WORKSHOP

Πώς μπορούμε να βελτιώσουμε τις εκβάσεις των ασθενών με ρευματοειδή αρθρίτιδα;

Αθανάσιος Κουτρούμπας, Ρευματολόγος Βόλος
Χρήστος Κουτσιανάς, Επιστ. Συνεργάτης Β΄ΠΠ Κλινικής ΕΚΠΑ, ΓΝΑ «Ιπποκράτειο»

JAKa-GR-00162-E | June 2023

Disclosures

Τιμητική αμοιβή από την εταιρία AbbVie για τη σημερινή παρουσίαση

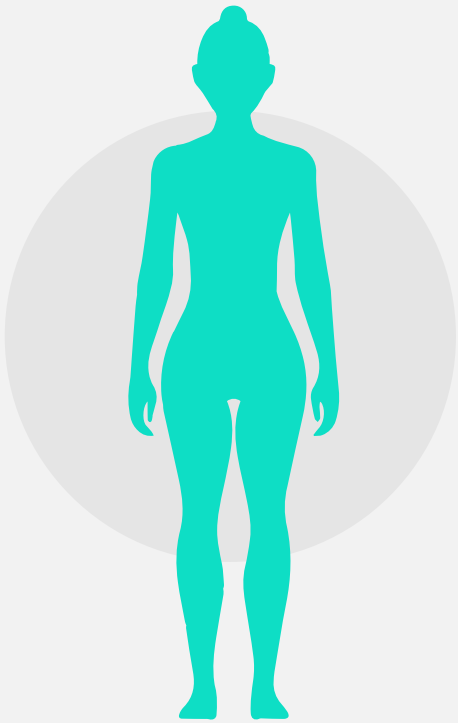
<u>Αθανάσιος Κουτρούμπας</u>

Την τελευταία διετία τιμητικές αμοιβές για εκπόνηση ομιλιών, και ερευνητικές και συμβουλευτικές υπηρεσίες από τις εταιρείες Elpen, UCB, Amgen, Pfizer, GSK.

<u>Χρήστος Κουτσιανάς</u>

- <u>Honoraria for lectures</u>: Roche, Genesis Pharma, Abbvie, Novartis, Genesis Pharma, Eli-Lilly, Pfizer, Aenorasis, UCB
- <u>Honoraria for advisory boards</u>: Genesis Pharma, Pfizer, Abbvie, Viatris, Aenorasis
- <u>Hospitality</u>: Eli-Lilly, Novartis, Viatris, UCB, Genesis Pharma, Abbvie
- <u>Research</u>: Sub-investigator: Roche, UCB, Eli-Lilly, Novartis, BMS, Pfizer, Genesis Pharma, AMGEN, MSD, Abbvie, Aenorasis

Patient Case #1



Woman, 33 yo. Non smoker

Early RA- ACPA+
DAS 28 (baseline)=5,8

MTX sc 20 mg

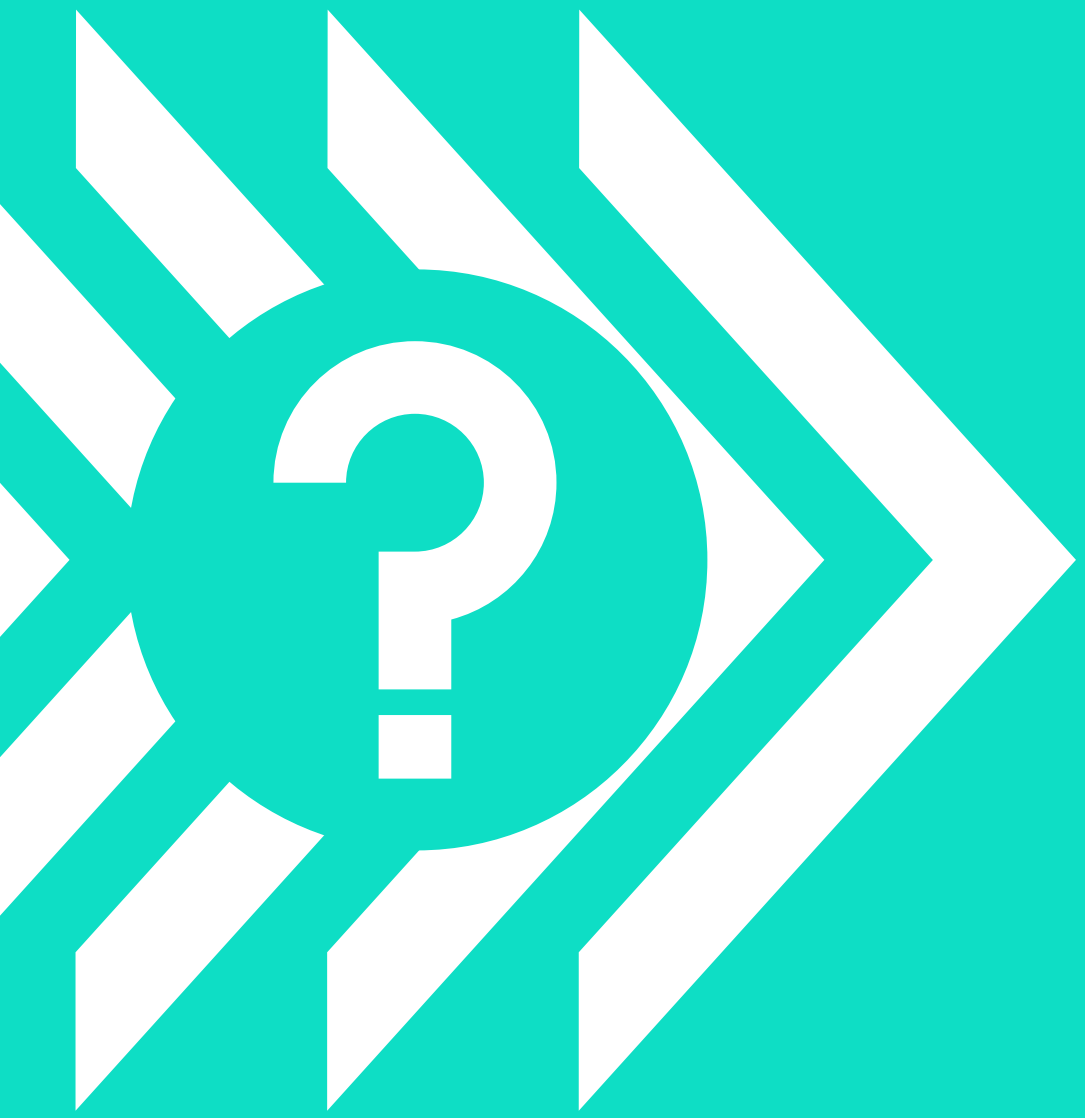
DAS 28 (6 month)=2,9

Wrist and 2 MCP synovitis

No pain

What's next?

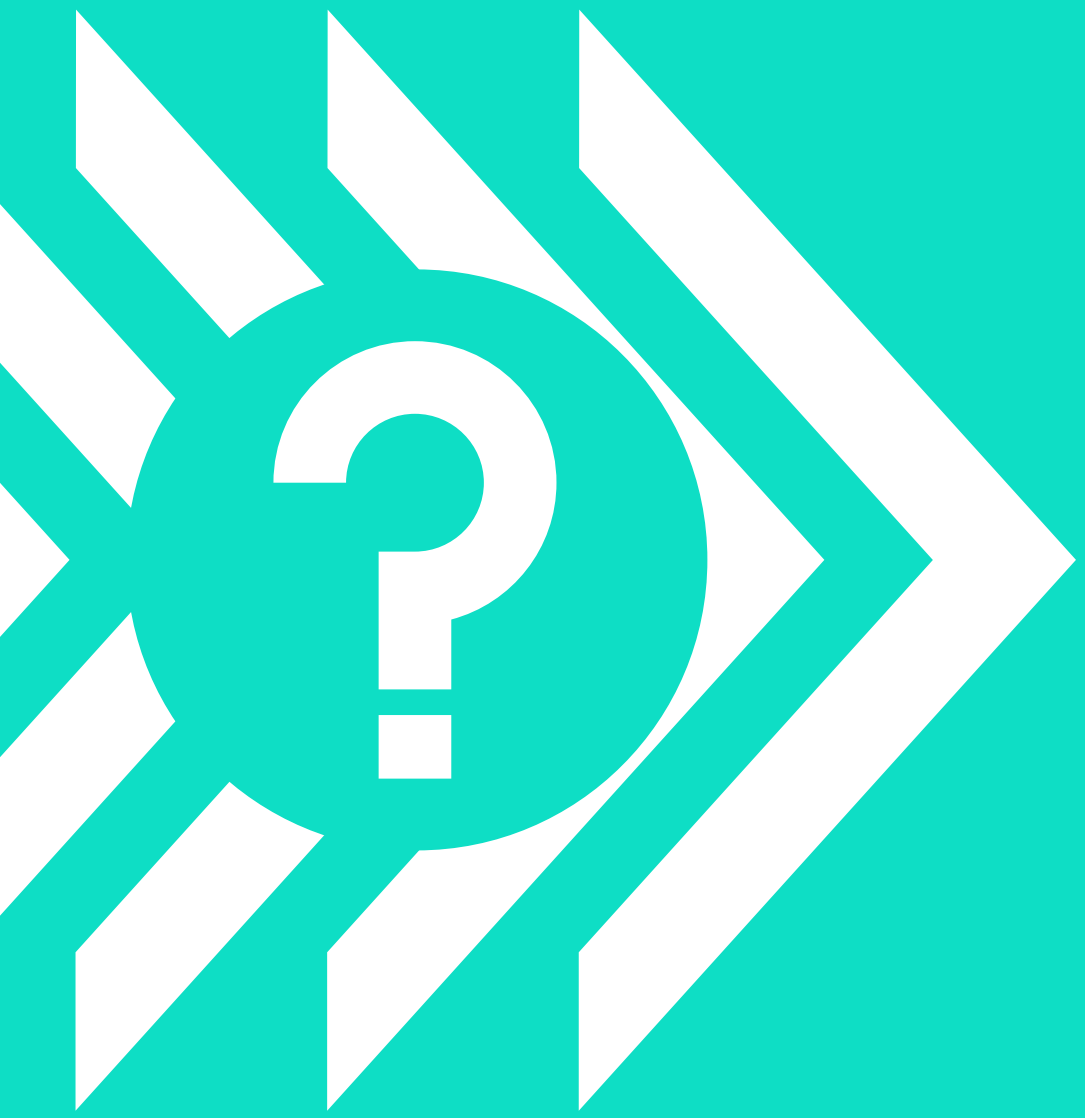
Polling Question



What's next?

1. Wait for another 6 months
2. Biologic therapy?
3. Targeted treatments?

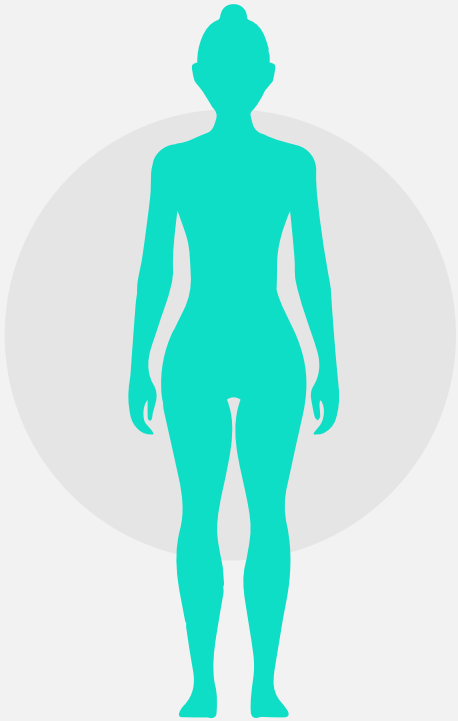
Polling Question



If biologic/targeted treatments:

1. TNF- inh
2. CTLA4 Ag
3. Anti IL-6
4. Anti CD-20
5. JAK-I (non-selective)
6. JAK-I (selective)

Remission vs low disease activity



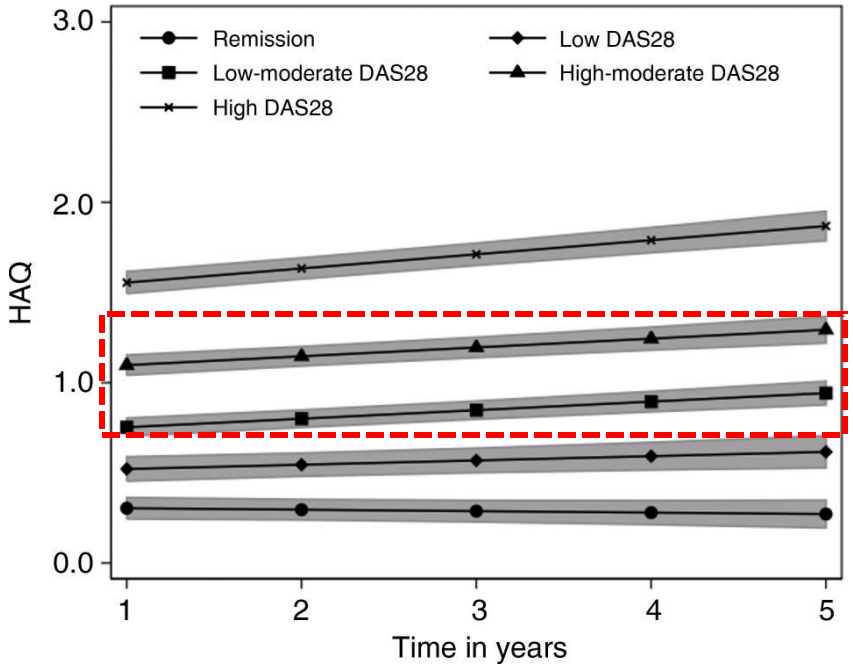
When to stop up-titration?

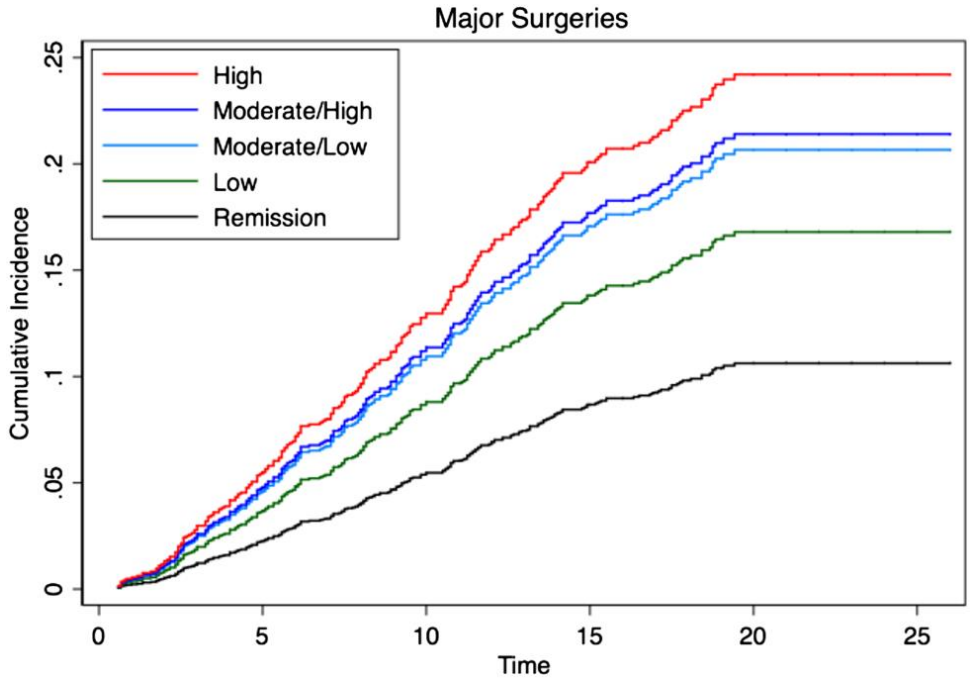
Acceptable disease activity levels for optimal outcomes on MTX: Remission (Low disease activity)

Early RA

Early RA patients' cohorts (2 inception cohorts, 1986-2012)

Patients on medium disease activity compared to low-remission have higher functional decline and double risk for major orthopedic surgeries





Nikiphorou E, et al. Ann Rheum Dis 2016;75:2080

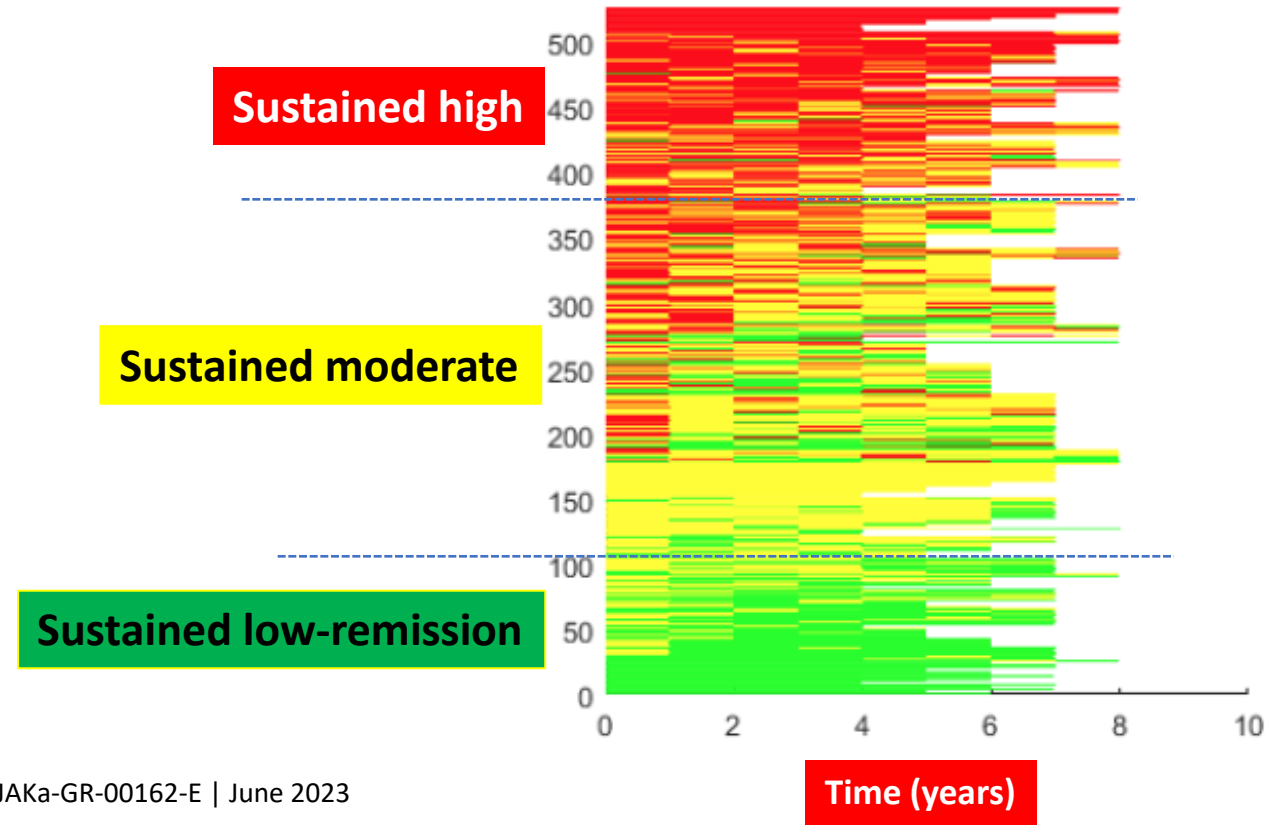
Established, highly active disease on TNFi: analysis for **persistent** disease activity

During a 5 years follow-up:

20% on sustained remission-LDA (>50% of the evaluation on remission-low DAS28)

bDMARDs established RA – Greek Patients

Figure 1a. Cohort patients' disease activity (DAS28) course.

