Η αναστολή της IL-17 στην ψωριασική αρθρίτιδα

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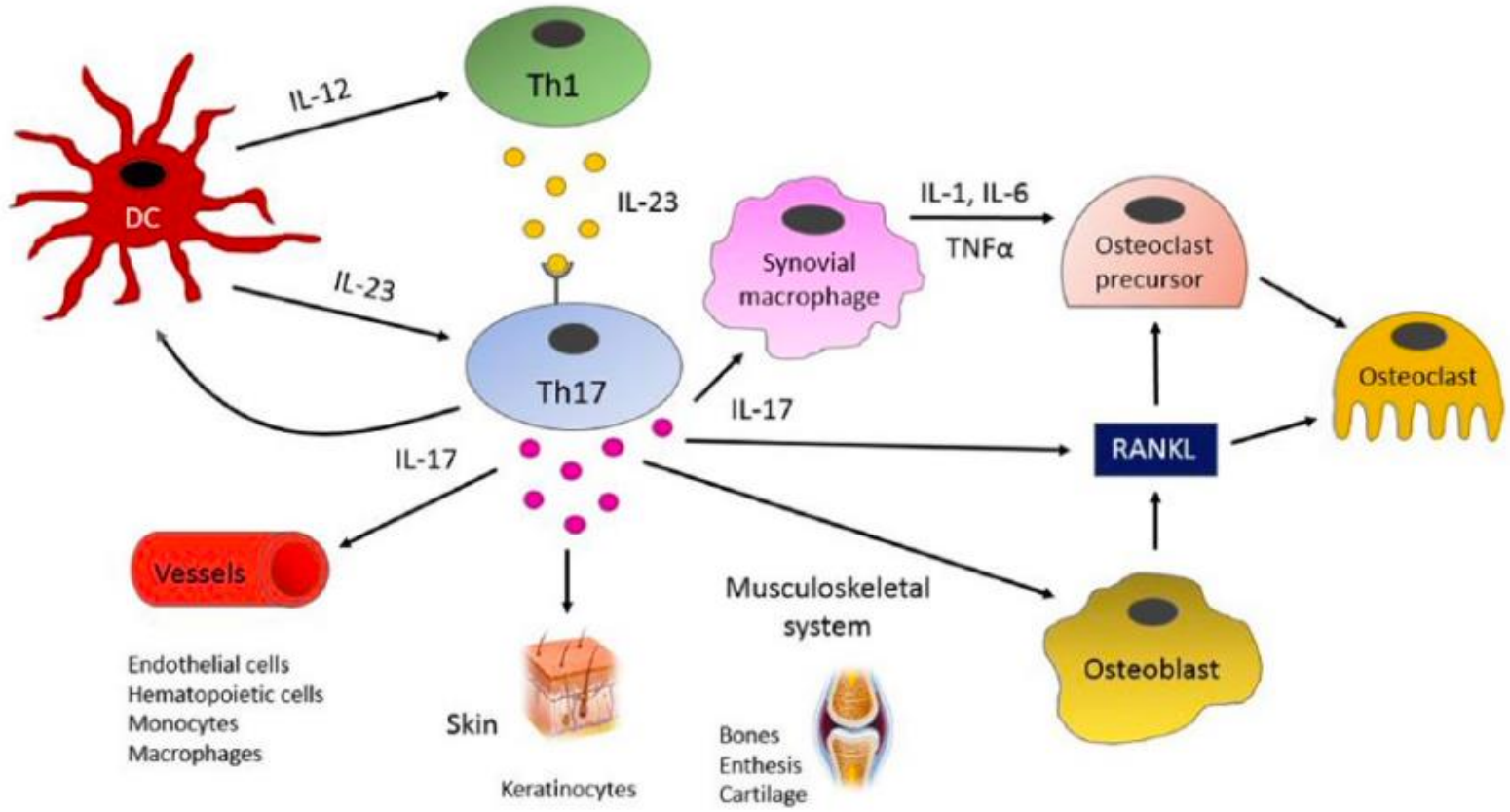
Ρευματολόγος

ΓΝΑ «Γ. Γεννηματάς»

Σύγκρουση συμφερόντων

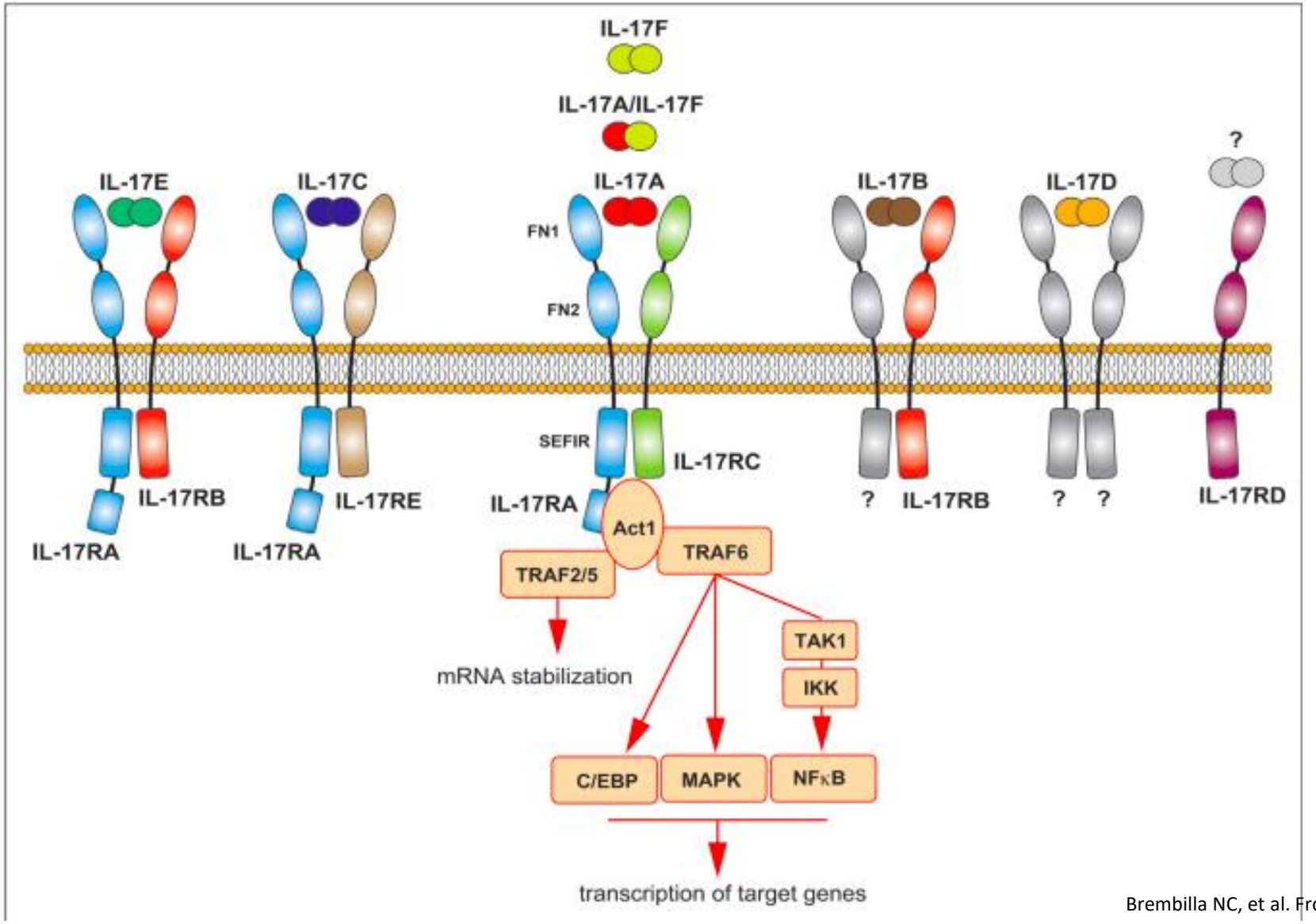
- Καμία για την παρούσα ομιλία

Ο ρόλος της IL-17 στην παθοφυσιολογία της ψωρίασης και ψωριασικής αρθρίτιδας



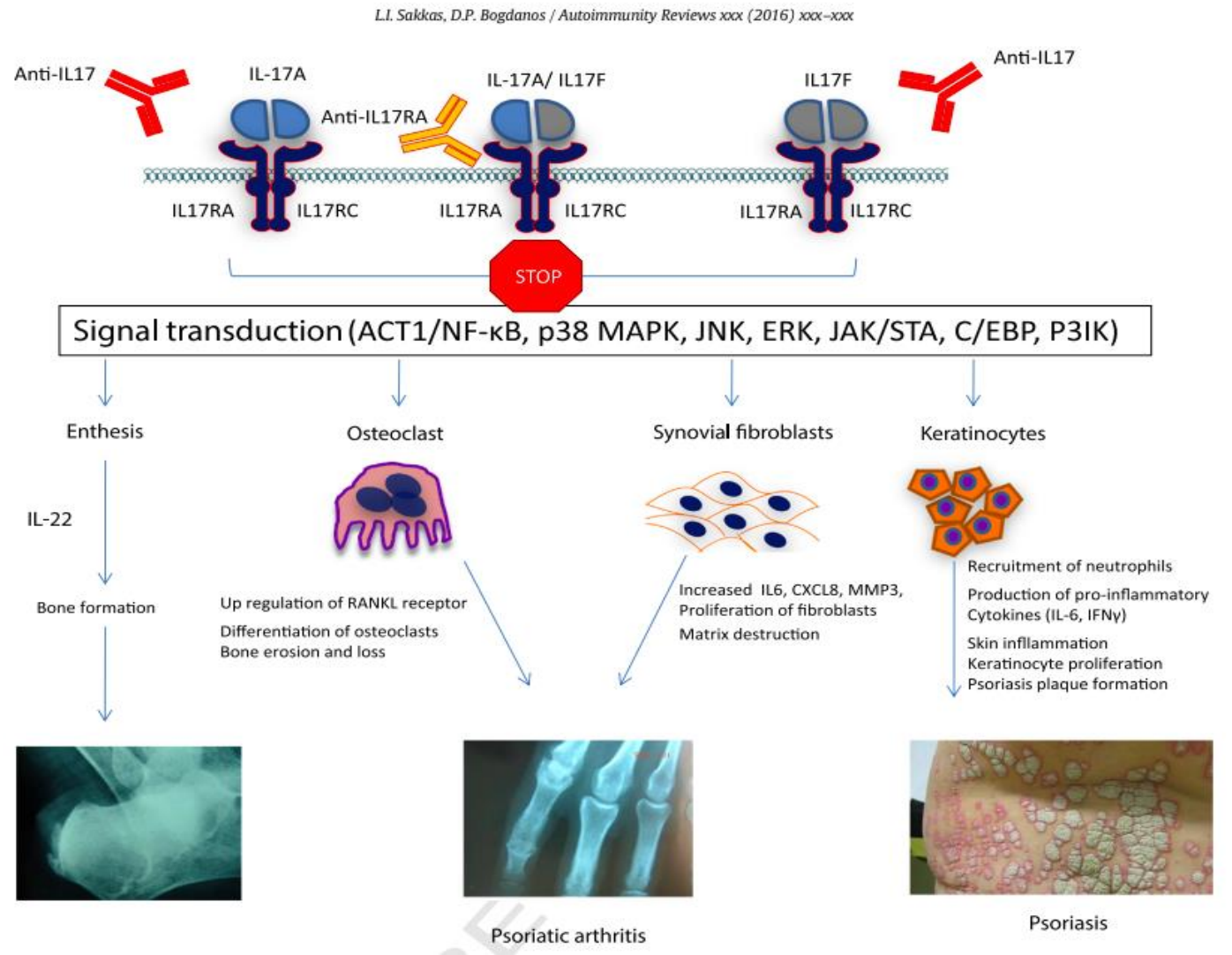
Montoya LG, et al. Ther Adv Musculoskel Dis 2018; 10(9) 169–180

Η οικογένεια της IL-17

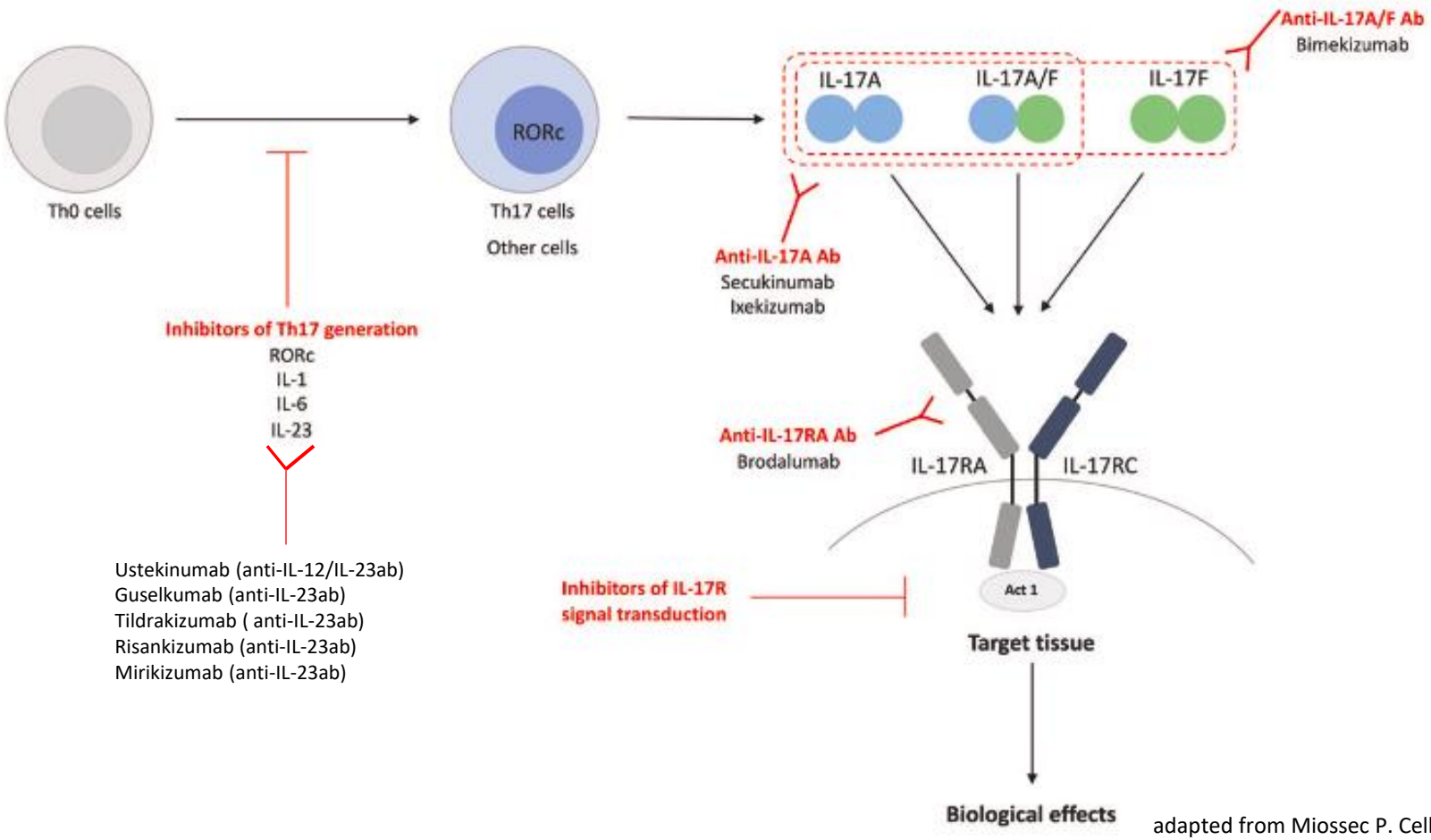


Brembilla NC, et al. Frontiers in Immunology 2018; 9: 1682

Ο ρόλος της IL-17 στην παθοφυσιολογία της ψωρίασης και ψωριασικής αρθρίτιδας

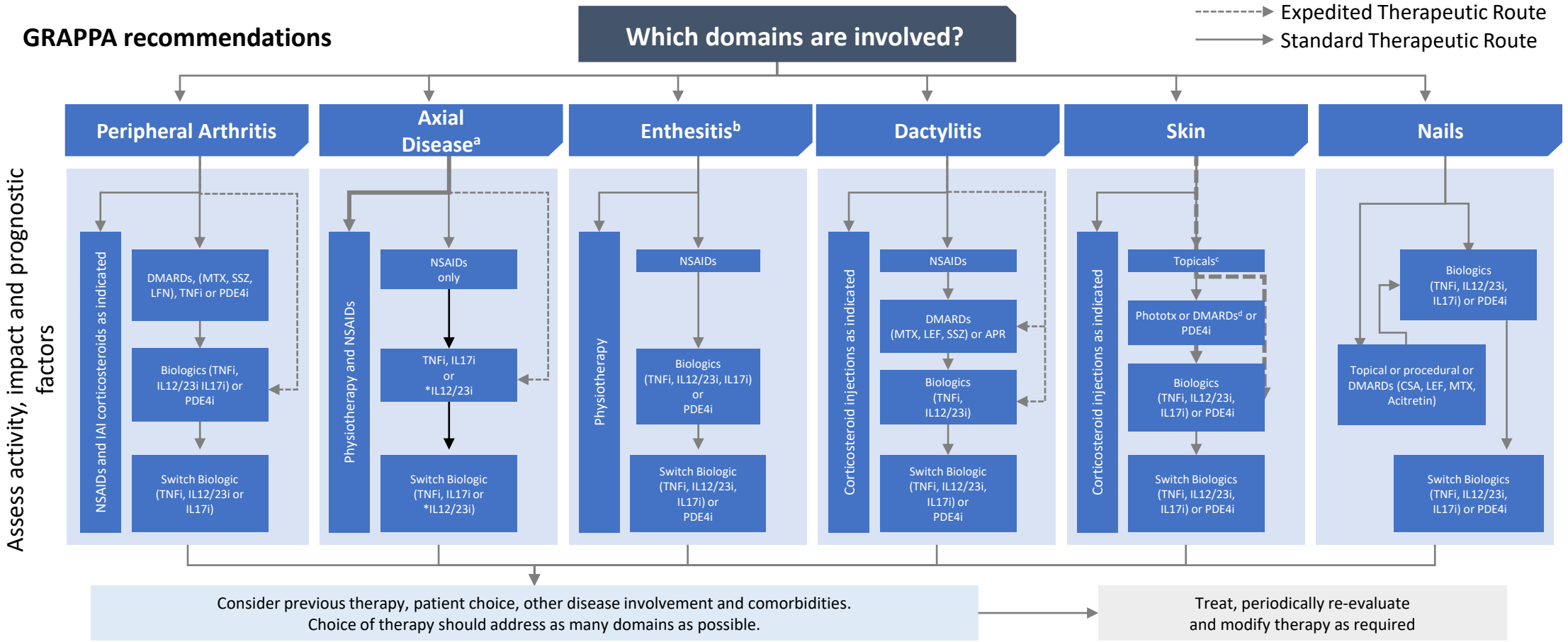


Άμεση κι έμμεση αναστολή της Il-17



adapted from Miossec P. Cellular & Molecular Immunology 2021; 18:860 – 8

Η αξιολόγηση όλων των σημείων και συμπτωμάτων είναι βασική για τη διαχείριση της Ψωριασικής Αρθρίτιδας

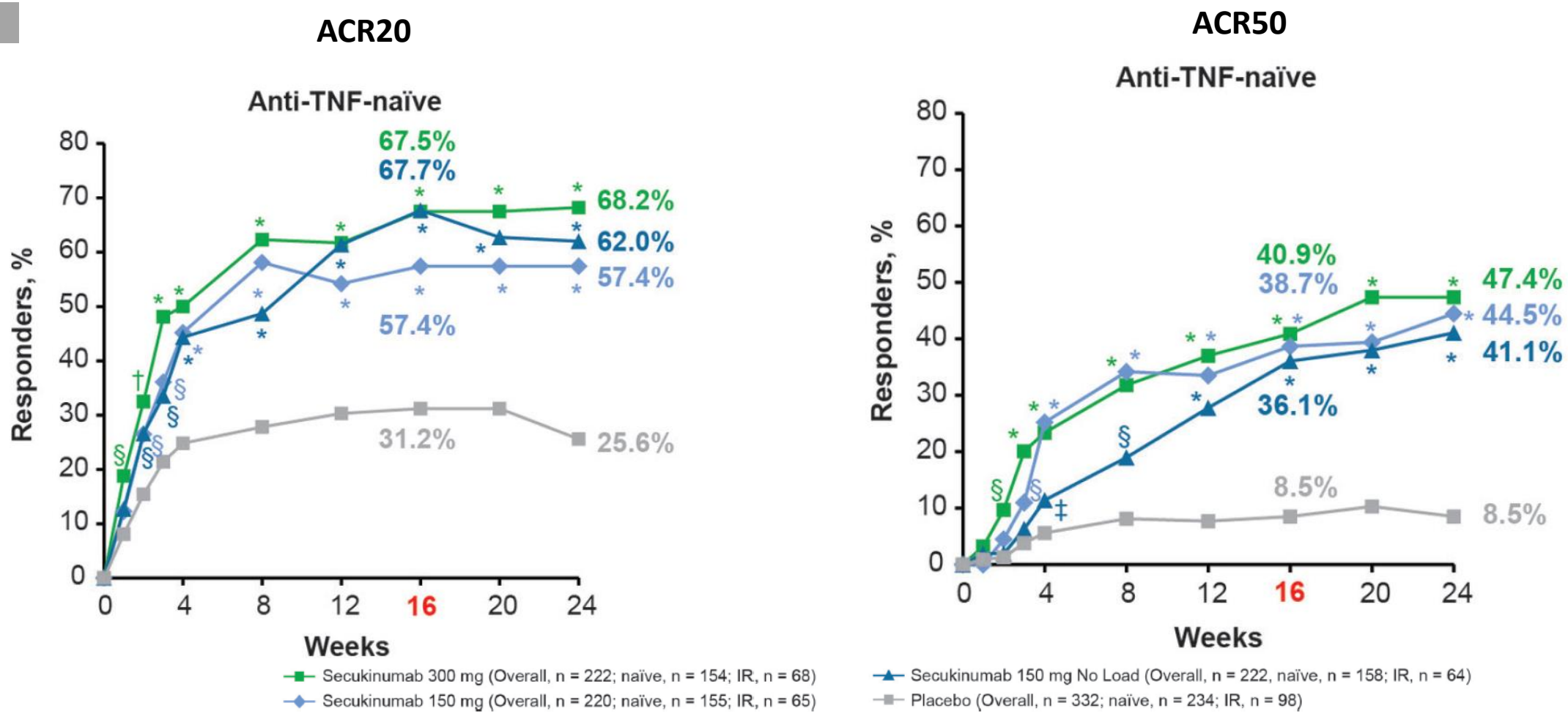


CSA, cyclosporine A; DMARD, disease-modifying anti-rheumatic drug; IAI, intra-articular injection; IL12/23i, interleukin 12/23 inhibitor; IL17i, interleukin 17 inhibitor; LFN, leflunomide; MTX, methotrexate; NSAID, non-steroidal anti-inflammatory drug; PDE4i, phosphodiesterase 4 inhibitor; phototx, phototherapy; SSZ, sulfasalazine; TNFi, tumor necrosis factor inhibitor. [a]No direct evidence for therapies in axial PsA, recommendations based on axial SpA literature; [b]Corticosteroid injections: consider on an individual basis due to potential for serious side effects; no clear evidence for efficacy; [c]Keratolytics, steroids, vitamin D analogues, emollients calcineurini; [d]MTX, CSA Acitretin, Fumaric acid esters

Coates LC, et al. *Arthritis Rheumatol.* 2016;68:1060–71.

>50% των πρωτοθεραπευόμενων ασθενών με secukinumab πέτυχαν ταχεία ανταπόκριση κατά ACR20 ήδη από τις 4 εβδομάδες θεραπείας

FUTURE 5



ACR20 & ACR50 response rates from baseline up to week 24 in anti-TNF naive. *P<0.0001; †p<0.001; §p<0.01; ‡p<0.05 unadjusted p values versus placebo (Statistical analysis was based on logistic regression. Missing values and placebo patients rescued at week 16 were imputed as non-responders.) aThe primary endpoint was ACR20 response in the overall population at week 16. ACR20/50/70, ≥20/50/70% improvement from baseline in American College of Rheumatology response criteria.

Mease P, et al. Ann Rheum Dis 2018;77:890–897. doi:10.1136/annrheumdis-2017-212687

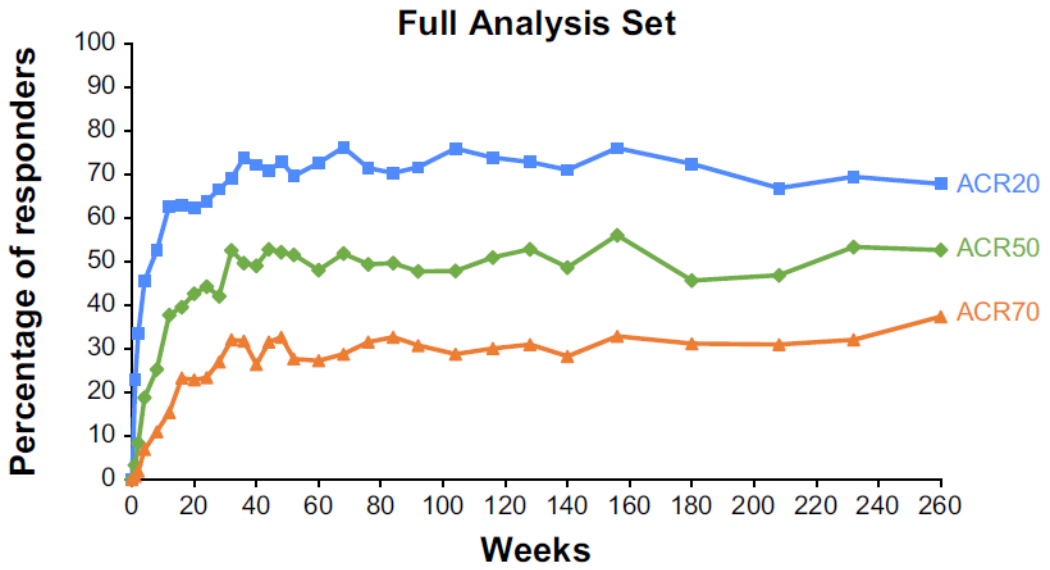
*Ομάδα ασθενών που είχαν λάβει προηγουμένως έως 3 αντι-TNF παράγοντες

>50% των σε θεραπεία με secukinumab πέτυχαν και διατήρησαν ανταπόκριση κατά ACR50 έως τα 5 έτη θεραπείας

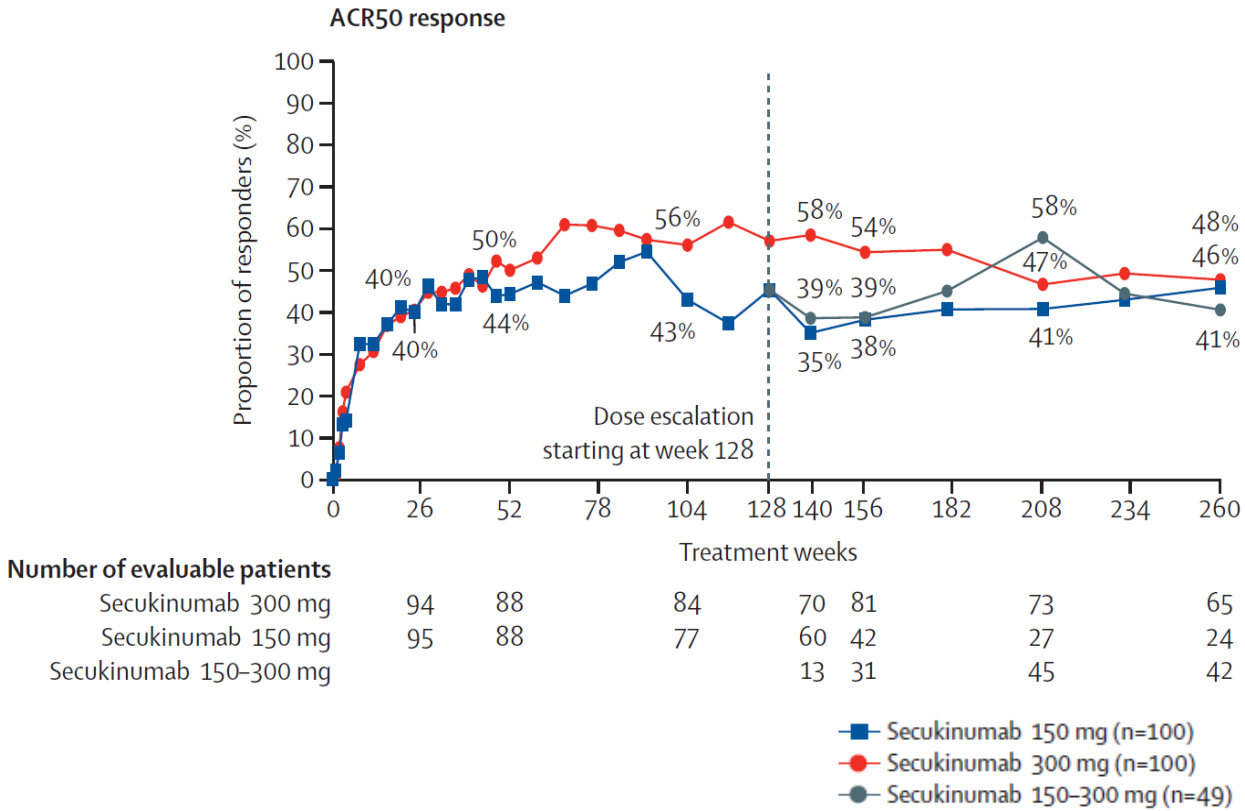
FUTURE 1 & FUTURE 2

FUTURE 1 (n=606 @ BL), 1/3 had IR to prior anti-TNF (up to 3 TNFi)
- At wk 104, 460 patients entered the 3-year extension study
- 132/161 (82%) of those who were originally randomised to secukinumab 150 mg, completed 5 years treatment
- Data are reported as observed.

