ΑΝΑΣΚΟΠΗΣΗ (YEAR IN REVIEW)
Ρευματοειδής Αρθρίτιδα

Χάρης Παπαγόρας

Ρευματολόγος

Επίκουρος Καθηγητής Ρευματολογίας

Τμήμα Ιατρικής ΔΠΘ

Βόλος, 1 Ιουνίου 2018

Δήλωση συμφερόντων

Δεν υπάρχει κάποια σύγκρουση συμφερόντων για αυτήν την ομιλία

Εκπαιδευτικές-ερευνητικές-συμβουλευτικές επιχορηγήσεις την τελευταία διετία:

- MSD, Roche, Abbvie, Novartis, Genesis, UCB

ARTHRITIS & RHEUMATOLOGY
Vol. 69, No. 8, August 2017, pp 1566–1575
DOI 10.1002/art.40090

Twenty-Year Outcome and Association Between Early Treatment and Mortality and Disability in an Inception Cohort of Patients With Rheumatoid Arthritis

Results From the Norfolk Arthritis Register

James M. Gwinnutt,[1] Deborah P. M. Symmons,[2] Alexander J. MacGregor,[3] Jacqueline R. Chipping,[3] Tarnya Marshall,[3] Mark Lunt,[1] and Suzanne M. M. Verstappen[1]