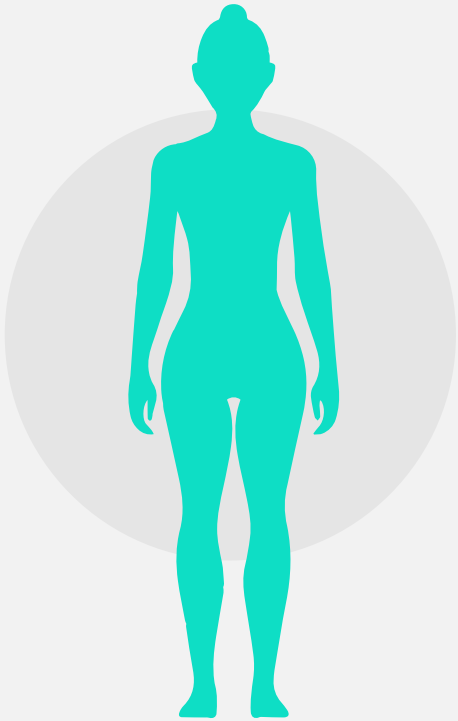


Red: DAS28 >5.1
Yellow: DAS28 ≤5.1 & DAS28 >3.2
Green: DAS28 ≤3.2

Course ≥50% red: 142 (27% sHDA)
Course ≥50% yellow: 295 (56% sMDA)
Course ≥50% green: 90 (17% sRLDA)

Genitsaridi et al. Arthritis Research & Therapy (2020) 22:226

Remission vs low disease activity



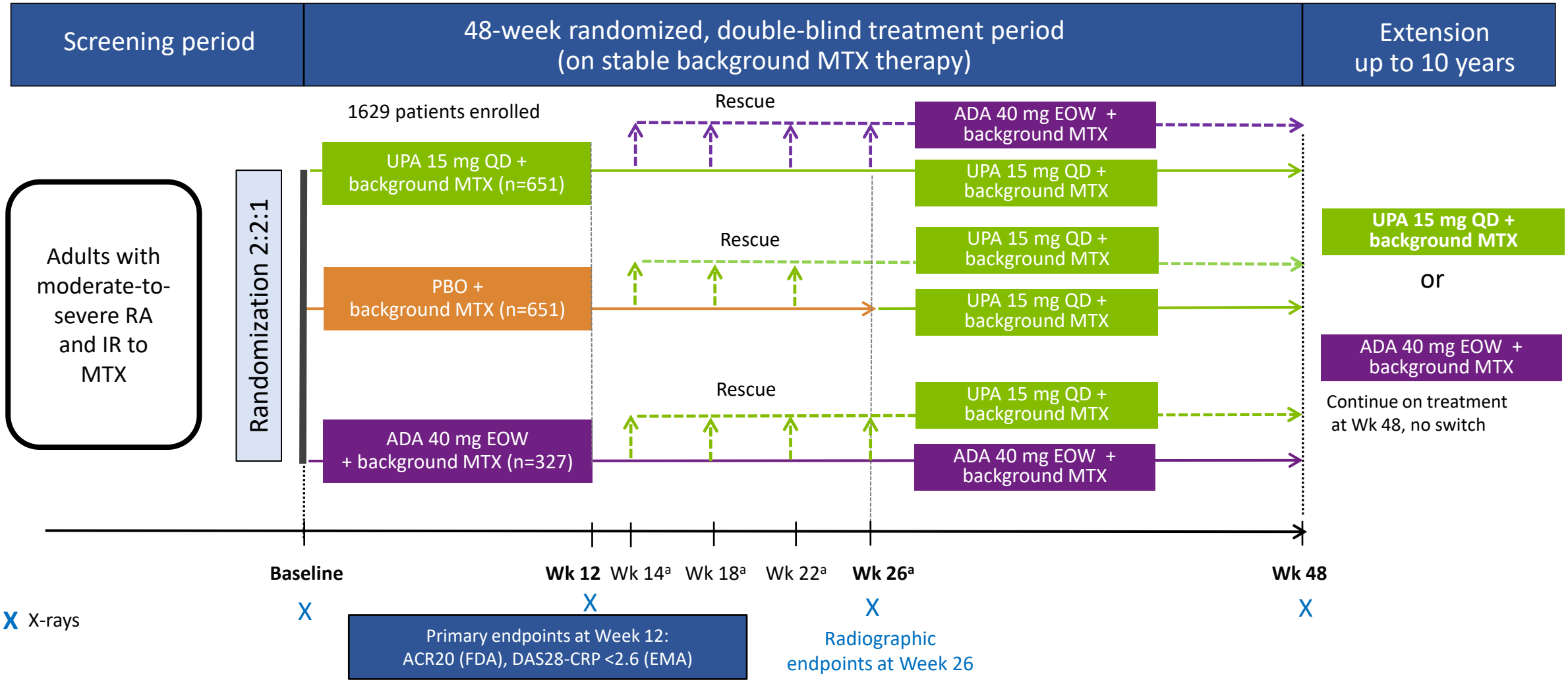
Which tool do you trust/ use? (SDAI, CDAI, DAS28, RAPID, Boolean remission...)

Assessment of tools- are those tools objective, or are they influenced by (among others):

- Pain
- Depression
- Patient personality
- Comorbidities
- Deformities

What is the best target for the specific patient?

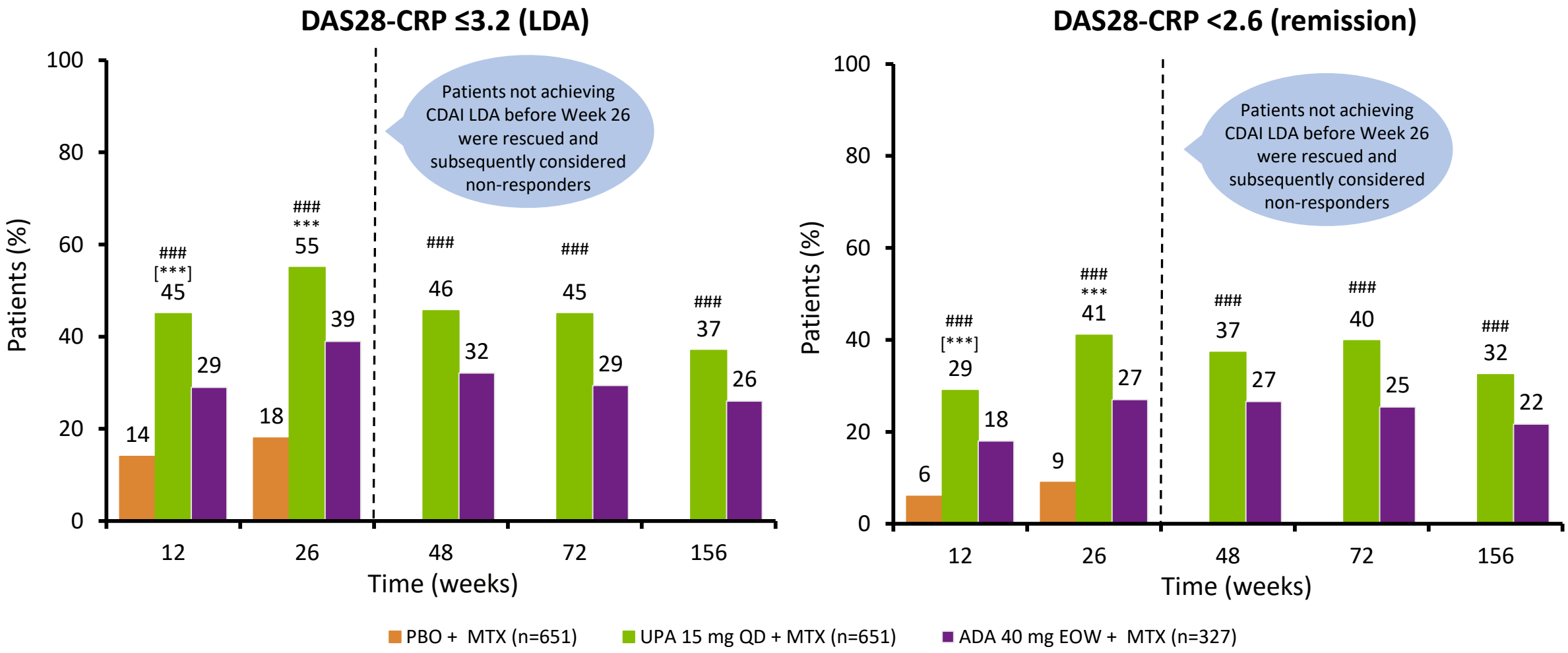
SELECT-COMPARE: Study design[1,2]



[a]Rescue criteria: At Weeks 14, 18, and 22 if <20% improvement in TJC and SJC; at Week 26 if CDAI >10
ACR20, 20% improvement in ACR criteria; CDAI, Clinical Disease Activity Index; DAS28-CRP, Disease Activity Score of 28 joints with C-reactive protein; EMA, European Medicines Agency; EOW, end of week; FDA, Food and Drug Administration; UPA, upadacitinib; Wk, week

1. Fleischmann, RM et al. Ann Rheum Dis 2019;78:1454–62;
2. Clinicaltrials.gov. NCT02629159

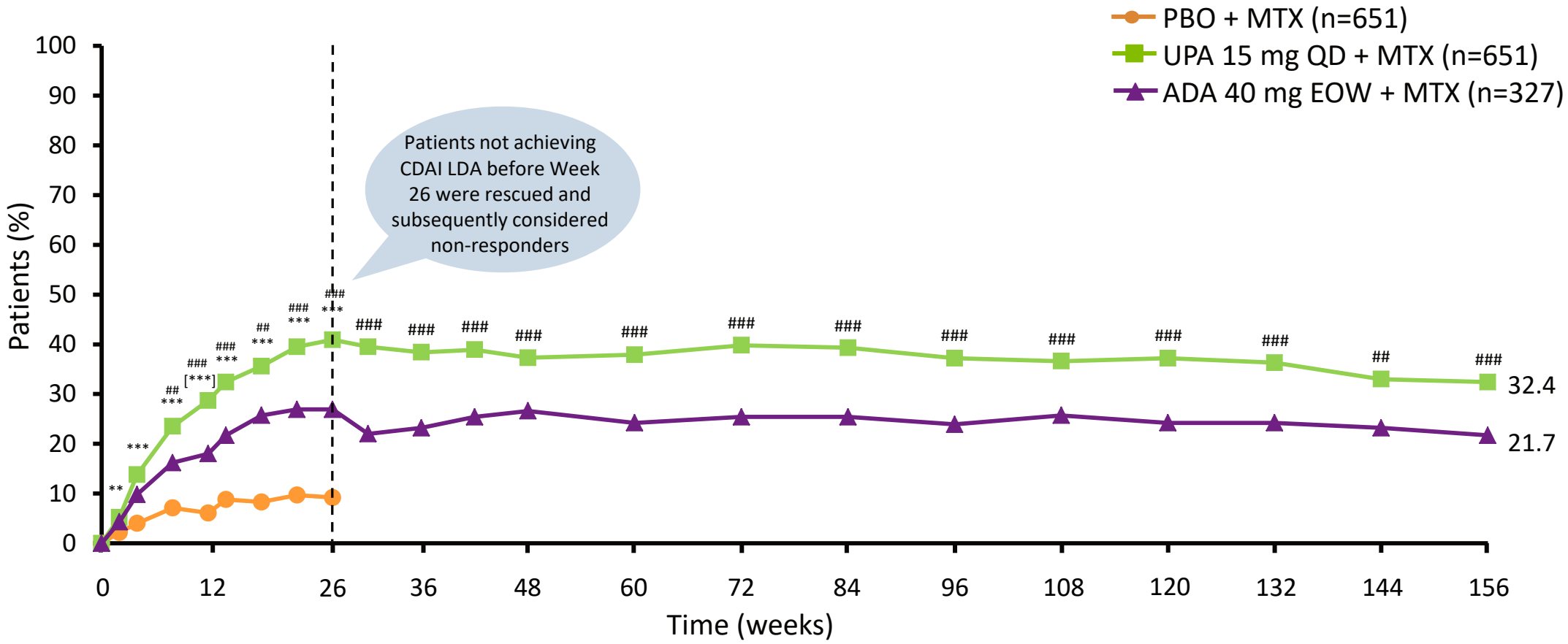
SELECT-COMPARE:
DAS28-CRP LDA and remission over 156 weeks (NRI)[1–3]



Full analysis set; n-values apply to NRI data set only. Treatment groups are by initial randomization. NRI was used for patients who were rescued or prematurely discontinued study drug, as well as for missing data. Vertical line at Week 26 indicates the end of the PBO-controlled period
Comparisons adjusted for multiplicity: [***]p≤0.001 vs PBO
Comparisons unadjusted for multiplicity: Nominal ***p≤0.001 vs PBO; ###p≤0.001 vs ADA

1. Fleischmann R, et al. Arthritis Rheum 2019;71:1788–800;
2. Fleischmann R, et al. Ann Rheum Dis 2019;78:1454–62;
3. Fleischmann R, et al. EULAR 2021;Poster POS0087

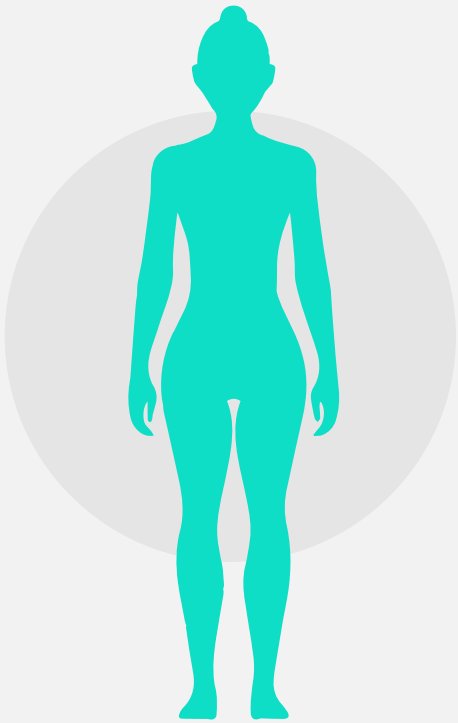
SELECT-COMPARE: DAS28-CRP remission (<2.6) over 156 weeks (NRI)[1–3]



Full analysis set; n-values apply to NRI data set only. Treatment groups are by initial randomization. NRI was used for patients who were rescued or prematurely discontinued study drug, as well as for missing data. Vertical line at Week 26 indicates the end of the PBO-controlled period
Comparisons adjusted for multiplicity: [***] p<0.001 vs PBO
Comparisons unadjusted for multiplicity: **p<0.01; ***p<0.001 vs PBO; ##p<0.01; ###p<0.001 vs ADA

1. Fleischmann R, et al. Arthritis Rheum 2019;71:1788–800;
2. Fleischmann R, et al. EULAR 2021;Poster POS0087;

Patient Case #2



Man, 62 yo.