FUTURE 2 (n=397 @ BL), 35% had IR to prior anti-TNF (up to 3 TNFi)
- The study was designed as 5-yr study from the beginning
- 248/397 (>62%) of those who were originally randomised to secukinumab 75 mg, 150 mg, or 300 mg completed 5 years treatment
- Data are reported as observed.



Dose received	1	52	104	156	180	208	232	260
150 mg	153	155	146	155	137	126	87	74
150 → 300 mg	0	0	0	0	1	19	44	57



Number of evaluable patients							
Secukinumab 300 mg	94	88	84	70	81	73	65
Secukinumab 150 mg	95	88	77	60	42	27	24
Secukinumab 150–300 mg				13	31	45	42

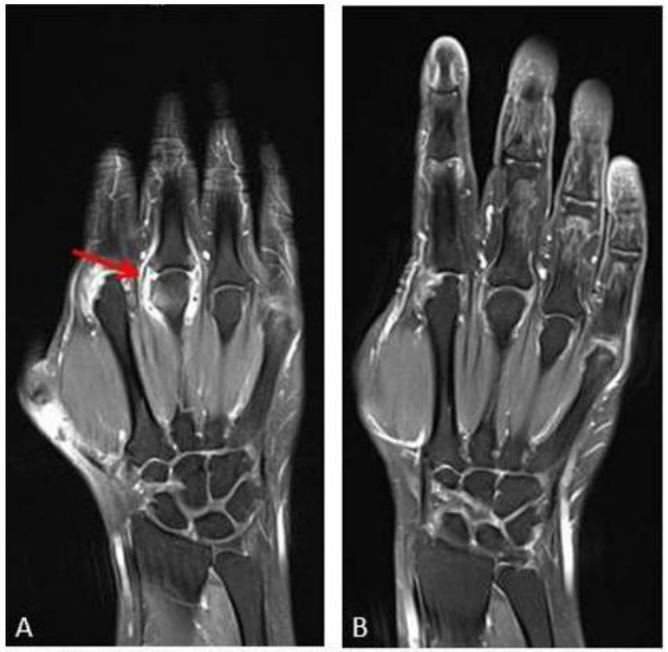
Secukinumab 150 mg (n=100)
Secukinumab 300 mg (n=100)
Secukinumab 150–300 mg (n=49)

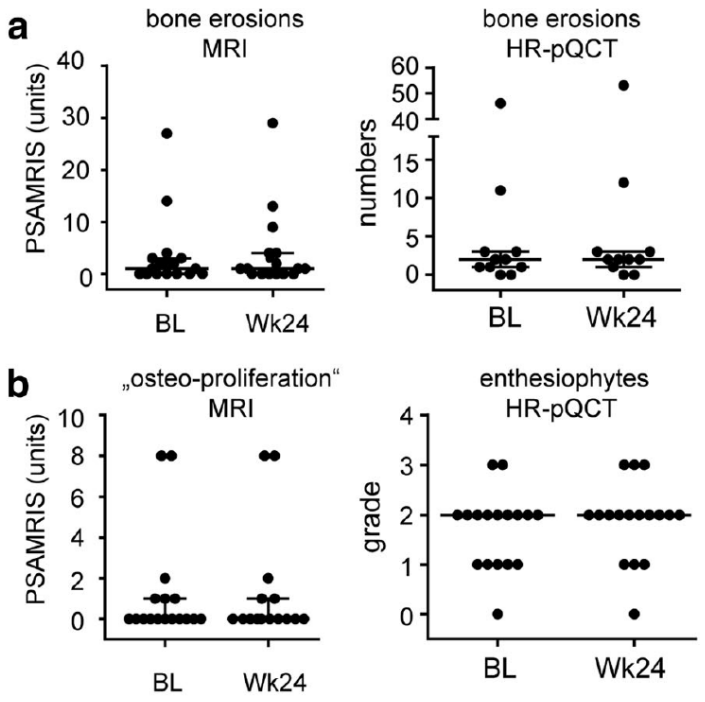
Observed data presented through 260 weeks. ACR 20/50/70, American College of Rheumatology criteria for 20%/50%/70% improvement in disease activity; Original randomised treatment groups shown and include patients who had dose escalation from 150 mg to 300 mg based on physician's judgement from Week 128 or 156 onwards

Mease PJ, et al. *ACR Open Rheumatology*, Vol. 0, No. 0, Month 2019, pp 1–8. DOI:10.1002/acr2.11097; McInnes et al., Lancet Rheumatol 2020;2: e227–35

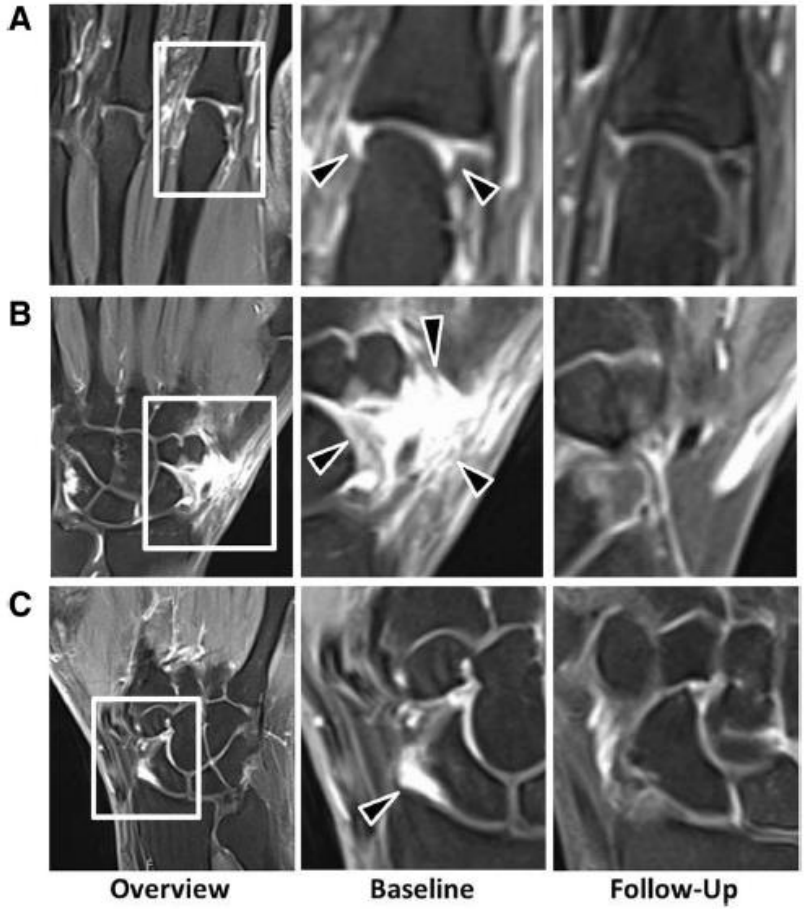
Η σεκουκινουμάμπη βελτιώνει σημαντικά τα ευρήματα σε MRI και US της φλεγμονής των αρθρώσεων σε ασθενείς με ΨΑ

PSARTROS





IVEPSA



A. Baseline coronal T1W fs pos-Gd image shows synovial and periarticular thickness and enhancement (arrow), indicating active synovitis and periarticular inflammation.
B. B. follow up image after 24 weeks treatments shows resolution of the periarticular inflammation and only residual synovial enhancement.

BMP, bone morphogenic proteins; IL-22, interleukin 22; PTHrP, parathyroid hormone related-peptide; MSC, mesenchymal stem cell
E. Kampylafka, et al. Poster FRI0625 EULAR, Madrid, 14-17 June 2017; Kampylafka et al. Arthritis Research & Therapy (2019) 21:178.

Αναστολή της ακτινογραφικής εξέλιξης σε >80% των ασθενών με ενεργό ΨΑ σε θεραπεία με secukinumab

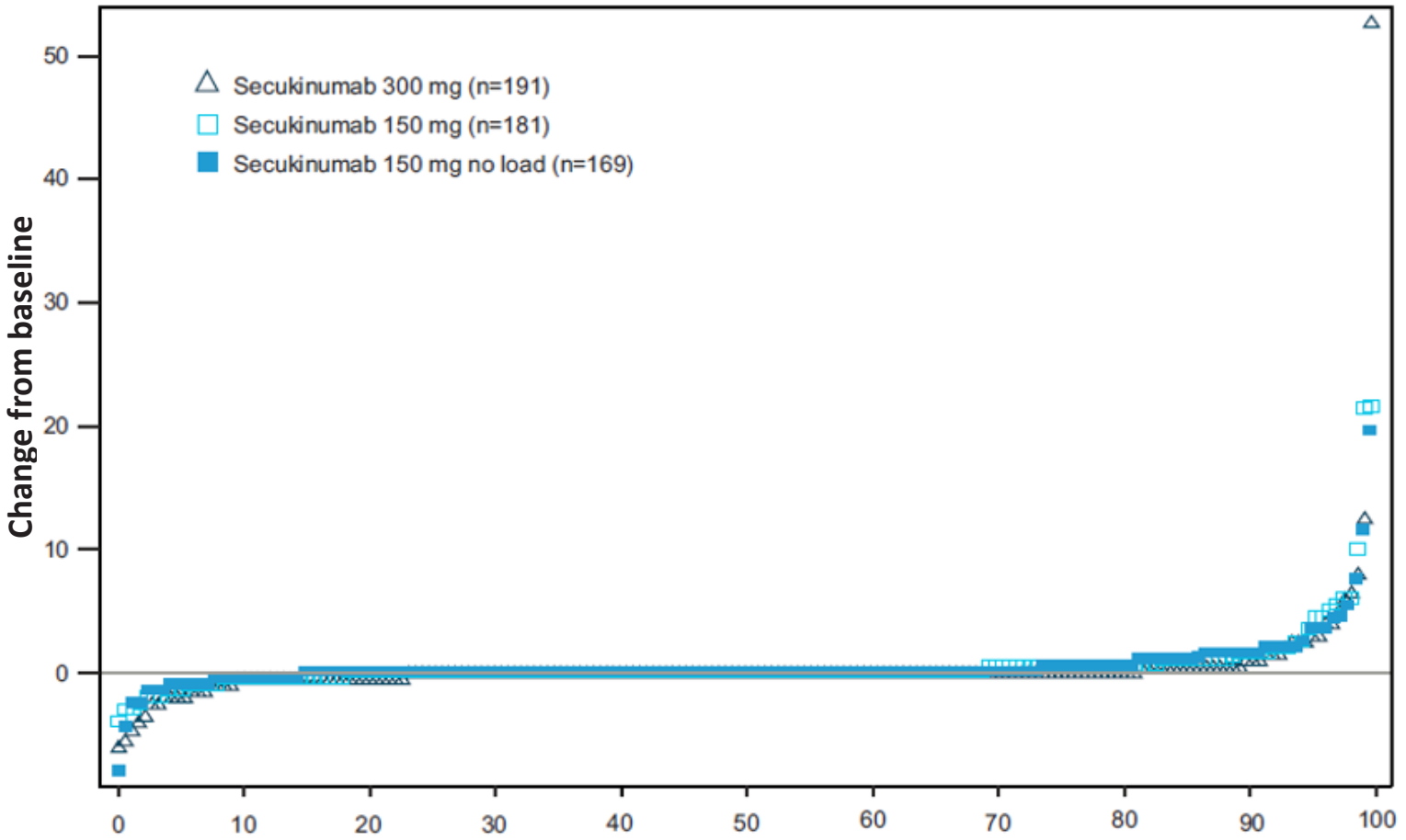
FUTURE 5

Proportion of patients with no radiographic progression at 2 years:

*Change from baseline in mTSS ≤0.5: **89.5%** (300 mg), **82.3%** (150 mg), and **81.1%** (150 mg no load)*

*Change from baseline in mTSS ≤0.0: **81.2%** (300 mg), **69.1%** (150 mg) and **73.4%** (150 mg no load)*

Cumulative probability plot (vdH-mTSS change from baseline)

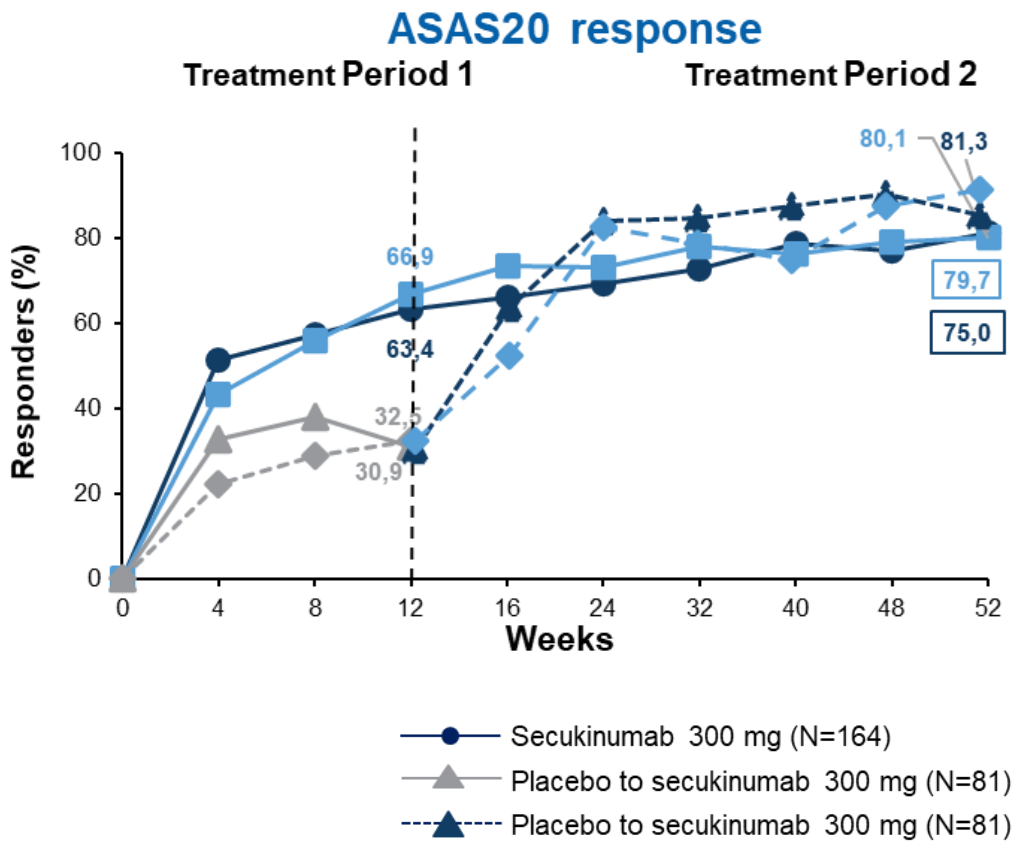


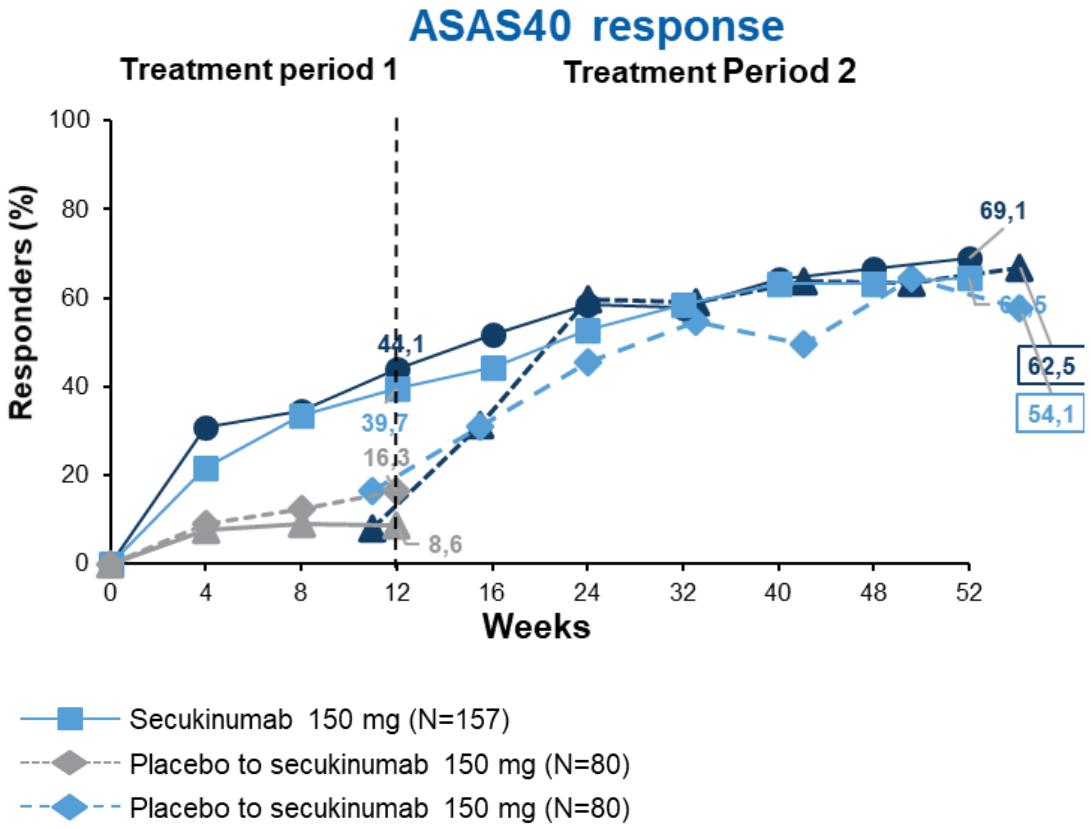
150 mg and 150 mg no load groups included 77 and 79 patients with radiographic results, respectively, who had dose escalation at Week 52 or later
TNF-IR, TNF-inadequate response. One anti-TNF-IR patient in 300 mg group is an outlier. mTSS change from baseline is 52.67

Mease PJ, et al. RMD Open 2021;7:e001600. doi:10.1136/rmdopen-2021-001600

>60% των ασθενών πέτυχε ανταπόκριση ASAS20, κλινικά σημαντική, ήδη από την εβδομάδα 12 θεραπείας με σεκουκινουμάμπη

MAXIMISE



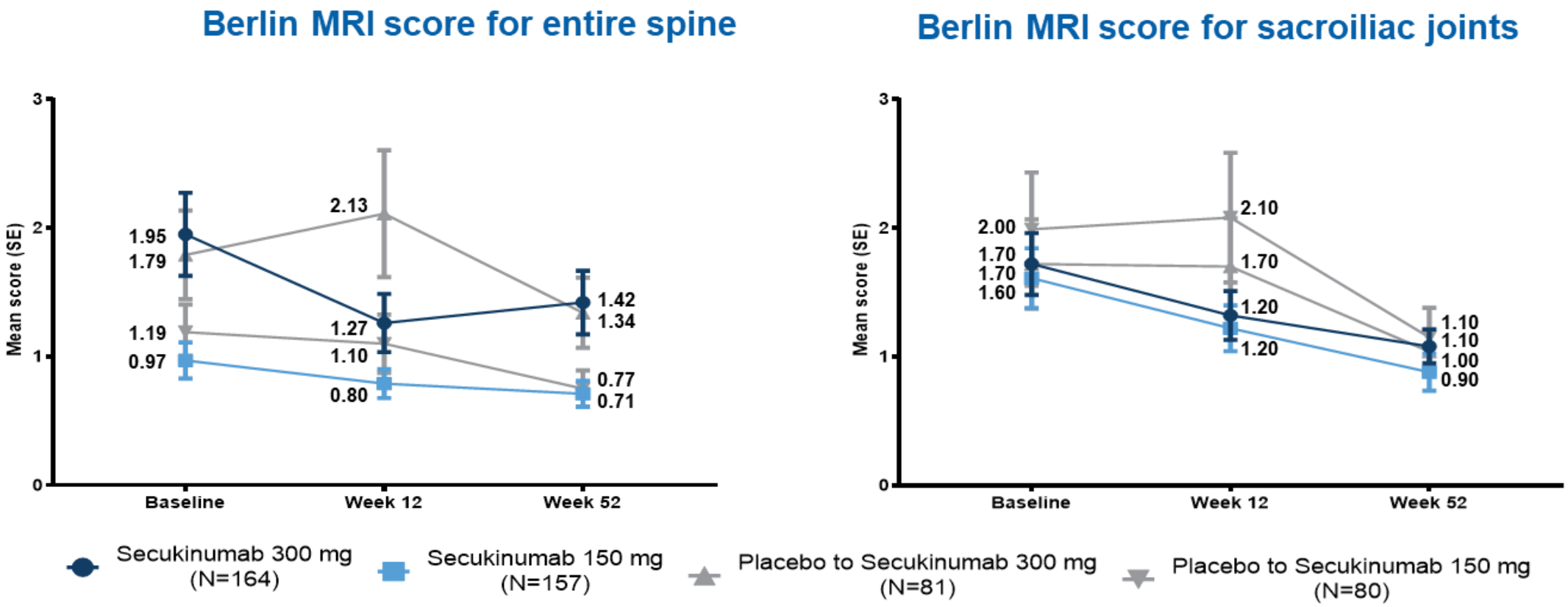


*Full Analysis Set, as observed;
ASAS, Assessment of Spondyloarthritis international Society

Baraliakos X, et al. Ann Rheum Dis 2021;80:582–590.

Η σεκουκινουμάμπη μείωσε τη φλεγμονή τόσο στην ΣΣ όσο και στις ιερολαγόνιες αρθρώσεις (σύμφωνα με το total Berlin MRI score)

MAXIMISE

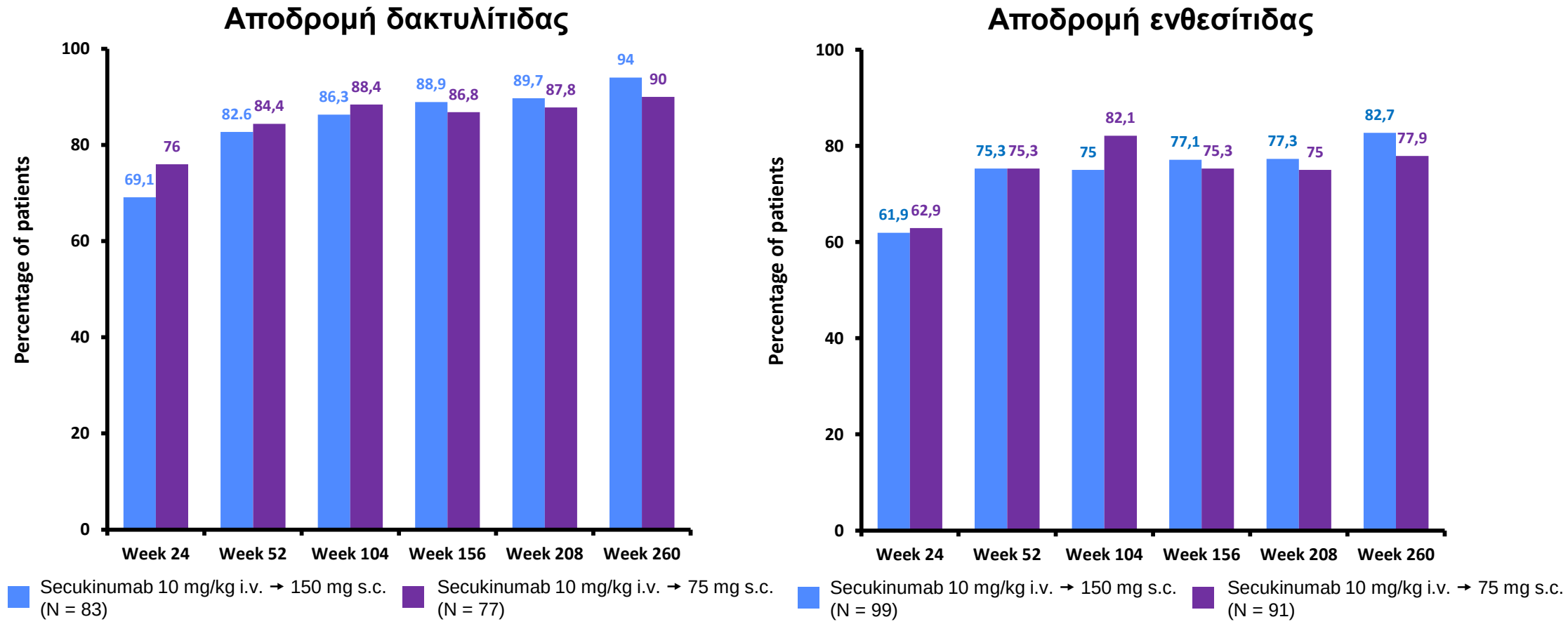


*Full Analysis Set.
MRI, magnetic resonance imaging; SI, sacroiliac

Baraliakos X, et al. Ann Rheum Dis 2021;80:582–590.

Αποδρομή δακτυλίτιδας και ενθεσίτιδας με διατήρηση της αποτελεσματικότητας έως τα 5 έτη σε ασθενείς σε θεραπεία με secukinumab

FUTURE 1

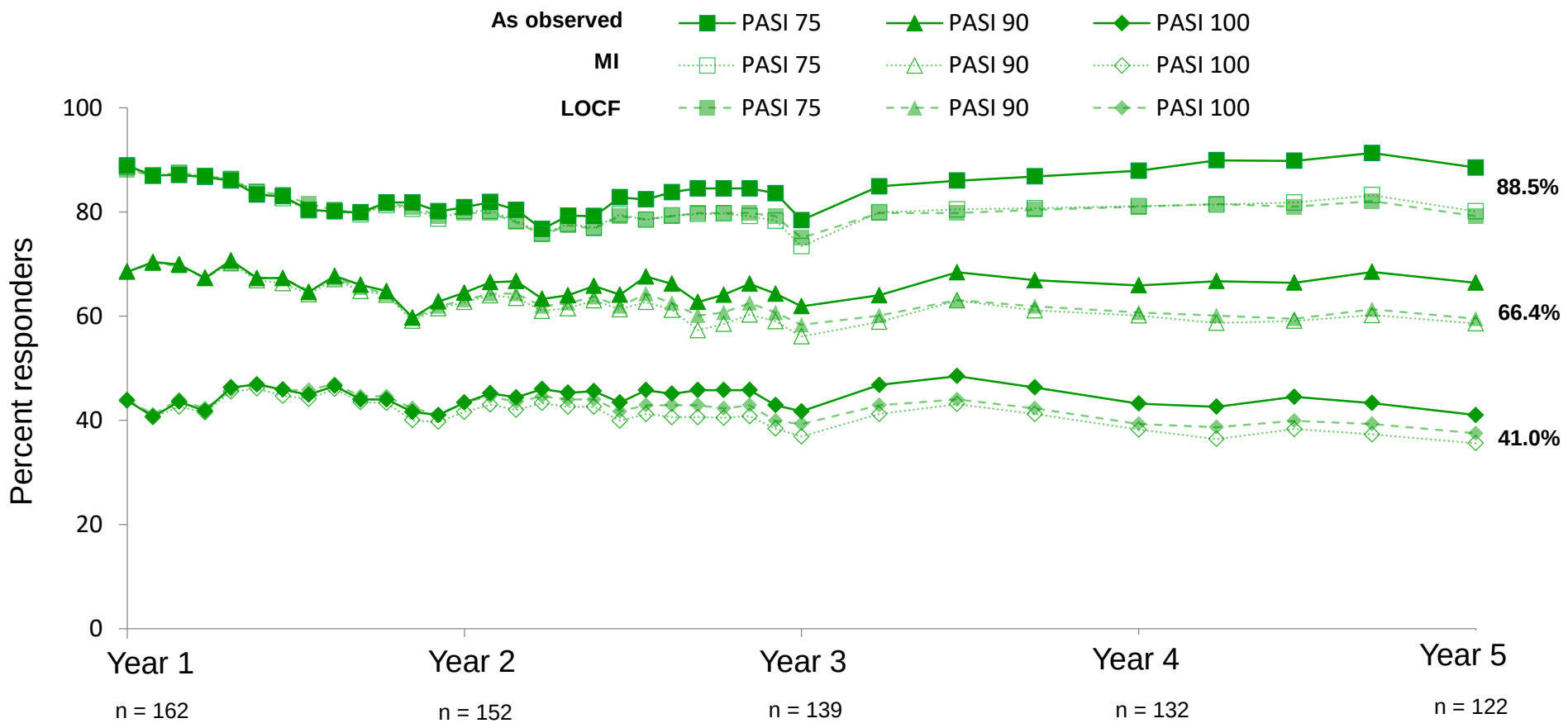


Original randomized patients who had these symptoms at baseline are shown. Includes patients who had dose escalation from 75mg to 150/300 mg, and from 150 mg to 300 mg based on physician's judgement from Week 156 onwards.

