Νέα δεδομένα/ενδιαφέρουσες εξελίξεις στις Σπονδυλοαρθρίτιδες

ΝΙΚΟΛΑΟΣ ΚΟΥΓΚΑΣ
ΕΠΙΚ. ΕΠΙΜΕΛΗΤΗΣ Β΄
ΡΕΥΜΑΤΟΛΟΓΙΚΗ ΚΛΙΝΙΚΗ ΠΑΓΝΗ

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DOI 10.1002/acr.24025

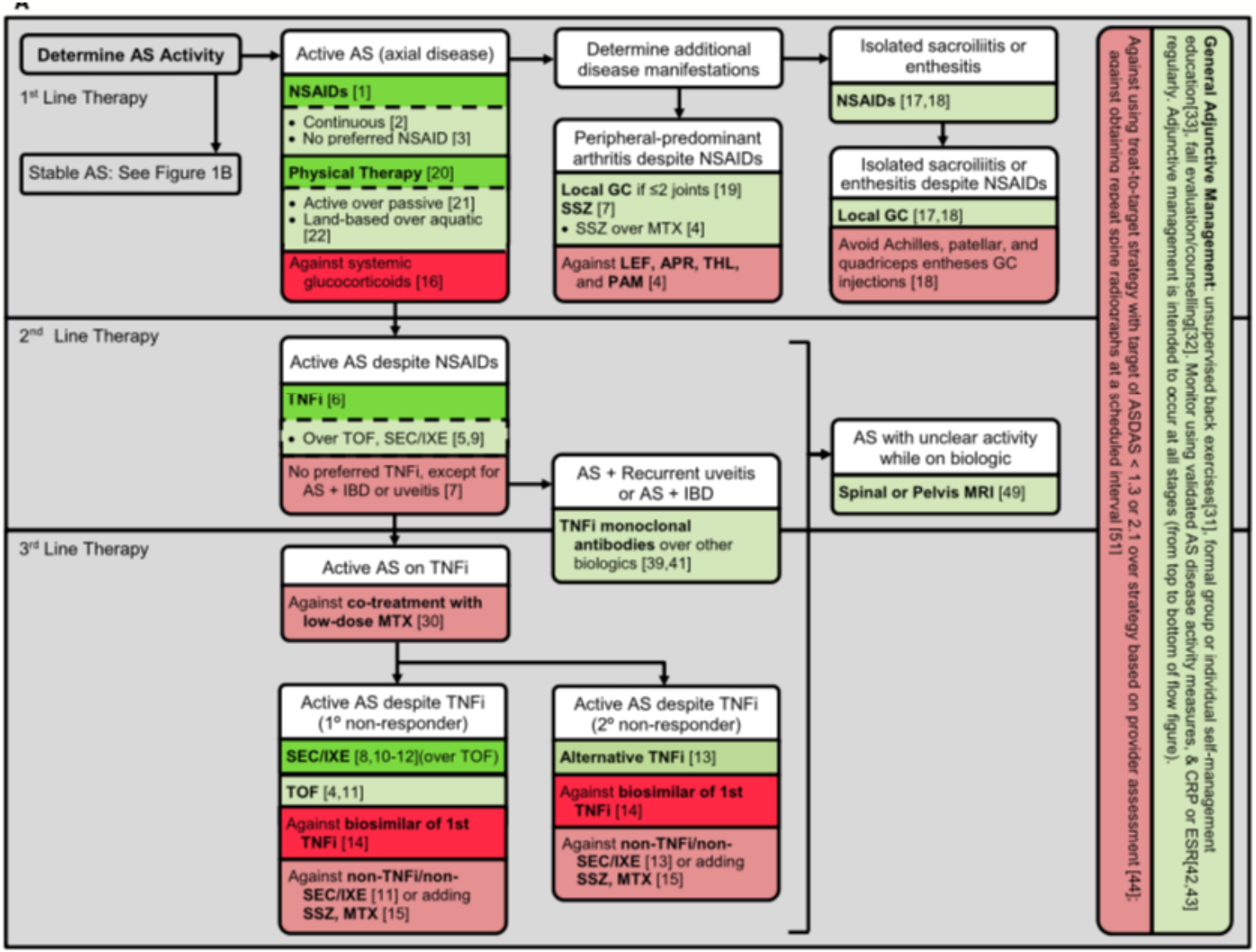
AMERICAN COLLEGE of RHEUMATOLOGY
Empowering Rheumatology Professionals