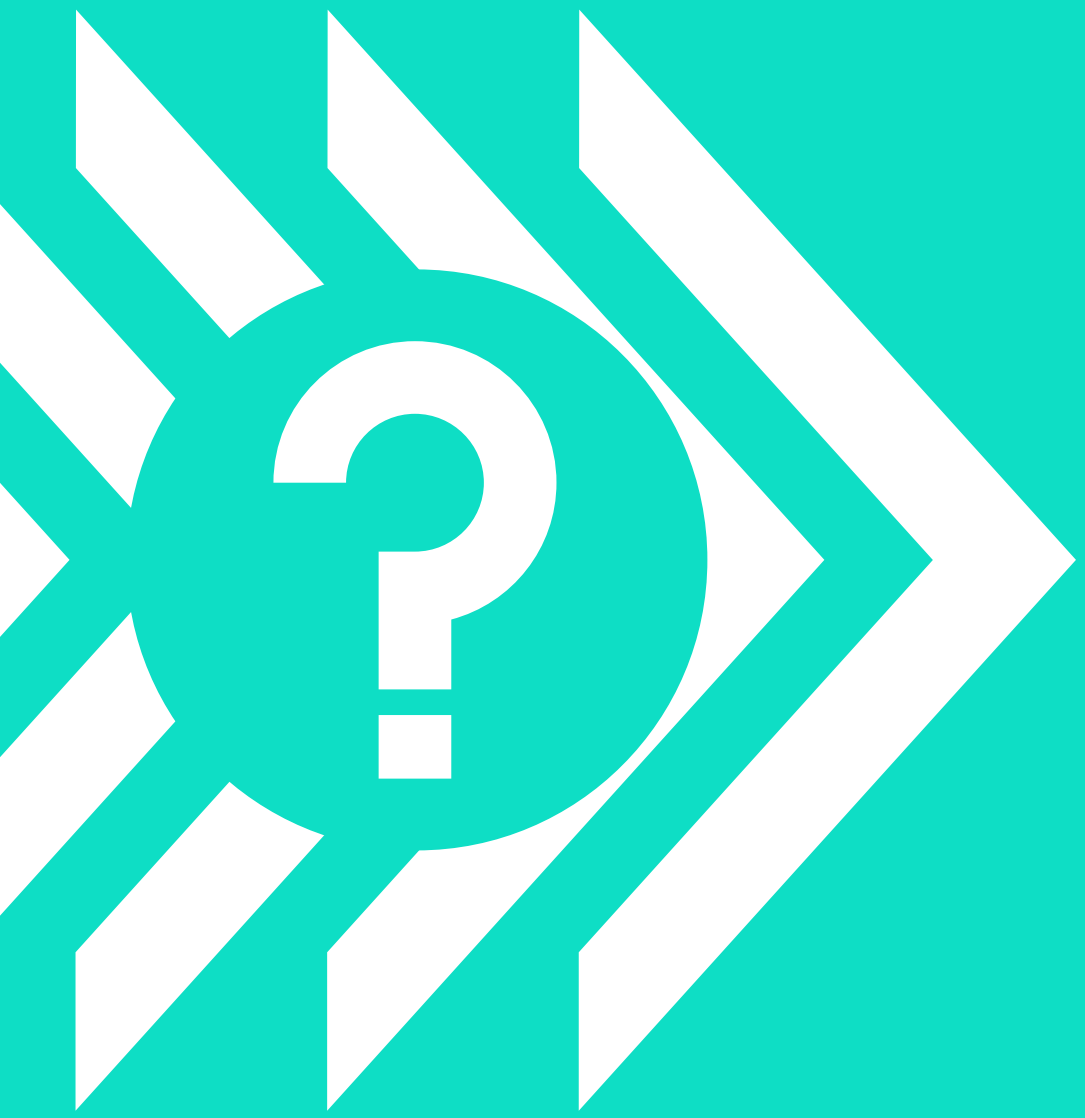
Hypertension/ Atrial fibrillation/ Hyperlipidemia/ Smoker
Early RA- ACPA+
DAS 28 (baseline)=5,8

MTX sc 20 mg + Prezolon 2.5 mg/day

DAS 28 (6 month)=2,9

What's next?

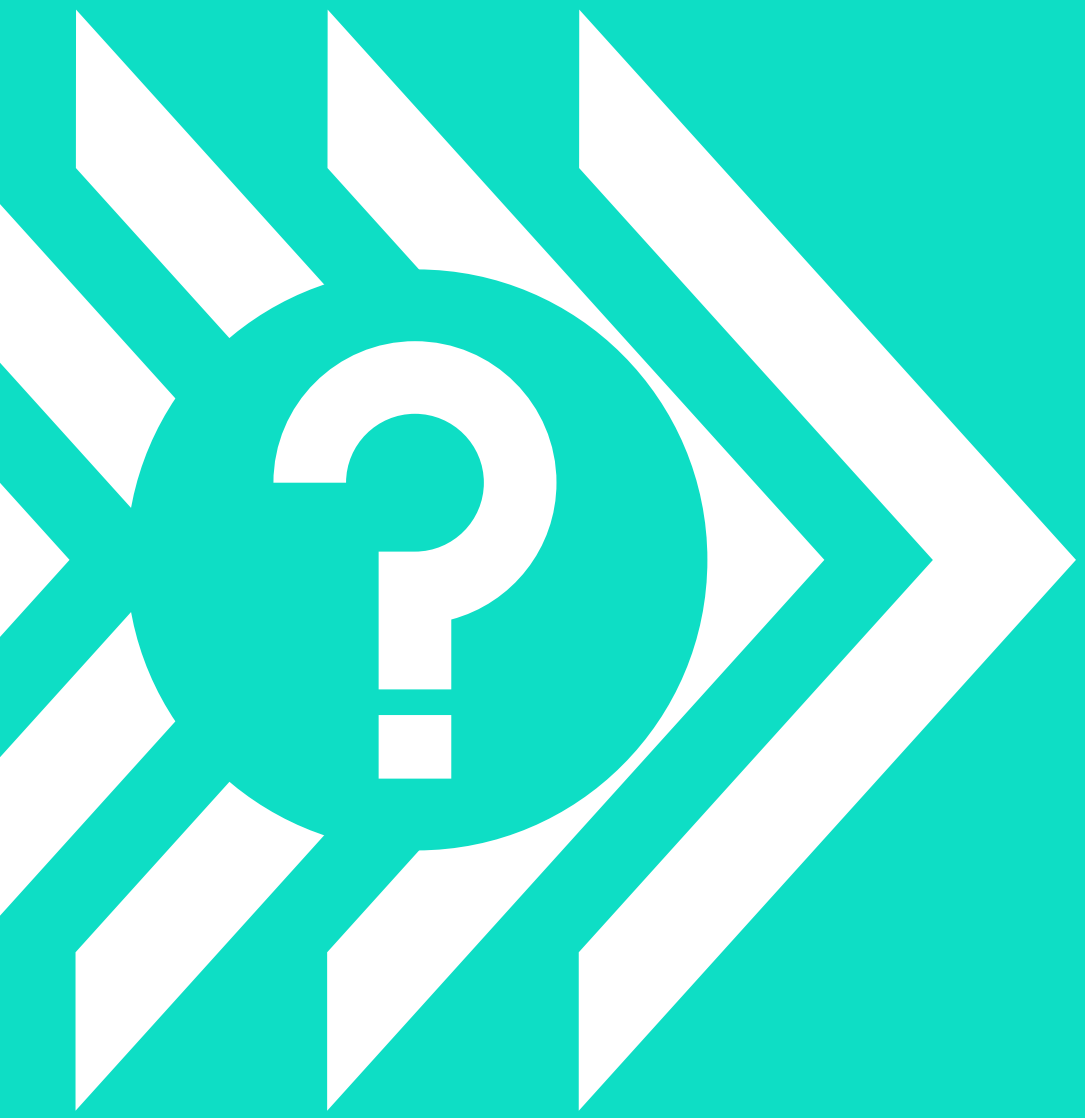
Polling Question



What's next?

1. Wait for another 6 months
2. Biologic therapy?
3. Targeted treatments?

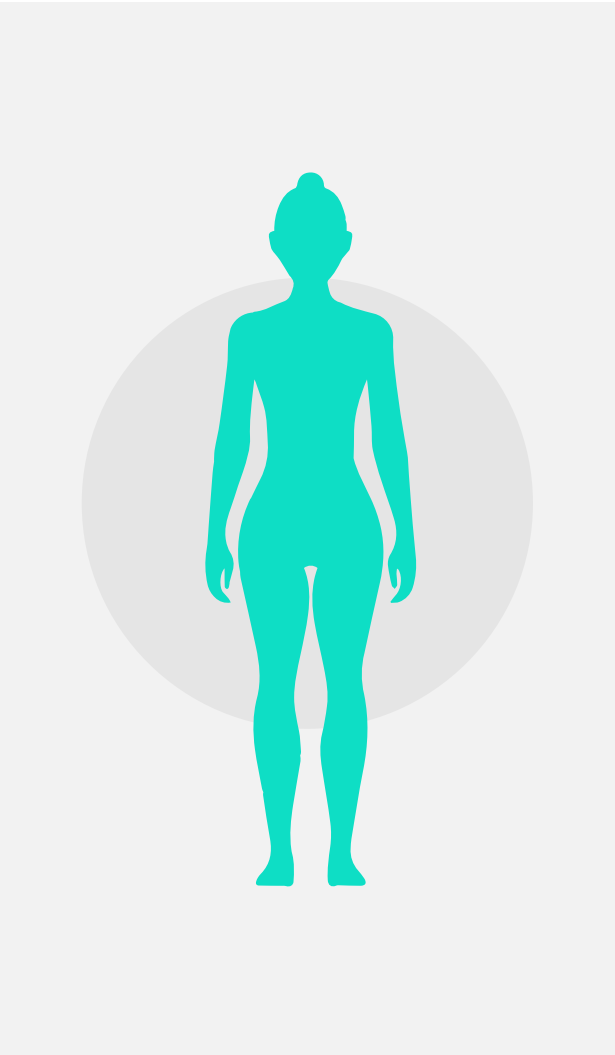
Polling Question



If biologic/targeted treatments:

1. TNF- inh
2. CTLA4 Ag
3. Anti IL-6
4. Anti CD-20
5. JAK-I (non-selective)
6. JAK-I (selective)

Holistic approach



- Pain
- Depression
- Disability
- Functional impairment
- Cognitive decline
- Accessibility
- Exercise
- Comorbidities (cardiovascular, osteoporosis, lung,….)
- Smoking cessation
- Vaccinations
- Cancer risk assessment (mammograms, PAP smear, PSA tests, colonoscopy etc)
- ……..

RMD Open
Rheumatic & Musculoskeletal Diseases

ORIGINAL RESEARCH

Safety profile of upadacitinib over 15 000 patient-years across rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and atopic dermatitis

Gerd R Burmester ,[1] Stanley B Cohen ,[2] Kevin L Winthrop ,[3] Peter Nash ,[4] Alan D Irvine,[5,6] Atul Deodhar,[3] Eduardo Mysler,[7] Yoshiya Tanaka ,[8] John Liu,[9] Ana P Lacerda,[9] Hannah Palac,[9] Tim Shaw,[10] Philip J Mease ,[11] Emma Guttman-Yassky[12]

To cite: Burmester GR, Cohen SB, Winthrop KL, *et al.* Safety profile of upadacitinib over 15 000 patient-years across rheumatoid arthritis, psoriatic arthritis, ankylosing

ABSTRACT

Objective To evaluate the long-term safety profile for upadacitinib across rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS) and atopic dermatitis (AD).

Methods Safety data from clinical trials of upadacitinib

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Upadacitinib is a Janus kinase (JAK) inhibitor with established efficacy in adults with rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS) and ulcerative colitis and adults and

RMD Open: first published as 10.1136/rmdopen-2022-002735 on 8 Februar

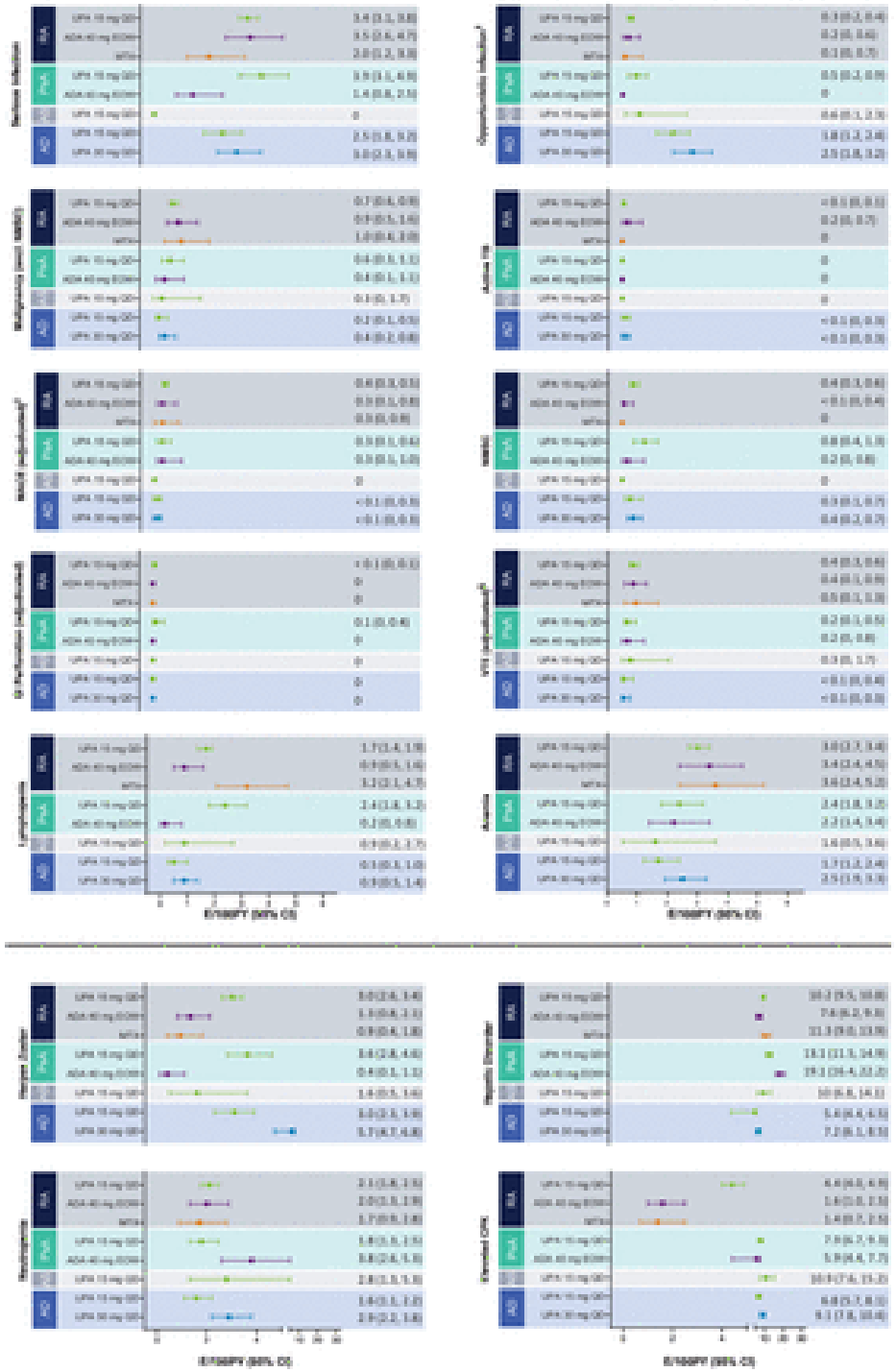
Inflammatory arthritis

RMD Open
Rheumatic & Musculoskeletal Diseases

ORIGINAL RESEARCH

Safety profile of upadacitinib over 15 000 patient-years across rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and atopic dermatitis

Gerd R Burmester ,[1] Stanley B Cohen ,[2] Kevin L Winthrop ,[3] Peter Nash ,[4] Alan D Irvine,[5,6] Atul Deodhar,[5] Eduardo Mysler,[7] Yoshiya Tanaka ,[8] John Liu,[9] Ana P Lacerda,[9] Hannah Palac,[9] Tim Shaw,[10] Philip J Mease ,[11] Emma Guttman-Yassky[12]



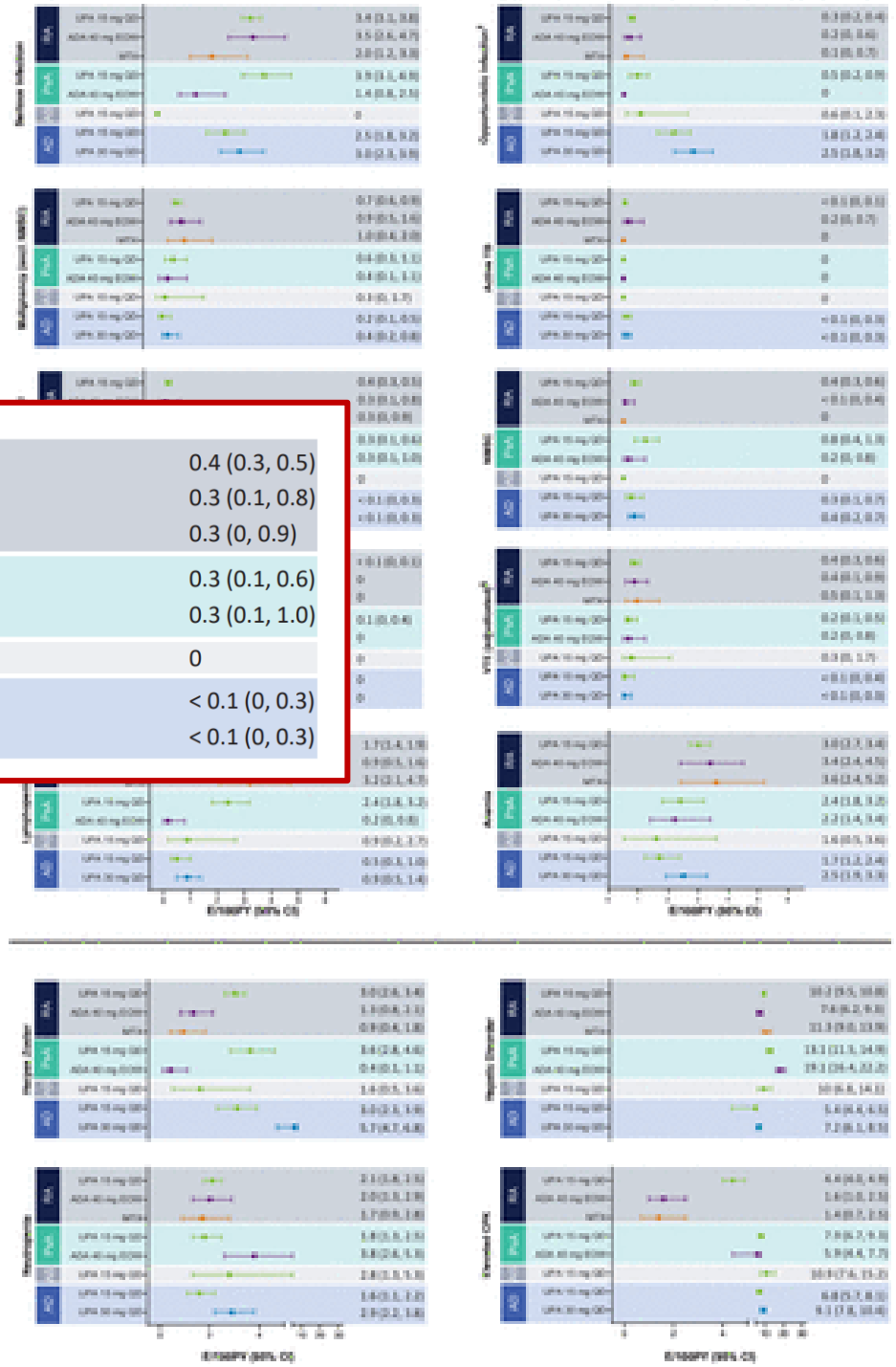
Inflammatory arthritis

RMD Open
Rheumatic & Musculoskeletal Diseases

ORIGINAL RESEARCH

Safety profile of upadacitinib over 15 000 patient-years across rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and atopic dermatitis