Mease, et al. ACR/ARHP Annual Meeting 2018, Chicago, United States, Oct 19–24, 2018, #2568; Mease PJ, et al. ACR Open Rheumatology, Vol. 0, No. 0, Month 2019, pp 1–8. DOI:10.1002/acr2.11097;
McInnes et al., Lancet Rheumatol 2020;2: e227–35

Σημαντικές και παρατεταμένες βελτιώσεις της δερματικής προσβολή σε ασθενείς με ψωρίαση έως τα 5 έτη θεραπείας με σεκουκινουμάμπη

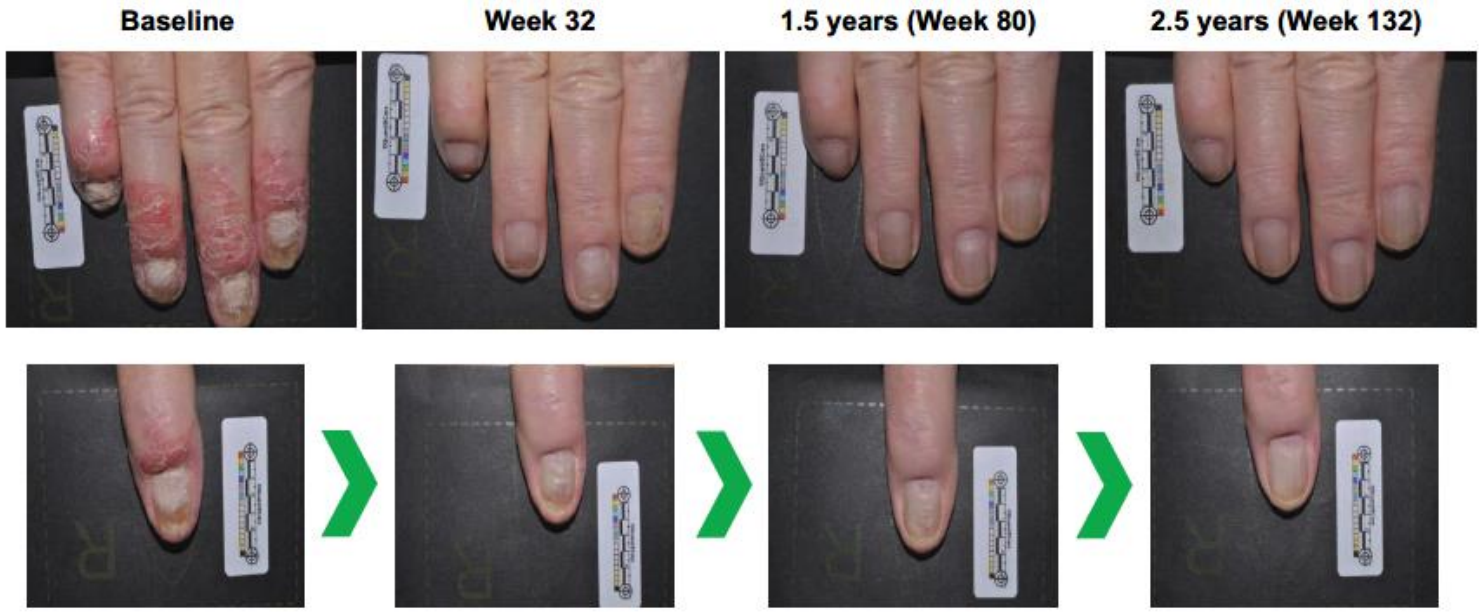
SCULPTURE

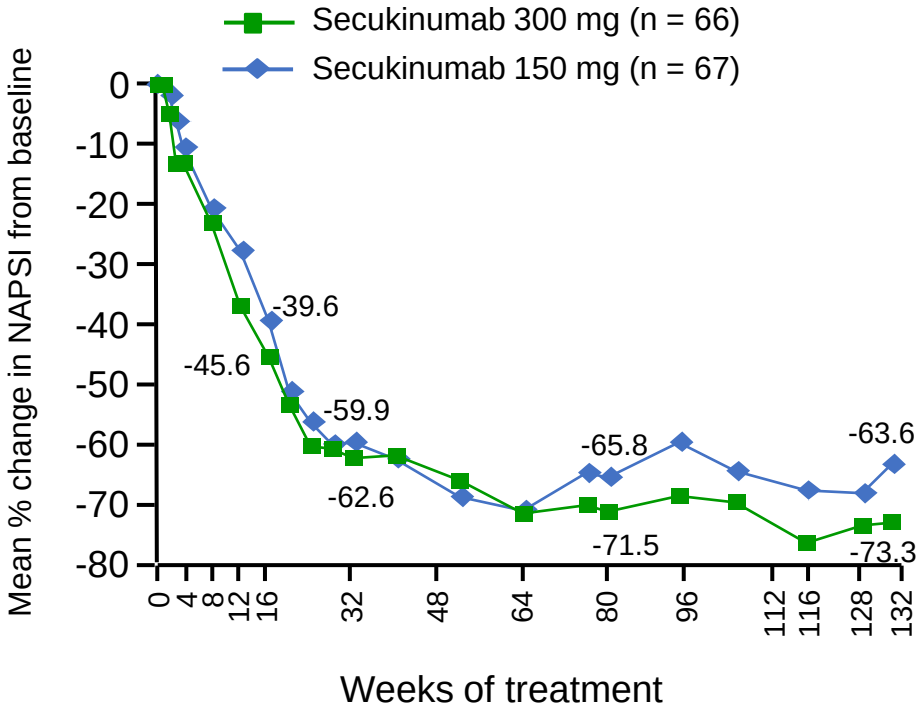


- Bissonette R, et al. J Eur Acad Dermatol Venereol. 2018; 32(9): 1507–1514.
- LOCF, last observation carried forward; MI, multiple imputation; n, number of evaluable patients in the as observed analysis (the number of evaluable patients in the MI and LOCF analyses was 168 at each time point); PASI, Psoriasis Area and Severity Index score.

Σημαντικές και παρατεταμένες βελτιώσεις κατά NAPSI σε ασθενείς με ψωριασική ονυχία έως τα 2,5 έτη θεραπείας με σεκουκινουμάμπη

TRANSFIGURE





- NAPSI, Nail Psoriasis Severity Index.
  Images from a representative patient receiving secukinumab 300 mg in the trial over time.
  Long-term data are as observed.

- Reich K, et al. Br J Dermatol . 2021;184(3):425-436

Τα ανεπιθύμητα συμβάντα ήταν συγκρίσιμα σε όλες τις ενδείξεις χωρίς κάποιο νέο σήμα ασφάλειας

Table II. Summary of pooled safety data from secukinumab clinical trials

Characteristic	Psoriasis Any secukinumab N = 8,819	Psoriatic arthritis Any secukinumab N = 2,678	Ankylosing spondylitis Any secukinumab N = 1,140
Exposure (days), mean (SD)	623.9 (567.7)	816.2 (580.7)	1,130.1 (583.0)
Exposure (days), median (min–max)	366.0 (1.0–1,982.0)	671.0 (8.0–1,984.0)	1,037.0 (1.0–1,991.0)
Death, *n* (%)	14 (0.2)	11 (0.4)	9 (0.8)
Discontinuations due to adverse events, *n* (%)	466 (5.3)	162 (6.0)	88 (7.7)
Exposure-adjusted incidence rate/100 PY (95% CI)			
Any adverse event	224.9 (219.8, 230.1)	159.2 (152.7, 166.0)	125.5 (117.8, 133.5)
Any serious adverse event	7.0 (6.6, 7.5)	8.2 (7.4, 9.0)	5.8 (5.0, 6.7)
Most common adverse events, IR (95% CI)			
Nasopharyngitis	22.6 (21.8, 23.5)	11.6 (10.7, 12.6)	10.7 (9.48, 12.0)
Headache	7.3 (6.8, 7.8)	3.8 (3.3, 4.4)	3.8 (3.2, 4.6)
Diarrhoea	4.2 (3.9, 4.6)	3.9 (3.4, 4.5)	4.0 (3.3, 4.7)
Upper respiratory tract infection	5.3 (4.9, 5.7)	8.8 (8.0, 9.6)	4.5 (3.8, 5.3)
Adverse events of special interest, IR (95% CI)			
Serious infections[a]	1.4 (1.2, 1.6)	1.8 (1.5, 2.2)	1.2 (0.9, 1.6)
Candida infections[b]	2.9 (2.7, 3.2)	1.5 (1.2, 1.9)	0.7 (0.5, 1.1)
Opportunistic infections[c]	0.19 (0.1, 0.3)	0.18 (0.1, 0.3)	0.14 (0.1, 0.3)
Inflammatory bowel disease[d]	0.01 (0.0, 0.1)	0.03 (0.0, 0.1)	0.03 (0.0, 0.2)
Crohn's disease[d]	0.1 (0.05, 0.2)	0.1 (0.04, 0.2)	0.4 (0.2, 0.7)
Ulcerative colitis[d]	0.1 (0.08, 0.2)	0.1 (0.04, 0.2)	0.2 (0.1, 0.5)
Major adverse cardiovascular event[e]	0.4 (0.3, 0.5)	0.4 (0.3, 0.6)	0.7 (0.4, 1.0)
Uveitis[d]	0.01 (0.0, 0.05)	0.1 (0.04, 0.2)	1.2 (0.9, 1.7)
Malignancy[f]	0.9 (0.7, 1.0)	1.0 (0.77, 1.3)	0.5 (0.3, 0.8)

[a]Rates for system organ class. [b]Rates for high-level terms. [c]Opportunistic infections were bronchopulmonary aspergillosis, cytomegalovirus gastroenteritis, gastrointestinal candidiasis, herpes zoster cutaneous disseminated, herpes zoster infection neurological, mycobacterium avium complex infection, oesophageal candidiasis, pneumocystis jirovecii pneumonia, toxoplasmosis, tuberculosis. [d]Rates for preferred terms. [e]Rates for Novartis Medical Dictionary for Regulatory Activities (MedDRA) query terms. [f]Rates for standardized MedDRA query terms – "malignancies and unspecified tumour".
CI: confidence interval; IR: incidence rate; N: total number of patients per group; *n*: number of patients with an event; PY: patient-years; SD: standard deviation.

Gottlieb AB, et al. *Acta Derm Venereol*. 2022. doi: 10.2340/actadv.v102.563.

SERENA

Μελέτη SERENA: Υψηλό ποσοστό παραμονής στη θεραπεία με σεκουκινουμάμπη για ασθενείς με ΨΑ και ΑΣ στην καθημερινή κλινική πρακτική στα 2 έτη θεραπείας

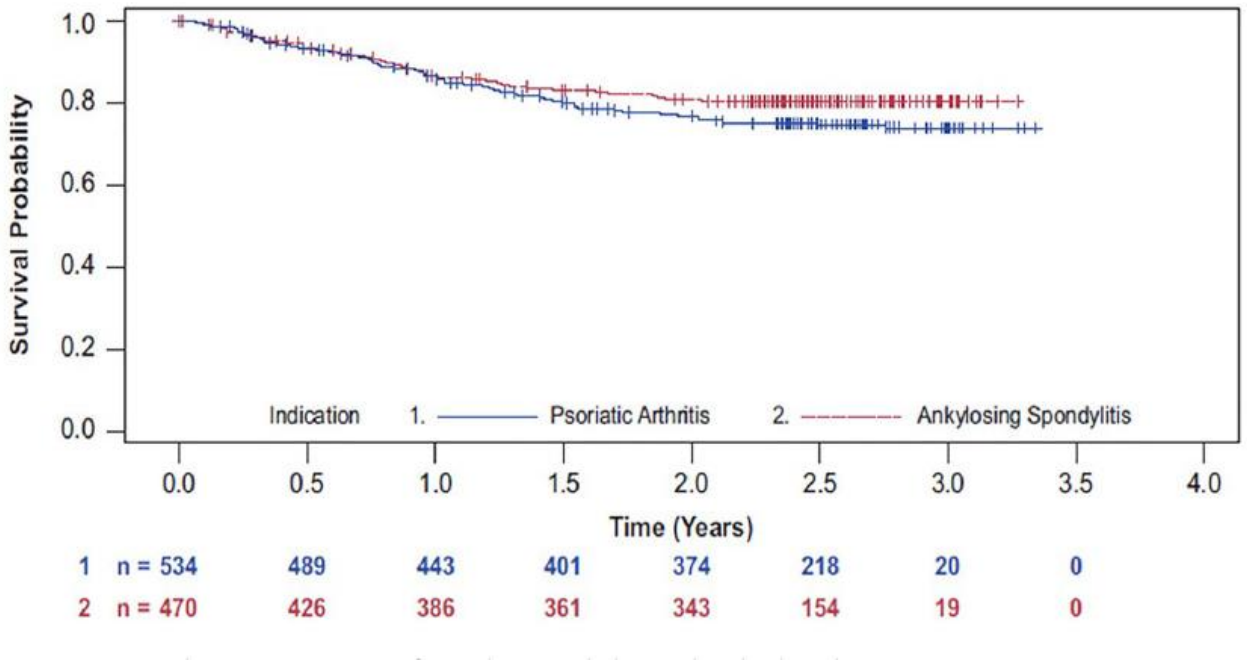


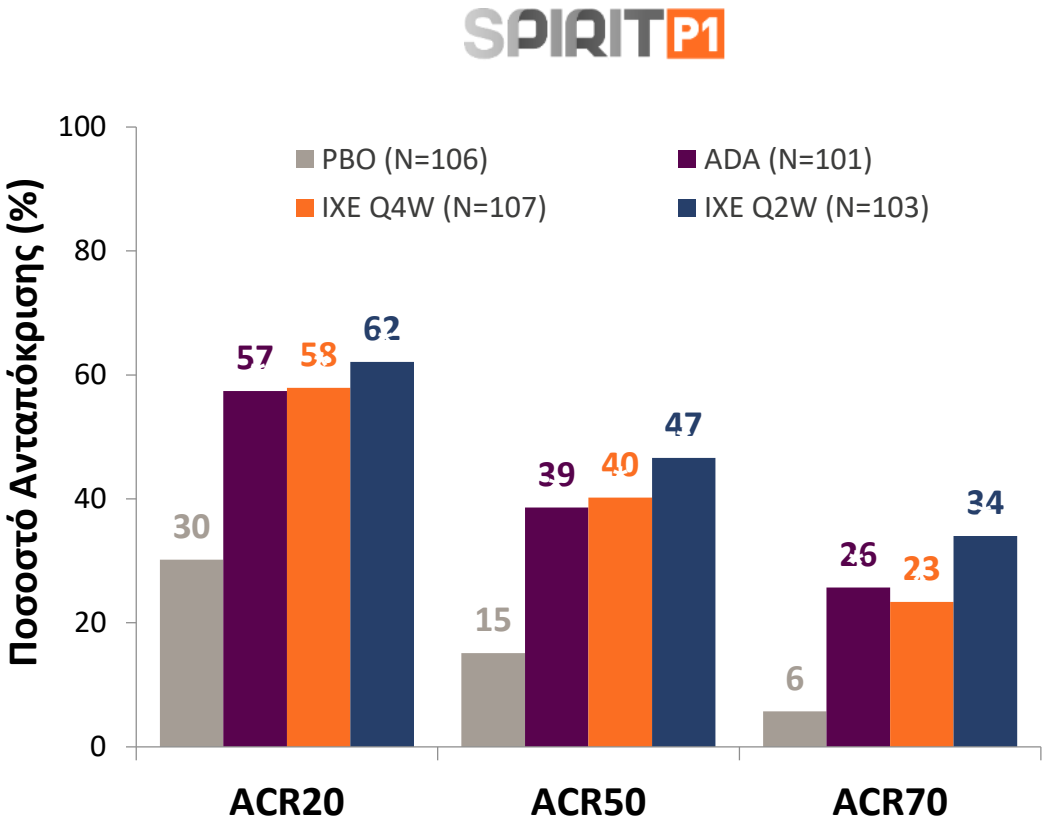
Table 2 Efficacy responses with secukinumab in PsA and AS cohort up to 2 years

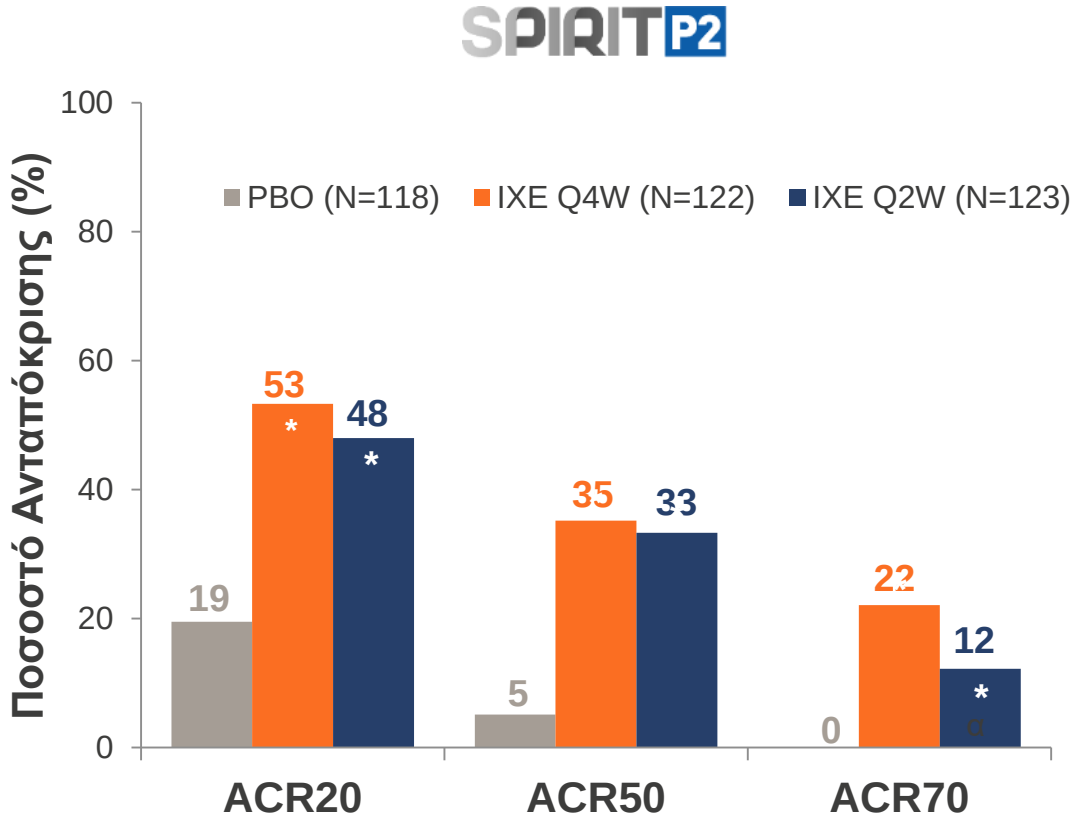
Endpoints	Baseline	Year 1	Year 2
PsA (N = 534)			
Swollen joint count, mean ± SD (M)	3.3 ± 5.8 (203)	2.7 ± 4.6 (164)	2.9 ± 5.8 (105)
Tender joint count, mean ± SD (M)	6.3 ± 9.4 (203)	6.5 ± 9.7 (165)	5.6 ± 7.2 (105)
Presence of dactylitis, n/M (%)	33/519 (6.4)	15/422 (3.6)	12/298 (4.0)
Presence of enthesitis, n/M (%)	54/278 (19.4)	39/281 (13.9)	28/183 (15.3)
Total pain (VAS 0–100), mean ± SD (M)	31.9 ± 24.4 (431)	31.0 ± 25.3 (370)	28.4 ± 24.2 (245)
PGA 0/1 response, n/M (%)	197/307 (64.2)	216/303 (71.3)	152/191 (79.6)
Nail involvement, n/M (%)	96/521 (18.4)	44/419 (10.5)	32/300 (10.7)
HAQ-DI, mean ± SD (M)	0.84 ± 0.71(398)	0.82 ± 0.71 (313)	0.77 ± 0.68 (208)
FACIT Fatigue, mean ± SD (M)	34.2 ± 11.4(399)	34.4 ± 12.1 (310)	36.6 ± 10.5 (205)

Η σεκουκινουμάμπη επέδειξε υψηλά ποσοστά παραμονής στη θεραπεία, καλή και διατηρημένη αποτελεσματικότητα και ευνοϊκό προφίλ ασφάλειας χωρίς νέα σήματα ασφάλειας

Rheumatol Ther (2022) 9:1129–1142

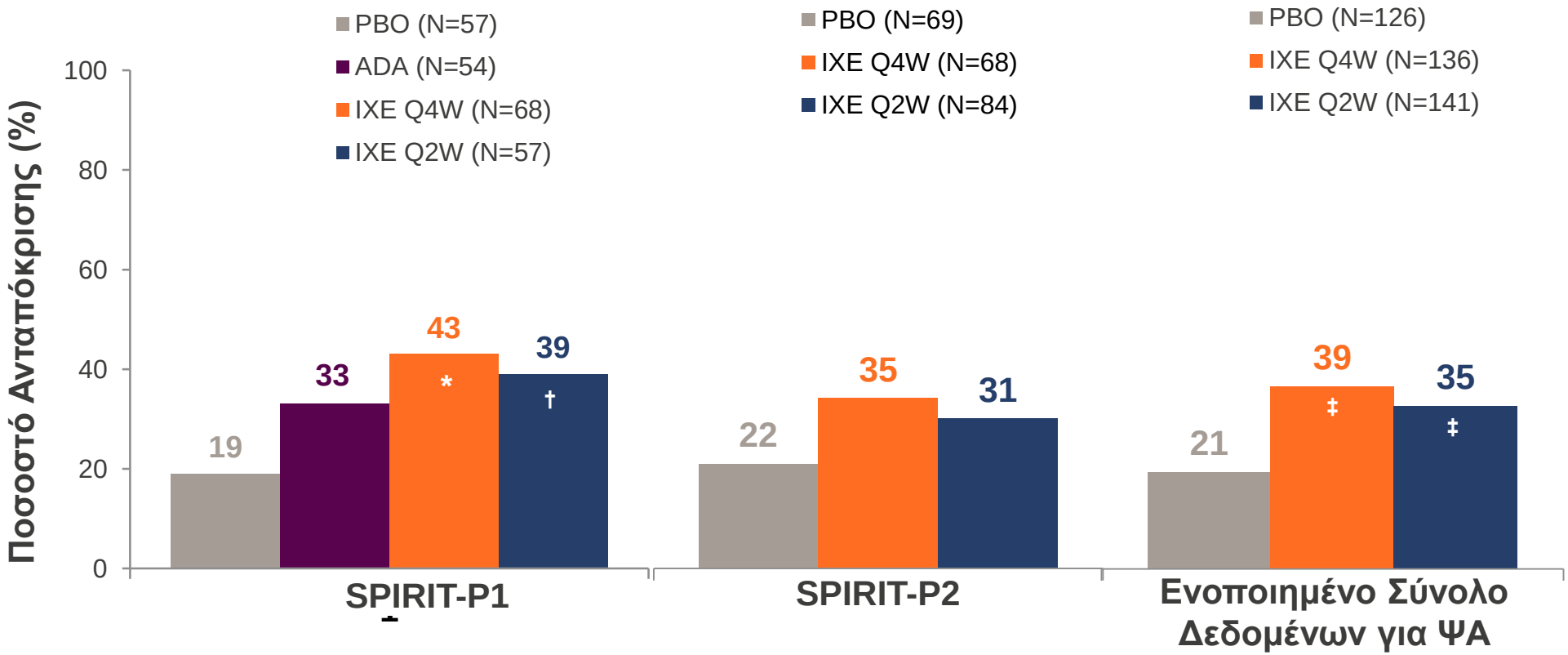
Σημαντικά περισσότεροι ασθενείς που έλαβαν θεραπεία με το ixekizumab πέτυχαν ανταπόκριση ACR έναντι εκείνων που έλαβαν εικονικό φάρμακο την Εβδομάδα 24





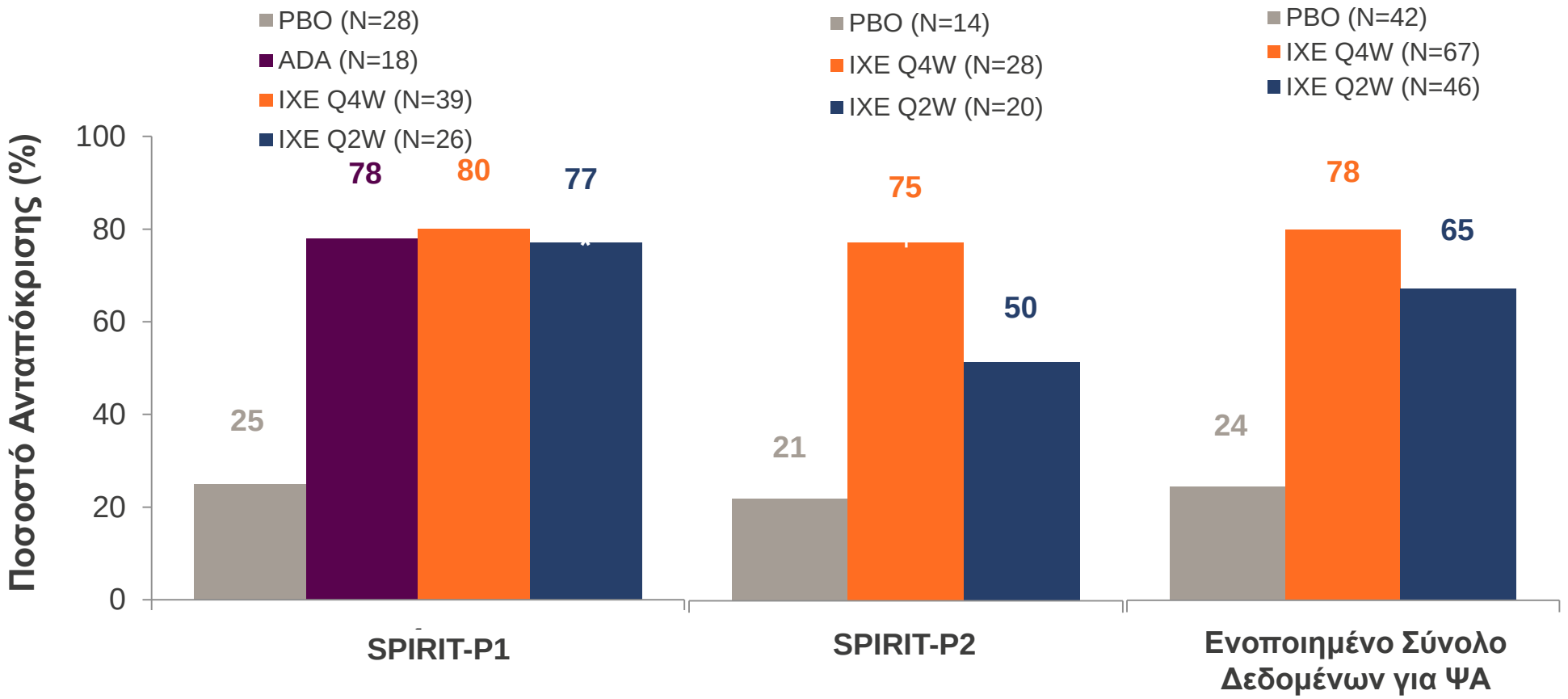
*p≤0,001 έναντι του PBO.
Η ADA αντιπροσωπεύει έναν δραστικό παράγοντα αναφοράς. Η μελέτη δεν είχε ισχύ για τον έλεγχο της ισοδυναμίας ή της μη κατωτερότητας των ομάδων δραστικής θεραπείας μεταξύ τους, συμπεριλαμβανομένων του IXE έναντι της ADA.
1. Mease PJ, et al. *Ann Rheum Dis*. 2017;76:79-87. 2. Nash P, et al. *Lancet*. 2017;389:2317-2327.