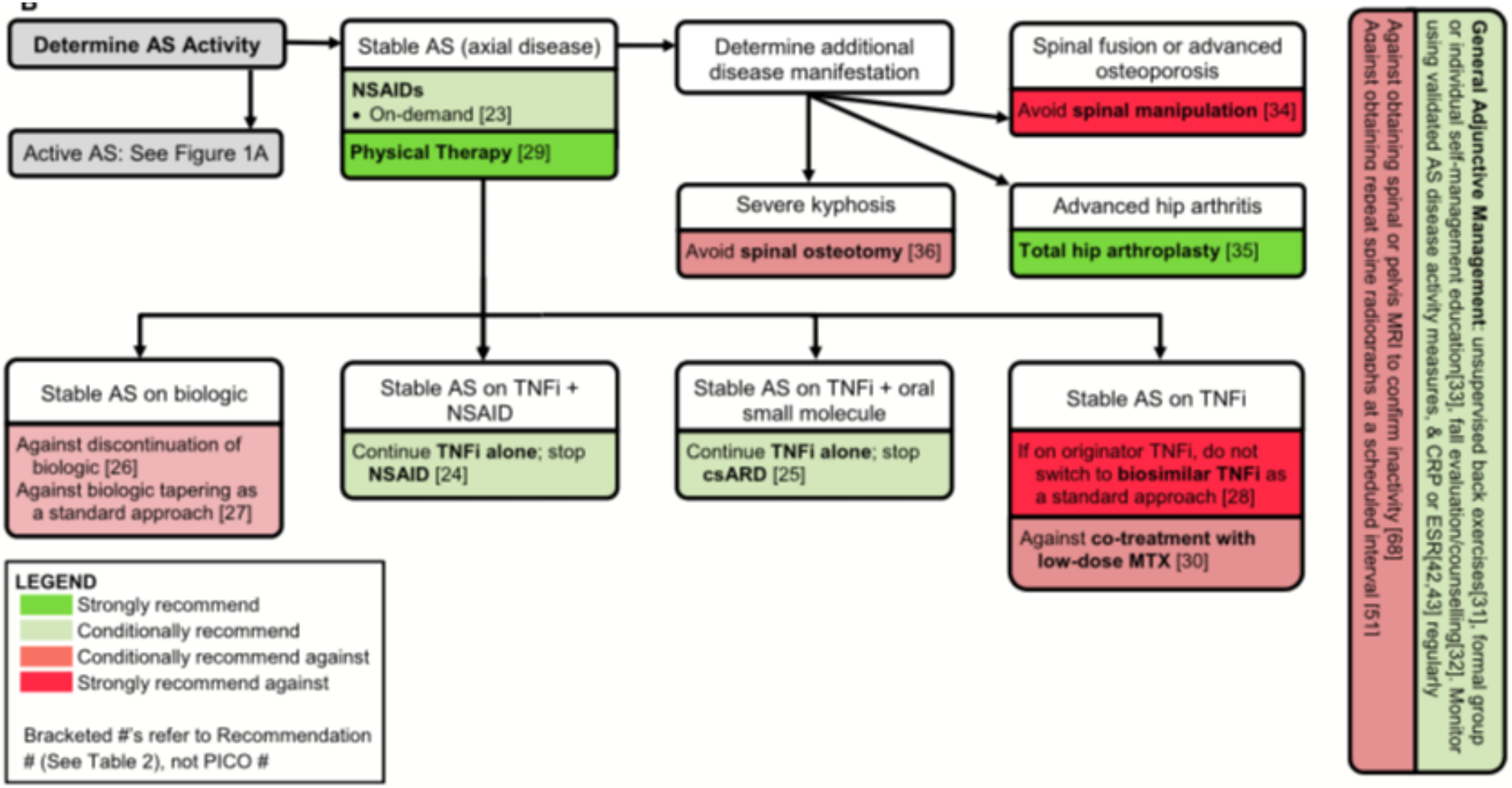
SPECIAL ARTICLE

2019 Update of the American College of Rheumatology/ Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis

Key points

- Χρήση νέων βιολογικών παραγόντων (secukinumab, ixekizumab, tofacitinib και TNFi biosimilars)
- Θέση ΜΣΑΦ και DMARDs
- Θεραπευτική προσέγγιση εξω αρθρικών εκδηλώσεων
- Στρατηγική αποκλιμάκωσης θεραπείας σε σταθερή νόσο
- Ρόλος της απεικόνισης στην παρακολούθηση των ασθενών


A
Determine AS Activity
1st Line Therapy
Stable AS: See Figure 1B
Active AS (axial disease)
NSAIDs [1]
• Continuous [2]
• No preferred NSAID [3]
Physical Therapy [20]
• Active over passive [21]
• Land-based over aquatic [22]
Against systemic glucocorticoids [16]
Determine additional disease manifestations
Peripheral-predominant arthritis despite NSAIDs
Local GC if ≤2 joints [19]
SSZ [7]
• SSZ over MTX [4]
Against LEF, APR, THL, and PAM [4]
Isolated sacroiliitis or enthesitis
NSAIDs [17,18]
Isolated sacroiliitis or enthesitis despite NSAIDs
Local GC [17,18]
Avoid Achilles, patellar, and quadriceps entheses GC injections [18]
2nd Line Therapy
Active AS despite NSAIDs
TNFi [6]
• Over TOF, SEC/IXE [5,9]
No preferred TNFi, except for AS + IBD or uveitis [7]
AS + Recurrent uveitis or AS + IBD
TNFi monoclonal antibodies over other biologics [39,41]
AS with unclear activity while on biologic
Spinal or Pelvis MRI [49]
3rd Line Therapy
Active AS on TNFi
Against co-treatment with low-dose MTX [30]
Active AS despite TNFi (1° non-responder)
SEC/IXE [8,10-12](over TOF)
TOF [4,11]
Against biosimilar of 1st TNFi [14]
Against non-TNFi/non-SEC/IXE [11] or adding SSZ, MTX [15]
Active AS despite TNFi (2° non-responder)
Alternative TNFi [13]
Against biosimilar of 1st TNFi [14]
Against non-TNFi/non-SEC/IXE [13] or adding SSZ, MTX [15]
General Adjunctive Management: unsupervised back exercises[31], formal group or individual self-management education[33], fall evaluation/counselling[32]. Monitor using validated AS disease activity measures, & CRP or ESR[42,43] regularly. Adjunctive management is intended to occur at all stages (from top to bottom of flow figure).
Against using treat-to-target strategy with target of ASDAS < 1.3 or 2.1 over strategy based on provider assessment [44]; against obtaining repeat spine radiographs at a scheduled interval [51]


Determine AS Activity
Active AS: See Figure 1A
Stable AS (axial disease)
NSAIDs
• On-demand [23]
Physical Therapy [29]
Determine additional disease manifestation
Spinal fusion or advanced osteoporosis
Avoid spinal manipulation [34]
Severe kyphosis
Avoid spinal osteotomy [36]
Advanced hip arthritis
Total hip arthroplasty [35]
Stable AS on biologic
Against discontinuation of biologic [26]
Against biologic tapering as a standard approach [27]
Stable AS on TNFi + NSAID
Continue TNFi alone; stop NSAID [24]
Stable AS on TNFi + oral small molecule
Continue TNFi alone; stop csARD [25]
Stable AS on TNFi
If on originator TNFi, do not switch to biosimilar TNFi as a standard approach [28]
Against co-treatment with low-dose MTX [30]
LEGEND
Strongly recommend
Conditionally recommend
Conditionally recommend against
Strongly recommend against
Bracketed #'s refer to Recommendation # (See Table 2), not PICO #
General Adjunctive Management: unsupervised back exercises[31], formal group or individual self-management education[33], fall evaluation/counselling[32]. Monitor using validated AS disease activity measures, & CRP or ESR[42,43] regularly
Against obtaining spinal or pelvis MRI to confirm inactivity [68]
Against obtaining repeat spine radiographs at a scheduled interval [51]