Gerd R Burmester ,[1] Stanley B Cohen ,[2] Kevin L Winthrop ,[3] Peter Nash ,[4] Alan D Irvine,[5,6] Atul Deodhar,[3] Eduardo Mysler,[7] Yoshiya Tanaka ,[8] John Liu,[9] Ana P Lacerda,[9] Hannah Palac,[9] Tim Shaw,[10] Philip J Mease ,[11] Emma Guttman-Yassky[12]



Burmester, RMD Open 2022

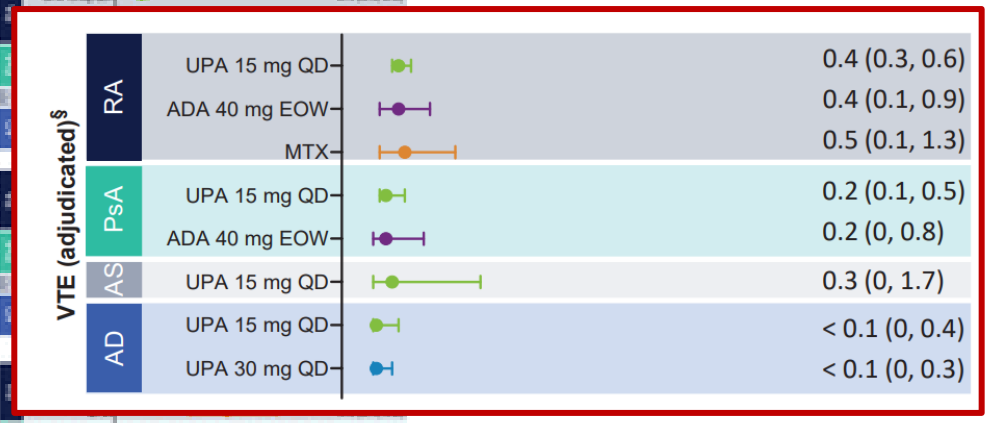
Inflammatory arthritis

RMD Open
Rheumatic & Musculoskeletal Diseases

ORIGINAL RESEARCH

Safety profile of upadacitinib over 15 000 patient-years across rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and atopic dermatitis

Gerd R Burmester ,[1] Stanley B Cohen ,[2] Kevin L Winthrop ,[3] Peter Nash ,[4] Alan D Irvine,[5,6] Atul Deodhar,[3] Eduardo Mysler,[7] Yoshiya Tanaka ,[8] John Liu,[9] Ana P Lacerda,[9] Hannah Palac,[9] Tim Shaw,[10] Philip J Mease ,[11] Emma Guttman-Yassky[12]



Burmester, RMD Open 2022

Inflammatory arthritis

RMD Open
Rheumatic & Musculoskeletal Diseases

ORIGINAL RESEARCH

Safety profile of upadacitinib over 15 000 patient-years across rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and atopic dermatitis

Gerd R Burmester ,[1] Stanley B Cohen ,[2] Kevin L Winthrop ,[3] Peter Nash ,[4] Alan D Irvine,[5,6] Atul Deodhar,[3] Eduardo Mysler,[7] Yoshiya Tanaka ,[8] John Liu,[9] Ana P Lacerda,[9] Hannah Palac,[9] Tim Shaw,[10] Philip J Mease ,[11] Emma Guttman-Yassky[12]

Parameter, n (%)	RA			PsA		AS	AD	
	UPA 15 mg QD N=3209	ADA 40 mg EOW N=579	MTX N=314	UPA 15 mg QD N=907	ADA 40 mg EOW N=429	UPA 15 mg QD N=182	UPA 15 mg QD N=1340	UPA 30 mg QD N=1353
Age (years), mean (SD)	54.3 (12.0)	54.1 (11.7)	53.3 (12.9)	51.5 (12.1)	51.4 (12.0)	45.3 (12.5)	31.9 (15.2)	33.0 (16.0)
Age ≥65 years	643 (20.0)	106 (18.3)	58 (18.5)	129 (14.2)	67 (15.6)	11 (6.0)	48 (3.6)	68 (5.0)
Number of CV risk factors†								
0	739 (23.0)	133 (23.0)	82 (26.1)	150 (16.5)	90 (21.0)	36 (19.8)	635 (47.4)	697 (51.5)
1	1073 (33.4)	202 (34.9)	105 (33.4)	308 (34.0)	140 (32.6)	73 (40.1)	486 (36.3)	439 (32.4)
2	883 (27.5)	160 (27.6)	82 (26.1)	251 (27.7)	118 (27.5)	54 (29.7)	173 (12.9)	166 (12.3)
3	394 (12.3)	63 (10.9)	36 (11.5)	151 (16.6)	56 (13.1)	18 (9.9)	38 (2.8)	45 (3.3)
4+	120 (3.7)	21 (3.6)	9 (2.9)	47 (5.2)	25 (5.8)	1 (0.5)	8 (0.6)	6 (0.4)
Presence of any CV risk factor	2470 (77.0)	446 (77.0)	232 (73.9)	757 (83.5)	339 (79.0)	146 (80.2)	705 (52.6)	656 (48.5)
Prior CV event	384 (12.0)	62 (10.7)	27 (8.6)	116 (12.8)	40 (9.3)	19 (10.4)	67 (5.0)	70 (5.2)
History of hypertension	1301 (40.5)	252 (43.5)	112 (35.7)	403 (44.4)	179 (41.7)	35 (19.2)	149 (11.1)	123 (9.1)
Diabetes mellitus	382 (11.9)	61 (10.5)	31 (9.9)	122 (13.5)	47 (11.0)	8 (4.4)	26 (1.9)	27 (2.0)
Tobacco/nicotine use‡	1221 (38.0)	199 (34.4)	120 (38.2)	385 (42.4)	163 (38.0)	100 (54.9)	418 (31.2)	418 (30.9)
Elevated LDL-C (≥3.36 mmol/L)	869 (27.2)	170 (29.4)	86 (27.5)	253 (28.7)	121 (28.7)	43 (23.8)	197 (14.9)	185 (14.0)
Lowered HDL-C (<1.034 mmol/L)	354 (11.0)	53 (9.2)	39 (12.4)	176 (19.6)	95 (22.4)	34 (18.7)	178 (13.4)	168 (12.5)

OPEN ACCESS

CLINICAL SCIENCE

Safety profile of upadacitinib in patients at risk of cardiovascular disease: integrated post hoc analysis of the SELECT phase III rheumatoid arthritis clinical programme

Roy Fleischmann,[1] Jeffrey R Curtis,[2] Christina Charles-Schoeman ,[3] Eduardo Mysler,[4] Kunihiro Yamaoka,[5] Christophe Richez ,[6] Hannah Palac,[7] Deanne Dilley,[7] Jianzhong Liu,[7] Sander Strengholt,[7] Gerd Burmester [8]

Table 1 Baseline demographics and disease characteristics

n (%), unless specified	Overall population			Higher CV risk population			SELECT-COMPARE higher CV risk population	
	upadacitinib 15 mg QD±csDMARDs (n=3209)	adalimumab 40 mg EOW+MTX (n=579)	MTX monotherapy (n=314)	upadacitinib 15 mg QD±csDMARD(s) (n=1717)	adalimumab 40 mg EOW+MTX (n=320)	MTX monotherapy (n=162)	upadacitinib 15 mg QD+MTX (n=649)	adalimumab 40 mg EOW+MTX (n=177)
Female	2581 (80.4)	470 (81.2)	240 (76.4)	1331 (77.5)	254 (79.4)	114 (70.4)	501 (77.2)	133 (75.1)
Mean (SD) age (years)	54.3 (12.0)	54.2 (11.7)	53.3 (12.9)	61.4 (7.3)	60.6 (7.2)	61.6 (7.7)	61.1 (7.2)	60.9 (7.6)
Age ≥65 years	643 (20.0)	106 (18.3)	58 (18.5)	543 (31.6)	89 (27.8)	54 (33.3)	202 (31.1)	52 (29.4)
Mean (SD) BMI (kg/m^2)	29.1 (6.7)*	29.4 (7.1)	28.0 (6.3)	29.8 (6.5)*	30.4 (6.9)	28.7 (6.6)	29.7 (6.4)	29.4 (6.3)
BMI ≥30 kg/m^2	1200 (37.4)*	227 (39.2)	97 (30.9)	722 (42.1)*	144 (45.0)	56 (34.6)	267 (41.1)	67 (37.9)
Race								
White	2784 (86.8)	504 (87.0)	256 (81.5)	1480 (86.2)	284 (88.8)	129 (79.6)	570 (87.8)	162 (91.5)
Black or African–American	170 (5.3)	39 (6.7)	12 (3.8)	118 (6.9)	27 (8.4)	9 (5.6)	41 (6.3)	11 (6.2)
Asian	191 (6.0)	30 (5.2)	37 (11.8)	86 (5.0)	7 (2.2)	21 (13.0)	24 (3.7)	3 (1.7)
Other	64 (2.0)	6 (1.0)	9 (2.9)	33 (1.9)	2 (0.6)	3 (1.9)	14 (2.2)	1 (0.6)
Geographical region								
North America	815 (25.4)	122 (21.1)	46 (14.6)	537 (31.3)	79 (24.7)	29 (17.9)	148 (22.8)	39 (22.0)
Rest of the world	2394 (74.6)	457 (78.9)	268 (85.4)	1180 (68.7)	241 (75.3)	133 (82.1)	501 (77.2)	138 (78.0)
Mean (SD) time since diagnosis (years)	8.5 (8.4)†	8.2 (8.0)	2.6 (5.1)	9.5 (9.0)	8.9 (8.8)	2.9 (6.1)	8.9 (8.4)	8.8 (9.4)
Mean (SD) CDAI‡	39.7 (12.7)	41.1 (13.3)	40.5 (13.3)	39.8 (12.6)	41.6 (13.4)	39.8 (13.8)	40.4 (12.7)	40.2 (13.9)
Mean (SD) DAS28(CRP)§	5.8 (1.0)	5.9 (1.0)	5.9 (1.0)	5.8 (0.9)	5.9 (1.0)	5.8 (1.0)	5.8 (0.9)	5.9 (1.0)
RF positive	2439 (76.1)¶	456 (78.8)	232 (73.9)	1312 (76.5)¶	249 (77.8)	115 (71.0)	521 (80.3)	141 (79.7)
ACPA positive	2505 (78.2)**	455 (78.6)	236 (75.2)	1318 (76.9)**	247 (77.2)	116 (71.6)	521 (80.4)	138 (78.0)
Prior bDMARD use	952 (29.7)	55 (9.5)	0	544 (31.7)	30 (9.4)	0	54 (8.3)	17 (9.6)
Prior TNFi therapy	819 (25.5)	37 (6.4)	0	478 (27.8)	22 (6.9)	0	42 (6.5)	12 (6.8)
Other bDMARD therapy	304 (9.5)	20 (3.5)	0	168 (9.8)	8 (2.5)	0	14 (2.2)	5 (2.8)
Concomitant csDMARD use								
MTX alone	2182 (68.0)	579 (100)	0	1181 (68.8)	320 (100)	0	647 (99.7)	177 (100)
MTX and other csDMARD	169 (5.3)	0	0	88 (5.1)	0	0	2 (0.3)	0
csDMARDs other than MTX	196 (6.1)	0	0	112 (6.5)	0	0	0	0
None	662 (20.6)	0	314 (100)	336 (19.6)	0	162 (100)	0	0
Other concomitant treatments								
Glucocorticoid	1763 (54.9)	350 (60.4)	164 (52.2)	900 (52.4)	195 (60.9)	85 (52.5)	379 (58.4)	114 (64.4)
Aspirin	270 (8.4)	36 (6.2)	24 (7.6)	250 (14.6)	34 (10.6)	19 (11.7)	92 (14.2)	18 (10.2)
Statin	369 (11.5)	55 (9.5)	26 (8.3)	322 (18.8)	49 (15.3)	24 (14.8)	108 (16.6)	19 (10.7)
Antithrombotic agent	316 (9.8)	42 (7.3)	26 (8.3)	290 (16.9)	38 (11.9)	21 (13.0)	102 (15.7)	20 (11.3)
Smoking status††								
Never smoked	1986 (61.9)	378 (65.5)	194 (61.8)	800 (46.6)	162 (50.9)	69 (42.6)	342 (52.7)	78 (44.6)
Ever smoked	1221 (38.1)	199 (34.5)	120 (38.2)	915 (53.4)	156 (49.1)	93 (57.4)	307 (47.3)	97 (55.4)
History of hypertension	1277 (39.8)	252 (43.5)	112 (35.7)	1106 (64.4)	225 (70.3)	96 (59.3)	429 (66.1)	123 (69.5)
History of diabetes mellitus	383 (11.9)	61 (10.5)	31 (9.9)	327 (19.0)	54 (16.9)	28 (17.3)	119 (18.3)	27 (15.3)
History of VTE	53 (1.7)	9 (1.6)	3 (1.0)	38 (2.2)	9 (2.8)	0	14 (2.2)	6 (3.4)
History of CV event	385 (12.0)	63 (10.9)	27 (8.6)	346 (20.2)	56 (17.5)	24 (14.8)	141 (21.7)	20 (11.3)
HDL-C <40 mg/dL	354 (11.0)	53 (9.2)	39 (12.4)	224 (13.0)	33 (10.3)	26 (16.0)	87 (13.4)	19 (10.7)

*Overall population, n=3205. Overall higher-risk population, n=1715.
†n = 3208.
‡Overall population: upadacitinib 15 mg QD, n=3040; adalimumab 40 mg EOW, n=546; MTX, n=299. Overall higher-risk population: upadacitinib 15 mg QD, n=1632; adalimumab 40 mg EOW, n=306; MTX, n=153. SELECT-COMPARE higher-risk population: upadacitinib 15 mg QD, n=618; adalimumab 40 mg EOW, n=170.
§Overall population: upadacitinib 15 mg QD: n=3192; adalimumab 40 mg EOW: n=575; MTX: n=314. Overall higher-risk population: upadacitinib 15 mg QD, n=1709; adalimumab 40 mg EOW, n=318; MTX, n=162. SELECT-COMPARE higher-risk population: upadacitinib 15 mg QD, n=646; adalimumab 40 mg EOW, n=176.
¶Overall population: n=3207. Overall higher-risk population: n=1716.
**Overall population: n=3203. Overall higher-risk population: n=1714.
††Overall population: upadacitinib 15 mg QD: n=3207; adalimumab 40 mg EOW: n=577; MTX: n=314. Overall higher-risk population: upadacitinib 15 mg QD: n=1715; adalimumab 40 mg EOW: n=318; MTX: n=162. SELECT-COMPARE higher-risk population: upadacitinib 15 mg QD: n=649; adalimumab 40 mg EOW: n=175.

Table 1 Baseline demographics and disease characteristics

n (%), unless specified	Overall population			Higher CV risk population			SELECT-COMPARE higher CV risk population	
	upadacitinib 15 mg QD±csDMARDs (n=3209)	adalimumab 40 mg EOW+MTX (n=579)	MTX monotherapy (n=314)	upadacitinib 15 mg QD±csDMARD(s) (n=1717)	adalimumab 40 mg EOW+MTX (n=320)	MTX monotherapy (n=162)	upadacitinib 15 mg QD+MTX (n=649)	adalimumab 40 mg EOW+MTX (n=177)
Race								
White	2784 (86.8)	504 (87.0)	256 (81.5)	1480 (86.2)	284 (88.8)	129 (79.6)	570 (87.8)	162 (91.5)
Black or African–American	170 (5.3)	39 (6.7)	12 (3.8)	118 (6.9)	27 (8.4)	9 (5.6)	41 (6.3)	11 (6.2)
Asian	191 (6.0)	30 (5.2)	37 (11.8)	86 (5.0)	7 (2.2)	21 (13.0)	24 (3.7)	3 (1.7)
Other	64 (2.0)	6 (1.0)	9 (2.9)	33 (1.9)	2 (0.6)	3 (1.9)	14 (2.2)	1 (0.6)
Geographical region								
North America	815 (25.4)	122 (21.1)	46 (14.6)	537 (31.3)	79 (24.7)	29 (17.9)	148 (22.8)	39 (22.0)
Rest of the world	2394 (74.6)	457 (78.9)	268 (85.4)	1180 (68.7)	241 (75.3)	133 (82.1)	501 (77.2)	138 (78.0)
Smoking status††								
Never smoked	1986 (61.9)	378 (65.5)	194 (61.8)	800 (46.6)	162 (50.9)	69 (42.6)	342 (52.7)	78 (44.6)
Ever smoked	1221 (38.1)	199 (34.5)	120 (38.2)	915 (53.4)	156 (49.1)	93 (57.4)	307 (47.3)	97 (55.4)
History of hypertension	1277 (39.8)	252 (43.5)	112 (35.7)	1106 (64.4)	225 (70.3)	96 (59.3)	429 (66.1)	123 (69.5)
History of diabetes mellitus	383 (11.9)	61 (10.5)	31 (9.9)	327 (19.0)	54 (16.9)	28 (17.3)	119 (18.3)	27 (15.3)
History of VTE	53 (1.7)	9 (1.6)	3 (1.0)	38 (2.2)	9 (2.8)	0	14 (2.2)	6 (3.4)
History of CV event	385 (12.0)	63 (10.9)	27 (8.6)	346 (20.2)	56 (17.5)	24 (14.8)	141 (21.7)	20 (11.3)
HDL-C <40 mg/dL	354 (11.0)	53 (9.2)	39 (12.4)	224 (13.0)	33 (10.3)	26 (16.0)	87 (13.4)	19 (10.7)
None	662 (20.6)	0	314 (100)	336 (19.6)	0	162 (100)	0	0
Other concomitant treatments								
Glucocorticoid	1763 (54.9)	350 (60.4)	164 (52.2)	900 (52.4)	195 (60.9)	85 (52.5)	379 (58.4)	114 (64.4)
Aspirin	270 (8.4)	36 (6.2)	24 (7.6)	250 (14.6)	34 (10.6)	19 (11.7)	92 (14.2)	18 (10.2)
Statin	369 (11.5)	55 (9.5)	26 (8.3)	322 (18.8)	49 (15.3)	24 (14.8)	108 (16.6)	19 (10.7)
Antithrombotic agent	316 (9.8)	42 (7.3)	26 (8.3)	290 (16.9)	38 (11.9)	21 (13.0)	102 (15.7)	20 (11.3)
Smoking status††								
Never smoked	1986 (61.9)	378 (65.5)	194 (61.8)	800 (46.6)	162 (50.9)	69 (42.6)	342 (52.7)	78 (44.6)
Ever smoked	1221 (38.1)	199 (34.5)	120 (38.2)	915 (53.4)	156 (49.1)	93 (57.4)	307 (47.3)	97 (55.4)
History of hypertension	1277 (39.8)	252 (43.5)	112 (35.7)	1106 (64.4)	225 (70.3)	96 (59.3)	429 (66.1)	123 (69.5)
History of diabetes mellitus	383 (11.9)	61 (10.5)	31 (9.9)	327 (19.0)	54 (16.9)	28 (17.3)	119 (18.3)	27 (15.3)
History of VTE	53 (1.7)	9 (1.6)	3 (1.0)	38 (2.2)	9 (2.8)	0	14 (2.2)	6 (3.4)
History of CV event	385 (12.0)	63 (10.9)	27 (8.6)	346 (20.2)	56 (17.5)	24 (14.8)	141 (21.7)	20 (11.3)
HDL-C <40 mg/dL	354 (11.0)	53 (9.2)	39 (12.4)	224 (13.0)	33 (10.3)	26 (16.0)	87 (13.4)	19 (10.7)