>30% των ασθενών που λάμβαναν θεραπεία με το ixekizumab εμφάνισαν υποχώρηση της ενθεσίτιδας (LEI=0) την Εβδομάδα 24



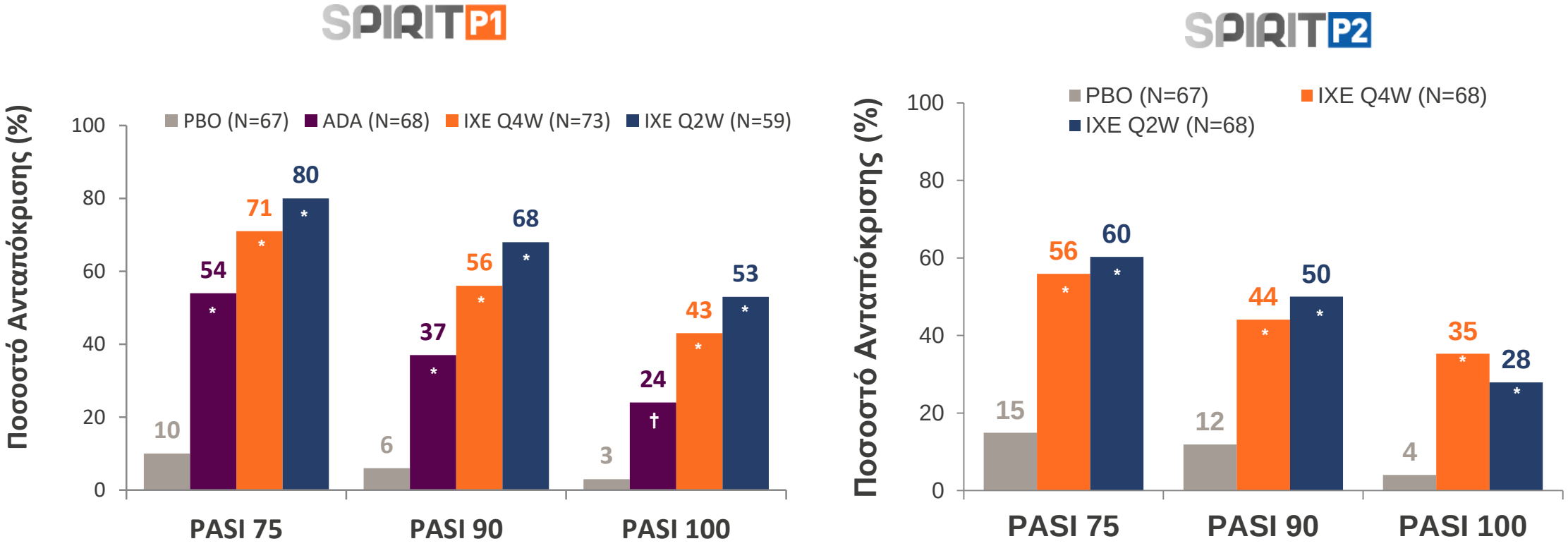
*p≤0,01 έναντι PBO, †p≤0,025 έναντι PBO, ‡p<0,05 έναντι PBO με τη χρήση ανάλυσης λογιστικής παλινδρόμησης.
ADA αντιπροσωπεύει έναν δραστικό παράγοντα αναφοράς. Η μελέτη δεν είχε ισχύ για τον έλεγχο της ισοδυναμίας ή της μη κατωτερότητας των ομάδων δραστικής θεραπείας μεταξύ τους, συμπεριλαμβανομένων του IXE έναντι της ADA.
1. Mease PJ, et al. *Ann Rheum Dis*. 2017;76:79-87. 2. Nash P, et al. *Lancet*. 2017;389:2317-2327. 3. Gladman DD, et al. *Arthritis Res Ther*. 2019;21:38.

Περισσότεροι ασθενείς που έλαβαν θεραπεία με ixekizumab εμφάνισαν υποχώρηση της δακτυλίτιδας και στις δύο μελέτες, σε σύγκριση με εκείνους τους ασθενείς που έλαβαν εικονικό φάρμακο (LDI-B=0) την Εβδομάδα 24



*p≤0,001 έναντι PBO, †p<0,005 έναντι PBO (η τιμή p για IXE Q4W έναντι PBO στη δοκιμή SPIRIT-P2 προέκυψε με τη χρήση της δοκιμασίας ακριβείας του Fisher).
Η ADA αντιπροσωπεύει έναν δραστικό παράγοντα αναφοράς. Η μελέτη δεν είχε ισχύ για τον έλεγχο της ισοδυναμίας ή της μη κατωτερότητας των ομάδων δραστικής θεραπείας μεταξύ τους, συμπεριλαμβανομένων του IXE έναντι της ADA.
1. Mease PJ, et al. *Ann Rheum Dis*. 2017;76:79-87. 2. Nash P, et al. *Lancet*. 2017;389:2317-2327. 3. Gladman DD, et al. *Arthritis Res Ther*. 2019;21:38.

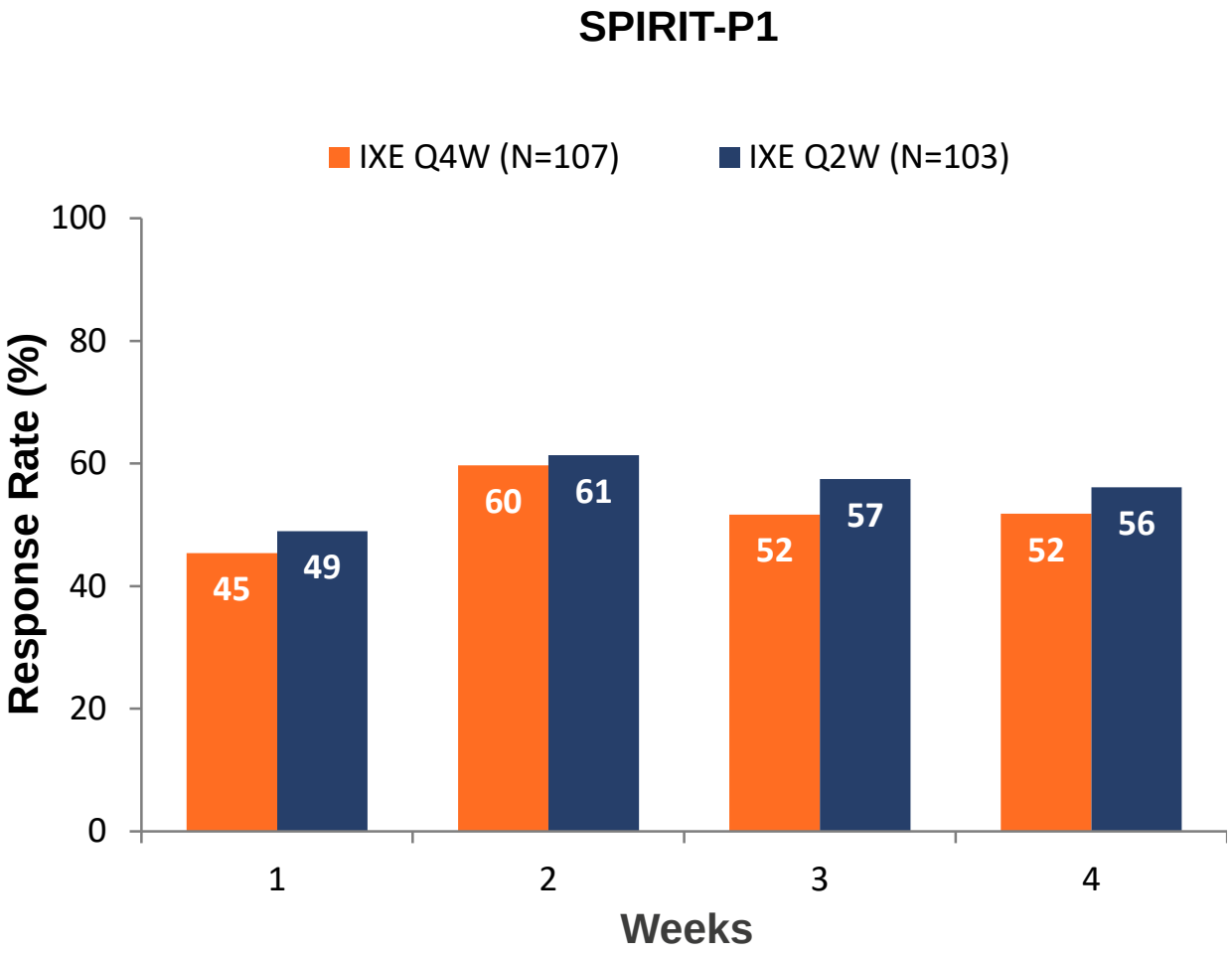
Περίπου το 30% έως 50% των ασθενών που έλαβαν θεραπεία με ixekizumab εμφάνισαν πλήρη υποχώρηση της ψωρίασης κατά πλάκας την Εβδομάδα 24

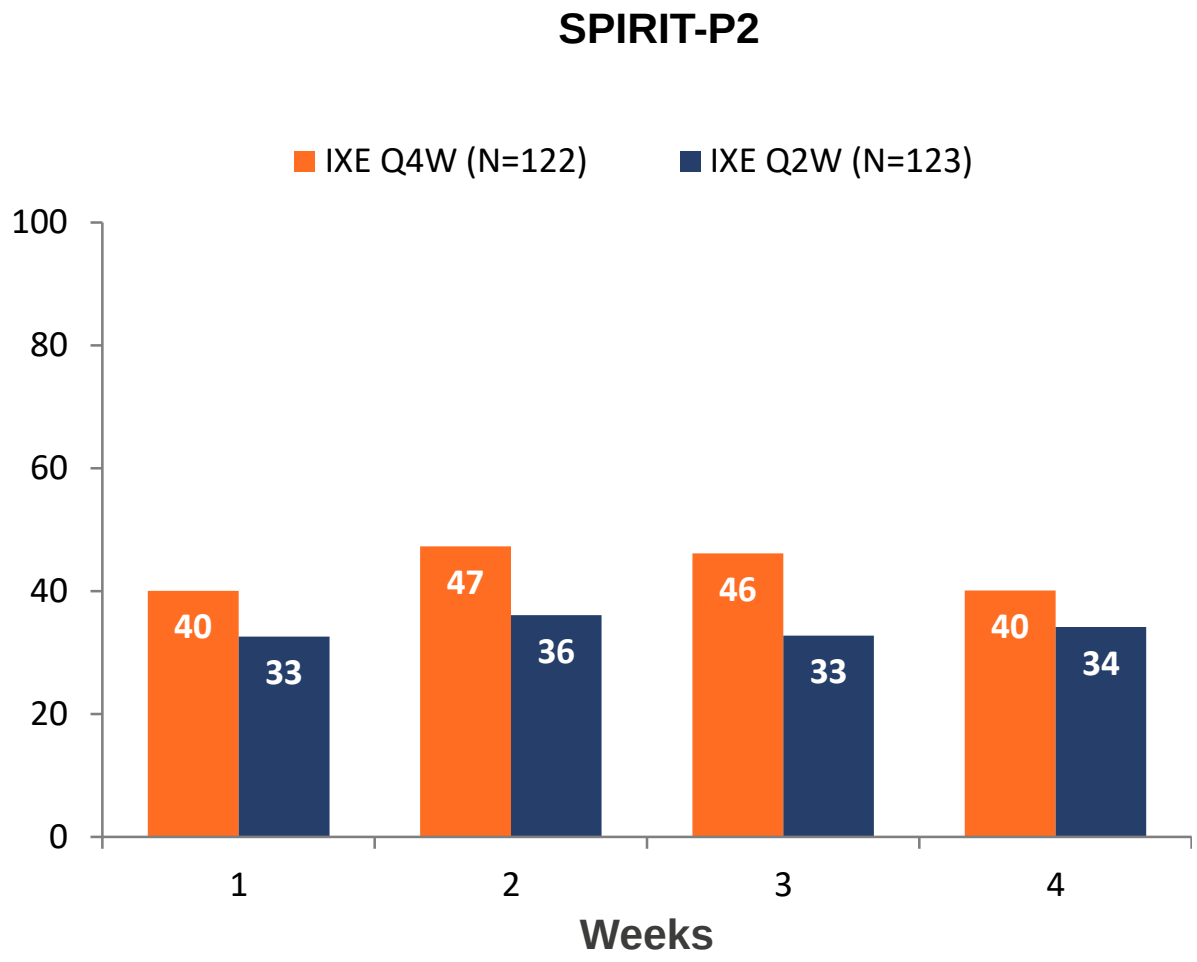


BSA ≥3% κατά την Έναρξη της Μελέτης

*p≤0,001 έναντι PBO, †p≤0,01 έναντι PBO.
Η ADA αντιπροσωπεύει έναν δραστικό παράγοντα αναφοράς. Η μελέτη δεν είχε ισχύ για τον έλεγχο της ισοδυναμίας ή της μη κατωτερότητας των ομάδων δραστικής θεραπείας μεταξύ τους, συμπεριλαμβανομένων του IXE έναντι της ADA.
1. Mease PJ, et al. *Ann Rheum Dis*. 2017;76:79-87. 2. Nash P, et al. *Lancet*. 2017;389:2317-2327.

Διατήρηση στον χρόνο σημαντικών κλινικών βελτιώσεων – ACR50



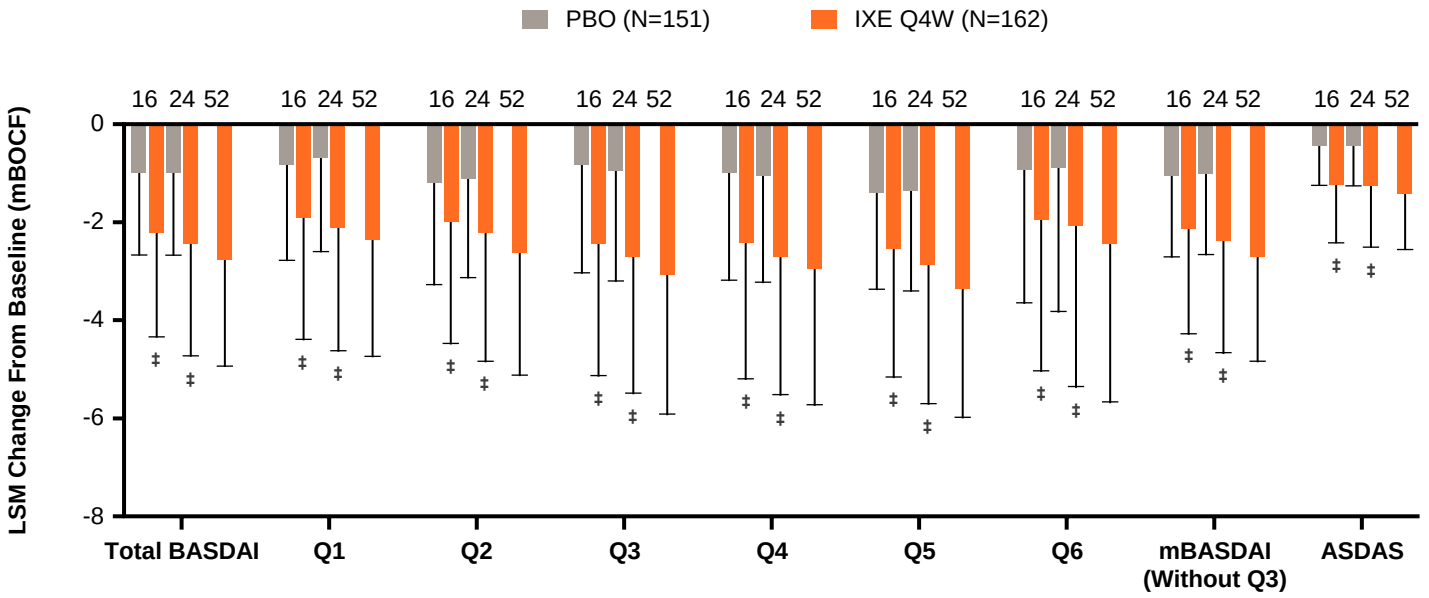


1. Chandran V, et al. *Rheumatology*. 2020;0:1-11. 2. Orbai AM, et al. Rheumatol Ther https://doi.org/10.1007/s40744-020-00261-0

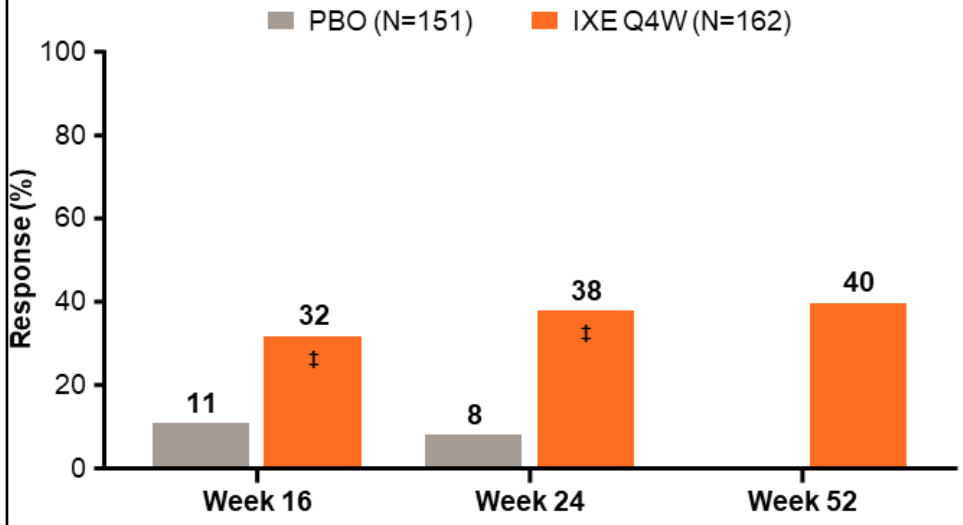
Μεταβολή των δεικτών ενεργότητας των συμπτωμάτων ενδεικτικών αξονικής προσβολής στην Ψωριασική Αρθρίτιδα από τις μελέτες SPIRIT-P1/P2

KEY RESULTS

Change From Baseline in BASDAI- and ASDAS-Related Endpoints in Patients With PsA With Axial Symptoms



BASDAI50 Response Rates in Patients With PsA With Axial Symptoms



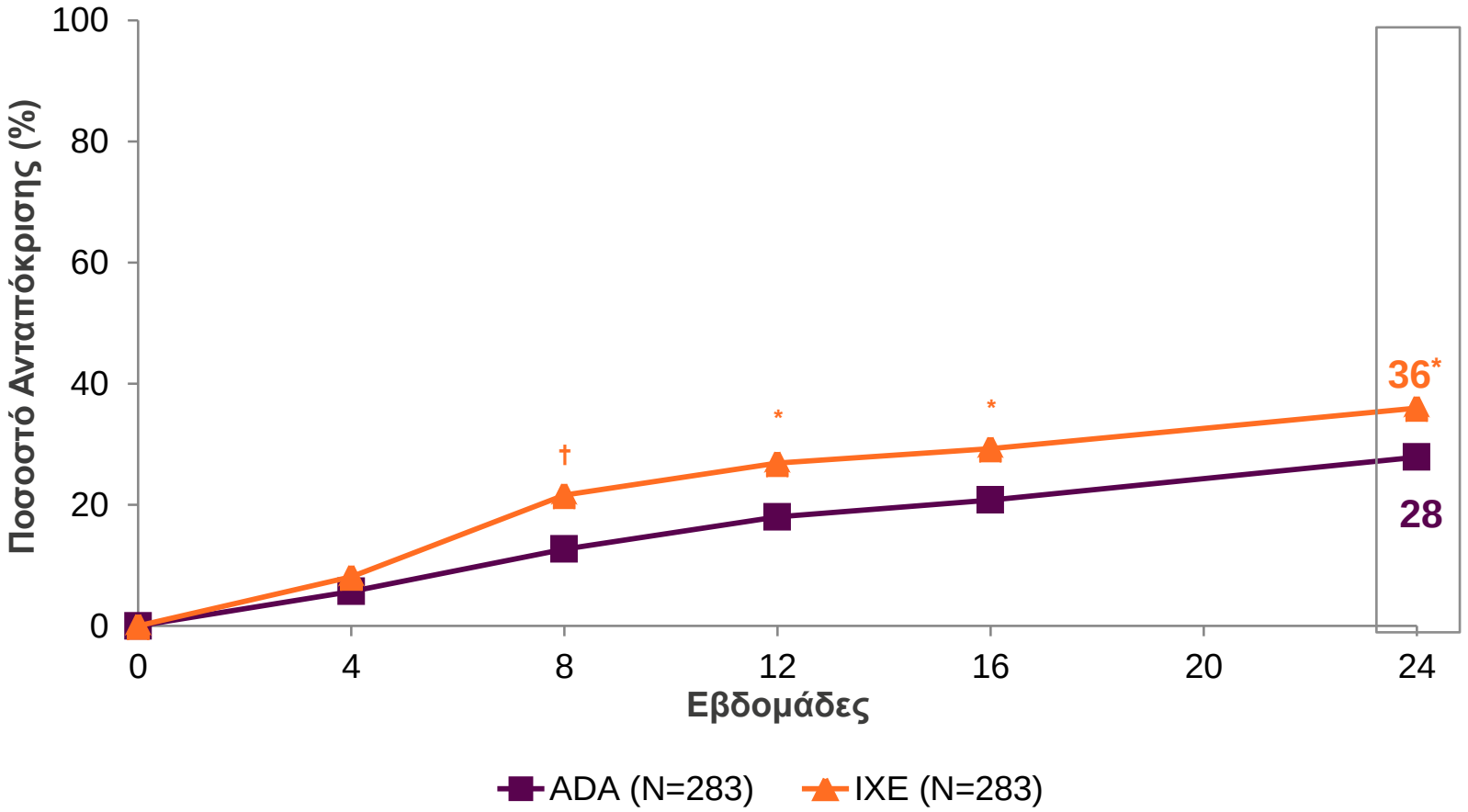
Ενοποιημένος πληθυσμός των μελετών και post hoc ανάλυση

Deodhar A et al, poster 1347, ACR Convergence 2021

Εκατοστιαία Αναλογία Ασθενών που Πέτυχαν Ταυτόχρονα Ανταπόκριση ACR50 και PASI 100 ανά Εβδομάδα Θεραπείας

Κύριο τελικό σημείο: Αναλογία ασθενών που λάμβαναν θεραπεία με ixekizumab και πέτυχαν ταυτόχρονα ανταπόκριση ACR50 και PASI 100 την Εβδομάδα 24

SPIRIT-H2H

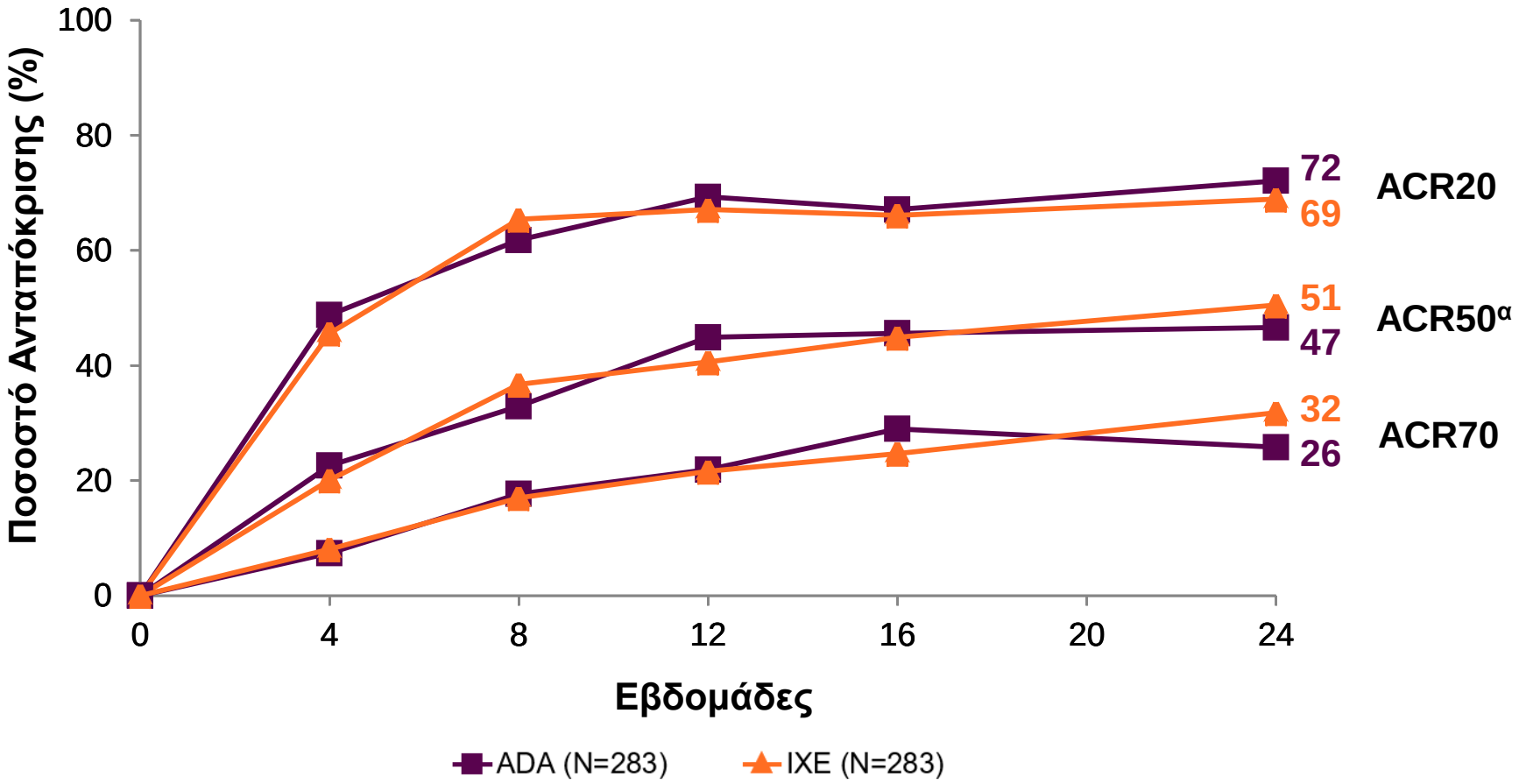


†p<0,01 έναντι ADA, *p<0,05 έναντι ADA.
H2H: Μελέτη Άμεσης Σύγκρισης
1. Mease PJ, et al. *Ann Rheum Dis.* 2020;79:123-131.