Ν= 602 ασθενείς που πληρούσαν (κατά την είσοδο) τα κριτήρια ACR/EULAR 2010

Περίοδος ένταξης 1990-1994

Επιβίωση

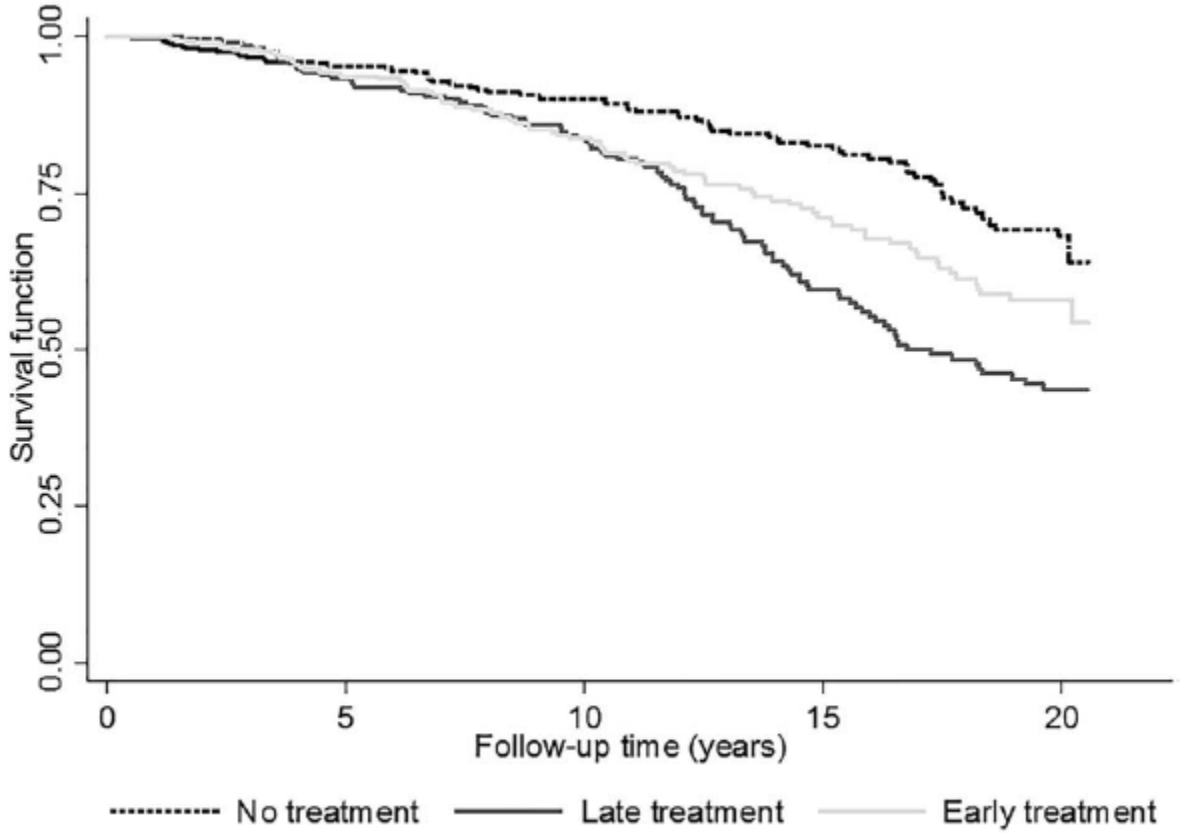


Figure 1. Survival curves for rheumatoid arthritis patients in the 3 treatment groups, after adjustment for age and sex.

Arthritis Rheumatol. 2017 Aug;69(8):1566-1575

Λειτουργικότητα

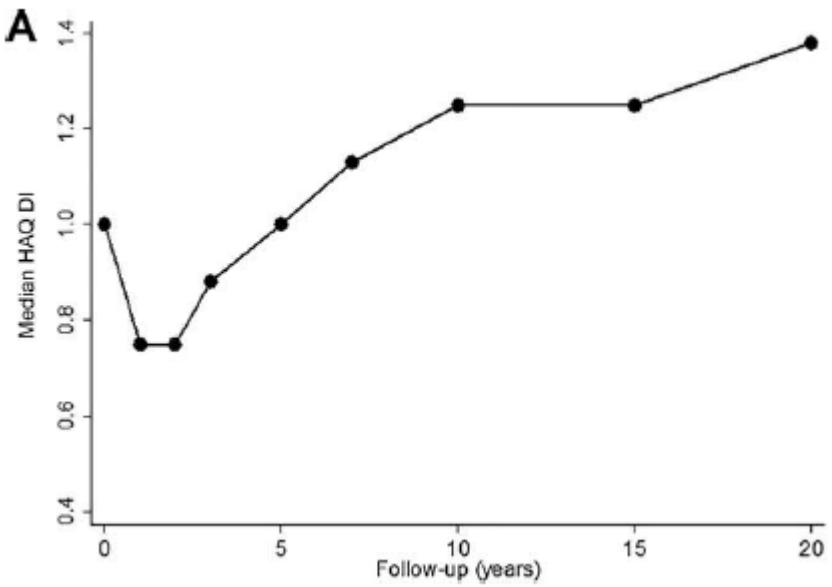


Table 3. Association between treatment regimen and the HAQ DI score over 20 years*

Model, treatment regimen	RA patients		Total cohort	
	No. of patients	β (95% CI)	No. of patients	β (95% CI)
Adjusted for age and sex				
NT	193	0	442	0
LT	249	0.27 (0.15, 0.39)	347	0.37 (0.28, 0.46)
ET	160	0.25 (0.11, 0.38)	211	0.36 (0.26, 0.47)
Fully adjusted†				
NT	193	0	442	0
LT	249	0.10 (0.02, 0.17)	347	0.11 (0.06, 0.17)
ET	160	0.03 (–0.06, 0.12)	211	0.04 (–0.03, 0.11)

Arthritis Rheumatol. 2017 Aug;69(8):1566-1575

ARTHRITIS & RHEUMATOLOGY
Vol. 69, No. 8, August 2017, pp 1560–1565
DOI 10.1002/art.40091

BRIEF REPORT

Rheumatoid Arthritis as the Underlying Cause of Death in Thirty-One Countries, 1987–2011: Trend Analysis of World Health Organization Mortality Database

Aliasghar A. Kiadaliri,[1] David T. Felson,[2] Tuhina Neogi,[2] and Martin Englund[3]