*Overall population, n=3205. Overall higher-risk population, n=1715.
†n = 3208.
‡Overall population: upadacitinib 15 mg QD, n=3040; adalimumab 40 mg EOW, n=546; MTX, n=299. Overall higher-risk population: upadacitinib 15 mg QD, n=1632; adalimumab 40 mg EOW, n=306; MTX, n=153. SELECT-COMPARE higher-risk population: upadacitinib 15 mg QD, n=618; adalimumab 40 mg EOW, n=170.
§Overall population: upadacitinib 15 mg QD: n=3192; adalimumab 40 mg EOW: n=575; MTX: n=314. Overall higher-risk population: upadacitinib 15 mg QD, n=1709; adalimumab 40 mg EOW, n=318; MTX, n=162. SELECT-COMPARE higher-risk population: upadacitinib 15 mg QD, n=646; adalimumab 40 mg EOW, n=176.
¶Overall population: n=3207. Overall higher-risk population: n=1716.
**Overall population: n=3203. Overall higher-risk population: n=1714.
††Overall population: upadacitinib 15 mg QD: n=3207; adalimumab 40 mg EOW: n=577; MTX: n=314. Overall higher-risk population: upadacitinib 15 mg QD: n=1715; adalimumab 40 mg EOW: n=318; MTX: n=162. SELECT-COMPARE higher-risk population: upadacitinib 15 mg QD: n=649; adalimumab 40 mg EOW: n=175.

Fleischmann, Ann RHeum Dis 2023

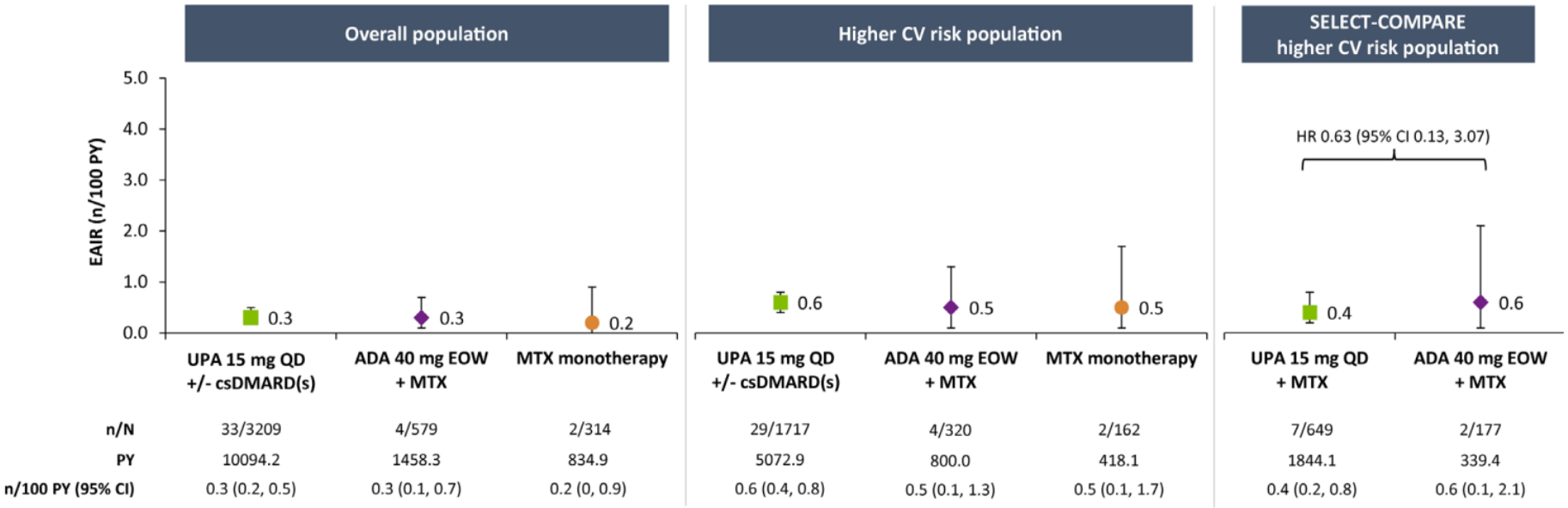
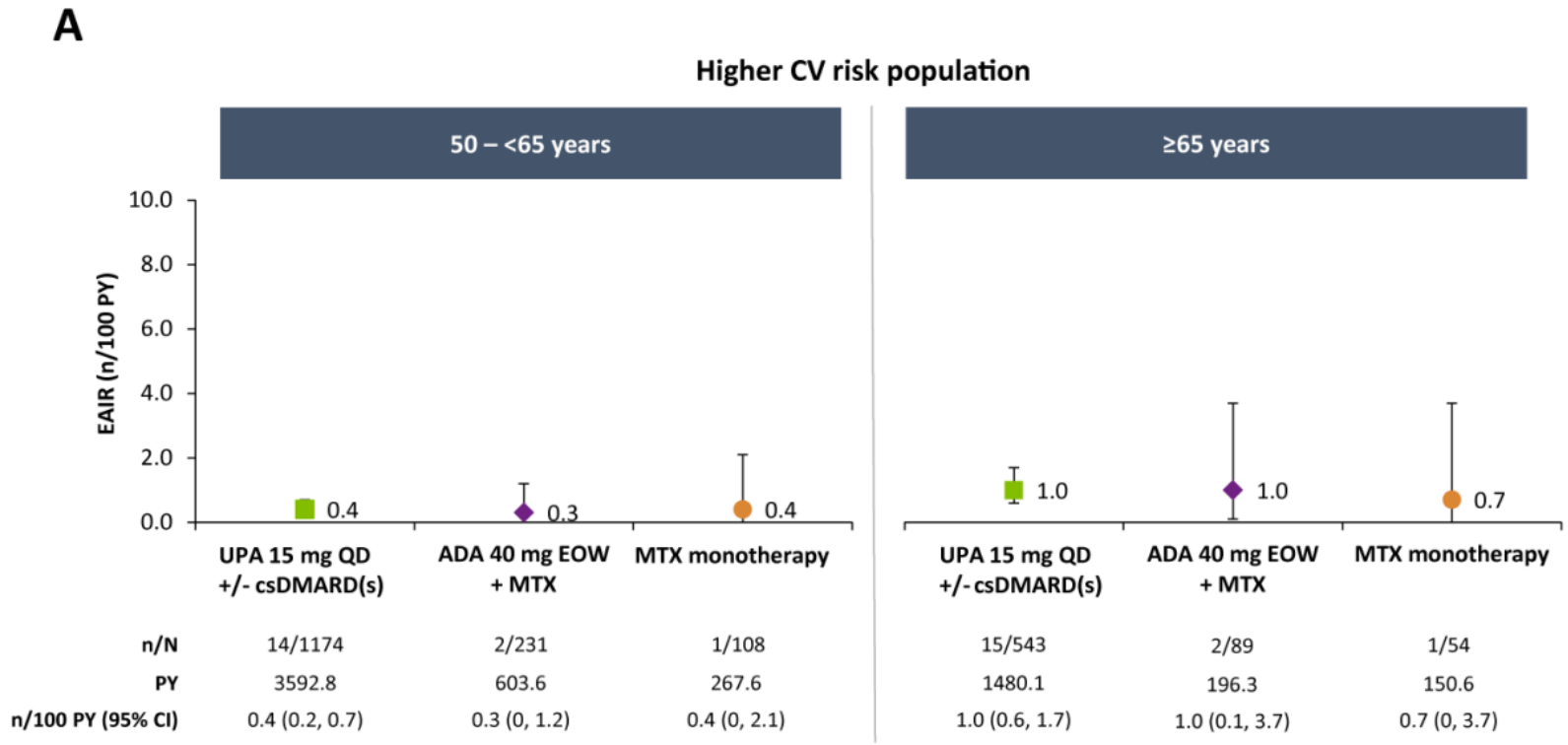


Figure 1 Exposure-adjusted incidence of adjudicated MACE. MACE defined as CV death (includes acute myocardial infarction, sudden cardiac death, heart failure, CV procedure-related death, death due to CV haemorrhage, fatal stroke, pulmonary embolism and other CV causes), non-fatal myocardial infarction and non-fatal stroke. ADA, adalimumab; csDMARD, conventional synthetic disease-modifying antirheumatic drug; CV, cardiovascular; EAIR, exposure-adjusted incidence rate; EOW, every other week; MACE, major adverse cardiovascular event; MTX, methotrexate; PY, patient-years; QD, once daily; UPA, upadacitinib.

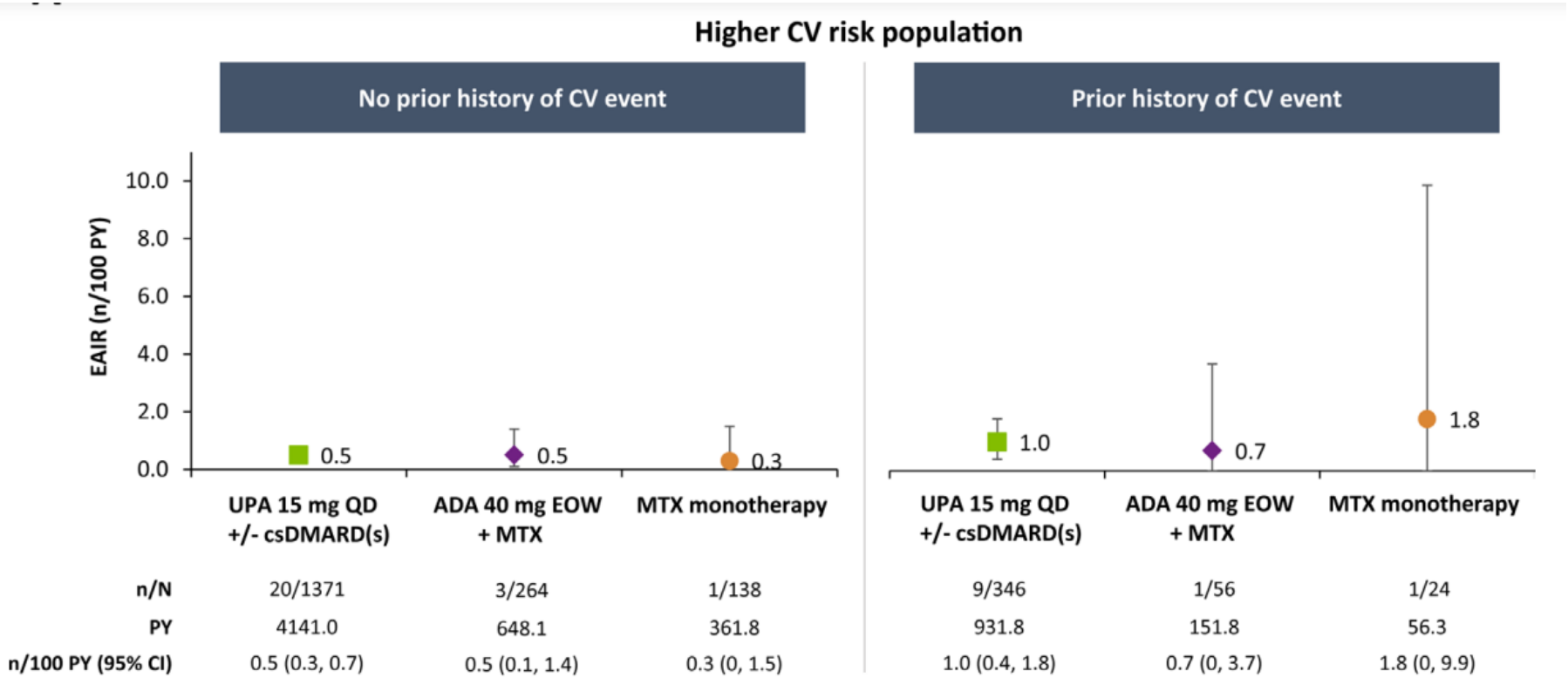
Fleischmann, Ann RHeum Dis 2023

Exposure-adjusted incidence of adjudicated MACE in higher CV risk populations by age



Fleischmann, Ann RHeum Dis 2023

Exposure-adjusted incidence of MACE in higher CV risk populations by medical history of a CV event



Fleischmann, Ann RHeum Dis 2023

Exposure-adjusted incidence of adjudicated VTE

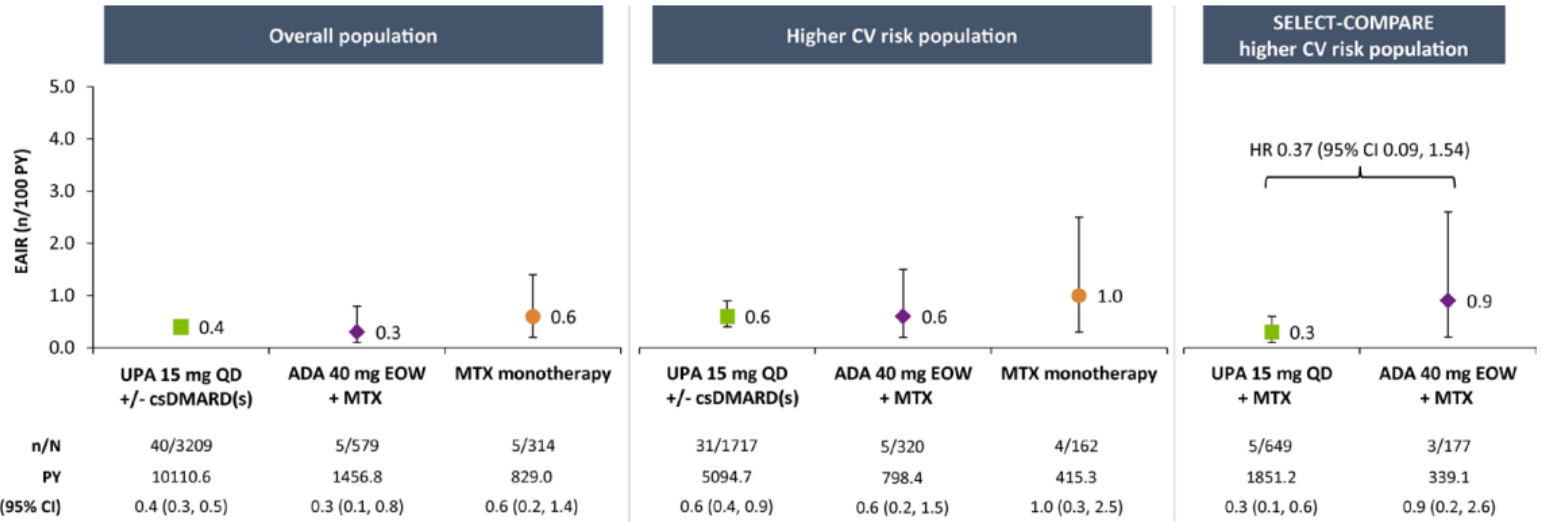
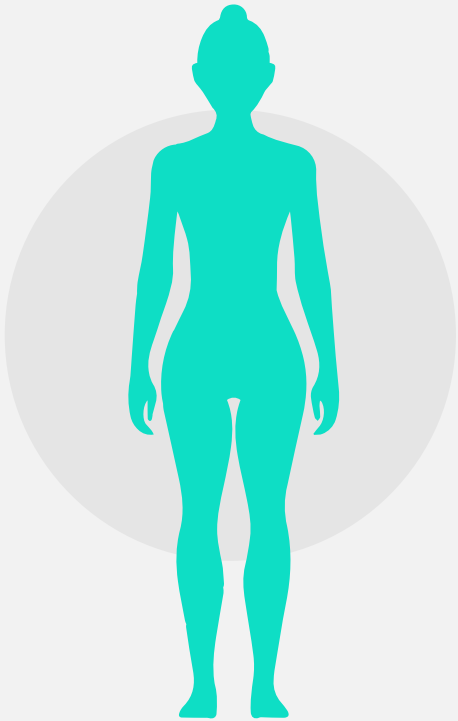


Figure 5 Exposure-adjusted incidence of adjudicated VTE. VTE events include deep vein thrombosis and pulmonary embolism. ADA, adalimumab; csDMARD, conventional synthetic disease-modifying antirheumatic drug; CV, cardiovascular; EAIR, exposure-adjusted incidence rate; EOW, every other week; MTX, methotrexate; PY, patient-years; QD, once daily; UPA, upadacitinib; VTE, venous thromboembolism.