Περιορισμοί

- ‘’Very low quality of evidence’ ’για πολλές συστάσεις
- Προτίμηση ασθενών
- Ελλιπή δεδομένα από μελέτες στη μη ακτινολογική αξονική σπονδυλοαρθρίτιδα
- Η εφαρμογή των συστάσεων πρέπει πάντοτε να εξατομικεύεται

AMERICAN COLLEGE OF RHEUMATOLOGY
EDUCATION • TREATMENT • RESEARCH

Arthritis Care & Research
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SPECIAL ARTICLE

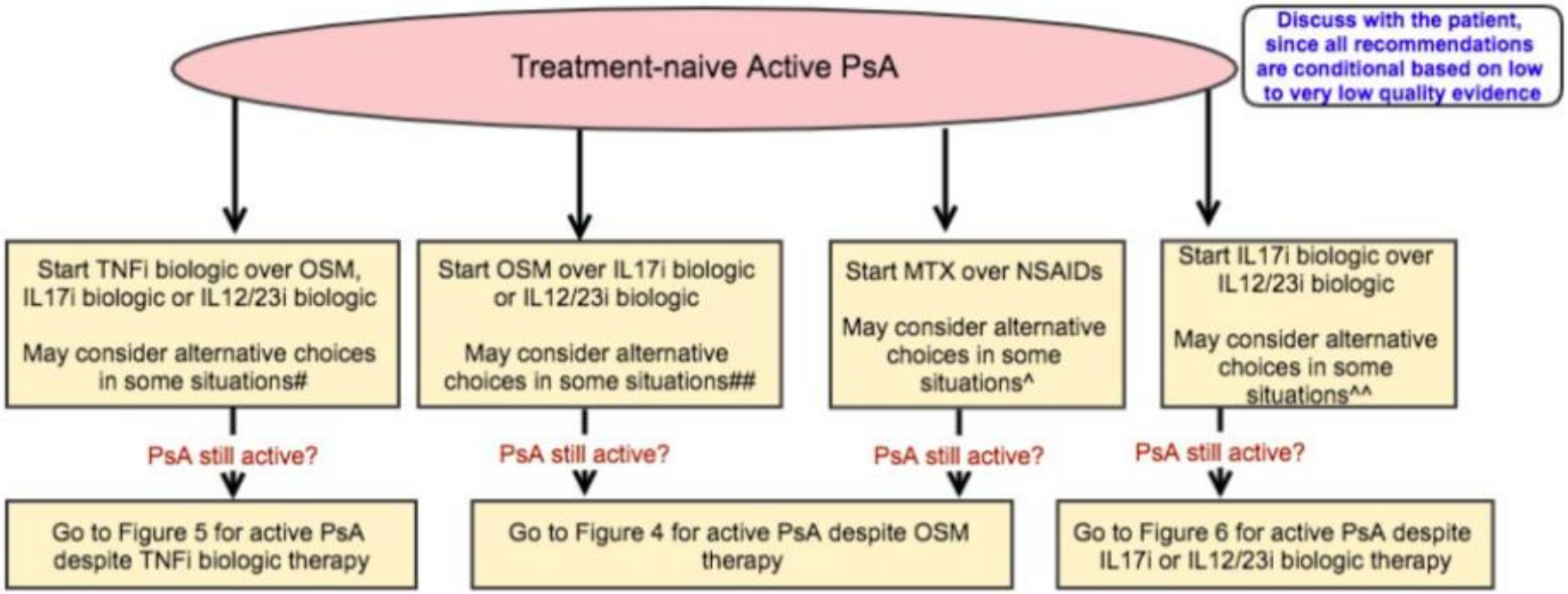
2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis

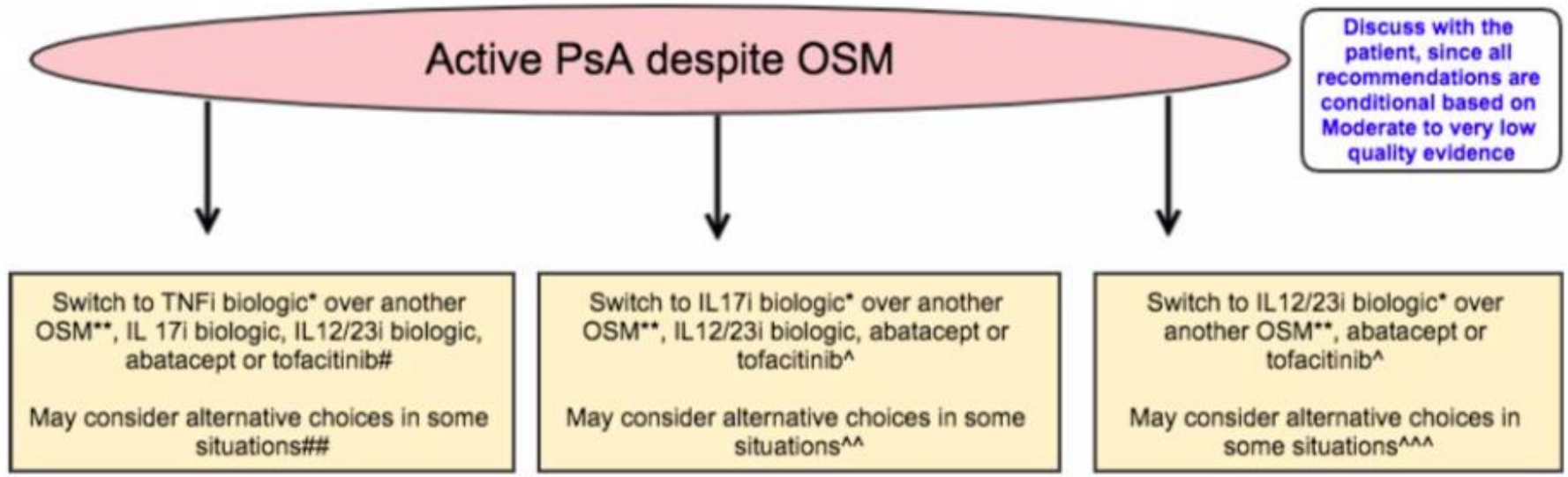
΄Σοβαρή νόσος" ορισμός

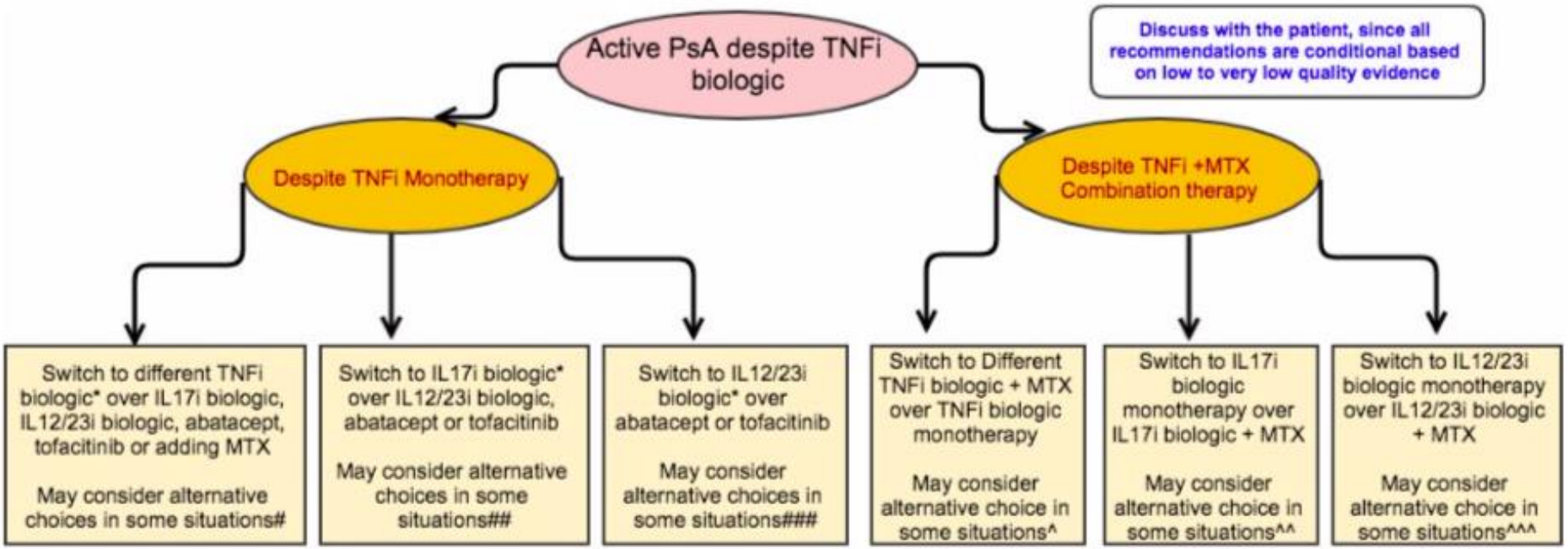
Severe Psoriatic Arthritis	Severe Psoriasis
• Erosive disease • Elevated markers of inflammation (ESR, CRP) attributable to PsA • Long-term damage that interferes with function (i.e., joint deformities) • Highly active disease that causes a major impairment in quality of life • Active PsA at many sites including dactylitis, enthesitis • Function-limiting PsA at a few sites • Rapidly progressive disease	• PASI of 12 or more • BSA of 5-10% or more • Significant involvement in specific areas • (e.g., face, hands or feet, nails, intertriginous areas, scalp) where the burden of the disease causes significant disability • Impairment of physical or mental functioning can warrant a designation of moderate-to-severe disease despite the lower amount of surface area of skin involved

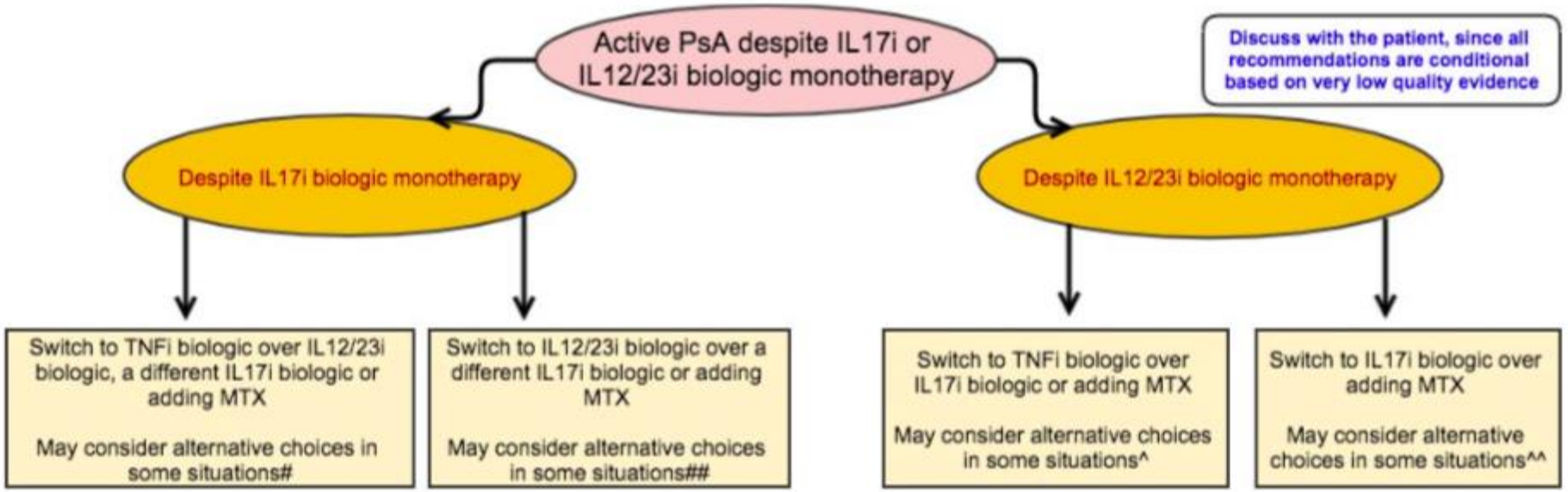
‘’Ενεργός νόσος” ορισμός

- 1 από τα ακόλουθα
  - Ενεργός αρθρίτιδα
  - Δακτυλίτιδα
  - Ενθεσίτιδα
  - Αξονική προσβολή
  - Ενεργός ψωρίαση ή/και ψωριασική ονυχία
  - Οφθαλμική προσβολή
  - ΙΦΝΕ


