντική μελλοντική κατεύθυνση στην έρευνα PsA

Best Pract Res Clin Rheumatol. 2021;35(2):101693.

Βιολογικά νέας γενιάς για τη θεραπεία της ψωρίασης και της ψωριασικής αρθρίτιδας

Dermatol Ther. 2021 Jan;34(1):e14660.

Table 1 – ***Summary of New Generation Drugs for Psoriasis and Psoriatic Arthritis ordered by target and associated risk of serious infections, based on clinical trials***

Target	Drug	Potential Infection	Risk of Serious Infection
JAK	Tofacitinib	Tuberculosis Extra- and intra-cellular bacterial infections Fungal infections Viral infections	Higher
	Upadacitinib		
IL-17A (ligand or receptor)	Secukinumab	Extracellular bacterial infections Sepsis Pneumoniae Fungal infections Mucocutaneous candida Opportunistic infections Herpes zoster Esophageal Candida Toxoplasmosis Mycobacterium avium complex	
	Ixekizumab		
	Brodalumab		
	Bimekizumab		
IL-23p19	Guselkumab	Extracellular bacterial infections Fungal infections	
	Tildrakizumab		
	Risankizumab		Lower
PDE-4	Apremilast	None reported	

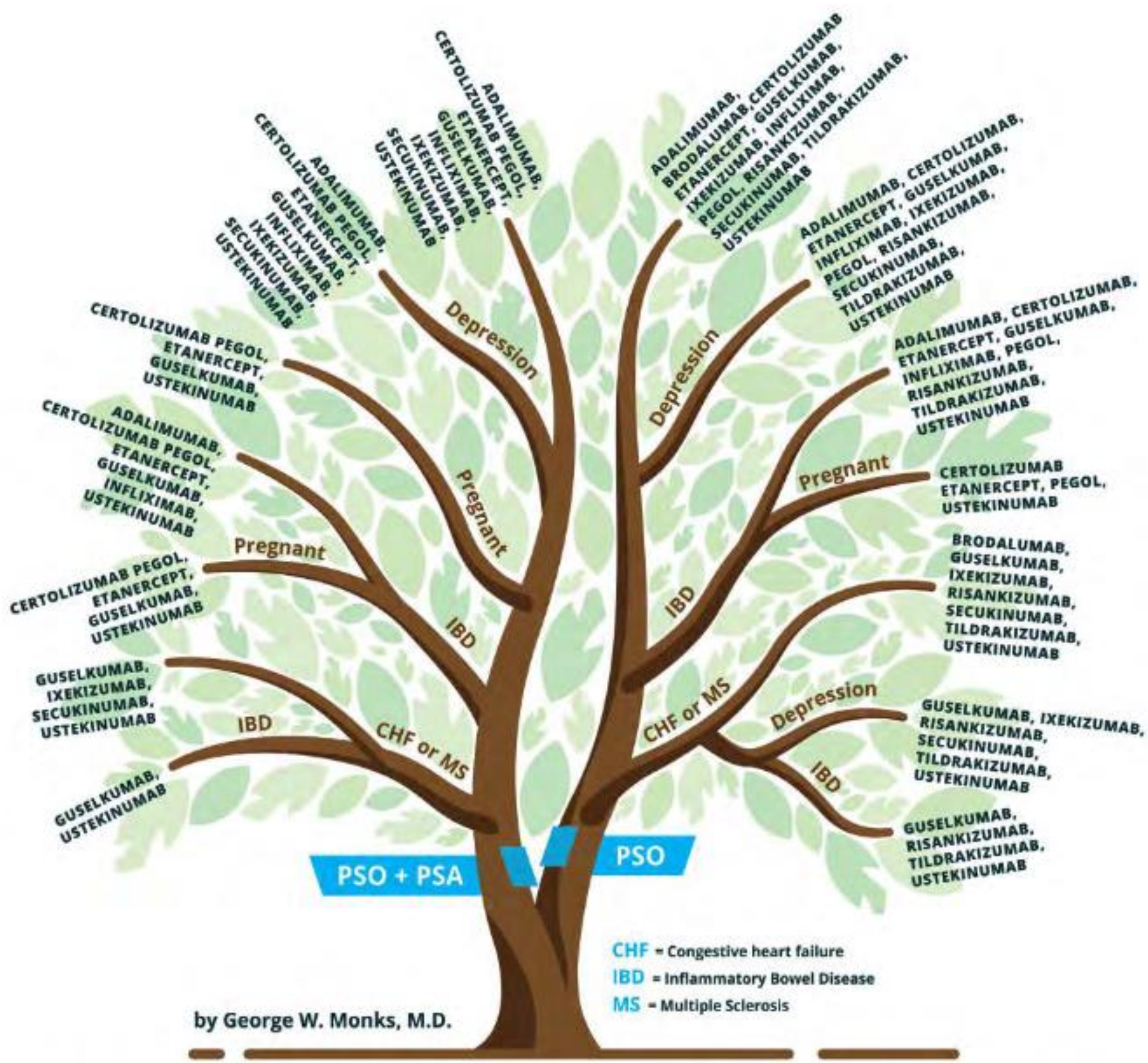
Abbreviations: JAK = Janus kinases; IL-17A = Interleukin-17A; IL-23p19 = p19 subunit of interleukin-23; PDE-4 = Phosphodiesterase 4