Fleischmann, Ann RHeum Dis 2023

Holistic approach



Safety concerns

Is age a specific concern?

Do you perform cardiovascular risk assessment?

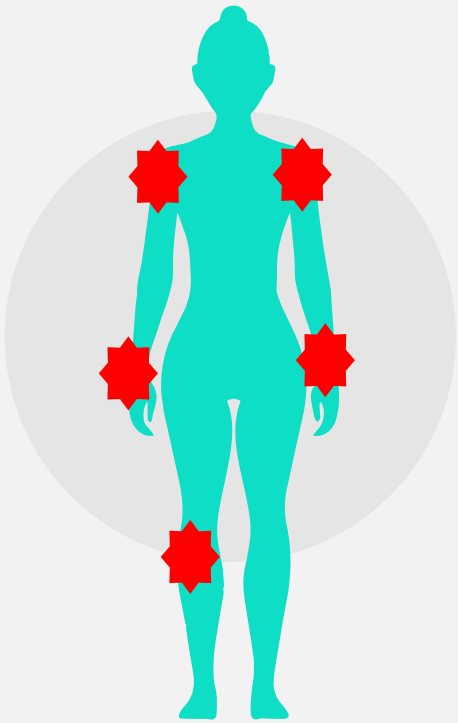
Which CV risk assessment tool do you use (Framingham risk score, SCORE, other?)

Do you feel comfortable with CV risk assessment, or would you refer to a specialist?

Who would that specialist be?

Could a structured tool (an APP?) help?

Patient Case #3



Ανθή, 44 ετών – μητέρα τριών παιδιών

Από 2 ετών αρθραλγίες σε περιφερικές αρθρώσεις με φλεγμονώδη τύπο
Οίδημα δακτύλων, νυχτερινή αφύπνιση
«Δυσκολεύεται να κάνει τις καθημερινές της δουλειές»

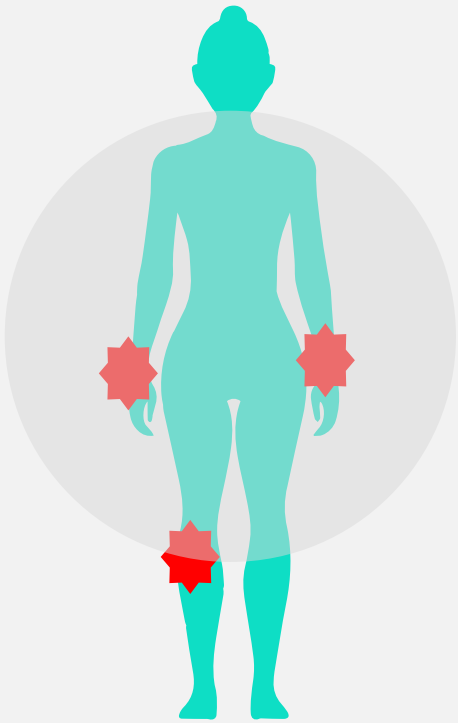
ESR: 35mm/hr, CRP: 8mg/L, RF(-), CCP (-)

Διάγνωση: **οροαρνητική ρευματοειδής αρθρίτιδα**

DAS28-CRP: 5.65
(TJC:14, SJC:6, VAS=80mm, CRP:8mg/L)
Έναρξη Prednisolone 15mg OD με σταδιακό tapering μέχρι διακοπής
MTX 15mg OWK

Επανεκτίμηση σε 12 εβδομάδες

Patient Case #3 ...continued



Επανεκτίμηση σε 12 εβδομάδες: μικρή βελτίωση

Παραμένει άλγος, ιδίως στις πηχεοκαρπικές και το ΔΕ γόνατο
ESR: 12mm/hr, CRP: 3mg/L

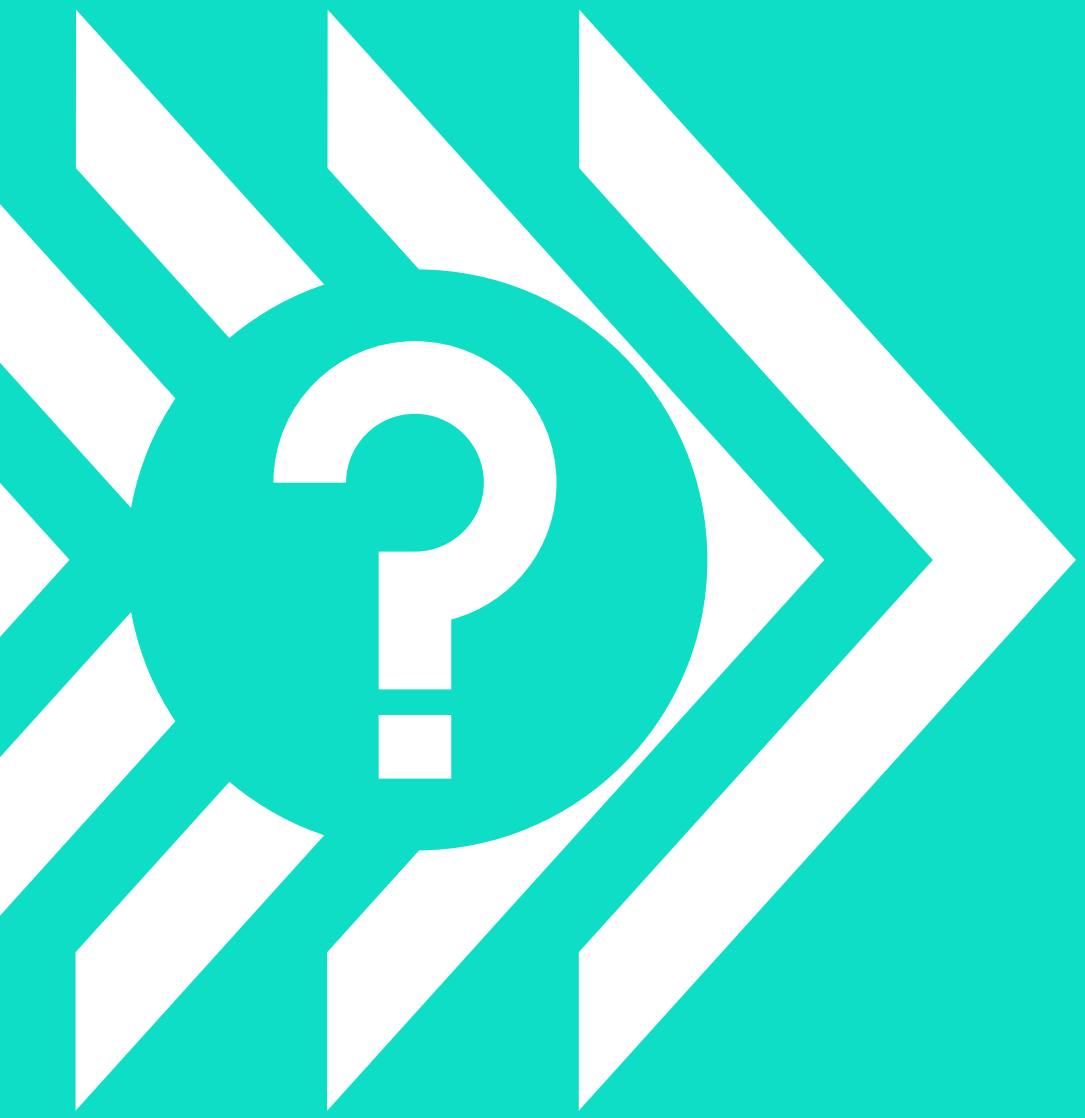
DAS28-CRP: 4.32
(TJC:5, SJC:3, VAS=80mm, CRP:3mg/L)

Έναρξη προωθημένης θεραπείας: adalimumab 40mg Q2W

Πολυσυμπτωματολογία: κακή διάθεση, χαμηλής ποιότητας ύπνος, δυσκολία να ανταπεξέλθει στην καθημερινότητα

Επανεκτίμηση σε τρεις μήνες

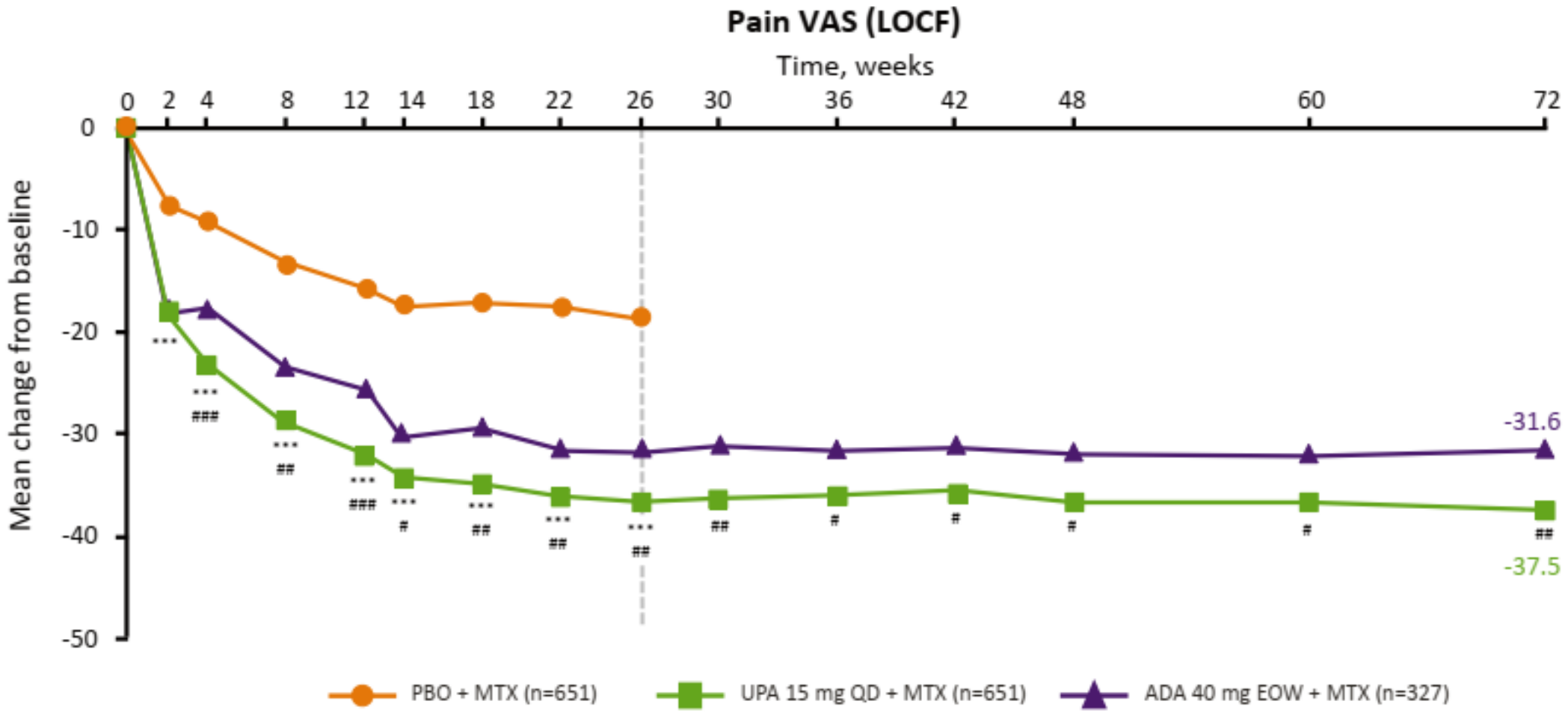
Question



Ποιο θεωρείτε ικανό διάστημα για να αξιολογήσετε την απάντηση ενός ασθενούς στη θεραπεία;

Από τι εξαρτάται η απάντησή σας στο παραπάνω ερώτημα;

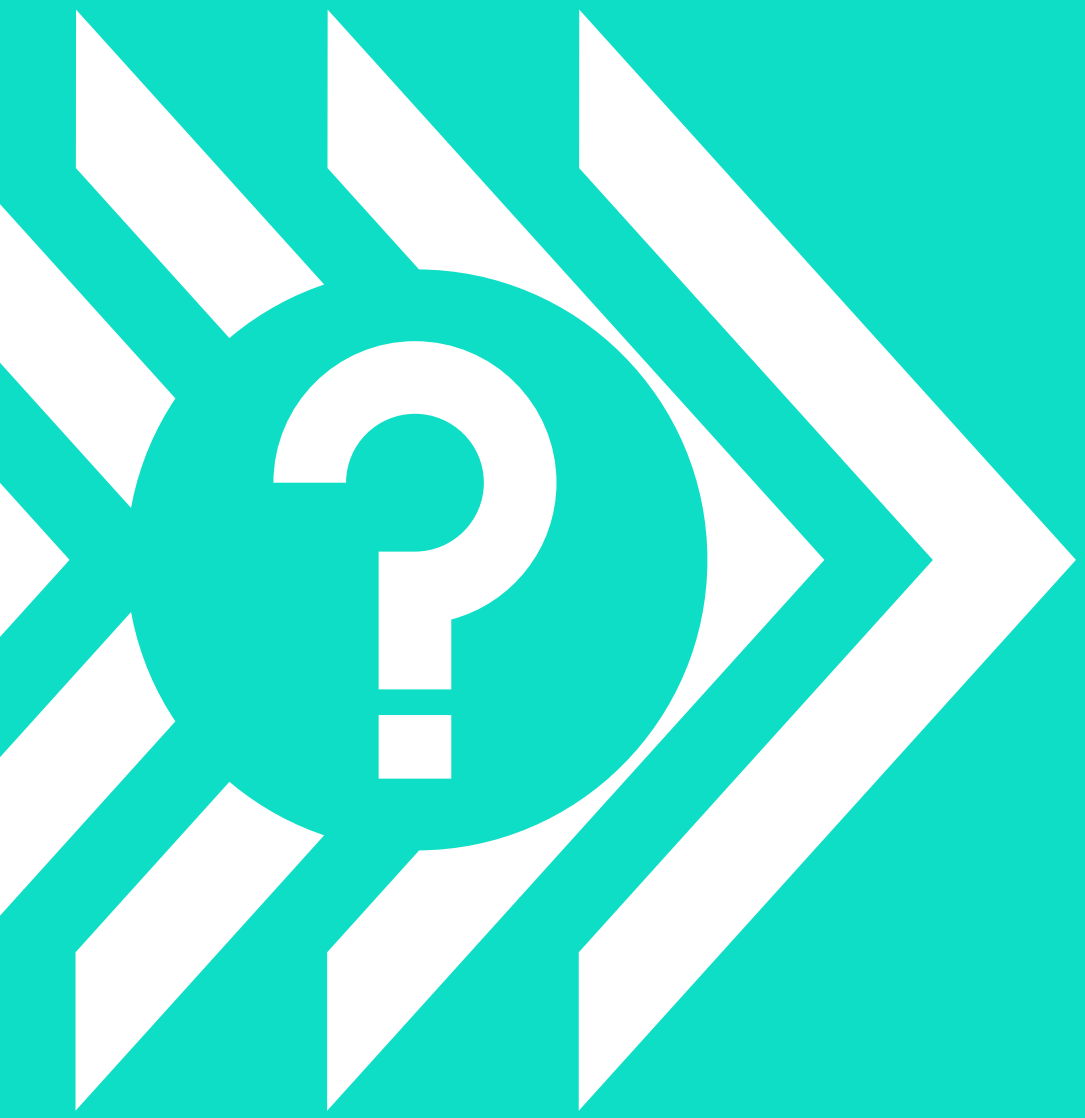
Rapid improvements in pain from baseline were demonstrated in MTX-IR patients with RA receiving UPA vs PBO



Full analysis set.
Comparisons not adjusted for multiplicity: ***nominal p≤0.001, UPA vs PBO; *nominal p≤0.05, **nominal p≤0.01, ***nominal p≤0.001, UPA vs ADA. ADA, adalimumab; EOW, every other week; IR, inadequate response; MTX, methotrexate; PBO, placebo; QD, once daily; RA, rheumatoid arthritis; UPA, upadacitinib; VAS, visual analog scale; LOCF, Last Observation Carried Forward.