Ανταπόκριση ACR20/50/70 ανά Εβδομάδα Θεραπείας

Μείζον δευτερεύον τελικό σημείο: Αναλογία ασθενών που λάμβαναν θεραπεία με ixekizumab και πέτυχαν ανταπόκριση ACR50 την Εβδομάδα 24

SPIRIT-H2H

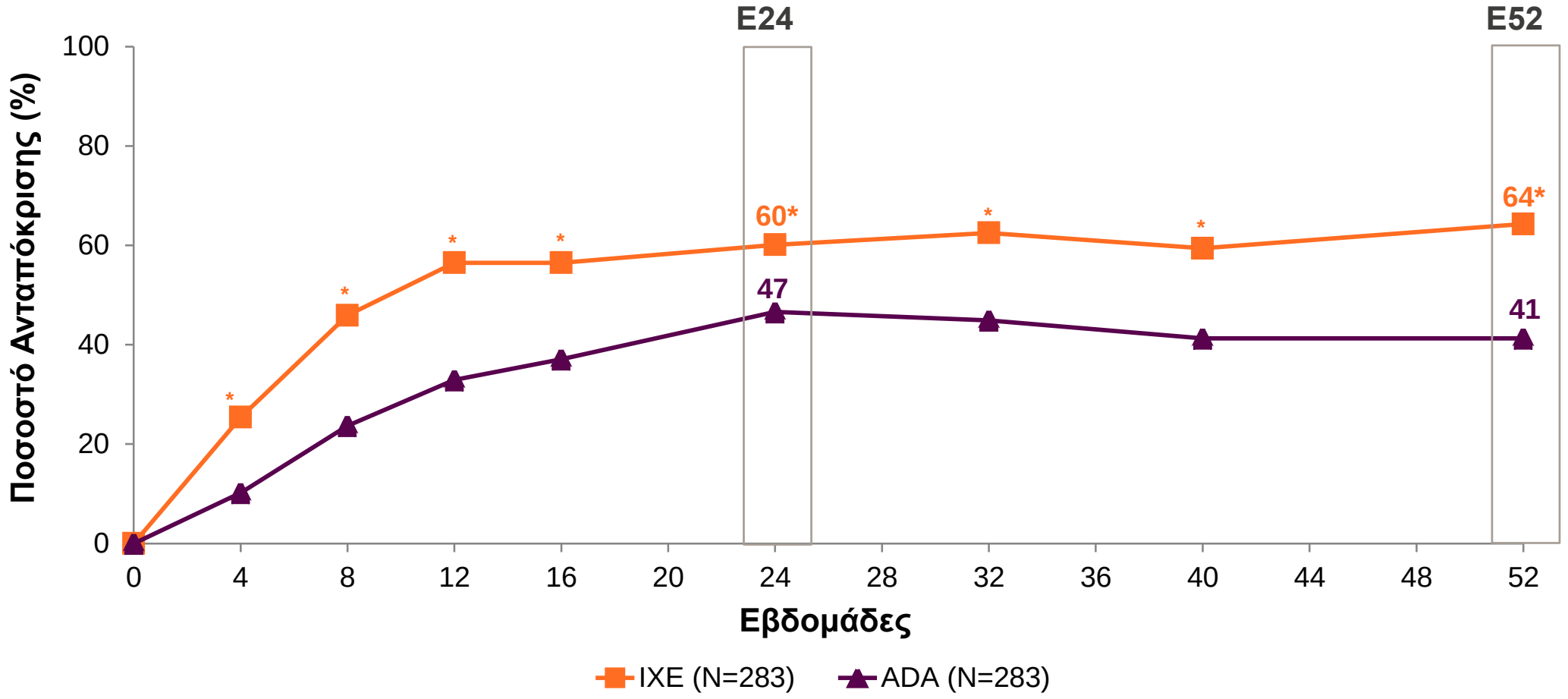


p=0,403 για IXE έναντι ADA την Εβδομάδα 24 για ACR20, p=0,338 για IXE έναντι ADA την Εβδομάδα 24 για ACR50, p=0,111 για IXE έναντι ADA την Εβδομάδα 24 για ACR70.
[α]Μία προσέγγιση σταθερού ορίου για τον έλεγχο μη κατωτερότητας, όπου το IXE θα κρινόταν μη κατώτερο της ADA εάν το κάτω φράγμα του αμφίπλευρου 95% CI για τη διαφορά των αναλογιών των ασθενών που παρουσίασαν ανταπόκριση ACR50 ενώ λάμβαναν IXE μείον τους ασθενείς που παρουσίασαν ανταπόκριση ACR50 ενώ λάμβαναν ADA ήταν μεγαλύτερο από το προκαθορισμένο όριο του −12,0%.
H2H: Μελέτη Άμεσης Σύγκρισης
1. Mease PJ, et al. Presented at: *EULAR 2019*. Abstract LB0005.

Ανταπόκριση PASI 100 ανά Εβδομάδα Θεραπείας

SPIRIT-H2H

Μείζον δευτερεύον τελικό σημείο: Αναλογία ασθενών που λάμβαναν θεραπεία με ixekizumab και πέτυχαν ανταπόκριση PASI100 την Εβδομάδα 24

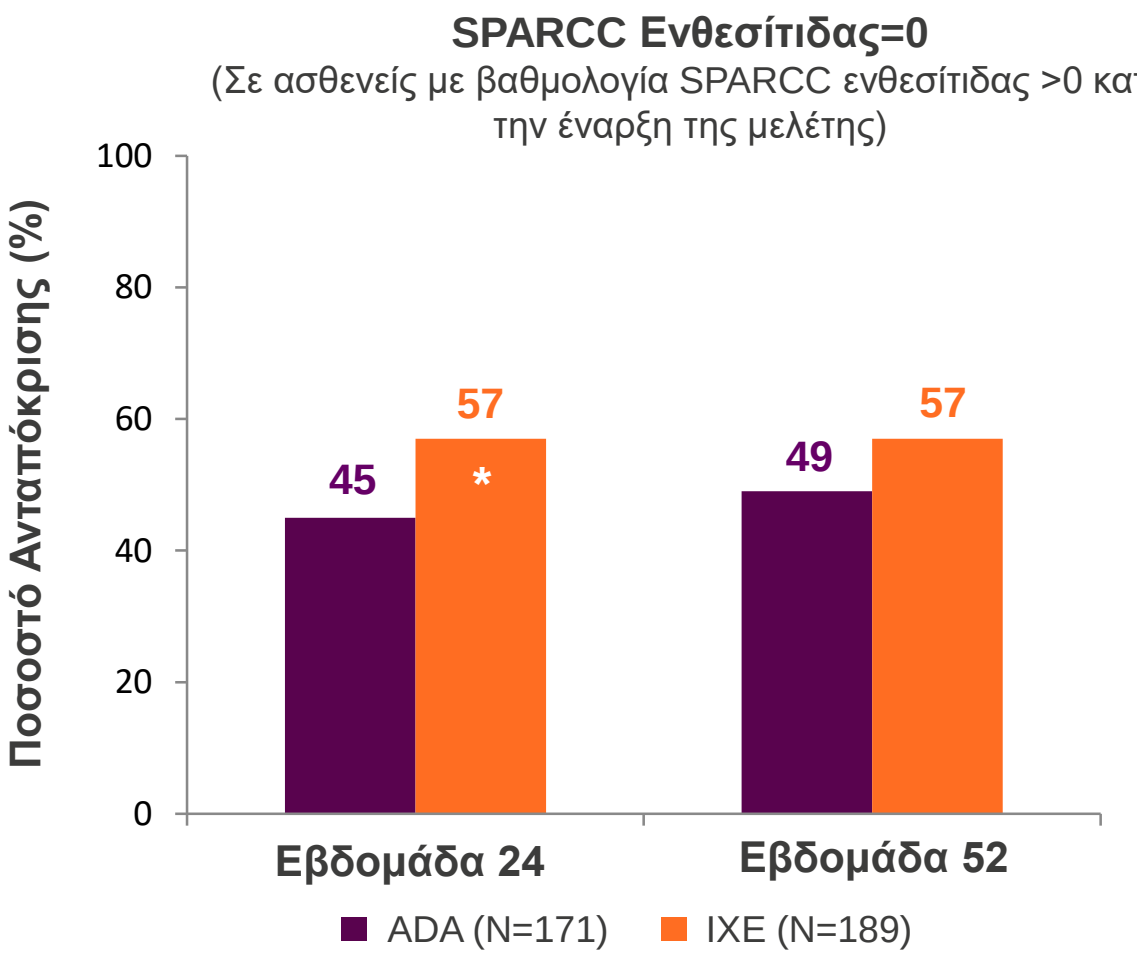


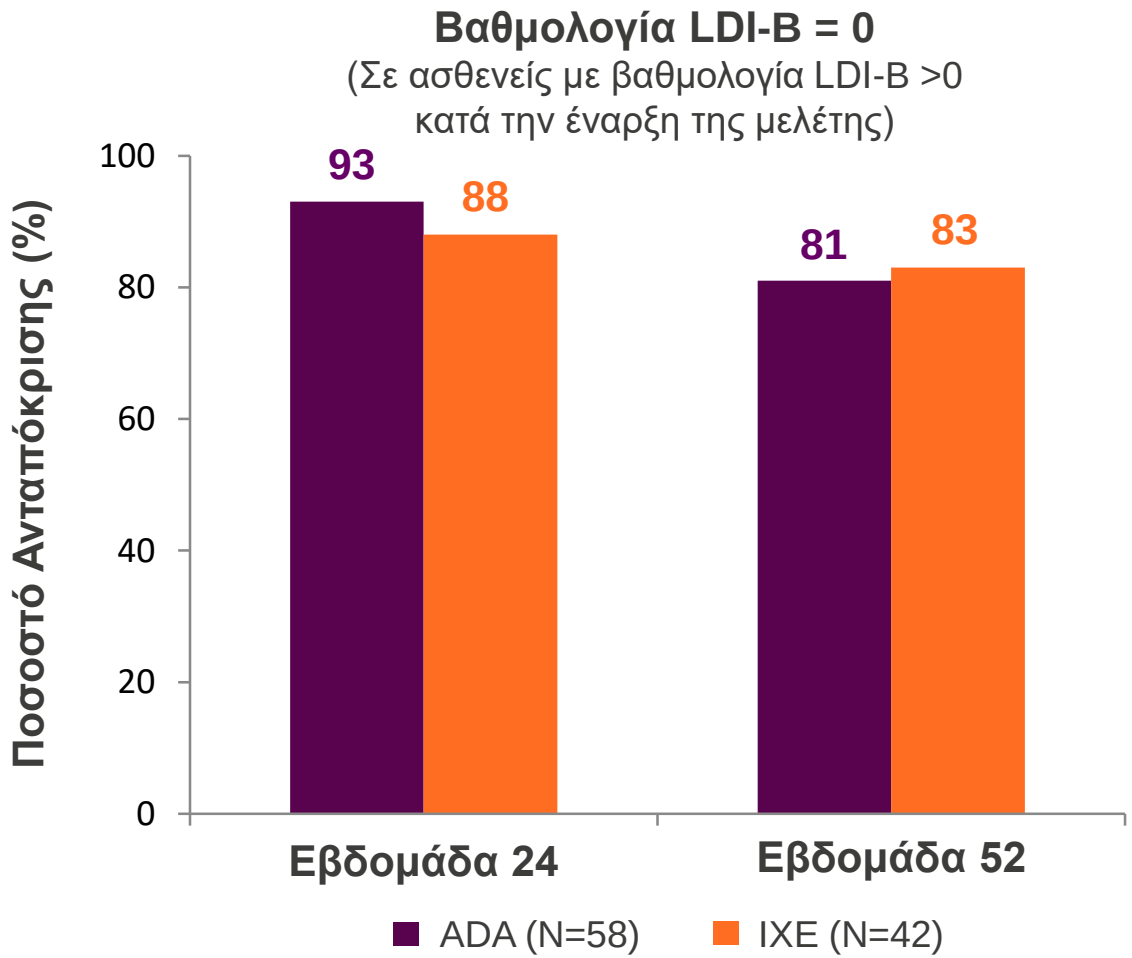
*p≤0,001 έναντι του ADA.
Χρησιμοποιήθηκε NRI για την απόδοση τιμής για όλα τα ελλείποντα δεδομένα, συμπεριλαμβανομένων των ασθενών που διέκοψαν τη θεραπεία ως μη ανταποκριθέντων.

1. Mease PJ, et al. *Ann Rheum Dis.* 2020;79:123-131. 2. Smolen J, et al. *Presented at the ACR/ARP Annual Meeting, 2019*. Late breaker presentation L20.

Υποχώρηση Ενθεσίτιδας (SPARCC=0) και Δακτυλίτιδας (LDI-B=0) τις Εβδομάδες 24 και 52

SPIRIT-H2H

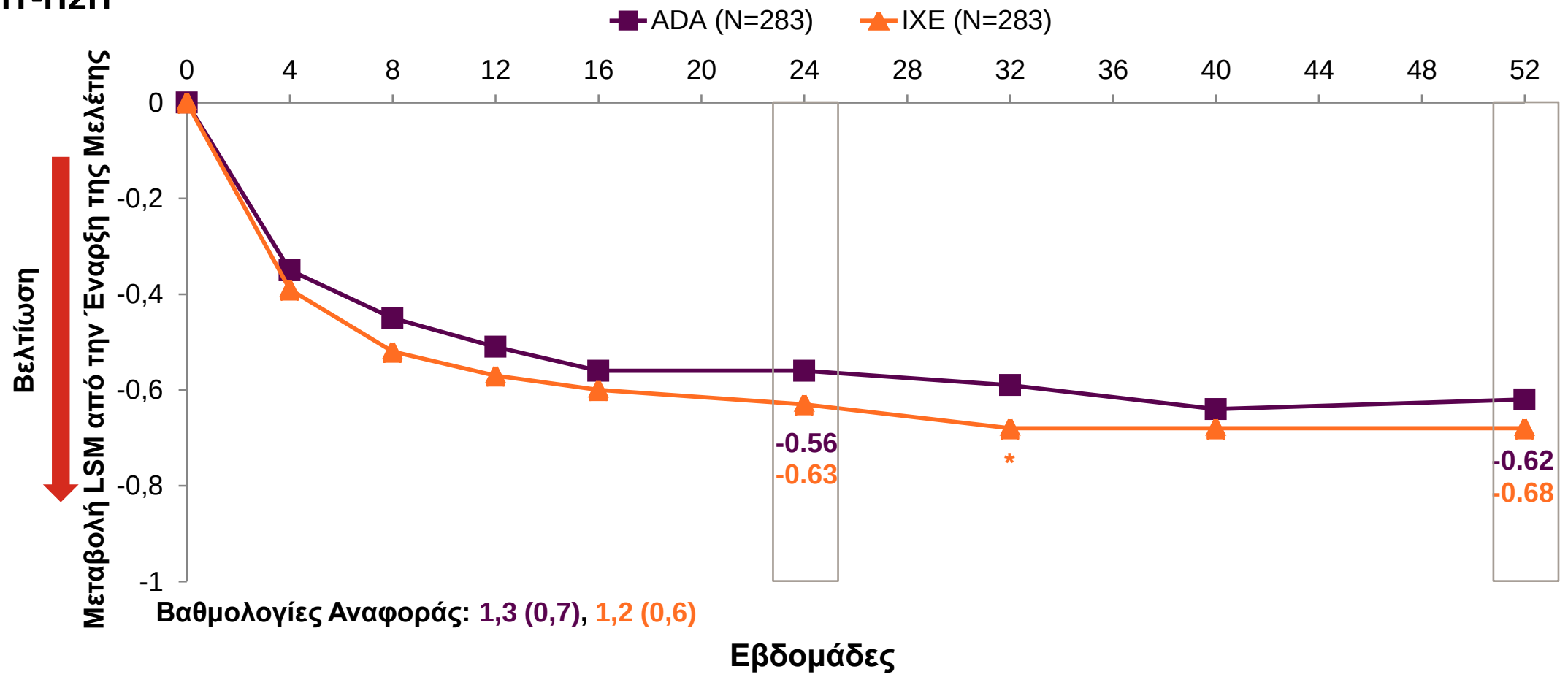




*p<0,05 έναντι του ADA.
Οι τιμές αναφοράς παρέχονται ως μέση τιμή (SD).
H2H: Μελέτη Άμεσης Σύγκρισης,
1. Mease PJ, et al. *Ann Rheum Dis.* 2020;79:123-131. 2. Smolen J, et al. *Presented at the ACR/ARP Annual Meeting, 2019*. Late breaker presentation L20.

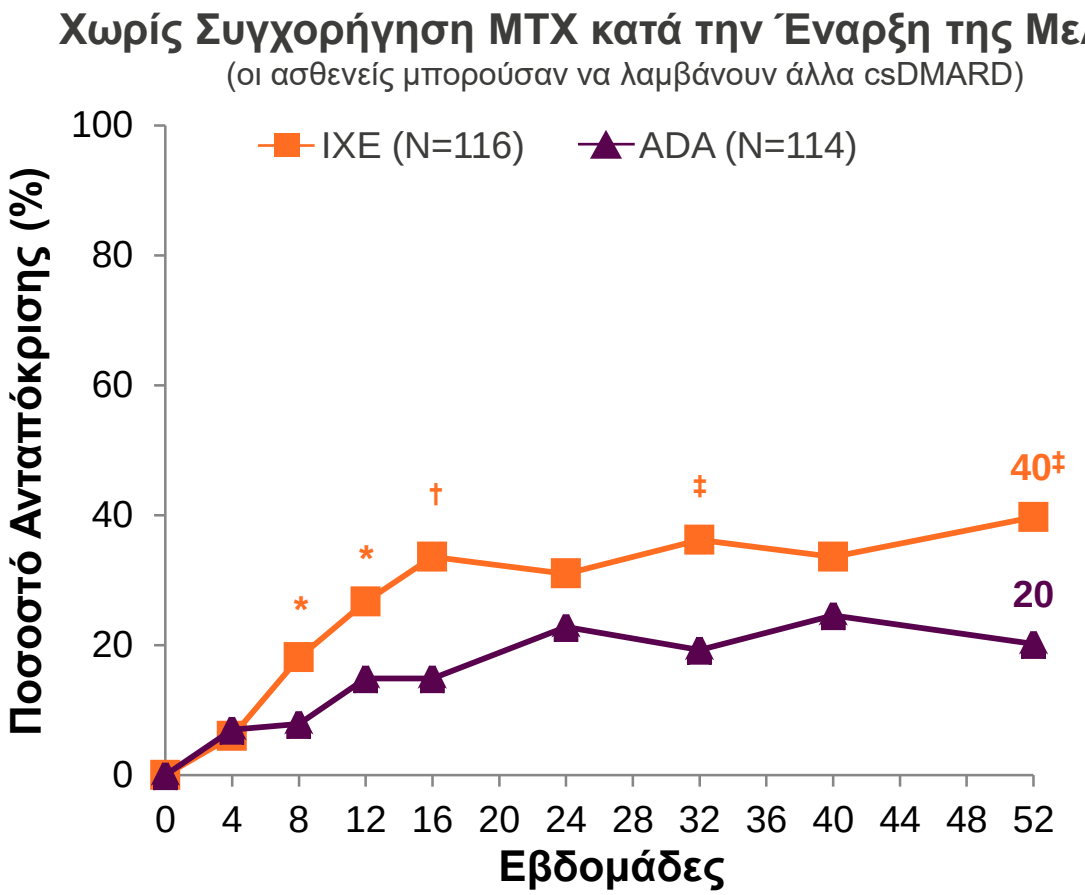
Μέση Μεταβολή του HAQ-DI από την Έναρξη της Μελέτης ανά Εβδομάδα Θεραπείας

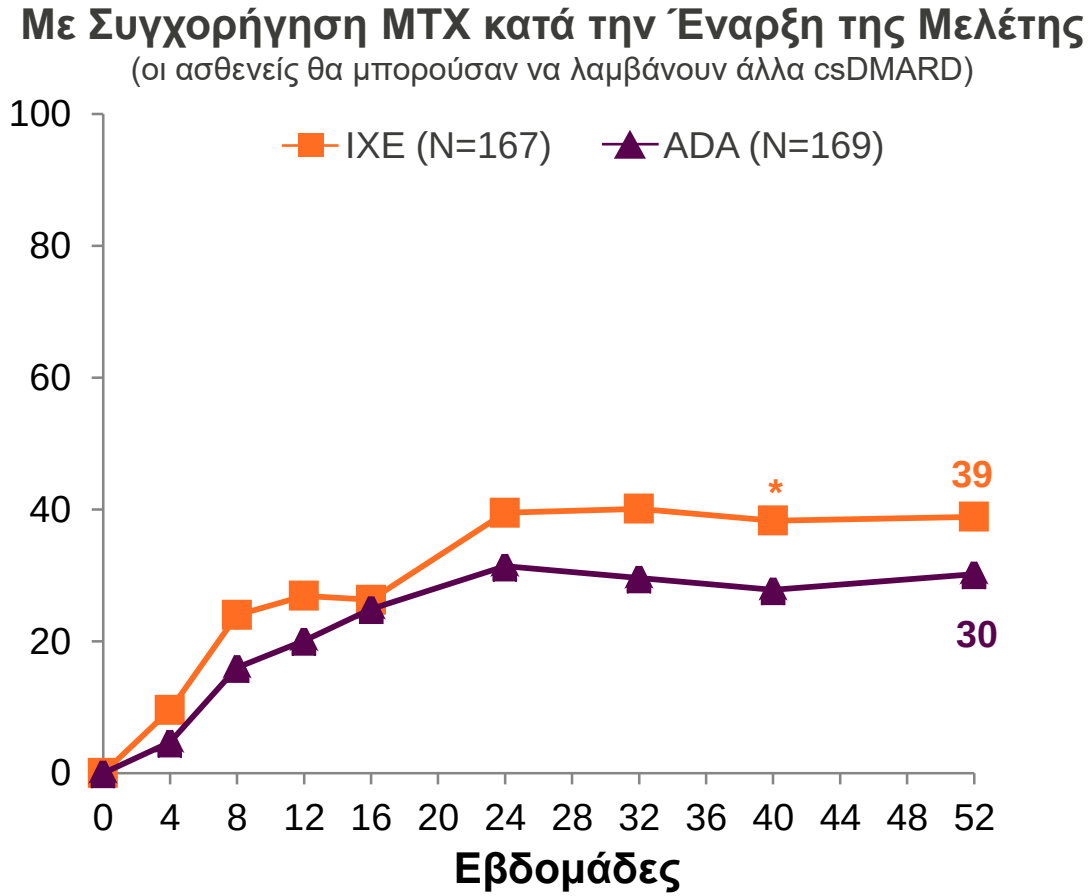
SPIRIT-H2H



*p<0,05 έναντι ADA. Τιμή p για ADA έναντι IXE την Εβδομάδα 52 = 0,176..
Smolen J, et al. *Presented at the ACR/ARP Annual Meeting, 2019*. Late breaker presentation L20.

Ταυτόχρονη Ανταπόκριση ACR50 και PASI 100 Έως και την Εβδομάδα 52 με Βάση τη Χρήση MTX κατά την Έναρξη της Μελέτη





Ασθενείς που λάμβαναν συγχορηγούμενη θεραπεία με csDMARD εκτός της MTX κατά την έναρξη της μελέτης, n (%) = 30 (11%) για ADA και 26 (9,2%) για IXE

*p<0,05 έναντι ADA, †p≤0,001 έναντι ADA, ‡p<0,01 έναντι ADA. Τιμή p για IXE έναντι ADA την Εβδομάδα 52 στην ομάδα συγχορηγούμενης MTX =0,108.
Τιμή p της αλληλεπίδρασης υποομάδας-θεραπείας την Εβδομάδα 16 = 0,019· σε όλα τα άλλα χρονικά σημεία: NS.
Στον έλεγχο αλληλεπίδρασης, μία τιμή p <0,1 θεωρείται στατιστικά σημαντική

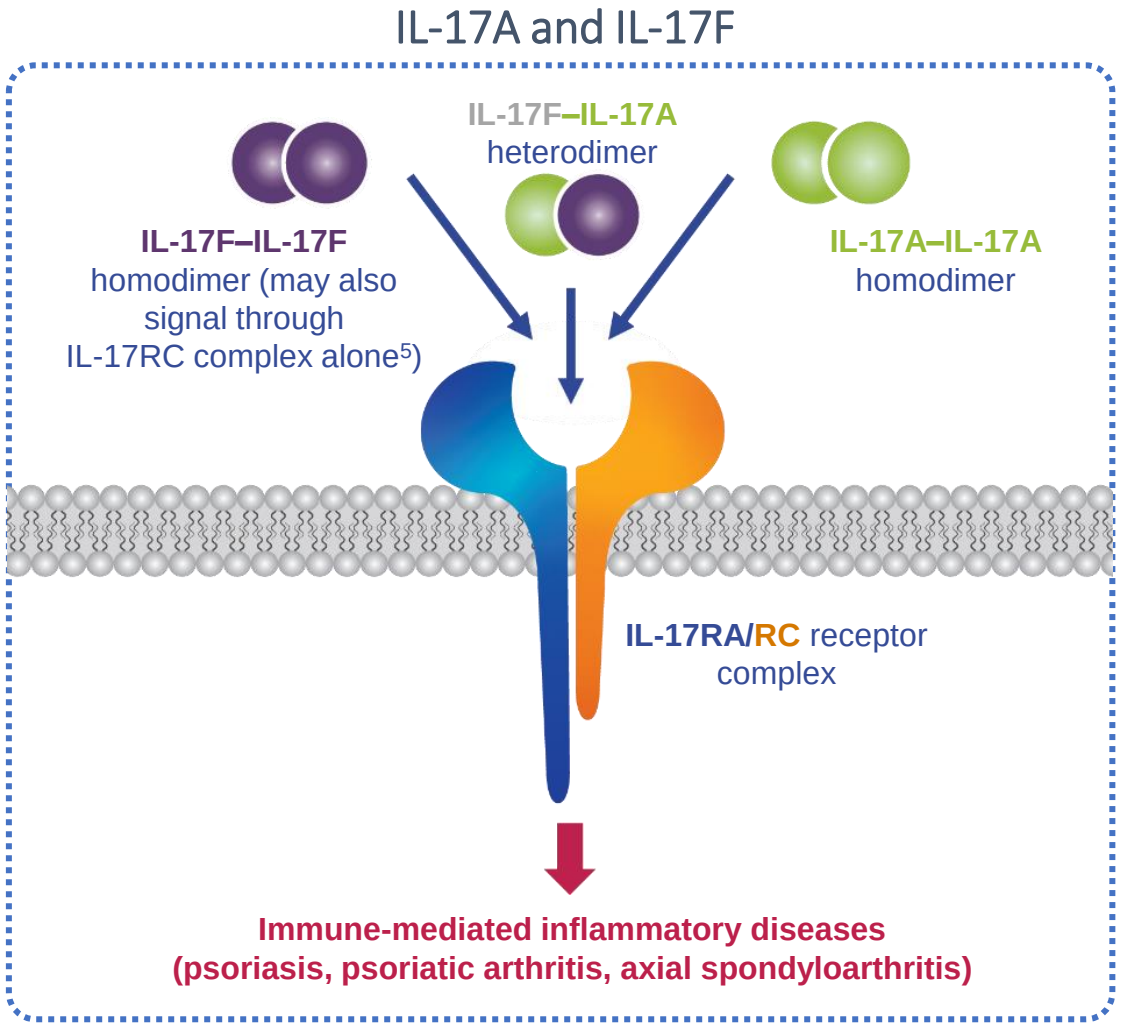
1. Smolen J, et al. *Presented at the ACR/ARP Annual Meeting, 2019*. Late breaker presentation L20. 2. Data on file, Eli Lilly and Company.

Ασφάλεια του ixekizumab σε ασθενείς με Ψωριασική Αρθρίτιδα: συνολικά δεδομένα από τέσσερις κλινικές δοκιμές με έκθεση άνω των 2000 ασθενο-ετών

	Συνολικός πληθυσμός του IXE στην Ψωριασική Αρθρίτιδα N=1401		
Σύνολο ασθενών-ετών έκθεσης	2247.7		
Μέση έκθεση (ημέρες)	586.4		
Επιλεγμένες Ανεπιθύμητες Ενέργειες	n (%)	EAIR	95% CI
Θάνατος*	6 (0.4)	0.3	0.1 to 0.6
ΑΕ που οδηγεί σε διακοπή (συμπεριλαμβανομένου του θανάτου)	115 (8.2)	5.1	4.3 to 6.1
ΣΑΕ[a]	134 (9.6)	6.0	5.0 to 7.1
Αλλεργικές αντιδράσεις/υπερευαισθησίες	2 (0.1)	0.1	0.0 to 0.4
Κακοήθειες	7 (0.5)	0.3	0.1 to 0.7
NMSC	0	0.0	0.0 to 0.4
Κακοήθειες εκτός από NMSC	7 (0.5)	0.3	0.1 to 0.7
Φλεγμονώδης νόσος του εντέρου	2 (0.1)	0.1	0.0 to 0.4
Κατάθλιψη	1 (0.1)	0.0	0.0 to 0.3
Αυτοκτονική συμπεριφορά/Αυτοτραυματισμός	0	0.0	0.0 to 0.4
MACE[d]	12 (0.9)	0.5	0.3 to 0.9
Κυτταροπενίες	0	0.0	0.0 to 0.4
Αντιδράσεις στο σημείο της ένεσης	156 (11.1)	6.9	5.9 to 8.1

Deodhar AA, et al. Ann Rheum Dis 2022;**0**:1–7. doi:10.1136/annrheumdis-2021-222027

Dual Inhibition of IL-17F in Addition to IL-17A Modulates Downstream Cytokine Production and Reduces Inflammation in *in Vitro* Models of PsA and axSpA



***In vitro* models* of PsA and axSpA show that inhibiting IL-17F in addition to IL-17A results in:**

- **Increased suppression of synoviocyte proinflammatory genes elevated in PsA**
- **Reduced migration of both adaptive and innate immune cell types**
- **Reduced periosteal stem cell bone formation**

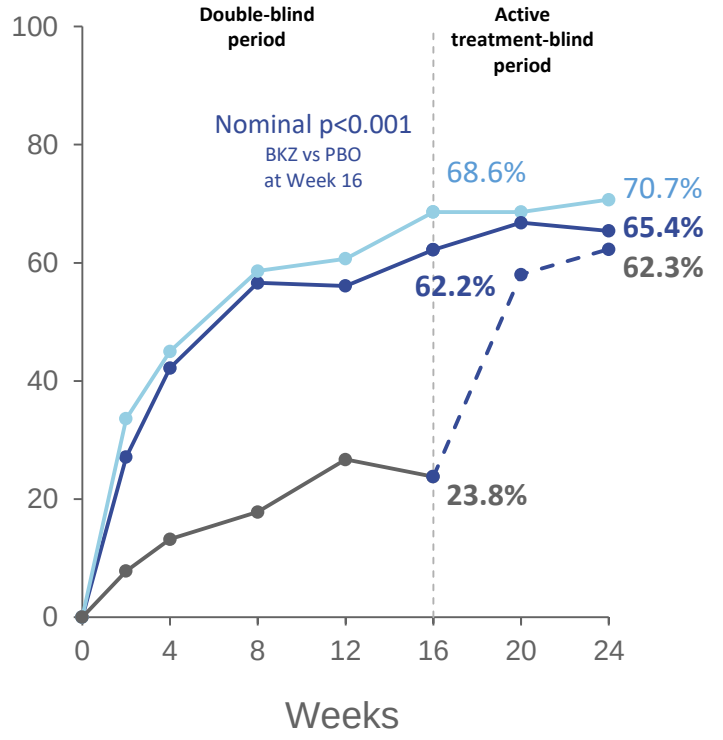
- *There are no head to head data comparing the clinical efficacy of BKZ vs IL-17A inhibitors in PsA or axSpA. IL: interleukin; IL-17R: Interleukin 17 receptor.