Δεδομένα από ΠΟΥ και τη βάση δεδομένων του ΟΗΕ για τις προοπτικές του πληθυσμού

Θνησιμότητα από PA

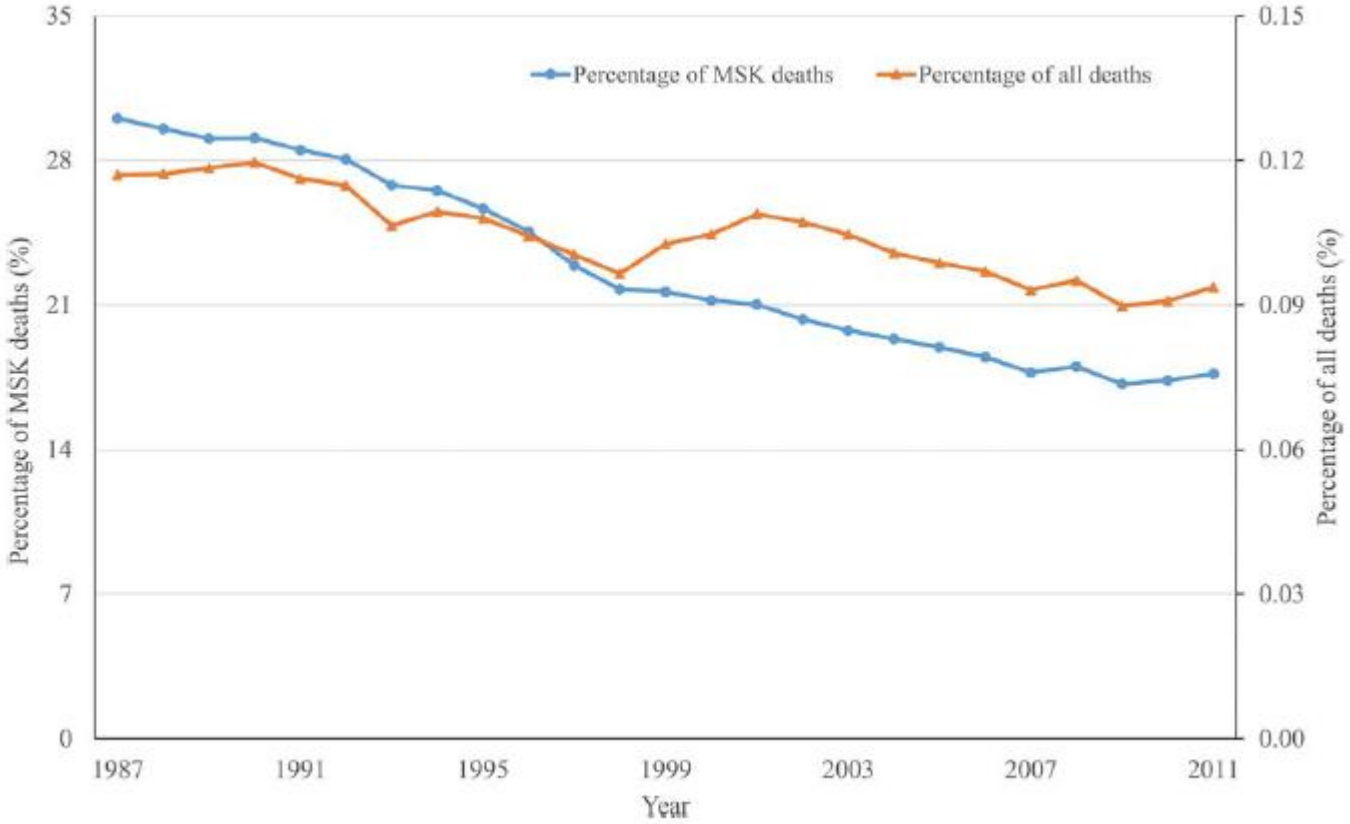