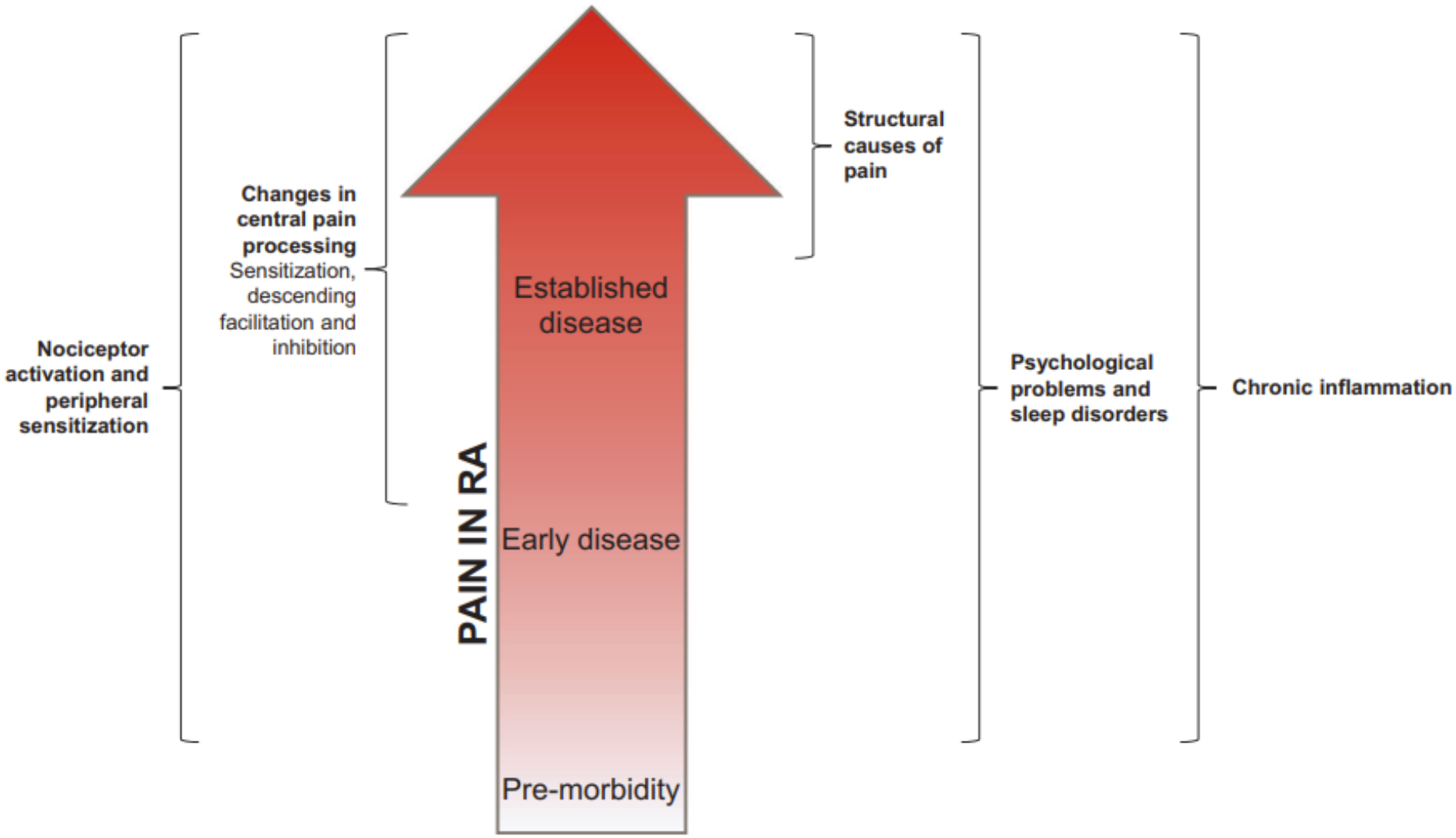
Fleischmann R et al. Poster presented at: EULAR 2020. Poster THU0201.

Question



Στην καθημερινή σας κλινική πρακτική, θα είχατε μέχρι τώρα μιλήσει με την ασθενή για τον πόνο ως έννοια μακριά από τη φλεγμονή;

Pain in Rheumatoid arthritis



Simon et al. Semin Arthritis Rheum 2021;51:278-84

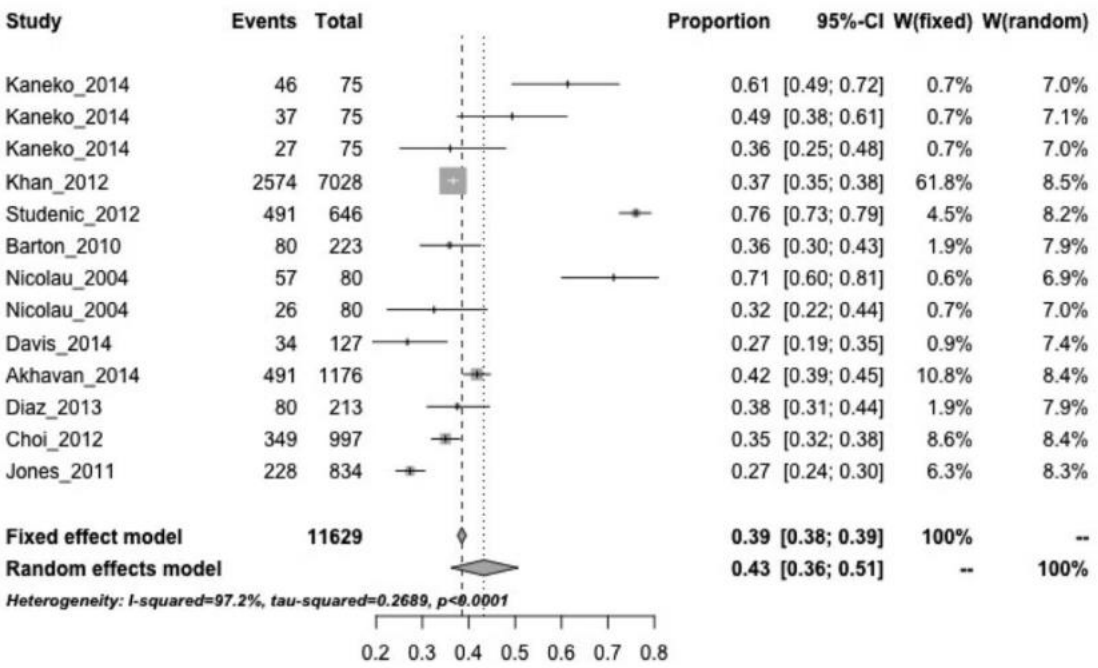
Are HCPs and patients after the same thing?

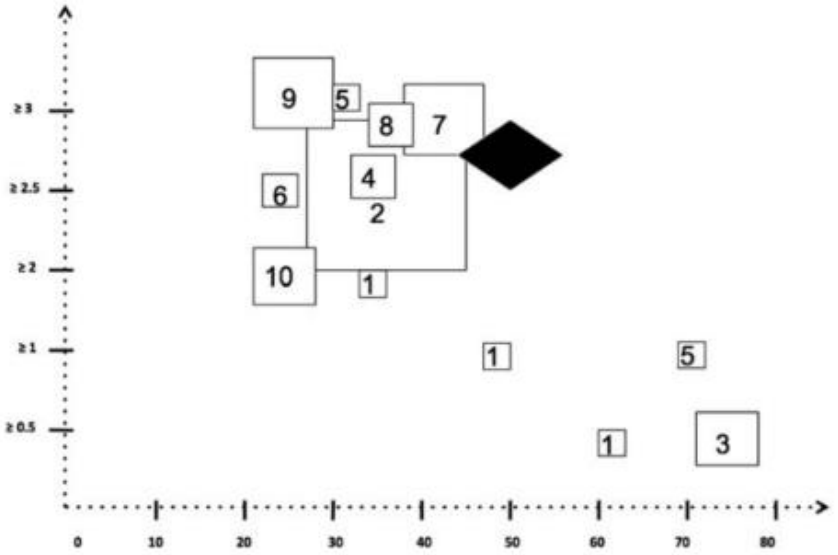
	Most important reasons to change treatment	Rheumatologist ranking	Patient ranking
Top 5 reasons for HCPs	Swollen joints	1	12
	DAS28 scores	2	17
	Rheumatologist impression of overall disease activity	3	8
	Worsening erosions in past year	4	27
	Disease activity now compared with 3 months ago	5	19
Top 5 reasons for patients	Physical functioning and mobility	7	**1**
	Patient's motivation to get better	23	**2**
	Patient's trust in their physician	45	**3**
	Patient's satisfaction with current DMARD	21	**4**
	Painful joints	13	**5**

[a]Dutch rheumatologists and patients with RA were surveyed
DAS28, Disease Activity Score – 28 joints; DMARD, disease-modifying antirheumatic drug; HCP, healthcare professional

Van Hulst L, et al. Arthritis Care Res 2011;63(10):1407–1414

Discordance in assessment between patient and HCPs





Διαφορά μεταξύ **patient's** και **physician's** global assessment

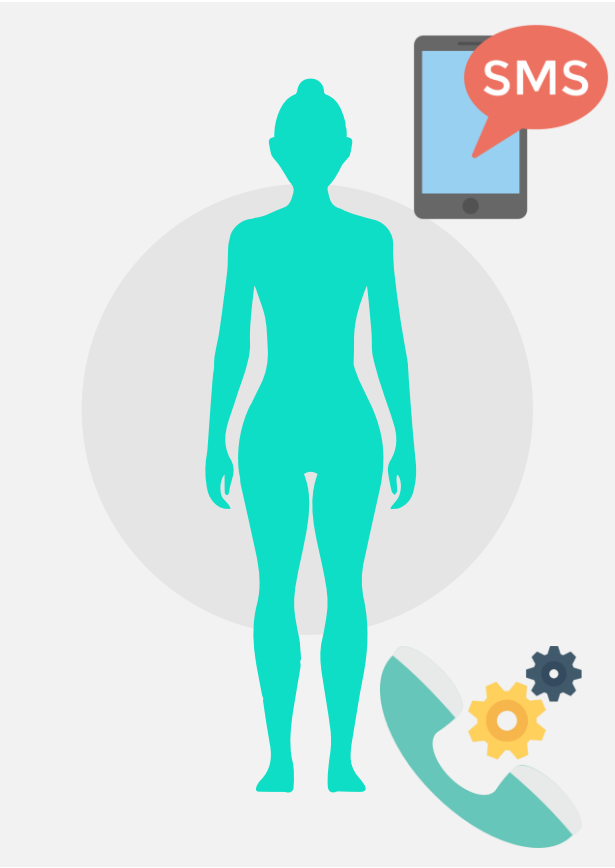
43% (36-51%)

Drivers of discordance:

- **depression**
- **health literacy**

Destieux et al. Arthritis Care Res 2016;68(12):1767–73

Patient case #3 … 2 months later...



Μήνυμα στο κινητό:

«Γιατρέ, το φάρμακο δε με έχει βοηθήσει καθόλου»

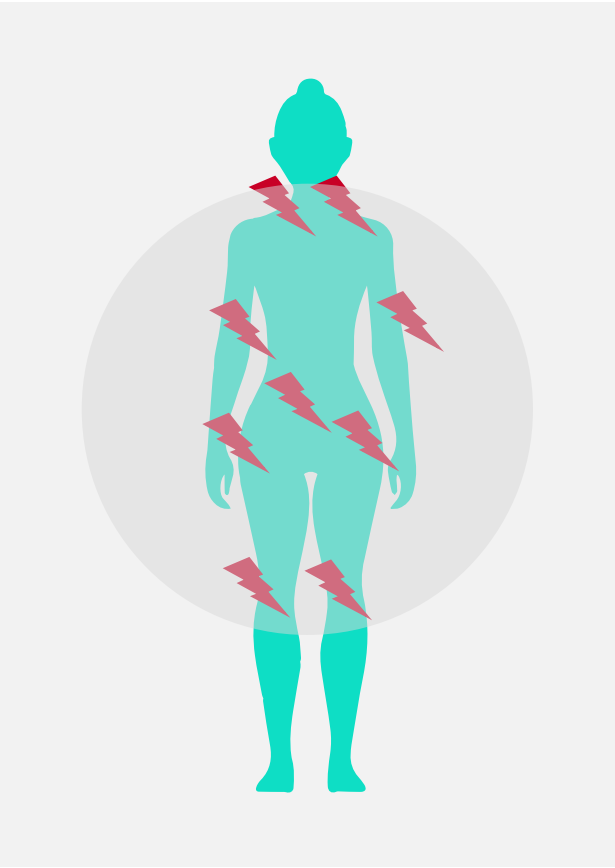
Τηλεφωνική επικοινωνία:
Η ασθενής περιγράφει σημαντικό άλγος σε διάφορες θέσεις και δυσκαμψία

Εργαστηριακός έλεγχος:

ESR: 10mm/hr, CRP: 2mg/L

Note: This is a fictitious patient case

Patient Case #3 ... 3 months later



«Γιατρέ, το φάρμακο δε με έχει βοηθήσει καθόλου»

DAS28-CRP: 4.56

(TJC:10, SJC:0, VAS=100mm, CRP:2mg/L)

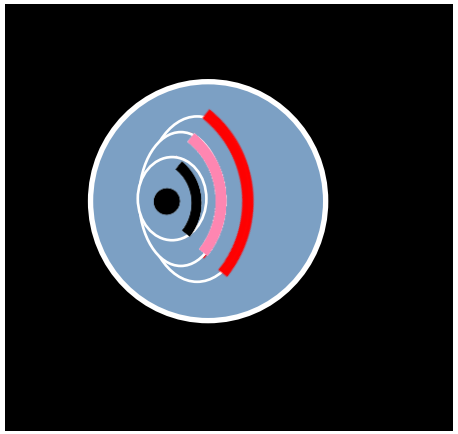
Αντικειμενικά δεν υπάρχει εικόνα υμενίτιδας

Έντονο άλγος σε πολλά σημεία, τόσο αρθρικά όσο και εξωαρθρικά

Εν διαστάσει με το σύντροφο

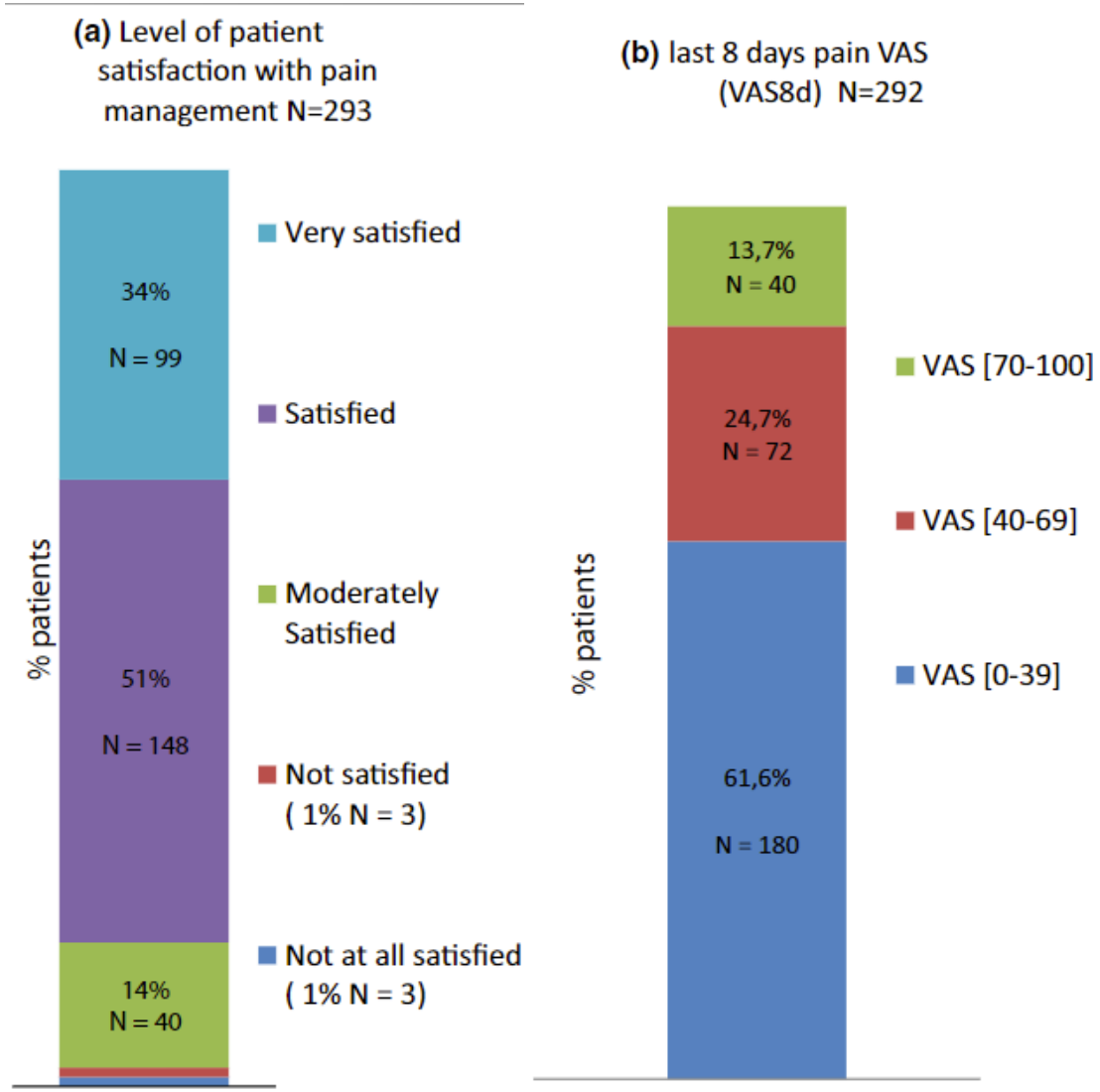
Pain causality in rheumatic diseases

Παθολογία στο επίπεδο της μυοσκελετικής δομής που πάσχει
- άρθρωση
- ένθεση
- αξονικός σκελετός



Απορρύθμιση του σήματος του πόνου κατά τη μεταφορά και επεξεργασία του από το νευρικό σύστημα:
- περιφερικό
- κεντρικό

Residual pain and its role in disease activity



4 από τους 10 ασθενείς με PA (η πλειοψηφία υπό βιολογική θεραπεία) είχαν VAS > 40mm

Vergne-Salle P et al. Eur J Pain. 2020

Residual pain and its role in disease activity

TABLE 3 Comparison of Rheumatoid arthritis patients with last 8 days average pain VAS < 40 and ≥ 40 mm/100 ($N = 292$)

	Pain VAS < 40		Pain VAS ≥ 40		
	Mean or %	*SD* or *n*	Mean or %	*SD* or *n*	*p*
Marital statut ($N = 292$)					
Single	26.7%	48	41.7%	46	0.0104*
Married or in relationship	73.3%	132	58.9%	66	
Activity ($N = 285$)					
Not working	43.7%	76	55.9%	62	0.0449*
In professional activity	56.3%	98	44.1%	49	
Disease duration (years) ($N = 291$)	13.1	9.1	13.5	10.5	0.7981#
ACPA or/and RF positivity ($N = 283$)	86.8	151	81.6	89	0.2420#
ESR (mm/h) ($N = 289$)	12.1	12.3	17.0	17.7	0.0162#
HAQ score ($N = 289$)	0.9	0.6	1.5	0.7	<0.0001#
Steroids ($N = 292$)	36.7%	66	51.8%	58	0.011*
Pain sensory qualifiers score (/100) ($N = 272$)	12.6	11.7	30.8	18.6	<0.0001#
Pain emotional qualifiers score (/100) ($N = 273$)	14.2	19.0	41.8	24.5	<0.0001#
Anxiety score (HAD) ($N = 287$)	7.8	4.3	9.4	4.6	0.0039#
Depression score (HAD) ($N = 288$)	5.1	3.9	7.2	3.6	<0.0001#
Pain interference on (0–10)					
Mood ($N = 289$)	2.4	2.3	4.6	2.6	<0.0001#
Walk ($N = 288$)	2.5	2.3	6.1	2.4	<0.0001#
Work ($N = 290$)	3.2	2.3	6.7	2.0	<0.0001#
Relationship ($N = 290$)	1.6	2.0	2.9	2.7	<0.0001#
Sleep ($N = 290$)	2.1	2.4	5.4	3.2	<0.0001#
Enjoyment of life ($N = 290$)	1.8	2.2	3.4	3.0	<0.0001#
Beck depression inventory ($N = 291$)	5.8	5.7	8.2	7.3	0.0100#