Treatment-naive Active PsA
Discuss with the patient, since all recommendations are conditional based on low to very low quality evidence
Start TNFi biologic over OSM, IL17i biologic or IL12/23i biologic
May consider alternative choices in some situations#
Start OSM over IL17i biologic or IL12/23i biologic
May consider alternative choices in some situations##
Start MTX over NSAIDs
May consider alternative choices in some situations^
Start IL17i biologic over IL12/23i biologic
May consider alternative choices in some situations^^
PsA still active?
PsA still active?
PsA still active?
PsA still active?
Go to Figure 5 for active PsA despite TNFi biologic therapy
Go to Figure 4 for active PsA despite OSM therapy
Go to Figure 6 for active PsA despite IL17i or IL12/23i biologic therapy


Active PsA despite OSM
Discuss with the patient, since all recommendations are conditional based on Moderate to very low quality evidence
Switch to TNFi biologic* over another OSM**, IL 17i biologic, IL12/23i biologic, abatacept or tofacitinib#
May consider alternative choices in some situations##
Switch to IL17i biologic* over another OSM**, IL12/23i biologic, abatacept or tofacitinib^
May consider alternative choices in some situations^^
Switch to IL12/23i biologic* over another OSM**, abatacept or tofacitinib^
May consider alternative choices in some situations^^^


Active PsA despite TNFi biologic
Discuss with the patient, since all recommendations are conditional based on low to very low quality evidence
Despite TNFi Monotherapy
Despite TNFi +MTX Combination therapy
Switch to different TNFi biologic* over IL17i biologic, IL12/23i biologic, abatacept, tofacitinib or adding MTX
May consider alternative choices in some situations#
Switch to IL17i biologic* over IL12/23i biologic, abatacept or tofacitinib
May consider alternative choices in some situations##
Switch to IL12/23i biologic* over abatacept or tofacitinib
May consider alternative choices in some situations###
Switch to Different TNFi biologic + MTX over TNFi biologic monotherapy
May consider alternative choice in some situations^
Switch to IL17i biologic monotherapy over IL17i biologic + MTX
May consider alternative choice in some situations^^
Switch to IL12/23i biologic monotherapy over IL12/23i biologic + MTX
May consider alternative choice in some situations^^^


Active PsA despite IL17i or IL12/23i biologic monotherapy
Discuss with the patient, since all recommendations are conditional based on very low quality evidence
Despite IL17i biologic monotherapy
Despite IL12/23i biologic monotherapy
Switch to TNFi biologic over IL12/23i biologic, a different IL17i biologic or adding MTX
May consider alternative choices in some situations#
Switch to IL12/23i biologic over a different IL17i biologic or adding MTX
May consider alternative choices in some situations##
Switch to TNFi biologic over IL17i biologic or adding MTX
May consider alternative choices in some situations^
Switch to IL17i biologic over adding MTX
May consider alternative choices in some situations^^

Περιορισμοί

- ‘’Very low quality of evidence’’ για τις περισσότερες συστάσεις
- Χρήση κορτικοστεροειδών
- Φαρμακο-οικονομικά δεδομένα

EPIDEMIOLOGICAL SCIENCE

Treatment response and drug retention rates in 24 195 biologic-naïve patients with axial spondyloarthritis initiating TNFi treatment: routine care data from 12 registries in the EuroSpA collaboration

Σκοπός-μέθοδολογία

- Αποτελεσματικότητα και παραμονή στη θεραπεία του 1^{ου} anti-TNF σε naïve ασθενείς
- Δεδομένα από 12 Ευρωπαικά αρχεία καταγραφής ασθενών
- ASDAS inactive disease (<1.3), BASDAI <40 mm και ανταπόκριση κατά ASAS 20/40 στους 6, 12 και 24 μήνες παρακολούθησης
- Σε ασθενείς που ξεκίνησαν μετά το 2009 εφαρμογή και των νέων κριτηρίων της ASAS

Χαρακτηριστικά ασθενών στην έναρξη

Epidemiology

Table 1 Baseline characteristics of all patients and the axSpA subcohorts

	All patients		ASAS cohort*		NY cohort†		nr-axSpA cohort‡	
	No of patients with available data, n	Median (IQR) or percentage	No of patients with available data, n	Median (IQR) or percentage	No of patients with available data, n	Median (IQR) or percentage	No of patients with available data, n	Median (IQR) or percentage
Age, years	24195	41 (33–50)	6097	41 (33–50)	2935	43 (34–52)	1178	39 (31–48)
Male	24195	61%	6097	63%	2935	67%	1178	52%
HLA-B27	12620	74%	5645	76%	2595	70%	1104	69%
BMI, kg/m^2	10418	26 (23–29)	4699	26 (23–29)	2266	26 (23–29)	753	25 (23–29)
Concomitant csDMARD	23984	31%	6002	29%	2865	26%	1169	25%
Time since diagnosis, years	19091	2 (1–9)	5971	2 (1–8)	2884	3 (1–10)	1155	1 (0–3)
Current smoking	21049	23%	5755	27%	2822	27%	1121	26%

Χαρακτηριστικά ασθενών στην έναρξη

Table 1 Baseline characteristics of all patients and the axSpA subcohorts

	All patients		ASAS cohort*		NY cohort†		nr-axSpA cohort‡	
	No of patients with available data, n	Median (IQR) or percentage	No of patients with available data, n	Median (IQR) or percentage	No of patients with available data, n	Median (IQR) or percentage	No of patients with available data, n	Median (IQR) or percentage
Infliximab	6874	28%	1143	19%	580	20%	194	16%
Etanercept	6034	25%	1165	19%	647	22%	230	20%
Adalimumab	6936	29%	2176	36%	1050	36%	410	35%
Certolizumab	1107	5%	240	4%	77	3%	60	5%
Golimumab	3244	14%	1373	23%	581	20%	284	24%
Start before 2009	5784	24	0	0	0	0	0	0
Start 2009–2011	5061	21	1586	26	941	32	345	29
Start 2012–2014	6092	25	2123	35	932	32	500	42
Start 2015–2017	7258	30	2388	39	1062	36	333	28