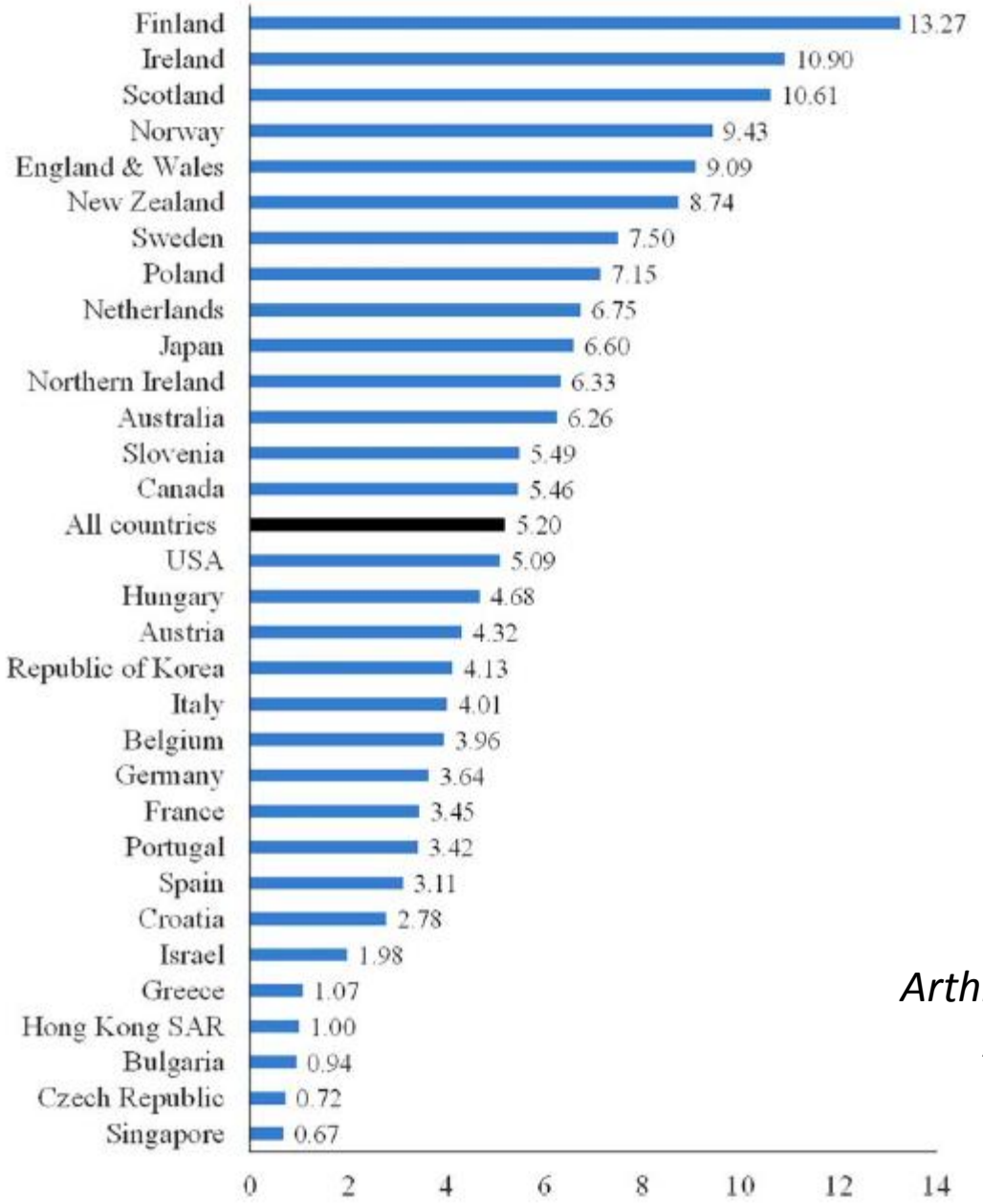
Figure 1. Changes in the proportion of rheumatoid arthritis deaths from musculoskeletal (MSK) disorders and all deaths, 1987–2011.