1. Glatt S et al. Ann Rheum Dis. 2018;77:523–532. 2. Shaw. Psoriasis Gene to Clinic 2017. London, United Kingdom. Oral Presentation. 3. Shah et al. RMD Open. 2020;6(2):e001306. 4. Yang XO et al. J Exp Med. 2008;1063–1075. 5. Goepfert A et al. Immunity. 2020;52(3):499–512.e5.

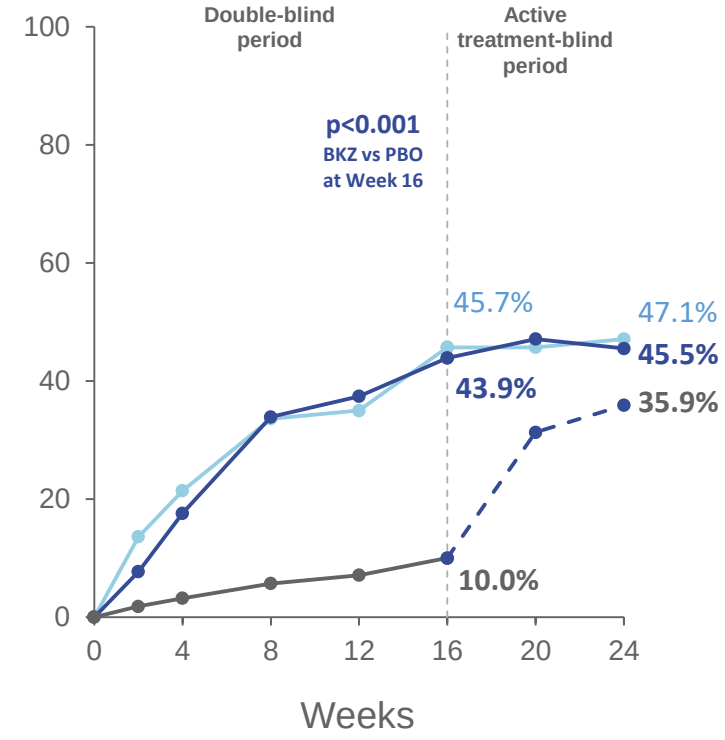
Σημαντικά περισσότεροι ασθενείς που έλαβαν θεραπεία με το bimekizumab πέτυχαν ανταπόκριση ACR έναντι εκείνων που έλαβαν εικονικό φάρμακο την Εβδομάδα 16

BE OPTIMAL

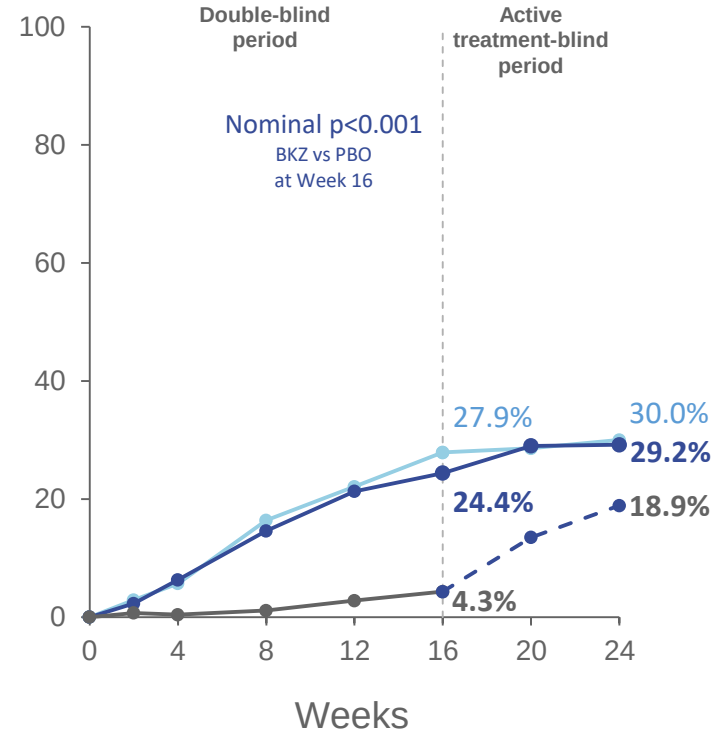
ACR20



Primary endpoint: ACR50



ACR70



— → ---- PBO → BKZ 160 mg Q4W (n=281)

— BKZ 160 mg Q4W (n=431)

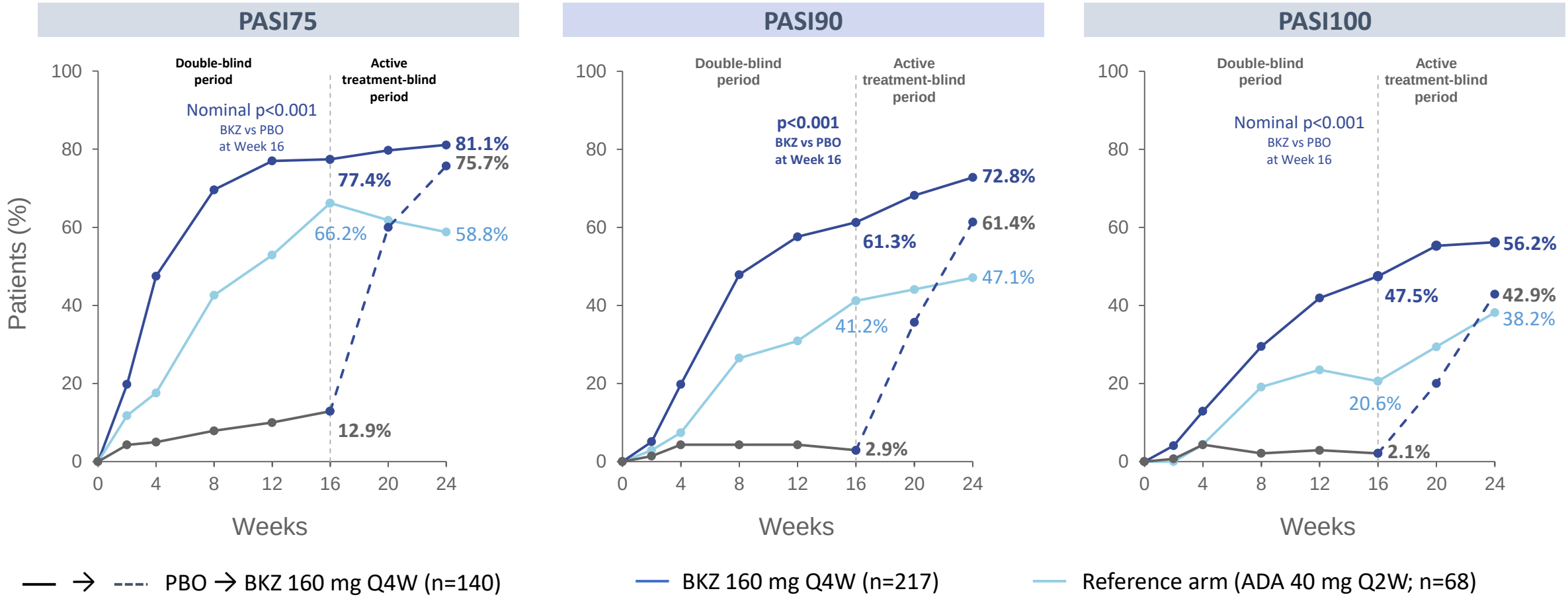
— Reference arm (ADA 40 mg Q2W; n=140)

Non-responder imputation. Randomised set. p values for BKZ vs placebo were obtained from logistic regression with treatment, bone erosion at baseline and region as factors. Nominal p values were not adjusted for multiplicity. The study was not powered for statistical comparisons of adalimumab to bimekizumab or adalimumab to placebo.

McInnes IB et al. EULAR 2022. Presentation LB0001.

>50% των ασθενών σε BKZ πέτυχαν PASI 100

BE OPTIMAL

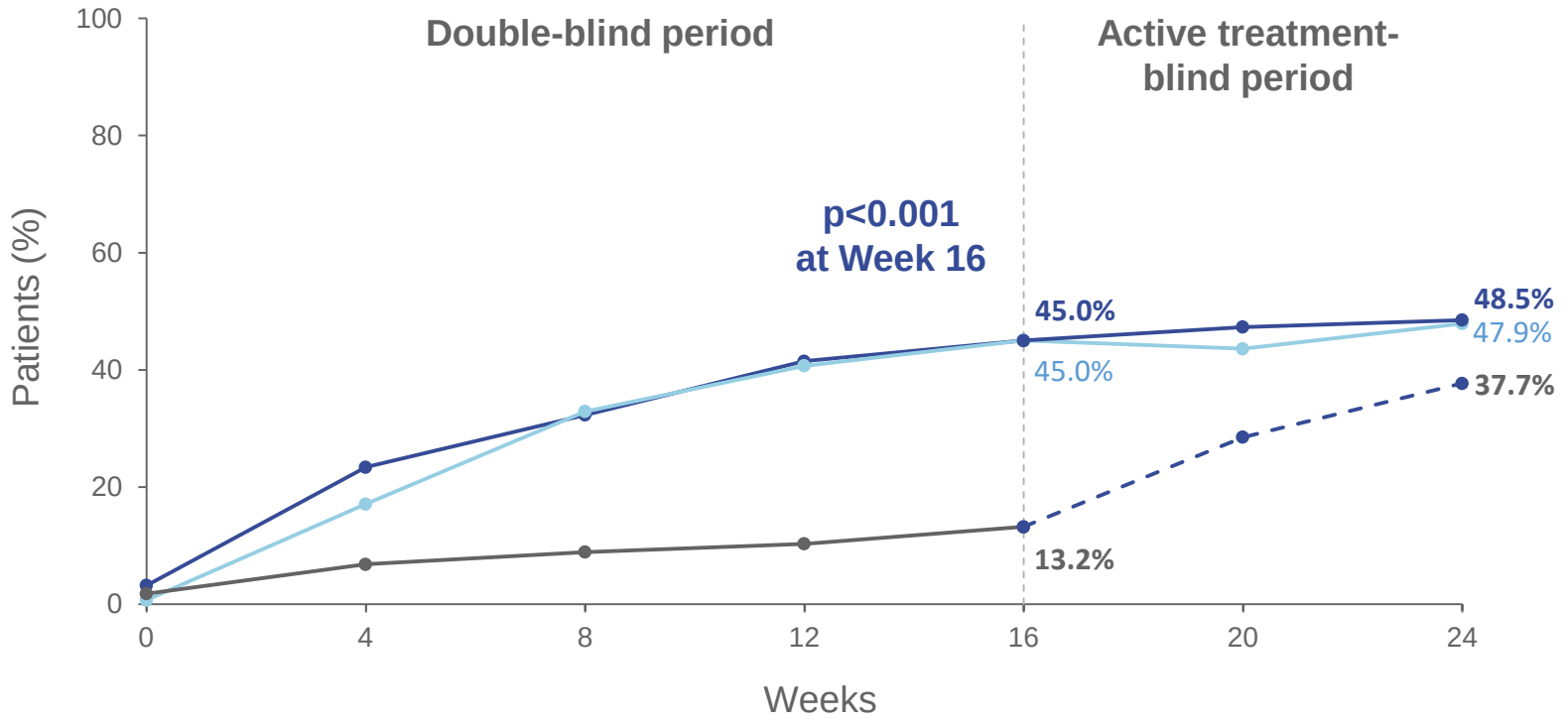


Non-responder imputation. Randomised set. In patients with PSO involving ≥3% of BSA at baseline. p values for BKZ vs placebo were obtained from logistic regression with treatment, bone erosion at baseline and region as factors. Nominal p values were not adjusted for multiplicity. The study was not powered for statistical comparisons of adalimumab to bimekizumab or adalimumab to placebo.

McInnes IB et al. EULAR 2022. Presentation LB0001.

Σημαντικά περισσότεροι ασθενείς που έλαβαν BMK πέτυχαν MDA έναντι εκείνων που έλαβαν εικονικό φάρμακο την Εβδομάδα 16

BE OPTIMAL



MDA response defined as achievement of at least 5 of the 7 following criteria:

- Tender joint count ≤1
- Swollen joint count ≤1
- Psoriasis Area and Severity Index ≤1* or body surface area ≤3%†
- Patient's Assessment of Arthritis Pain ≤15 mm
- Patient global assessment-PsA ≤20 mm
- Health Assessment Questionnaire–Disability Index ≤0.5
- Leeds Enthesitis Index ≤1

— → ---- PBO → BKZ 160 mg Q4W (n=281)

— BKZ 160 mg Q4W (n=431)

— Reference arm (ADA 40 mg Q2W; n=140)

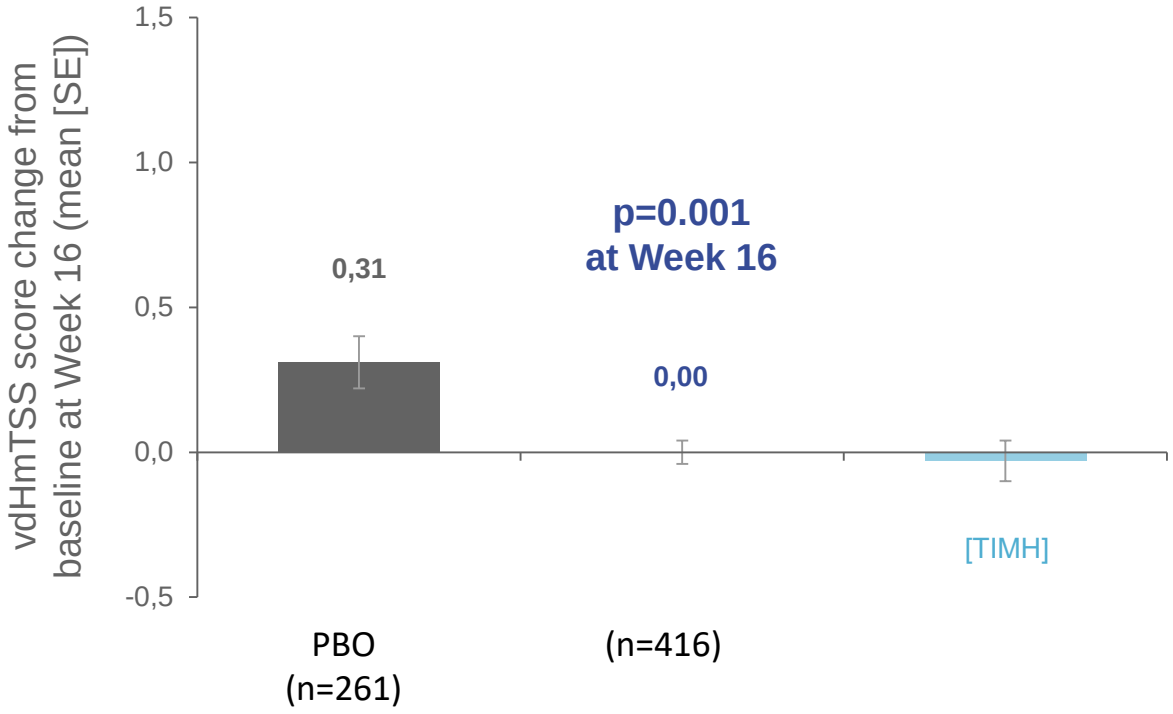
Non-responder imputation. **Patient's Assessment of Arthritis Pain and the Leeds Enthesitis Index were the instruments used to define patient pain and tender entheseal points in MDA, respectively, as per study protocol.**[1] Randomised set. p value for BKZ vs placebo was obtained from logistic regression with treatment, bone erosion at baseline and region as factors. The study was not powered for statistical comparisons of adalimumab to bimekizumab or adalimumab to placebo. *For patients with PSO involving ≥3% of BSA at baseline. †Subjects with BSA <3% at baseline will always meet the criteria PASI ≤1 or BSA ≤3% except in the cases where a BSA score >3% is observed.

McInnes IB et al. EULAR 2022. Presentation LB0001. 1. UCB Data on File (PA0010 Statistical Analysis Plan. Amendment 3. 2022. p85) – Data are available on request.

Σημαντικά περισσότεροι ασθενείς που έλαβαν BMK πέτυχαν αναστολή της εξέλιξης της δομικής βλάβης έναντι εκείνων που έλαβαν εικονικό φάρμακο την Εβδομάδα 16

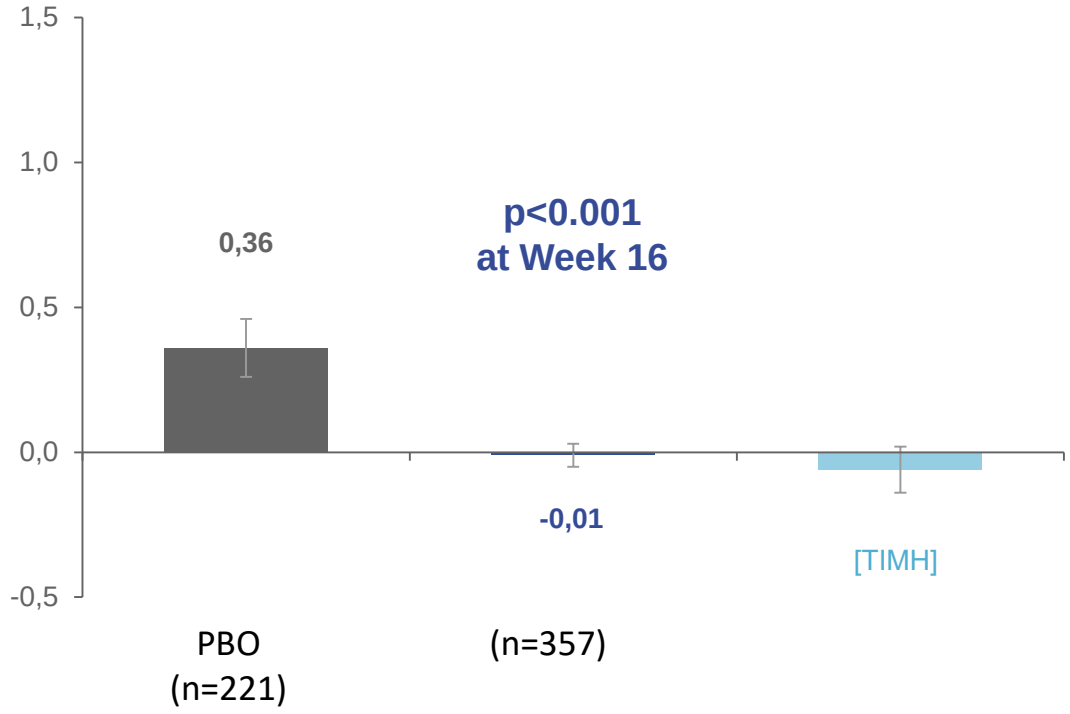
BE OPTIMAL

Overall population



At-risk population

Elevated hs-CRP (≥6 mg/L) and/or ≥1 bone erosion at baseline



Multiple imputation. Radiographic set. p values BKZ vs placebo were obtained from ANCOVA with treatment, bone erosion at baseline and region as fixed effects and the baseline value as covariate. The study was not powered for statistical comparisons of adalimumab to bimekizumab or adalimumab to placebo.

McInnes IB et al. EULAR 2022. Presentation LB0001.

Χωρίς κάποιο νέο σήμα ασφάλειας στις 24 εβδομάδες θεραπείας με BKZ

BE OPTIMAL

n (%)	Weeks 0–16			Weeks 0–24	
	Placebo (n=281)	BKZ 160 mg Q4W (n=431)	Reference Arm (ADA 40 mg Q2W; n=140)	BKZ 160 mg Q4W Total (n=702)*	Reference Arm (ADA 40 mg Q2W; n=140)
Any TEAE	139 (49.5)	258 (59.9)	83 (59.3)	395 (56.3)	96 (68.6)
Serious TEAEs	3 (1.1)	7 (1.6)	2 (1.4)	20 (2.8)	5 (3.6)
Discontinuation due to TEAEs	3 (1.1)	8 (1.9)	3 (2.1)	12 (1.7)	7 (5.0)
Drug-related TEAEs	35 (12.5)	101 (23.4)	34 (24.3)	149 (21.2)	43 (30.7)
Severe TEAEs	0	4 (0.9)	3 (2.1)	10 (1.4)	3 (2.1)
Deaths	0	0	0	0	0

Safety set. *Includes patients who switched from placebo to BKZ (events after switch only).

McInnes IB et al. EULAR 2022. Presentation LB0001.
1. Ritchlin CT et al. Lancet. 2020;395(10222):427–40.
2. Coates LC et al. Ann Rheum Dis. 2021;80:779–780(POS1022).

Χωρίς κάποιο νέο σήμα ασφάλειας στις 24 εβδομάδες θεραπείας με BKZ

BE OPTIMAL

n (%)	Weeks 0–16			Weeks 0–24	
	Placebo (n=281)	BKZ 160 mg Q4W (n=431)	Reference Arm (ADA 40 mg Q2W; n=140)	BKZ 160 mg Q4W Total (n=702)*	Reference Arm (ADA 40 mg Q2W; n=140)
Most frequently reported TEAEs (≥3% in any treatment arm)[†]					
Nasopharyngitis	13 (4.6)	40 (9.3)	7 (5.0)	58 (8.3)	12 (8.6)
Upper respiratory tract infection	18 (6.4)	21 (4.9)	3 (2.1)	31 (4.4)	5 (3.6)
Headache	7 (2.5)	20 (4.6)	2 (1.4)	26 (3.7)	3 (2.1)
Diarrhoea	7 (2.5)	16 (3.7)	5 (3.6)	21 (3.0)	5 (3.6)
Hypertension	11 (3.9)	12 (2.8)	4 (2.9)	19 (2.7)	4 (2.9)
ALT elevation	2 (0.7)	3 (0.7)	7 (5.0)	5 (0.7)	8 (5.7)
Oral herpes	3 (1.1)	5 (1.2)	3 (2.1)	7 (1.0)	6 (4.3)
Injection site erythema	0	1 (0.2)	4 (2.9)	2 (0.3)	5 (3.6)
Fungal Infections[‡]	4 (1.4)	20 (4.6)	1 (0.7)	40 (5.7)	1 (0.7)
***Candida* infections**[§]	2 (0.7)	11 (2.6)	0	22 (3.1)	0
Adjudicated MACE	0	0	0	1 (0.1)	0
Adjudicated IBD	0	0	0	1 (0.1)[‖]	0

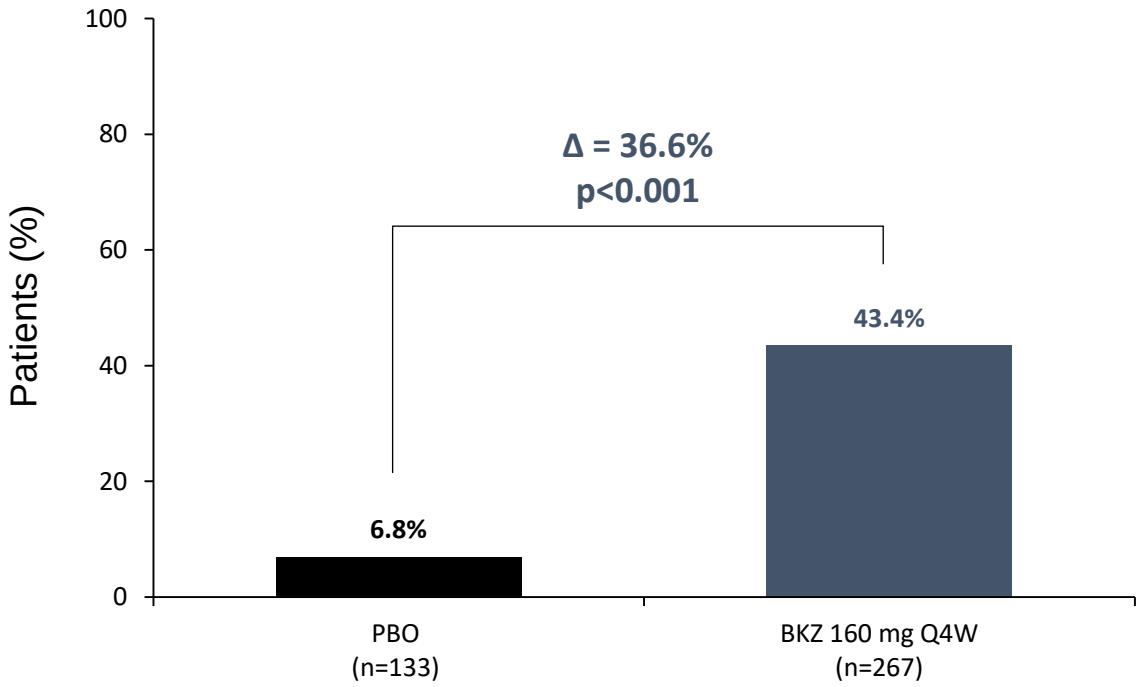
Safety set. *Includes patients who switched from placebo to BKZ (events after switch only). [†]TEAEs ≥3% in any treatment arm are reported by preferred term. [‡]No fungal infections were systemic. [§]All infections were mild to moderate and none were serious, 1 BKZ patient discontinued. [‖]One case of probable IBD in a patient with no prior history of IBD.

McInnes IB et al. EULAR 2022. Presentation LB0001.
1. Ritchlin CT et al. Lancet. 2020;395(10222):427–40.
2. Coates LC et al. Ann Rheum Dis. 2021;80:779–780(POS1022).