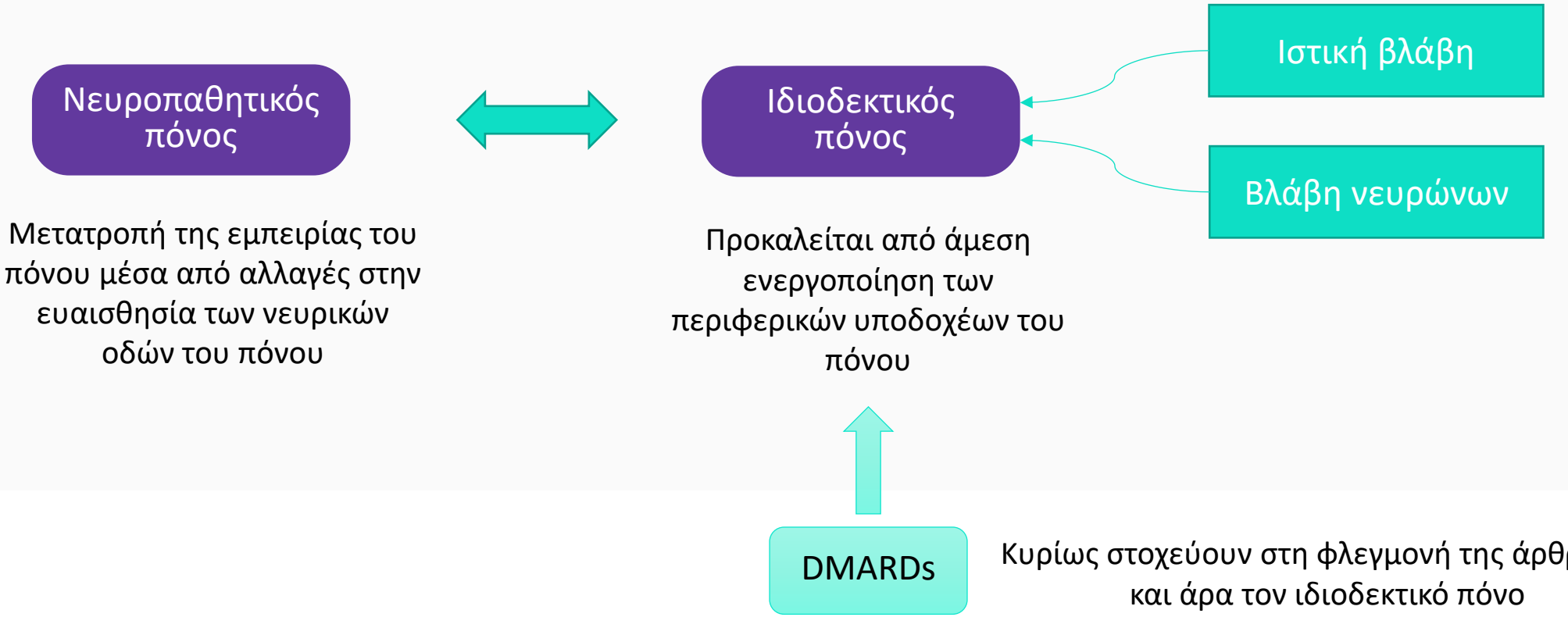
Ασθενείς με υψηλότερο πόνο είχαν μεγαλύτερη πιθανότητα να:

- **είναι single**
- **είναι άνεργοι**
- **έχουν χαμηλότερη ποιότητα ζωής**
- **έχουν κατάθλιψη**
- **έχουν άγχος**

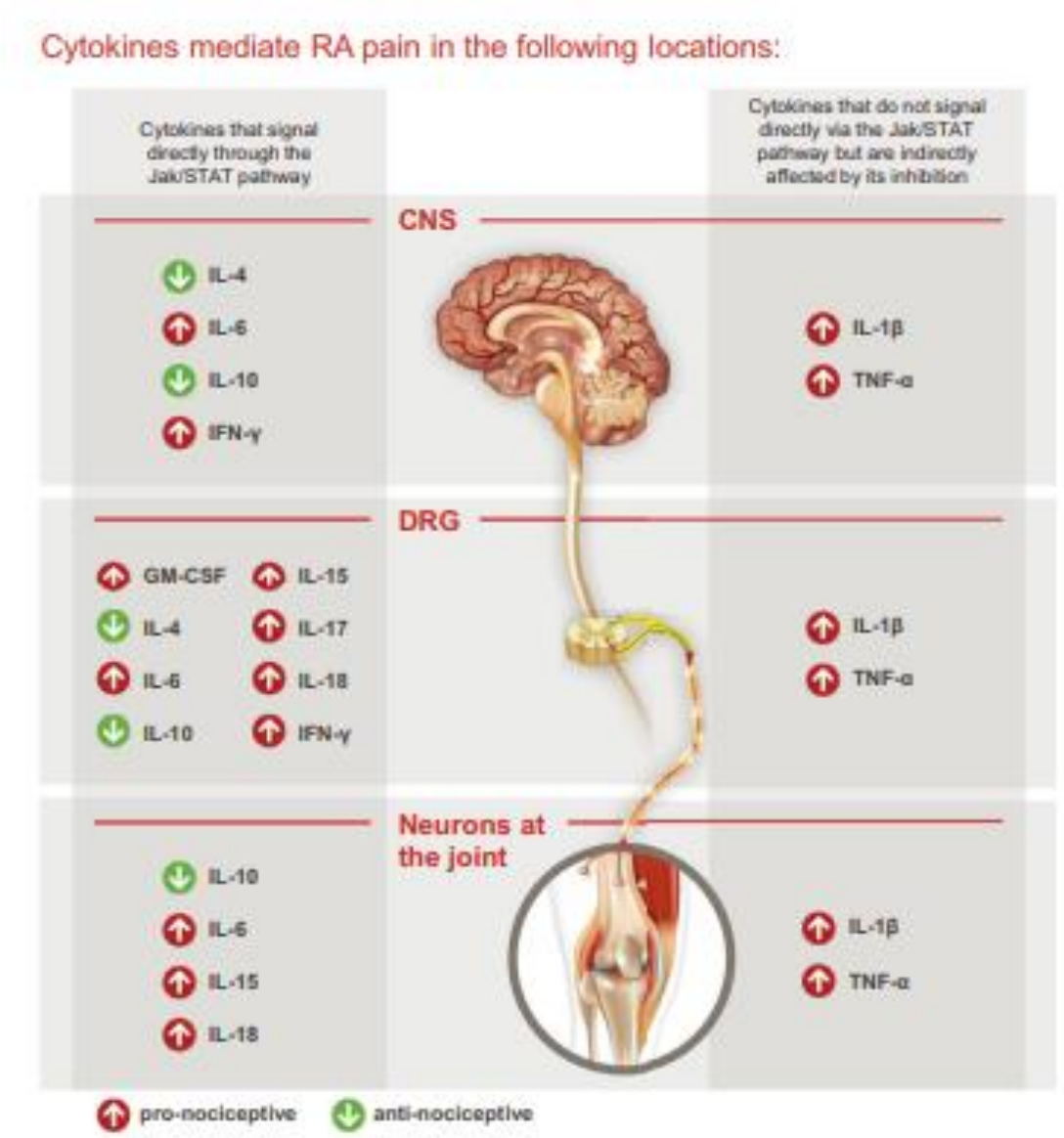
Vergne-Salle P et al. Eur J Pain. 2020

Neuropathic and nociceptive pain

Στις φλεγμονώδεις αρθρίτιδες συνυπάρχουν συχνά νευροπαθητικός και ιδιοδεκτικός πόνος



JAK/STAT pathway cytokines and rheumatoid arthritis pain



Simon et al. Semin Arthritis Rheum 2021;51:278-84

JAK inhibitors and nociceptive pain signalling

JAK/STAT and nociceptive cytokine signalling in RA / N. Crispino & F. Ciccia

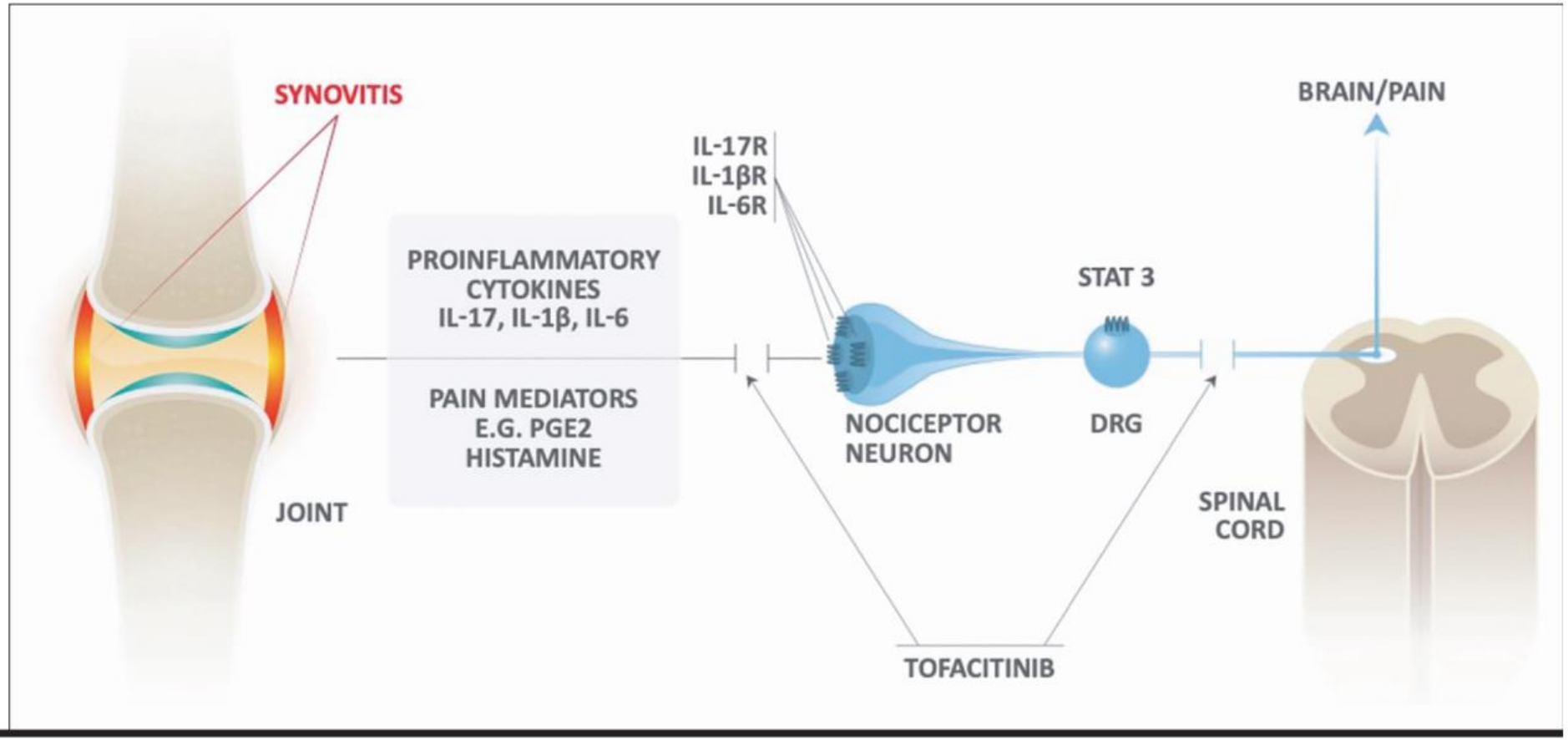
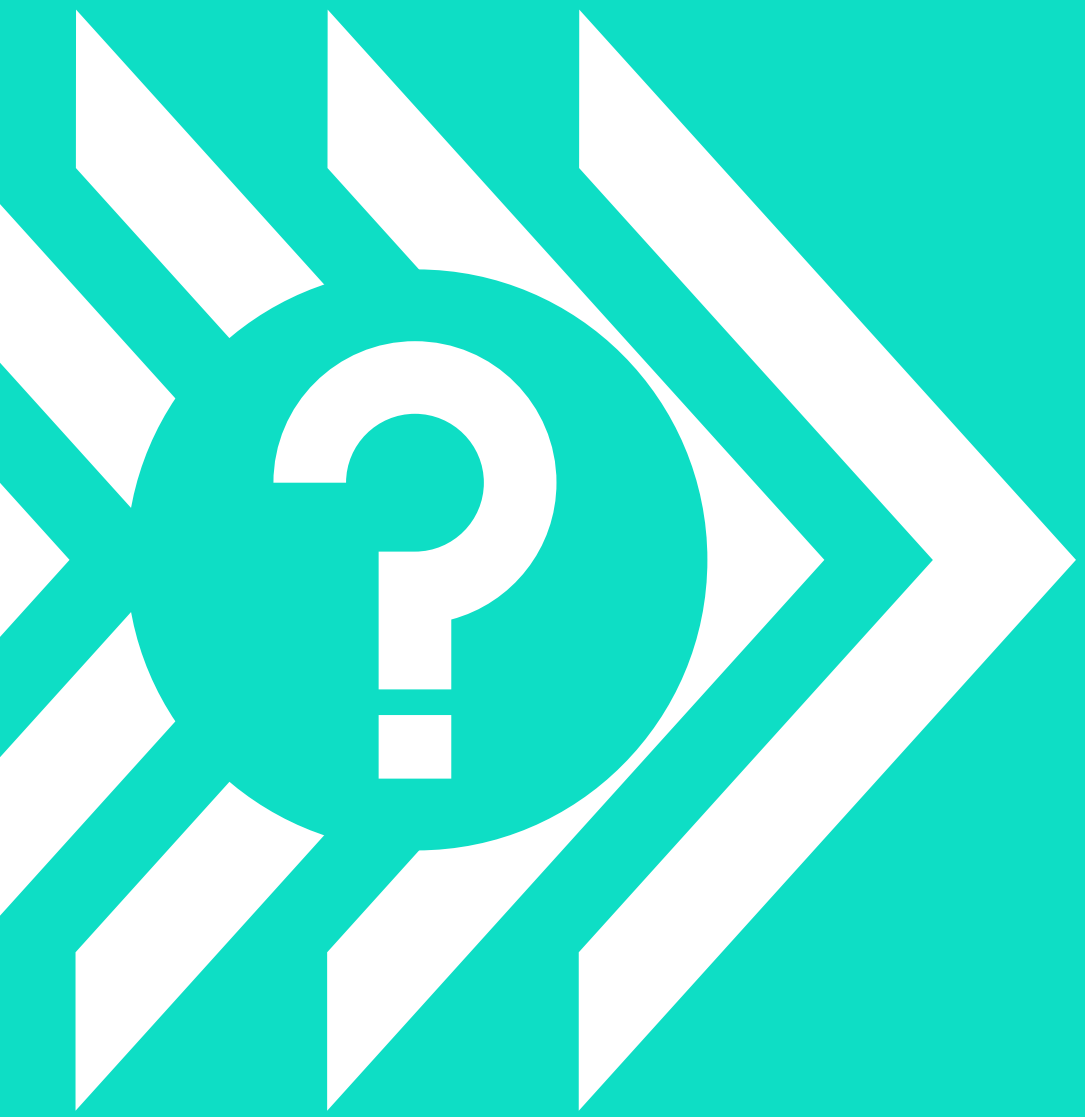


Fig. 1. Schema showing the hypothesised role of tofacitinib in modulating inflammation and nociception.

Crispino et al Clin Exp Rheumatol 2021

Question



Πόσο εύκολο είναι να γεφυρωθεί το κενό μεταξύ των πεποιθήσεων του ασθενούς και του ιατρού;

Πόσο εφικτό είναι το “shared decision making” στην καθημερινή κλινική πρακτική;

Shared Decision Making

Is shared decision making happening in clinical consultations?

Barriers:

- Clinicians' perceived patient preferences & knowledge regarding DMARDs
- Disagreement in T2T practice:
  - physicians aiming for LDA and remission
  - patients aiming for QoL and pain

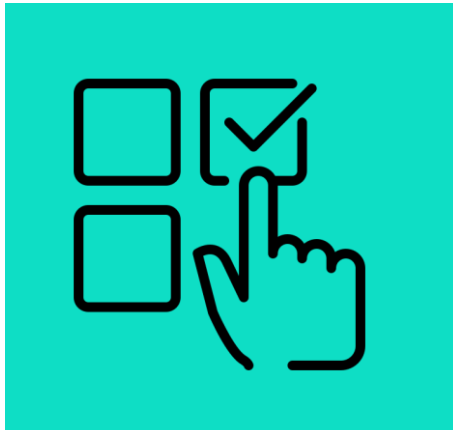
How can these barriers be overcome?

Designing Innovative Strategies to Foster Shared Decision Making

- Advances in decision aids
- Setting shared goals to foster SDM
- Identifying preference phenotypes

Burton et al Curr Opin Rheumatol. 2020 May ; 32(3): 273–278

Shared decision making



Το **επίπεδο συμμετοχής** του ασθενούς στη συναπόφαση

- είναι διαφορετικό για κάθε ασθενή
- μπορεί να αλλάξει κατά τη διάρκεια της παρακολούθησης και στην πορεία της νόσου

Βασικός παράγοντας είναι η **επικοινωνία** μεταξύ του ασθενούς και του ιατρού και η ανάπτυξη **εμπιστοσύνης**.

Matthews et al. Arthritis Care Res 2016;68(3): 318-24

Thank You

Please complete the evaluation form