Χαρακτηριστικά ασθενών στην έναρξη

Table 1 Baseline characteristics of all patients and the axSpA subcohorts

	All patients		ASAS cohort*		NY cohort†		nr-axSpA cohort‡	
	No of patients with available data, n	Median (IQR) or percentage	No of patients with available data, n	Median (IQR) or percentage	No of patients with available data, n	Median (IQR) or percentage	No of patients with available data, n	Median (IQR) or percentage
CRP, mg/L	18552	10 (4–23)	5159	13 (5–26)	2446	13 (5–27)	1003	7 (2–19)
CRP >10 mg/L	18552	48%	5159	56%	2446	56%	1003	40%
BASDAI, mm	14442	59 (44–72)	5014	64 (51–76)	2442	66 (52–77)	994	65 (50–78)
BASMI, mm	4551	24 (10–40)	1937	20 (10–40)	1037	30 (10–50)	605	20 (10–30)
BASFI, mm	11548	46 (26–66)	4187	51 (33–69)	1840	53 (34–70)	762	48 (29–68)
ASDAS, units	7678	3.6 (2.9–4.2)	3139	4.0 (3.3–4.6)	1394	4.1 (3.3–4.7)	561	3.9 (3.1–4.6)
VAS pain, mm	15332	65 (45–80)	4249	70 (52–82)	1927	75 (58–90)	911	70 (52–86)
VAS fatigue, mm	10718	69 (49–80)	3650	70 (51–85)	1434	77 (60–90)	853	72 (51–86)

Αποτελέσματα

Epidemiology

Table 3 Retention and response rates in patients with axial spondyloarthritis

	All patients	ASAS cohort*	NY cohort†	nr-axSpA cohort‡
	Retention rates	Retention rates	Retention rates	Retention rates
6 months (95%CI)	88% (87% to 88%)	89% (88% to 90%)	90% (89% to 91%)	84% (82% to 86%)
12 months (95%CI)	80% (79% to 80%)	81% (80% to 82%)	83% (82% to 85%)	73% (70% to 76%)
24 months (95%CI)	73% (72% to 73%)	74% (73% to 76%)	76% (74% to 78%)	64% (62%–67%)

Αποτελέσματα

Table 3 Retention and response rates in patients with axial spondyloarthritis

	All patients		ASAS cohort*		NY cohort†		nr-axSpA cohort‡	
	Crude§	LUNDEX adjusted ¶	Crude§	LUNDEX adjusted¶	Crude§	LUNDEX adjusted¶	Crude§	LUNDEX adjusted¶
ASDAS inactive disease at 6 months	33%	27%	30%	25%	25%	21%	26%	20%
ASDAS inactive disease at 12 months	35%	24%	33%	23%	29%	21%	31%	19%
ASDAS inactive disease at 24 months	38%	19%	38%	18%	32%	16%	37%	15%
BASDAI <40 at 6 months	72%	59%	73%	60%	71%	60%	64%	50%
BASDAI <40 at 12 months	75%	51%	76%	52%	73%	52%	70%	43%
BASDAI <40 at 24 months	77%	38%	79%	37%	76%	37%	71%	29%
ASAS 20/40 at 6 months	64%/49%	52%/40%	68%/54%	56%/45%	64%/48%	54%/41%	57%/42%	45%/33%
ASAS 20/40 at 12 months	67%/53%	46%/36%	70%/57%	48%/39%	66%/52%	47%/37%	63%/49%	39%/30%
ASAS 20/40 at 24 months	68%/54%	34%/27%	73%/59%	34%/28%	67%/51%	33%/25%	69%/53%	28%/22%

The Journal of Rheumatology

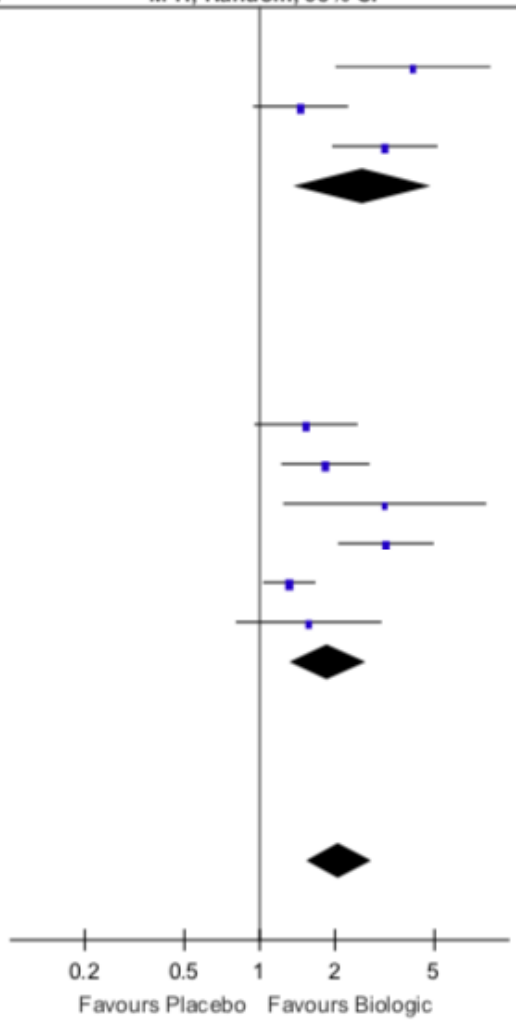
Treatment of Dactylitis and Enthesitis in Psoriatic Arthritis with Biologic Agents: A Systematic Review and Meta-Analysis