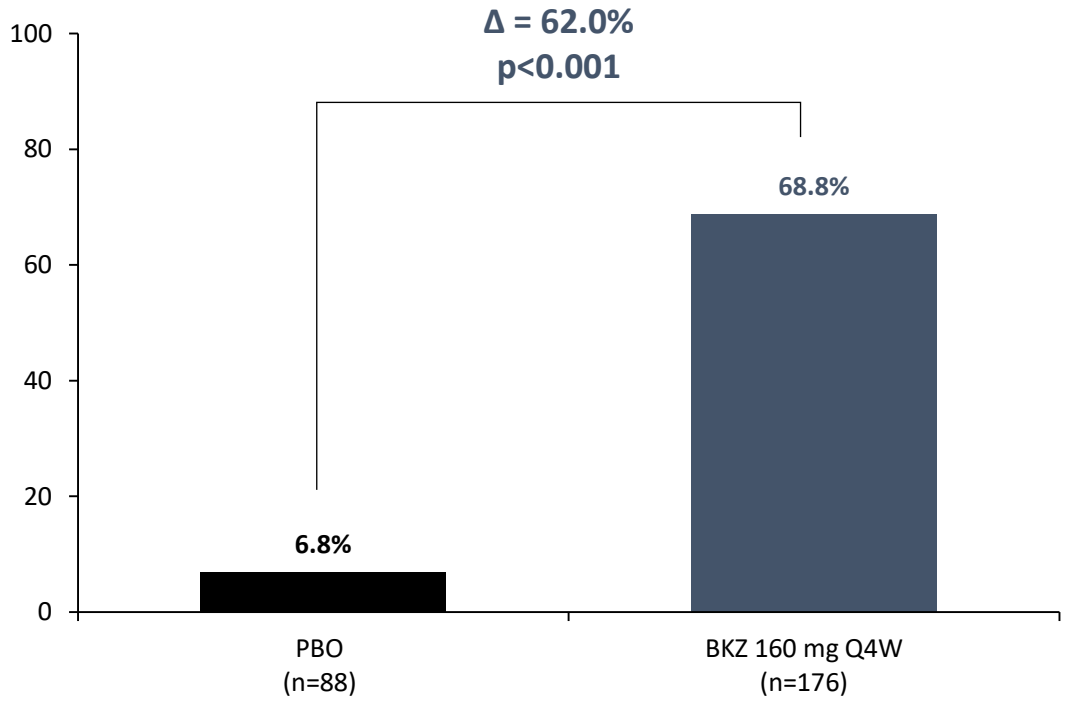
BE COMPLETE

Σημαντικά περισσότεροι ασθενείς που έλαβαν θεραπεία με το BKZ πέτυχαν ανταπόκριση ACR και PASI έναντι εκείνων που έλαβαν εικονικό φάρμακο την Εβδομάδα 16

Primary Endpoint: ACR50



PASI90*



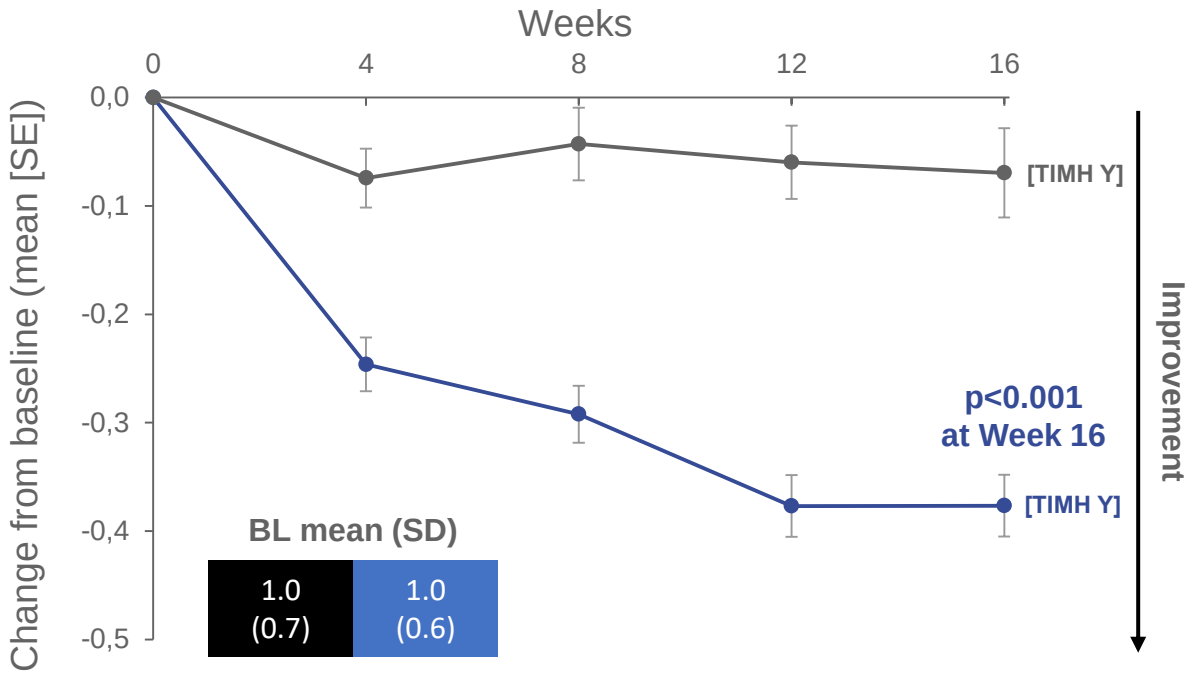
Non-responder imputation.
Randomised set. p values were obtained from logistic regression with treatment, prior TNF inhibitor exposure and region as factors. *In patients with PSO involving ≥3% BSA at baseline.

Merola JF et al. EULAR 2022. Presentation OP0255.

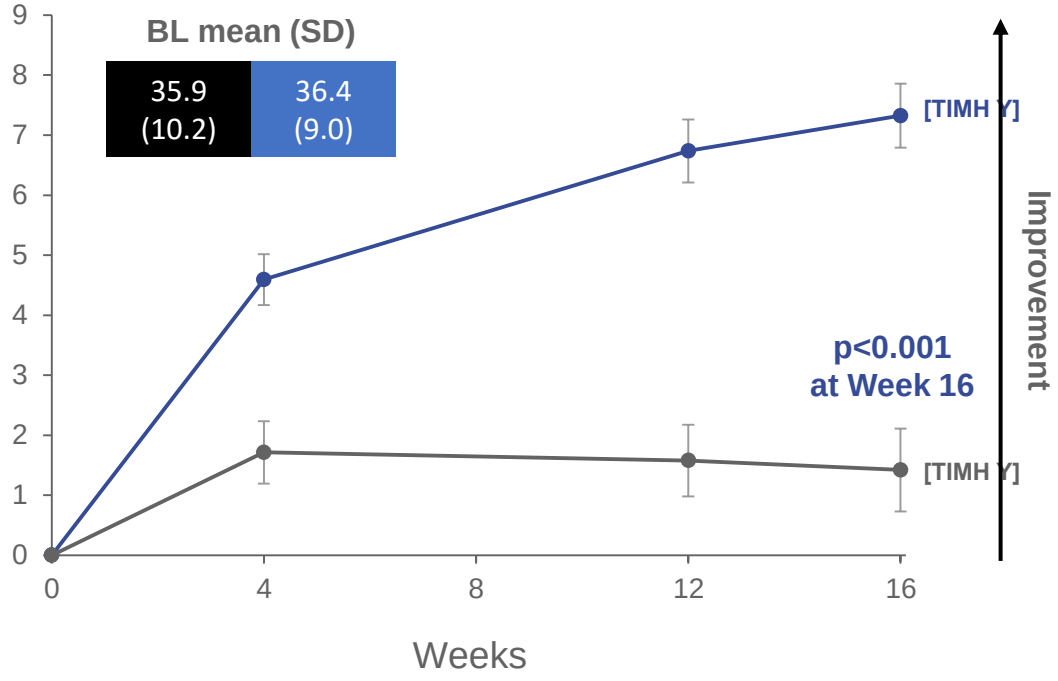
Σημαντικά μεγαλύτερες λειτουργικές βελτιώσεις με το BKZ έναντι του εικονικού φαρμάκου την εβδομάδα 16

BE COMPLETE

HAQ-DI CfB



SF-36 PCS CfB

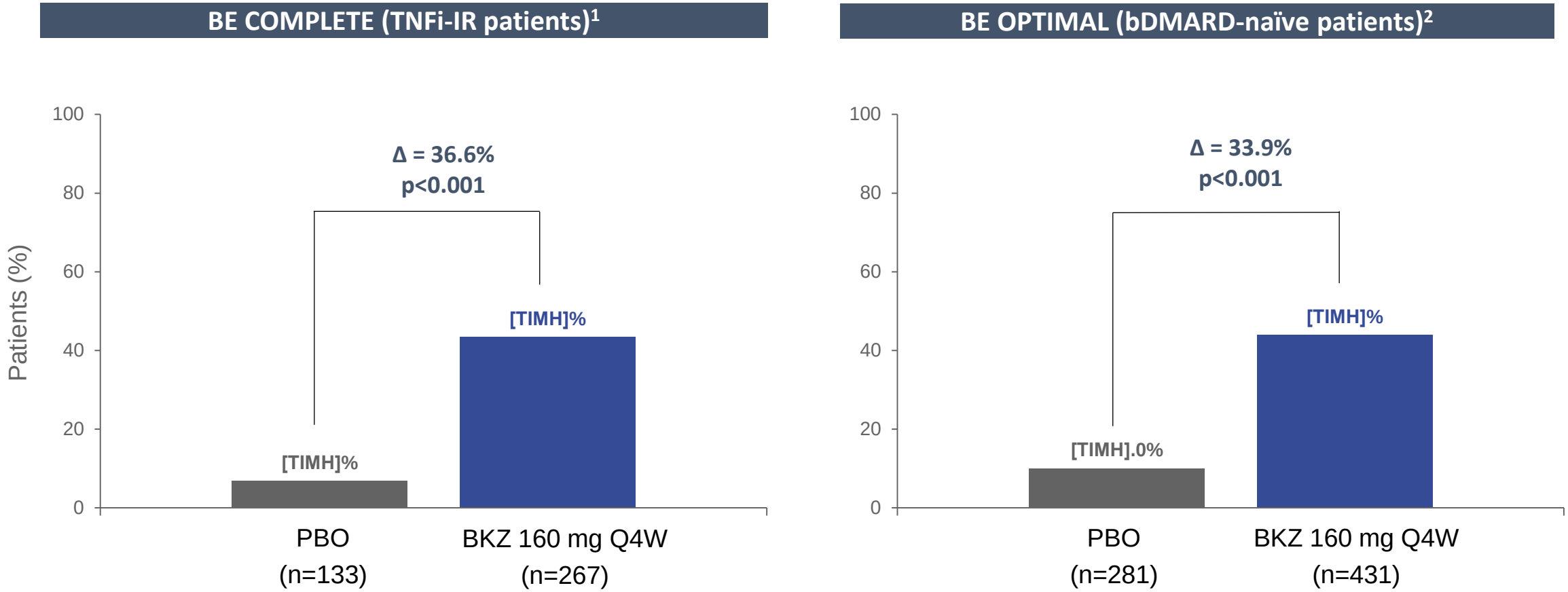


PBO (n=133) BKZ 160 mg Q4W (n=267)

Multiple imputation.
Randomised set. p value obtained from logistic regression with treatment, prior TNF inhibitor exposure and region as factors.

Merola JF et al. EULAR 2022. Presentation OP0255.

Παρόμοια αποτελέσματα κατά ACR50 μεταξύ BE COMPLETE (TNFi-IR) και BE OPTIMAL (bDMARD-naïve) την εβδομάδα 16



Non-responder imputation.
Randomised set. p value for BE COMPLETE was obtained from logistic regression with treatment, prior TNF inhibitor exposure and region as factors. p value for BE OPTIMAL was obtained from logistic regression with treatment, bone erosion at baseline and region as factors.

1. Merola JF et al. EULAR 2022. Presentation OP0255.
2. McInnes IB et al. EULAR 2022. Presentation LB0001.

Χωρίς κάποιο νέο σήμα ασφάλειας στις 24 εβδομάδες θεραπείας με BKZ

BE COMPLETE

n (%)	PBO (n=132)*	BKZ 160 mg Q4W (n=267)
Any TEAE	44 (33.3)	107 (40.1)
Serious TEAEs	0	5 (1.9)
Discontinuation due to TEAEs	0	2 (0.7)
Drug-related TEAEs	4 (3.0)	35 (13.1)
Severe TEAEs	0	5 (1.9)
Deaths	0	0
Most frequently reported TEAEs on the BKZ arm		
Nasopharyngitis	1 (0.8)	10 (3.7)
Oral candidiasis†	0	7 (2.6)
Upper respiratory tract infection	2 (1.5)	6 (2.2)

Safety set. *One patient included in the randomised set was not counted in the safety set. †6 out of 7 cases classified by investigator as mild in intensity, 1 out of 7 cases classified as moderate in intensity; one case resulted in discontinuation. n: number of patients reporting at least one TEAE in that category.

Merola JF et al. EULAR 2022. Presentation OP0255.
1. Ritchlin CT et al. Lancet 2020;395(10222):427–440.
2. Coates LC et al. Ann Rheum Dis. 2021;80:779–780.

Brodalumab

Ενδείκνυται για τη θεραπεία της μέτριας έως σοβαρής ψωρίασης κατά πλάκας σε ενήλικες ασθενείς, οι οποίοι είναι υποψήφιοι για συστηματική θεραπεία.

OPEN ACCESS

CLINICAL SCIENCE

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

Philip J Mease [1], Philip S Helliwell [2], Kasper Fjellhaugen Hjuler [3], Kyle Raymond [4], Iain McInnes [5]

Handling editor Josef S Smolen

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/annrheumdis-2019-216835).

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Received 14 May 2020
Revised 12 August 2020
Accepted 18 August 2020

To cite: Mease PJ, Helliwell PS, Hjuler KF, *et al*. *Ann Rheum Dis* Epub ahead of print: [please include Day Month Year]. doi:10.1136/annrheumdis-2019-216835

ABSTRACT

Objective To compare the efficacy and safety of brodalumab, an interleukin-17 receptor subunit A inhibitor, with placebo, in patients with psoriatic arthritis (PsA).

Methods Adult patients with active PsA and inadequate response to, or intolerance to, conventional treatment were enrolled into two phase III studies (NCT02029495 and NCT02024646) and randomised 1:1:1 to receive subcutaneous brodalumab 140 mg or 210 mg or placebo at weeks 0, 1 and every 2 weeks up to 24 weeks. About 30% of patients had prior use of biologics. The primary endpoint for both studies was the American College of Rheumatology 20 (ACR20) response at week 16.

Results 962 patients were randomised across the studies prior to early termination due to sponsor decision. The primary endpoint was met in both studies. Based on comparable design and eligibility criteria, data from both studies were pooled. Significantly more patients achieved ACR20 at week 16 in both brodalumab treatment groups (45.8% and 47.9% for 140 mg and 210 mg, respectively) versus placebo (20.9%) (p<0.0001). Similar results were observed at week 24. Significantly higher proportions of patients receiving brodalumab achieved ACR50/70, Psoriasis Area and Severity Index 75/90/100 and resolution of dactylitis and enthesitis versus placebo (p<0.01). Adverse event rates were similar across treatments at week 16 (54.4%, 51.6% and 54.5% for placebo, brodalumab 140 mg and 210 mg, respectively). No new safety signals were reported.

Conclusion Brodalumab was associated with rapid and significant improvements in signs and symptoms of PsA versus placebo. Brodalumab was well tolerated, with a safety profile consistent with other interleukin-17 inhibitors.

Key messages

What is already known about this subject?
- Brodalumab has demonstrated efficacy in a phase II trial of patients with psoriatic arthritis (PsA).

What does this study add?
- These phase III trials summarise the efficacy and safety of brodalumab in a much larger population, namely 962 patients with PsA.

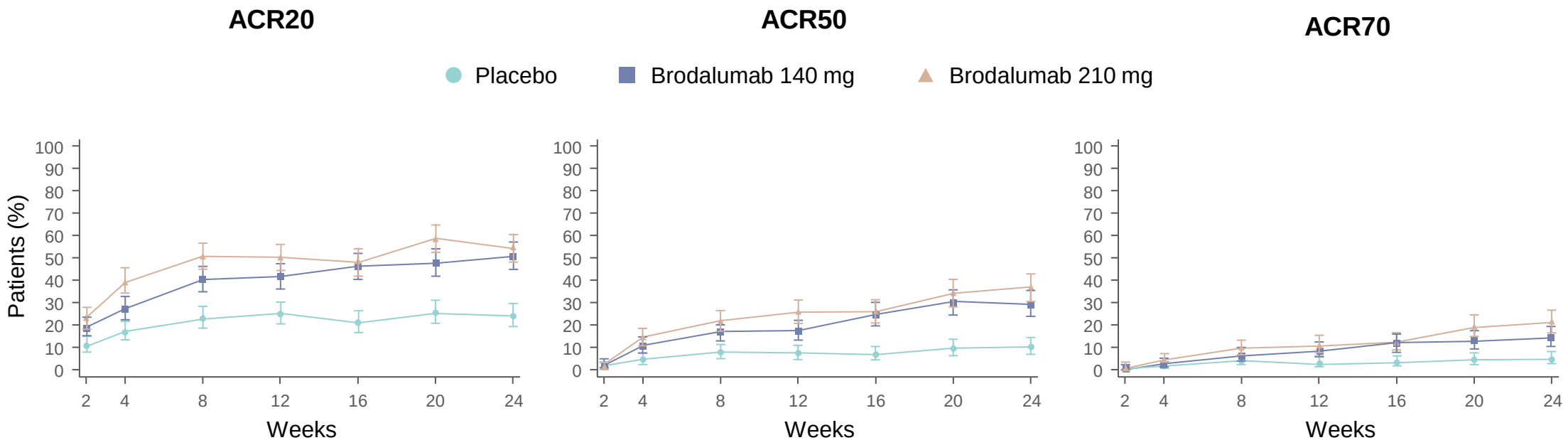
How might this impact on clinical practice or future developments?
- Receptor-level targeting of the interleukin-17 cytokine family involved in the pathogenesis of PsA by brodalumab results in clinically meaningful improvements in articular, enthesitis, dactylitis, skin and health-related domains. These trials provide important information for clinicians treating patients with PsA with brodalumab.

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory disorder that can affect the joints, tendon sheaths, entheses and axial skeleton.[1 2] PsA is a heterogeneous condition with different clinical phenotypes, varying in severity, disease course and numbers of affected joints.[3] Patients with PsA can experience substantial disability, with severe joint damage, digital deformation, functional impairment and impairment of quality of life (QoL).[4]

Current treatment guidelines recommend biologic disease-modifying antirheumatic drugs (DMARDs) as a treatment option on inadequate response following treatment with non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids and conventional synthetic DMARDs.[2 4] Despite the advent of therapeutics targeting tumour necrosis factor (TNF), interleukin (IL)-17A and IL-12/23,[5–7] and, more recently, Janus kinase and phosphodiesterase type 4, an unmet need remains in PsA as a significant proportion of patients either do not respond or eventually lose response to currently available therapies.[2 4 8] Brodalumab is a fully human monoclonal antibody with a unique mechanism of action that binds to the IL-17 receptor subunit A (IL-17RA) with high affinity and, as a consequence, blocks the action of multiple proinflammatory cytokines of the IL-17 family, beyond that of IL-17A alone. Brodalumab 210 mg is currently approved for the treatment of moderate-to-severe plaque psoriasis[9 10] in the USA, EU, Canada and certain Asian countries and for PsA currently only in Japan.[11] The efficacy and safety of brodalumab in PsA were evaluated in a phase II, randomised, double-blind, placebo-controlled trial (NCT 01516957).[12] Brodalumab 140 mg and 280 mg once every 2 weeks (Q2W) were associated with significantly greater improvements in clinical response (American College of Rheumatology 20 (ACR20); primary

Ποσοστά ανταποκρίσεων κατά ACR την Εβδ. 24



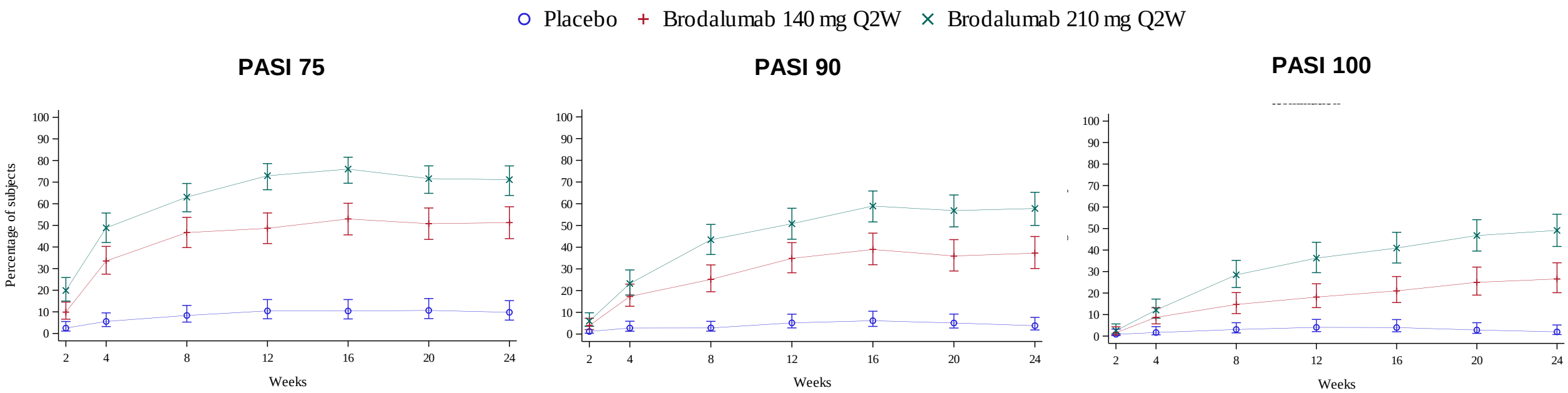
	Patients achieving ACR20 at week 24 (%)
Placebo	24.2
Brodalumab 140 mg	50.9
Brodalumab 210 mg	54.6

	Patients achieving ACR50 at week 24 (%)
Placebo	10.5
Brodalumab 140 mg	29.9
Brodalumab 210 mg	36.9

	Patients achieving ACR70 at week 24 (%)
Placebo	4.8
Brodalumab 140 mg	14.4
Brodalumab 210 mg	21.2

Full Analysis Set
GEE and NRI applied for reasons other than premature study termination.
GEE, generalised estimating equation model.
LEO data on file.

PASI scores την Εβδ. 24



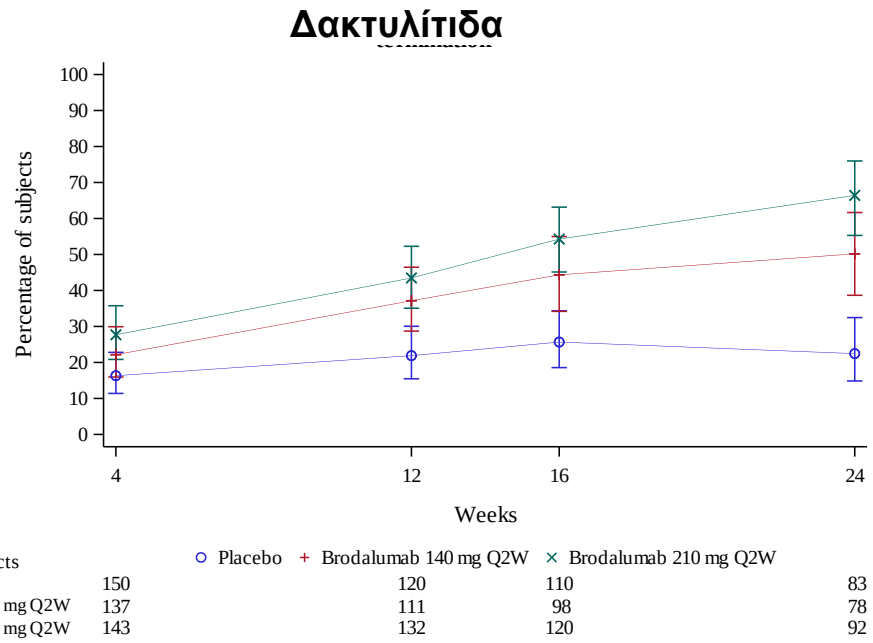
	Patients achieving PASI75 at week 24 (%)
Placebo	9.8
Brodalumab 140 mg	51.3
Brodalumab 210 mg	71.2

	Patients achieving PASI90 at week 24 (%)
Placebo	3.8
Brodalumab 140 mg	37.3
Brodalumab 210 mg	57.8

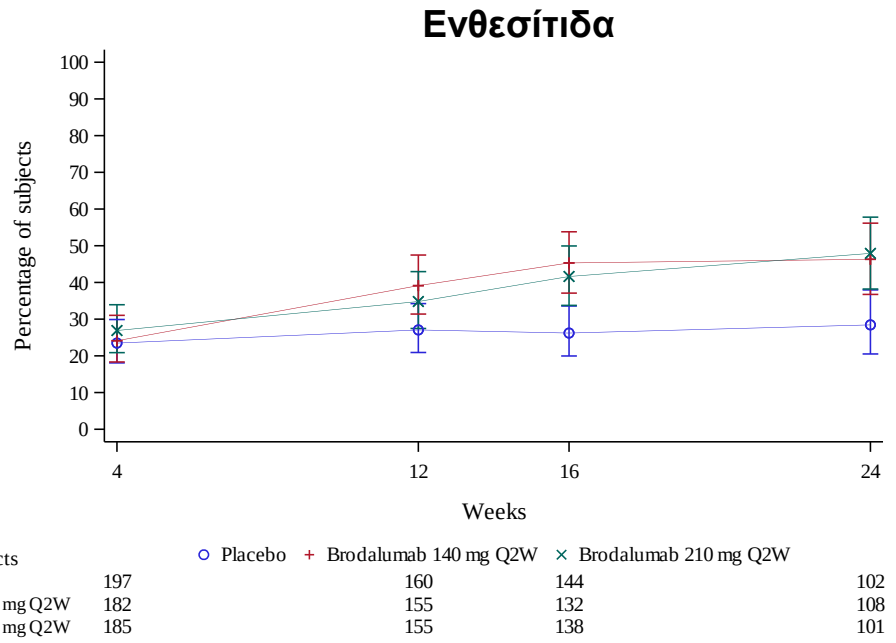
	Patients achieving PASI100 at week 24 (%)
Placebo	1.9
Brodalumab 140 mg	26.6
Brodalumab 210 mg	49.1

*p<0.0001 versus placebo. Psoriasis Efficacy Full Analysis Set. NRI has been applied following early withdrawal from study for reasons other than premature study termination. Intermittent missing data is assumed MCAR.
GEE has been used to estimate odds of response.
MCAR, missing completely at random.
LEO data on file.

Ανταποκρίσεις Ενθεσίτιδας & Δακτυλίτιδας την Εβδ. 24



No. subjects				
Placebo	150	120	110	83
Broda. 140 mg Q2W	137	111	98	78
Broda. 210 mg Q2W	143	132	120	92



No. subjects				
Placebo	197	160	144	102
Broda. 140 mg Q2W	182	155	132	108
Broda. 210 mg Q2W	185	155	138	101

	Patients achieving resolution of dactylitis at week 24 (%)
Placebo	22.7
Brodalumab 140 mg	41.6
Brodalumab 210 mg	43.8

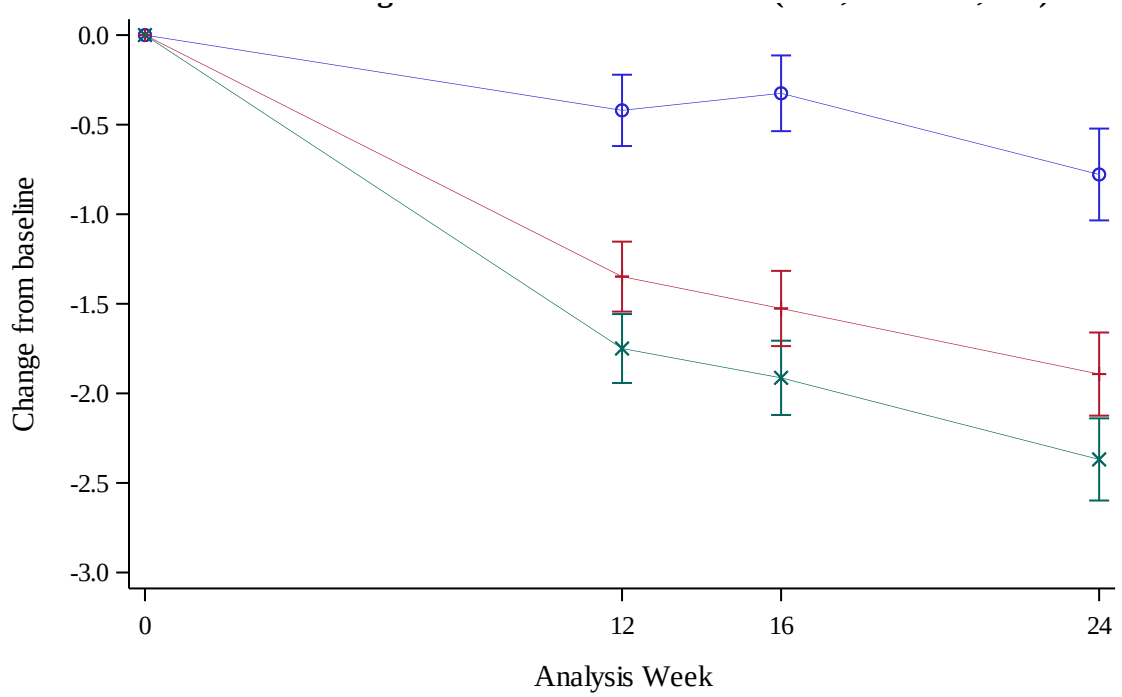
	Patients achieving resolution of enthesitis at week 24 (%)
Placebo	19.8
Brodalumab 140 mg	43.0
Brodalumab 210 mg	60.1

*p<0.0001 versus placebo. Enthesitis and Dactylitis Efficacy Full Analysis SetNRI has been applied following early withdrawal from study for reasons other than premature study termination. Intermittent missing data is assumed MCAR.
GEE has been used to estimate odds of response.
MCAR, missing completely at random.
LEO data on file.