Classification	Target molecule	Agent	Structure	FDA approval (approval in Japan)										
				Psoriasis	PsA	AS	RA	CD	UC	uveitis	Behcet D	HS	PG	PPP
TNF-inhibitor	TNF	Infliximab	chimeric IgG1	+ (+)	+ (+)	+ (+)	+ (+)	+ (+)	+ (+)	+ (+)	+ (+)	-	-	-
		Adalimumab	human IgG1	+ (+)	+ (+)	+ (+)	+ (+)	+ (+)	+ (+)	+ (+)	- (+)	+ (+)	applied	-
		certolizumab pegol	PEGylated, humanized Fab fragment	+ (+)	+ (+)	+ (-)	+ (+)	+ (-)	-	-	-	-	-	-
		Etanercept	fusion protein of TNFR and IgG1	+ (-)	+ (-)	+ (-)	+ (+)	-	-	-	-	-	-	-
IL-17 inhibitor	IL-17A	Secukinumab	human IgG1κ	+ (+)	+ (+)	+ (+)	-	-	-	-	-	Phase 3	-	-
		Ixekizumab	humanized IgG4	+ (+)	+ (+)	+ (+)	-	-	-	-	-	-	-	-
		ABY-035	affibody	Phase 2	-	-	-	-	-	-	-	-	-	-
		netakimab (BCD-085)	humanized IgG1	Phase 3	Phase 3	Phase 3	-	-	-	-	-	-	-	-
		vunakizumab (SHR-1314)	humanized IgG1k	Phase 2	-	-	-	-	-	-	-	-	-	-
	IL-17A/F	bimekizumab (UCB4940)	humanized IgG1	Phase 3	Phase 3	Phase 3	-	-	-	-	-	Phase 3	-	-
		sonelokinab (M1095)	bispecific nanobody	Phase 2b	-	-	-	-	-	-	-	-	-	-
	IL-17RA	Brodalumab	human IgG2	+ (+)	- (+)	- (+)	-	-	-	-	-	-	-	Phase 3
IL-12/23 inhibitor	IL-12/23 p40 subunit	Ustekinumab	human IgG1	+ (+)	+ (+)	-	-	+ (+)	+ (+)	-	-	-	-	-
IL-23 p19 inhibitor	IL-23 p19 subunit	Guselkumab	human IgG1	+ (+)	+ (+)	-	-	Phase 2/3	Phase 2/3	-	-	-	-	- (+)
		Risankizumab	humanized IgG1	+ (+)	- (+)	-	-	Phase 3	Phase 3	-	-	Phase 2	-	Phase 3
		Tildrakizumab	humanized IgG1	+ (+)	-	-	-	-	-	-	-	-	-	-
		mirikizumab (LY3074828)	humanized IgG4	Phase 3	-	-	-	Phase 3	Phase 3	-	-	-	-	-
IL-36 inhibitor	IL-36 receptor	spesolimab (BI 655130)[b]	humanized IgG1	-	-	-	-	-	Phase 2/3	-	-	-	-	Phase 2
		imsidolimab (ANB019)[b]	humanized Ig	-	-	-	-	-	-	-	-	-	-	Phase 2

J Dermatol. 2021 Jun;48(6):761-777.

Classification	Target molecule	Agent	Structure	FDA approval (approval in Japan)										
				Psoriasis	PsA	AS	RA	CD	UC	uveitis	Behcet D	HS	PG	PPP
PDE4 inhibitor	PDE4	Apremilast	small molecule	+ (+)	+ (+)	-	-	-	-	-	+ (+)[a]	-	-	-
		Roflumilast	small molecule	Phase 2	-	-	-	-	-	-	-	-	-	-
		Hemay005	small molecule	Phase 2	-	-	-	-	-	-	-	-	-	-
JAK inhibitor	JAK1/3	Tofacitinib	small molecule	-	+ (-)	-	+ (+)	-	+ (+)	-		-	-	-
	JAK1/2	Baricitinib	small molecule	-	-	-	+ (+)	-	-	-	-	-	-	-
	JAK1	upadacitinib (ABT-494)	small molecule	-	applied	Phase 3	+ (+)	Phase 3	Phase 3	-	-	Phase 2	-	-
	JAK1	Filgotinib	small molecule	-	Phase 3	Phase 3	applied	Phase 3	Phase 3	-	-	-	-	-
	TYK2	BMS-986165	small molecule	Phase 3	-	-	-	Phase 3	Phase 3	-	-	-	-	-
	TYK2	PF-06826647	small molecule	Phase 2	-	-	-	-	-	-	-	-	-	-
	TYK2/JAK1	brepocitinib (PF-06700841-00)	small molecule	Phase 2	-	-	-	-	-	-	-	-	-	-
Other inhibitors	RORgT	AUR101	small molecule	Phase 2	-	-	-	-	-	-	-	-	-	-
	RORgT	BI 730357	small molecule	Phase 2	-	-	-	-	-	-	-	-	-	-
	IRAK-4	CF101	small molecule	Phase 3	-	Phase 3	Phase 3	-	-	Phase 2	-	-	-	-

J Dermatol. 2021 Jun;48(6):761-777.



Monks G. et al, J Clin Aesthet Dermatol 2021

Συμπεράσματα

- Συναίνεση ότι η ψωρίαση έχει διάφορες συστημικές συνέπειες
- Επιβάλλει μια ολιστική και προληπτική προσέγγιση στην ψωρίαση
- Έγκαιρη εισαγωγή θεραπειών
- Προσέγγιση που επιτρέπει τον καλύτερο σχεδιασμό θεραπείας για τον καθένα
- Οι νεότερες διαθέσιμες θεραπείες αναμένεται να μειώσουν τις ακάλυπτες ανάγκες

Διαθέσιμες φαρμακολογικές θεραπείες

- Symptomatic therapies
- Oral treatments
- TNF inhibitors
- IL-12/23 inhibitor
- IL-17A inhibitors
- CTLA-4
- JAK/STAT inhibitor
- PDE4 inhibitor

Επιλογή θεραπείας με σκεπτικισμό

Ευχαριστώ !

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