Σκοπός-μέθοδολογία

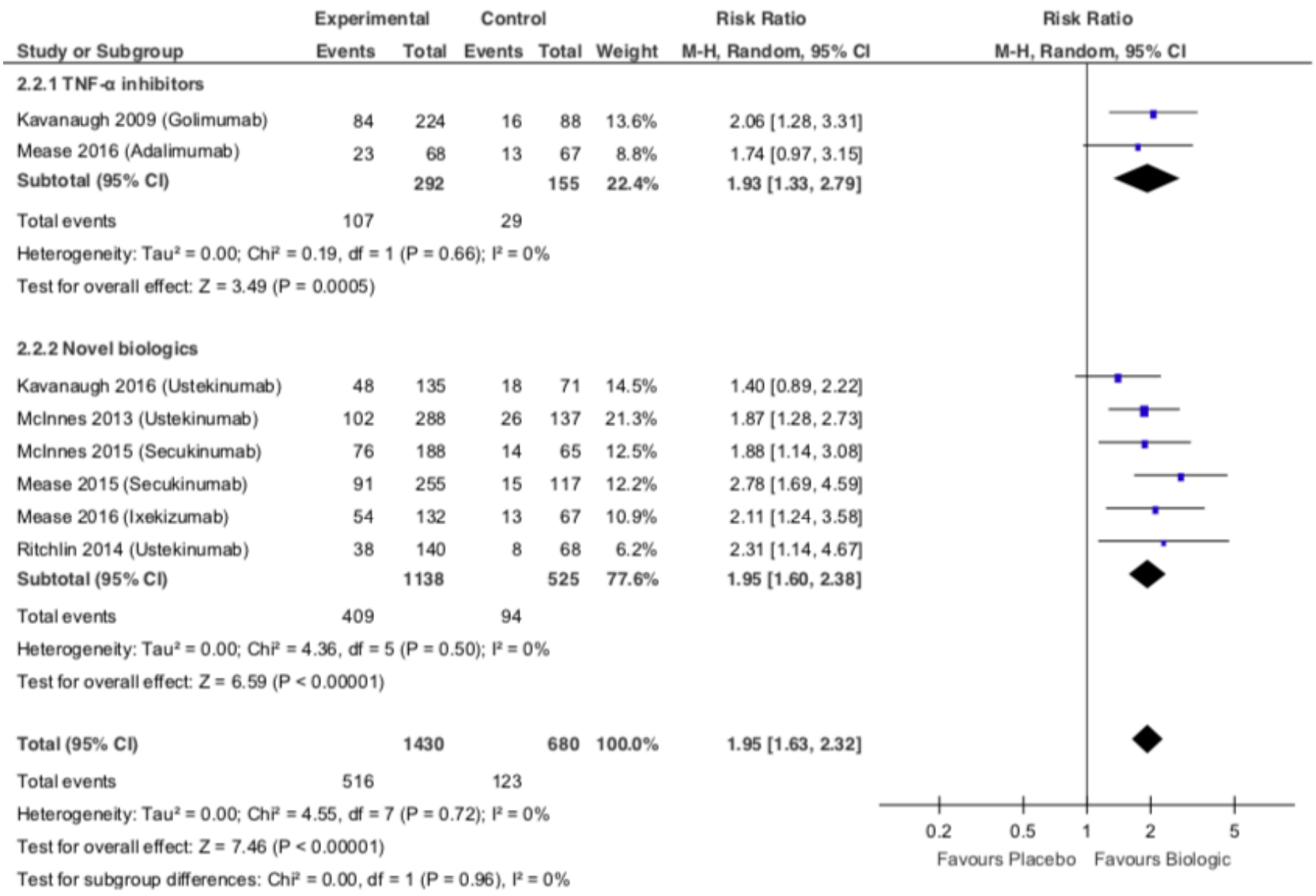
- Αποτελεσματικότητα 2 διαφορετικών κατηγοριών βιολογικών παραγόντων στη δακτυλίτιδα και την ενθεσίτιδα
- 19 μελέτες με συνολικά 7254 ασθενείς και τουλάχιστον 24 εβδομάδες παρακολούθησης
- Δεδομένα μέχρι τον 02/2018

Δακτυλίτιδα

Study or Subgroup	Biologic Events	Biologic Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.1 TNF-α inhibitors						
Antoni 2005 (Infliximab)	28	40	7	41	8.6%	4.10 [2.03, 8.29]
Kavanaugh 2009 (Golimumab)	57	99	15	38	12.3%	1.46 [0.95, 2.24]
Mease 2016 (Adalimumab)	42	54	14	57	11.6%	3.17 [1.97, 5.10]
Subtotal (95% CI)		**193**		**136**	**32.6%**	**2.57 [1.36, 4.84]**
Total events	127		36			
Heterogeneity: Tau² = 0.24; Chi² = 8.78, df = 2 (P = 0.01); I² = 77%						
Test for overall effect: Z = 2.92 (P = 0.004)						
1.2.2 Novel biologics						
Kavanaugh 2016 (Ustekinumab)	43	86	15	46	11.8%	1.53 [0.96, 2.44]
McInnes 2013 (Ustekinumab)	85	194	22	92	12.8%	1.83 [1.23, 2.73]
McInnes 2015 (Secukinumab)	52	111	4	27	6.4%	3.16 [1.25, 7.98]
Mease 2015 (Secukinumab)	109	208	19	116	12.3%	3.20 [2.08, 4.92]
Mease 2016 (Ixekizumab)	98	125	34	57	15.0%	1.31 [1.04, 1.66]
Ritchlin 2014 (Ustekinumab)	32	84	8	33	9.2%	1.57 [0.81, 3.05]
Subtotal (95% CI)		**808**		**371**	**67.4%**	**1.88 [1.33, 2.65]**
Total events	419		102			
Heterogeneity: Tau² = 0.12; Chi² = 17.51, df = 5 (P = 0.004); I² = 71%						
Test for overall effect: Z = 3.57 (P = 0.0004)						
Total (95% CI)		**1001**		**507**	**100.0%**	**2.07 [1.54, 2.80]**
Total events	546		138			
Heterogeneity: Tau² = 0.14; Chi² = 30.13, df = 8 (P = 0.0002); I² = 73%						
Test for overall effect: Z = 4.76 (P < 0.00001)						
Test for subgroup differences: Chi² = 0.73, df = 1 (P = 0.39), I² = 0%						