Psoriatic Arthritis Disease Activity Score (PASDAS) την Εβδ. 24

To Psoriatic Arthritis Disease Activity Score αποτελείται από τις παρακάτω κατηγορίες:

- Physician global VAS
- Patient global VAS
- SF-36 PCS
- Αριθμός Οιδηματωδών Αρθρώσεων
- Αριθμός Ευαίσθητων Αρθρώσεων
- Leeds Enthesitis Count
- Dactylitis count
- CRP



Psoriatic Arthritis Disease Activity Score (PASDAS):

(((0.18√ PGA) + (0.159√ PtGA) – (0.253 x √ SF-36-PCS) + (0.101 x LN (SJC + 1)) + (0.048 x LN (TJC + 1)) + (0.23 x LN (LEI +1)) + (0.37 LN (tender dactylitis count + 1)) + (0.102 x LN (CRP + 1)) +2) x 1.5

Helliwell et al. 2013 - Ann Rheum Dis. 2013 Jun;72(6) 986-91; Helliwell et al. 2014 - J Rheumatol. 2014 Jun;41(6) 1212-7

Προφίλ Ασφάλειας

Ανεπιθύμητες ενέργειες ανά κατηγορία μέχρι την Εβδ. 16

	Placebo (n=320)	Brodalumab 140 mg (n=318)	Brodalumab 210 mg (n=321)	All brodalumab (n=639)
Any AE, n (%)	174 (54.4)	164 (51.6)	175 (54.5)	339 (53.1)
Any SAE, n (%)	9 (2.8)	6 (1.9)	11 (3.4)	17 (2.7)
Any AE leading to discontinuation, n (%)	7 (2.2)	3 (0.9)	4 (1.2)	7 (1.1)
Any AE leading to interruption of treatment, n (%)	41 (12.8)	30 (9.4)	38 (11.8)	68 (10.6)

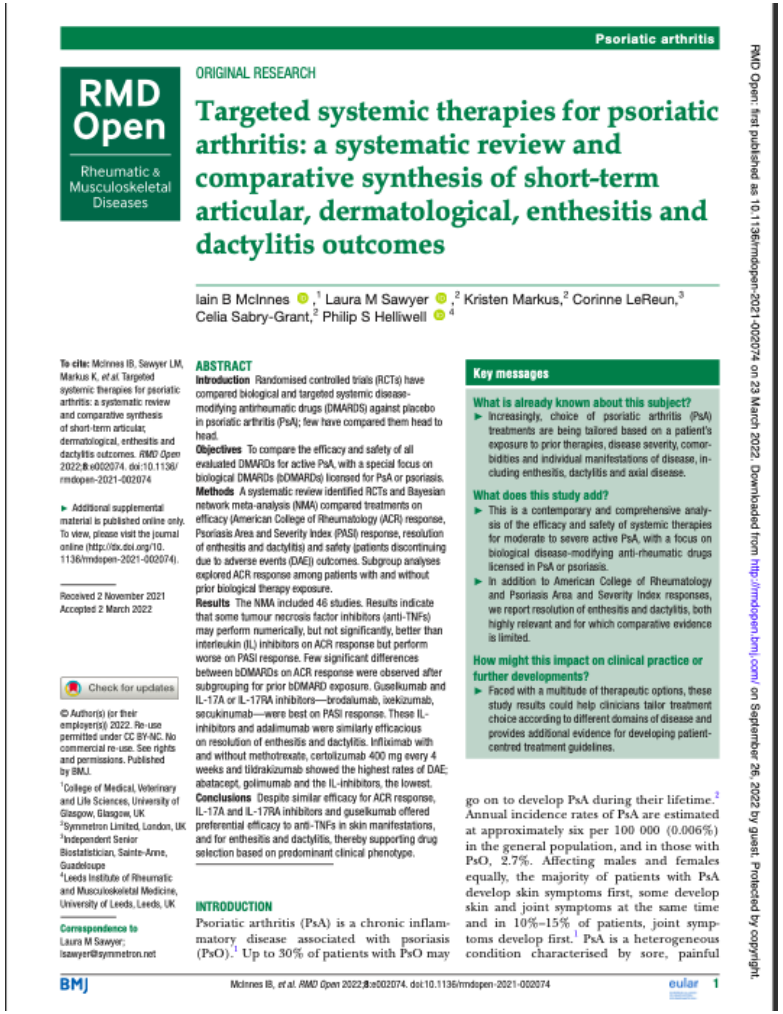
Πιο συχνές ανεπιθύμητες ενέργειες (≥5 patients per group) στο brodalumab (140 ή 210 mg):

- Διάρροια
- Ρινοφαρυγγίτιδα
- Κεφαλαλγία
- Υπέρταση
- Ρινίτιδα
- Λοιμώξεις Ανώτερου Αναπνευστικού

Subjects with multiple events in the same category are counted only once in that category.
AE, adverse event; SAE, serious AE.

1. LEO data on file. Table 11.3.2.1.1.; 2. Mease PJ et al. P0387 presented at the 26th EADV congress; September 13–17, 2017; Geneva, Switzerland;
3. Mease PJ et al. P0388 presented at the 26th EADV congress; September 13–17, 2017; Geneva, Switzerland.

Targeted systemic therapies for psoriatic arthritis: as systematic review



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

Iain B McInnes ,[1] Laura M Sawyer ,[2] Kristen Markus,[2] Corinne LeReun,[3] Celia Sabry-Grant,[2] Philip S Helliwell [4]

To cite: McInnes IB, Sawyer LM, Markus K, *et al*. Targeted systemic therapies for psoriatic arthritis: a systematic review and comparative synthesis of short-term articular, dermatological, enthesitis and dactylitis outcomes. *RMD Open* 2022;**8**:e002074. doi:10.1136/rmdopen-2021-002074

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/rmdopen-2021-002074).

Received 2 November 2021
Accepted 2 March 2022

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ABSTRACT

Introduction Randomised controlled trials (RCTs) have compared biological and targeted systemic disease-modifying antirheumatic drugs (DMARDS) against placebo in psoriatic arthritis (PsA); few have compared them head to head.

Objectives To compare the efficacy and safety of all evaluated DMARDs for active PsA, with a special focus on biological DMARDs (bDMARDs) licensed for PsA or psoriasis.

Methods A systematic review identified RCTs and Bayesian network meta-analysis (NMA) compared treatments on efficacy (American College of Rheumatology (ACR) response, Psoriasis Area and Severity Index (PASI) response, resolution of enthesitis and dactylitis) and safety (patients discontinuing due to adverse events (DAE)) outcomes. Subgroup analyses explored ACR response among patients with and without prior biological therapy exposure.

Results The NMA included 46 studies. Results indicate that some tumour necrosis factor inhibitors (anti-TNFs) may perform numerically, but not significantly, better than interleukin (IL) inhibitors on ACR response but perform worse on PASI response. Few significant differences between bDMARDs on ACR response were observed after subgrouping for prior bDMARD exposure. Guselkumab and IL-17A or IL-17RA inhibitors—brodalumab, ixekizumab, secukinumab—were best on PASI response. These IL-inhibitors and adalimumab were similarly efficacious on resolution of enthesitis and dactylitis. Infliximab with and without methotrexate, certolizumab 400 mg every 4 weeks and tildrakizumab showed the highest rates of DAE; abatacept, golimumab and the IL-inhibitors, the lowest.

Conclusions Despite similar efficacy for ACR response, IL-17A and IL-17RA inhibitors and guselkumab offered preferential efficacy to anti-TNFs in skin manifestations, and for enthesitis and dactylitis, thereby supporting drug selection based on predominant clinical phenotype.

Key messages

What is already known about this subject?
- Increasingly, choice of psoriatic arthritis (PsA) treatments are being tailored based on a patient's exposure to prior therapies, disease severity, comorbidities and individual manifestations of disease, including enthesitis, dactylitis and axial disease.

What does this study add?
- This is a contemporary and comprehensive analysis of the efficacy and safety of systemic therapies for moderate to severe active PsA, with a focus on biological disease-modifying anti-rheumatic drugs licensed in PsA or psoriasis.
- In addition to American College of Rheumatology and Psoriasis Area and Severity Index responses, we report resolution of enthesitis and dactylitis, both highly relevant and for which comparative evidence is limited.

How might this impact on clinical practice or further developments?
- Faced with a multitude of therapeutic options, these study results could help clinicians tailor treatment choice according to different domains of disease and provides additional evidence for developing patient-centred treatment guidelines.

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory disease associated with psoriasis (PsO).[1] Up to 30% of patients with PsO may go on to develop PsA during their lifetime.[2] Annual incidence rates of PsA are estimated at approximately six per 100 000 (0.006%) in the general population, and in those with PsO, 2.7%. Affecting males and females equally, the majority of patients with PsA develop skin symptoms first, some develop skin and joint symptoms at the same time and in 10%–15% of patients, joint symptoms develop first.[1] PsA is a heterogeneous condition characterised by sore, painful

-The NMA included 46 studies
-Some anti-TNFs may perform numerically, but not significantly, better than IL inhibitors on ACR response but perform worse on PASI response
-Few significant differences between bDMARDs on ACR response were after subgrouping for prior bDMARD exposure
-Guselkumab and IL-17A or IL-17RA inhibitors—brodalumab, ixekizumab, secukinumab—were best on PASI response
-These IL-inhibitors and adalimumab were similarly efficacious on resolution of enthesitis and dactylitis.
-Infliximab with and without methotrexate, certolizumab 400 mg every 4 weeks and tildrakizumab showed the highest rates of DAE
-Abatacept, golimumab and the IL-inhibitors, the lowest

Conclusions Despite similar efficacy for ACR response, IL-17A and IL-17RA inhibitors and guselkumab offered preferential efficacy to anti-TNFs in skin manifestations, and for enthesitis and dactylitis, thereby supporting drug selection based on predominant clinical phenotype.

Targeted systemic therapies for psoriatic arthritis: as systematic review

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

Iain B McInnes ,[1] Laura M Sawyer ,[2] Kristen Markus,[2] Corinne LeReun,[3] Celia Sabry-Grant,[2] Philip S Helliwell [4]

To cite: McInnes IB, Sawyer LM, Markus K, *et al*. Targeted systemic therapies for psoriatic arthritis: a systematic review and comparative synthesis of short-term articular, dermatological, enthesitis and dactylitis outcomes. *RMD Open* 2022;**8**:e002074. doi:10.1136/rmdopen-2021-002074

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/rmdopen-2021-002074).

Received 2 November 2021
Accepted 2 March 2022

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ABSTRACT

Introduction Randomised controlled trials (RCTs) have compared biological and targeted systemic disease-modifying antirheumatic drugs (DMARDS) against placebo in psoriatic arthritis (PsA); few have compared them head to head.

Objectives To compare the efficacy and safety of all evaluated DMARDs for active PsA, with a special focus on biological DMARDs (bDMARDs) licensed for PsA or psoriasis.

Methods A systematic review identified RCTs and Bayesian network meta-analysis (NMA) compared treatments on efficacy (American College of Rheumatology (ACR) response, Psoriasis Area and Severity Index (PASI) response, resolution of enthesitis and dactylitis) and safety (patients discontinuing due to adverse events (DAE)) outcomes. Subgroup analyses explored ACR response among patients with and without prior biological therapy exposure.

Results The NMA included 46 studies. Results indicate that some tumour necrosis factor inhibitors (anti-TNFs) may perform numerically, but not significantly, better than interleukin (IL) inhibitors on ACR response but perform worse on PASI response. Few significant differences between bDMARDs on ACR response were observed after subgrouping for prior bDMARD exposure. Guselkumab and IL-17A or IL-17RA inhibitors—brodalumab, ixekizumab, secukinumab—were best on PASI response. These IL-inhibitors and adalimumab were similarly efficacious on resolution of enthesitis and dactylitis. Infliximab with and without methotrexate, certolizumab 400 mg every 4 weeks and tildrakizumab showed the highest rates of DAE; abatacept, golimumab and the IL-inhibitors, the lowest.

Conclusions Despite similar efficacy for ACR response, IL-17A and IL-17RA inhibitors and guselkumab offered preferential efficacy to anti-TNFs in skin manifestations, and for enthesitis and dactylitis, thereby supporting drug selection based on predominant clinical phenotype.

Key messages

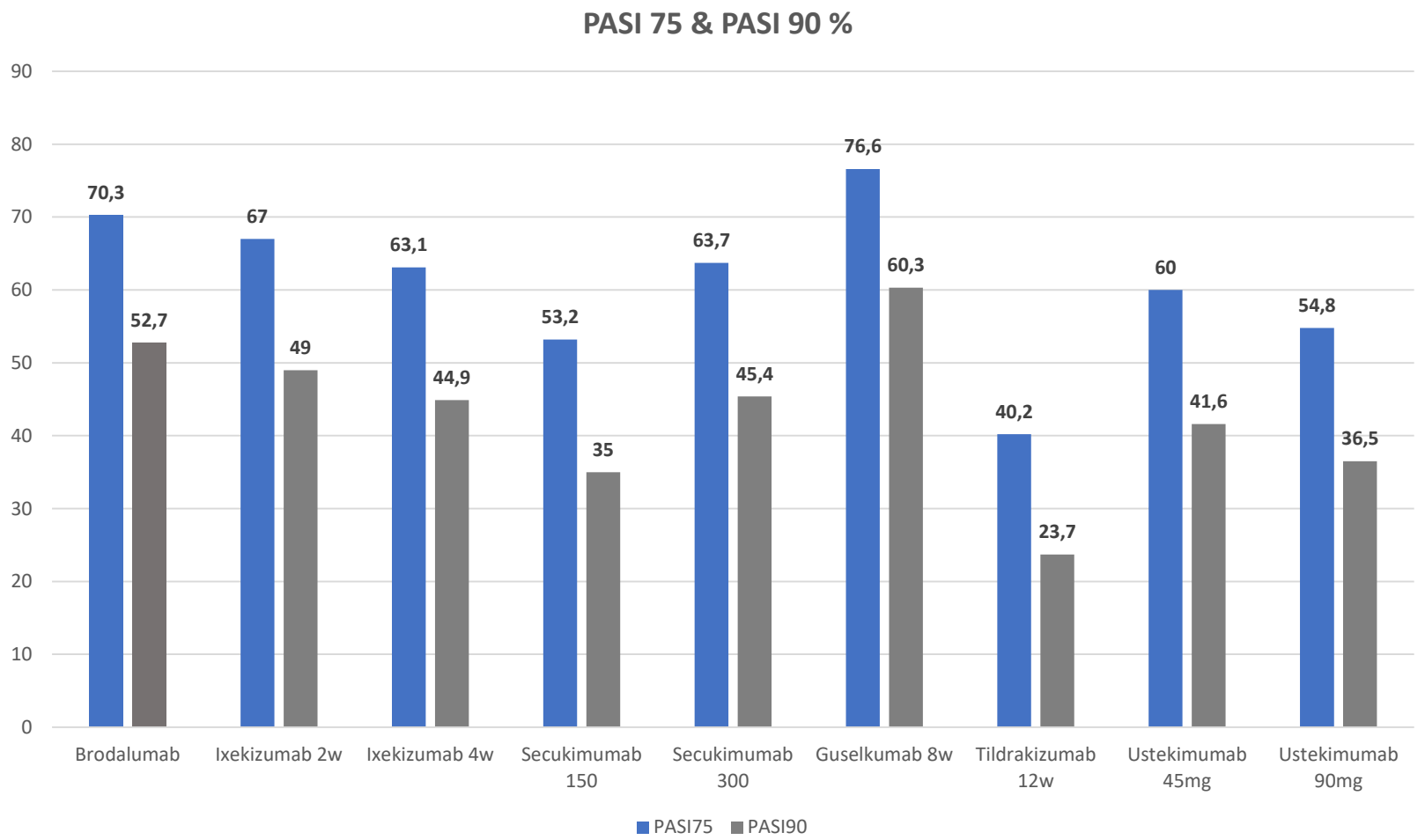
What is already known about this subject?
- Increasingly, choice of psoriatic arthritis (PsA) treatments are being tailored based on a patient's exposure to prior therapies, disease severity, comorbidities and individual manifestations of disease, including enthesitis, dactylitis and axial disease.

What does this study add?
- This is a contemporary and comprehensive analysis of the efficacy and safety of systemic therapies for moderate to severe active PsA, with a focus on biological disease-modifying anti-rheumatic drugs licensed in PsA or psoriasis.
- In addition to American College of Rheumatology and Psoriasis Area and Severity Index responses, we report resolution of enthesitis and dactylitis, both highly relevant and for which comparative evidence is limited.

How might this impact on clinical practice or further developments?
- Faced with a multitude of therapeutic options, these study results could help clinicians tailor treatment choice according to different domains of disease and provides additional evidence for developing patient-centred treatment guidelines.

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory disease associated with psoriasis (PsO).[1] Up to 30% of patients with PsO may go on to develop PsA during their lifetime.[2] Annual incidence rates of PsA are estimated at approximately six per 100 000 (0.006%) in the general population, and in those with PsO, 2.7%. Affecting males and females equally, the majority of patients with PsA develop skin symptoms first, some develop skin and joint symptoms at the same time and in 10%–15% of patients, joint symptoms develop first.[1] PsA is a heterogeneous condition characterised by sore, painful



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Targeted systemic therapies for psoriatic arthritis: as systematic review

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

Iain B McInnes ,[1] Laura M Sawyer ,[2] Kristen Markus,[2] Corinne LeReun,[3] Celia Sabry-Grant,[2] Philip S Helliwell [4]

To cite: McInnes IB, Sawyer LM, Markus K, *et al*. Targeted systemic therapies for psoriatic arthritis: a systematic review and comparative synthesis of short-term articular, dermatological, enthesitis and dactylitis outcomes. *RMD Open* 2022;**8**:e002074. doi:10.1136/rmdopen-2021-002074

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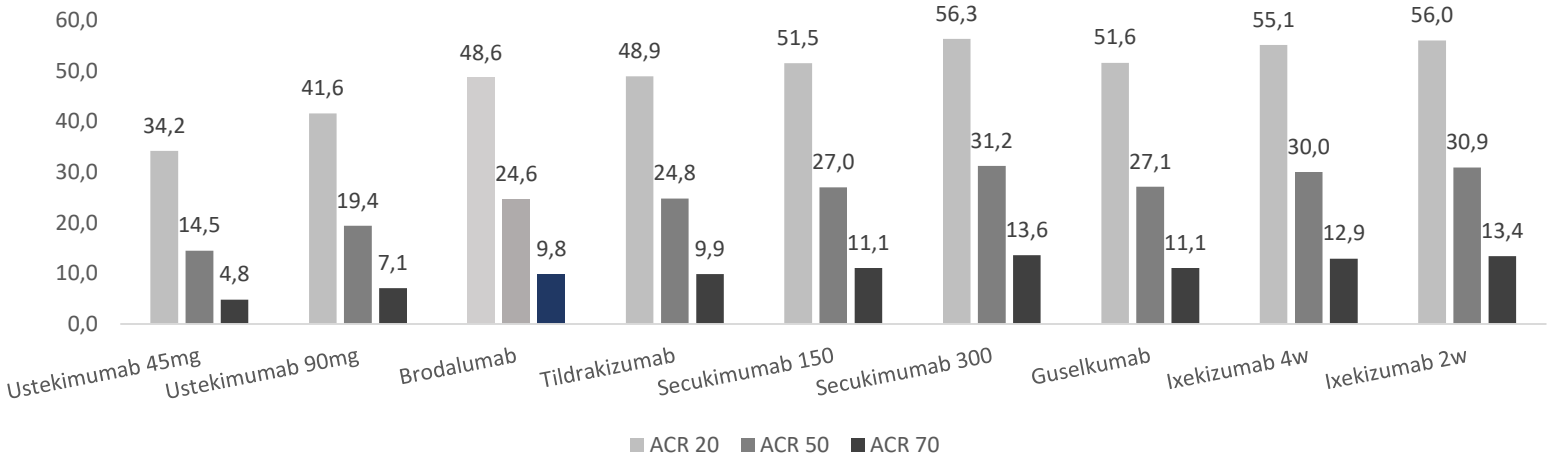
Ανταπόκριση δεικτών ACR



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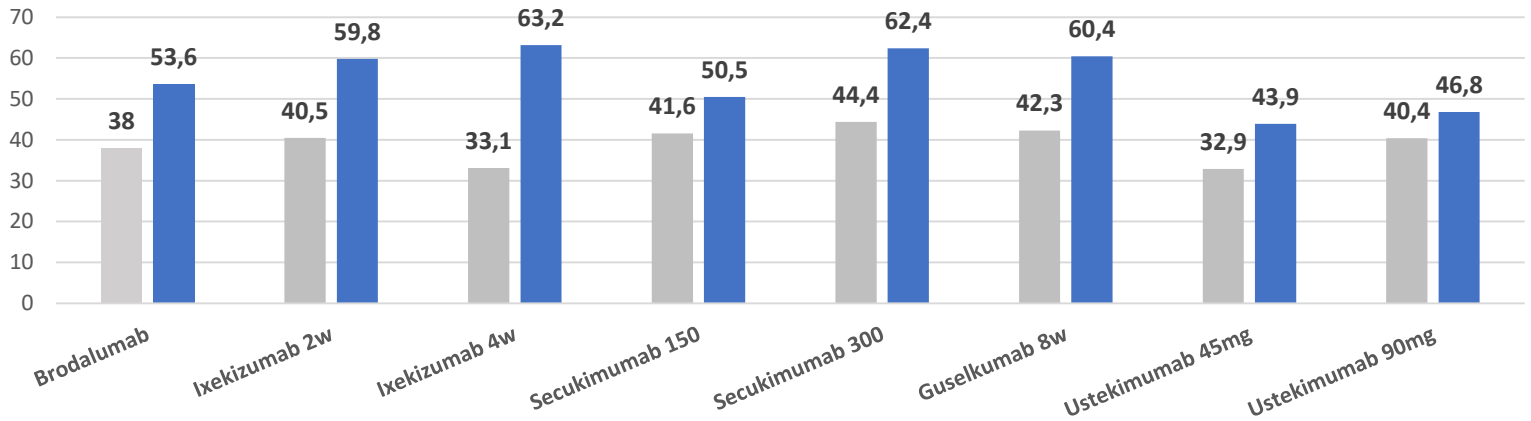

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Συστάσεις EULAR 2019 για ΨΑ

		Επίπεδο ενδείξεων	Βαθμός συστάσεων	Μεταβολές από Συστάσεις 2015
6.	Σε ασθενείς με **περιφερική αρθρίτιδα και ανεπαρκή ανταπόκριση** σε ≥1 csDMARD, θα πρέπει να ξεκινά θεραπεία με κάποιο bDMARD· **όταν υφίσταται σχετική προσβολή του δέρματος, μπορεί να είναι προτιμώμενη η χρήση ενός αναστολέα IL-17 ή ενός αναστολέα IL-12/23**	1β	B	**Τροποποιήθηκαν και συγχωνεύθηκαν**· δεν κάνουν διάκριση μεταξύ των bDMARD που χρησιμοποιούνται για την ΨΑ
7.	Σε ασθενείς με περιφερική αρθρίτιδα και ανεπαρκή ανταπόκριση σε ≥1 csDMARD και ≥1 bDMARD, ή όταν η χορήγηση ενός bDMARD δεν είναι κατάλληλη, μπορεί να εξεταστεί το ενδεχόμενο χρήσης ενός **αναστολέα JAK**	1β	B	**Νέο**
8.	Σε ασθενείς με ήπια νόσο* και ανεπαρκή ανταπόκριση σε ≥1 csDMARD†, για τους οποίους δεν είναι κατάλληλη η χορήγηση ούτε bDMARD ούτε αναστολέα JAK*, μπορεί να εξεταστεί το ενδεχόμενο χρήσης ενός **αναστολέα PDE4**	*5 †1β	B	**Τροποποιήθηκαν**· σύσταση για τη χρήση APR
9.	Σε ασθενείς με **αδιαμφισβήτητη ενθεσίτιδα** και ανεπαρκή ανταπόκριση σε ΜΣΑΦ ή τοπικές ενέσεις γλυκοκορτικοειδών, θα πρέπει να εξετάζεται το ενδεχόμενο θεραπείας με ένα bDMARD	1β	B	**Τροποποιήθηκαν**· αντικατάσταση της «ενεργού ενθεσίτιδας», παράλειψη της χρήσης TNFi στο πλαίσιο της ισχύουσας πρακτικής

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

Συστάσεις EULAR 2019 για ΨΑ

		Επίπεδο ενδείξεων	Βαθμός συστάσεων	Μεταβολές από Συστάσεις 2015
10.	Σε ασθενείς με κατά κύριο λόγο **αξονική νόσο** που είναι ενεργός και δεν ανταποκρίνεται επαρκώς στα ΜΣΑΦ, θα πρέπει να εξετάζεται το ενδεχόμενο θεραπείας με κάποιο bDMARD, το οποίο σύμφωνα με την ισχύουσα πρακτική είναι ένας αναστολέας TNF· όταν υφίσταται σχετική **προσβολή του δέρματος, μπορεί να είναι προτιμώμενη η χρήση ενός αναστολέα IL-17**	1β	Β	**Τροποποιήθηκε**· η διατύπωση ευθυγραμμίστηκε εν μέρει με τις συστάσεις αντιμετώπισης των ASAS/EULAR για την axSpA· προσθήκη προτίμησης ενός αναστολέα IL-17 για την περίπτωση προσβολής του δέρματος
11.	Σε ασθενείς που δεν παρουσιάζουν επαρκή ανταπόκριση ή παρουσιάζουν δυσανεξία σε κάποιο bDMARD, θα πρέπει να εξετάζεται το ενδεχόμενο **αλλαγής θεραπείας** σε κάποιο άλλο bDMARD ή tsDMARD*, συμπεριλαμβανομένης μίας αλλαγής θεραπείας εντός μίας φαρμακευτικής κατηγορίας†	*1β †4	Γ	**Τροποποιήθηκε**· επέκταση προηγούμενης σύστασης για την εισήγηση αλλαγής θεραπείας είτε σε κάποιο άλλο bDMARD είτε σε tsDMARD, ιδιαίτερα κάποιον αναστολέα JAK
12.	Σε ασθενείς με **διατηρούμενη ύφεση**, μπορεί να εξεταστεί το ενδεχόμενο προσεκτικής σταδιακής μείωσης της δόσης των DMARD	4	Γ	**Νέο**

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

Ανανεωμένες συστάσεις GRAPPA 2021

Indication	Strong recommendation for	Conditional recommendation for	Conditional recommendation against	Strong recommendation against	No recommendation: insufficient or conflicting evidence
Peripheral arthritis, DMARD naive	csDMARDs (except CsA), TNFi, IL-12/23i, IL-17i, IL-23i, JAKi, PDE4i	NSAIDs, oral GC, IA GC	–	–	–
Peripheral arthritis, DMARD inadequate response	TNFi, IL-12/23i, IL-17i, IL-23i, JAKi, PDE4i	csDMARDs, NSAIDs, oral GC, IA GC, CTLA4-Ig	–	–	–
Peripheral arthritis, bDMARD experienced	TNFi, IL-17i, IL-23i, JAKi	NSAIDs, oral GC, IA GC, IL-12/23i, PDE4i, CTLA4-Ig	–	–	–
Axial disease, bDMARD naive	NSAIDs, physiotherapy, simple analgesia, TNFi, IL-17i, JAKi	GC SIJ injections, bisphosphonates	PDE4i	csDMARDs	IL-12/23i, IL-23i
Enthesitis	TNFi, IL-12/23i, IL-17i, IL-23i, JAKi, PDE4i	NSAIDs, physiotherapy, MTX, CTLA4-Ig, GC injections (with extreme caution)	–	–	Other csDMARDs
Dactylitis	TNFi, IL-12/23i, IL-17i, IL-23i, JAKi, PDE4i	NSAIDs, GC injections, MTX, CTLA4-Ig	Other csDMARDs	–	–
Psoriasis (plaque)	Topical therapies, phototherapy, cdDMARDs (MTX, fumarate, fumaric acid esters, CsA), TNFi, IL-12/23i, IL-17i, IL-23i, PDE4i, JAKi	Acitretin	–	–	–
Nail psoriasis	TNFi, IL-12/23i, IL-17i, IL-23i, PDE4i	Topical GC, tacrolimus and calcipotriol combination or individual therapies, pulsed dye laser, csDMARDs (MTX, LEF, CsA), acitretin, JAKi	–	–	Topical CsA, tazarotene, fumarate, fumaric acid esters, UVA and UVB phototherapy, alitretinoin
IBD: Crohn's disease	TNFi (not ETN), IL-12/23i	IL-23i, JAKi, MTX	–	IL-17i	ETN
IBD: UC	TNFi (not ETN), IL-12/23i	IL-23i, JAKi, MTX	–	IL-17i	ETN, PDE4i
Uveitis	–	TNFi (not ETN), CsA, MTX	ETN	–	Other csDMARDs, IL-17i, IL-12/23i

Coates, L.C., et al. Nat Rev Rheumatol 2022;18:465–479


ευχαριστώ