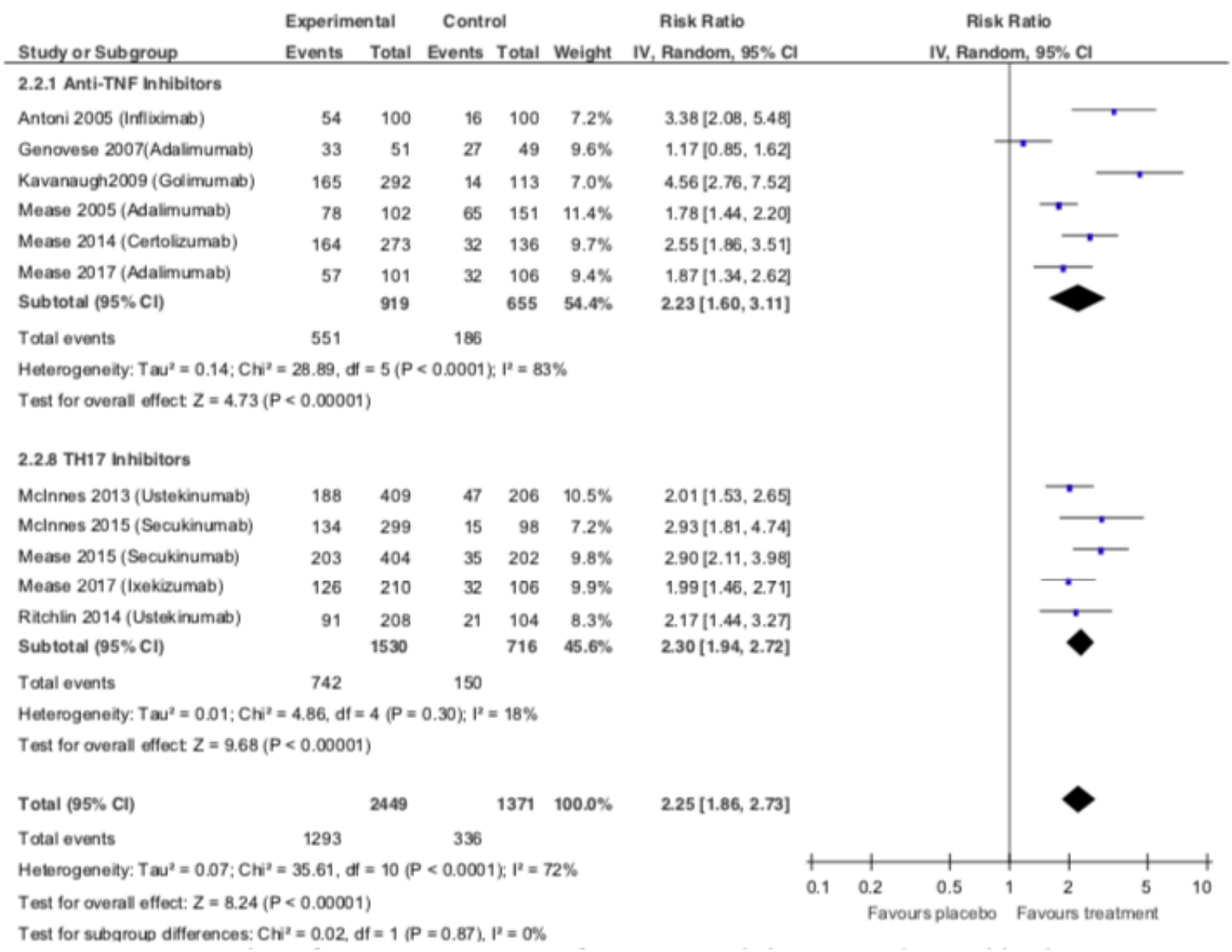


Ενθεσίτιδα



Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
2.2.1 TNF-α inhibitors						
Kavanaugh 2009 (Golimumab)	84	224	16	88	13.6%	2.06 [1.28, 3.31]
Mease 2016 (Adalimumab)	23	68	13	67	8.8%	1.74 [0.97, 3.15]
Subtotal (95% CI)		**292**		**155**	**22.4%**	**1.93 [1.33, 2.79]**
Total events	107		29			
Heterogeneity: Tau² = 0.00; Chi² = 0.19, df = 1 (P = 0.66); I² = 0%						
Test for overall effect: Z = 3.49 (P = 0.0005)						
2.2.2 Novel biologics						
Kavanaugh 2016 (Ustekinumab)	48	135	18	71	14.5%	1.40 [0.89, 2.22]
McInnes 2013 (Ustekinumab)	102	288	26	137	21.3%	1.87 [1.28, 2.73]
McInnes 2015 (Secukinumab)	76	188	14	65	12.5%	1.88 [1.14, 3.08]
Mease 2015 (Secukinumab)	91	255	15	117	12.2%	2.78 [1.69, 4.59]
Mease 2016 (Ixekizumab)	54	132	13	67	10.9%	2.11 [1.24, 3.58]
Ritchlin 2014 (Ustekinumab)	38	140	8	68	6.2%	2.31 [1.14, 4.67]
Subtotal (95% CI)		**1138**		**525**	**77.6%**	**1.95 [1.60, 2.38]**
Total events	409		94			
Heterogeneity: Tau² = 0.00; Chi² = 4.36, df = 5 (P = 0.50); I² = 0%						
Test for overall effect: Z = 6.59 (P < 0.00001)						
Total (95% CI)		**1430**		**680**	**100.0%**	**1.95 [1.63, 2.32]**
Total events	516		123			
Heterogeneity: Tau² = 0.00; Chi² = 4.55, df = 7 (P = 0.72); I² = 0%						
Test for overall effect: Z = 7.46 (P < 0.00001)						
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.96), I² = 0%						

ACR 20 24η εβδομάδα



Περιορισμοί-συμπεράσματα

- Μελέτες βιολογικών παραγόντων έναντι του placebo και όχι ‘’head to head’’
- Ομάδοποίηση 2 διαφορετικών κατηγοριών non-anti TNFa με πιθανό διαφορετικό τρόπο δράσης στα καταληκτικά σημεία-στόχους
- ‘’high quality evidence and low risk of bias’’ μελέτες που συμπεριελήφθηκαν

Παρόμοια αποτελεσματικότητα στην αντιμετώπιση της ενθεσίτιδας και της δακτυλίτιδας

Take home message

- 2 νέες θεραπευτικές συστάσεις με αρκετές αλλαγές αλλά με κριτική αντιμετώπιση
- Αξιόπιστα δεδομένα απο την καθημερινή κλινική πρακτική για την αποτελεσματικότητα και την παραμονή στη θεραπεία του 1^{ου} anti-TNF
- Παρόμοια αποτελεσματικότητα βιολογικών στην ενθεσίτιδα και τη δακτυλίτιδα