Συνολική μεταβολή της θνησιμότητας (προσαρμοσμένη για την ηλικία) από PA μεταξύ 1987 και 2011 στις 31 χώρες: -48,2%

Ελλάδα: +14,2%

Arthritis Rheumatol. 2017 Aug;69(8):1560-1565

Ετήσια θνησιμότητα από ΡΑ (προσαρμοσμένη ως προς την ηλικία) ανά εκατομμύριο πληθυσμού (1987-2011)



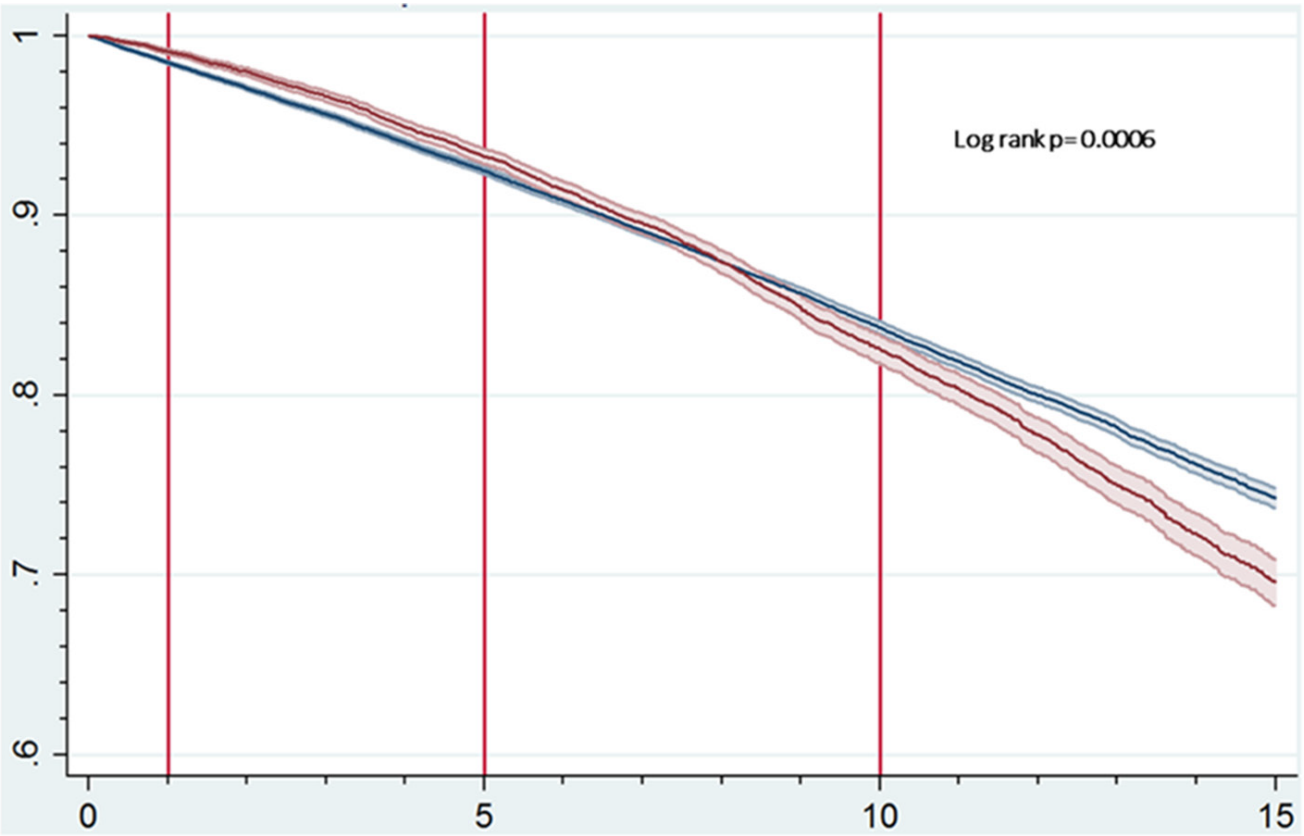
Arthritis Rheumatol. 2017 Aug;69(8):1560-1565

ARD Online First, published on September 26, 2017 as 10.1136/annrheumdis-2017-212131

EXTENDED REPORT

Mortality following new-onset Rheumatoid Arthritis: has modern Rheumatology had an impact?

Marie Holmqvist,[1] Lotta Ljung,[2] Johan Askling[1]



At risk at start of period	17512/78847	16062/71657	10282/45474	4737/21270	RA/
N deaths during period	146/1127	777/3630	869/3182	489/1592	General
Cumulative mortality	0.8%/1.4%	5%/6%	10%/10%	13%/12%	population

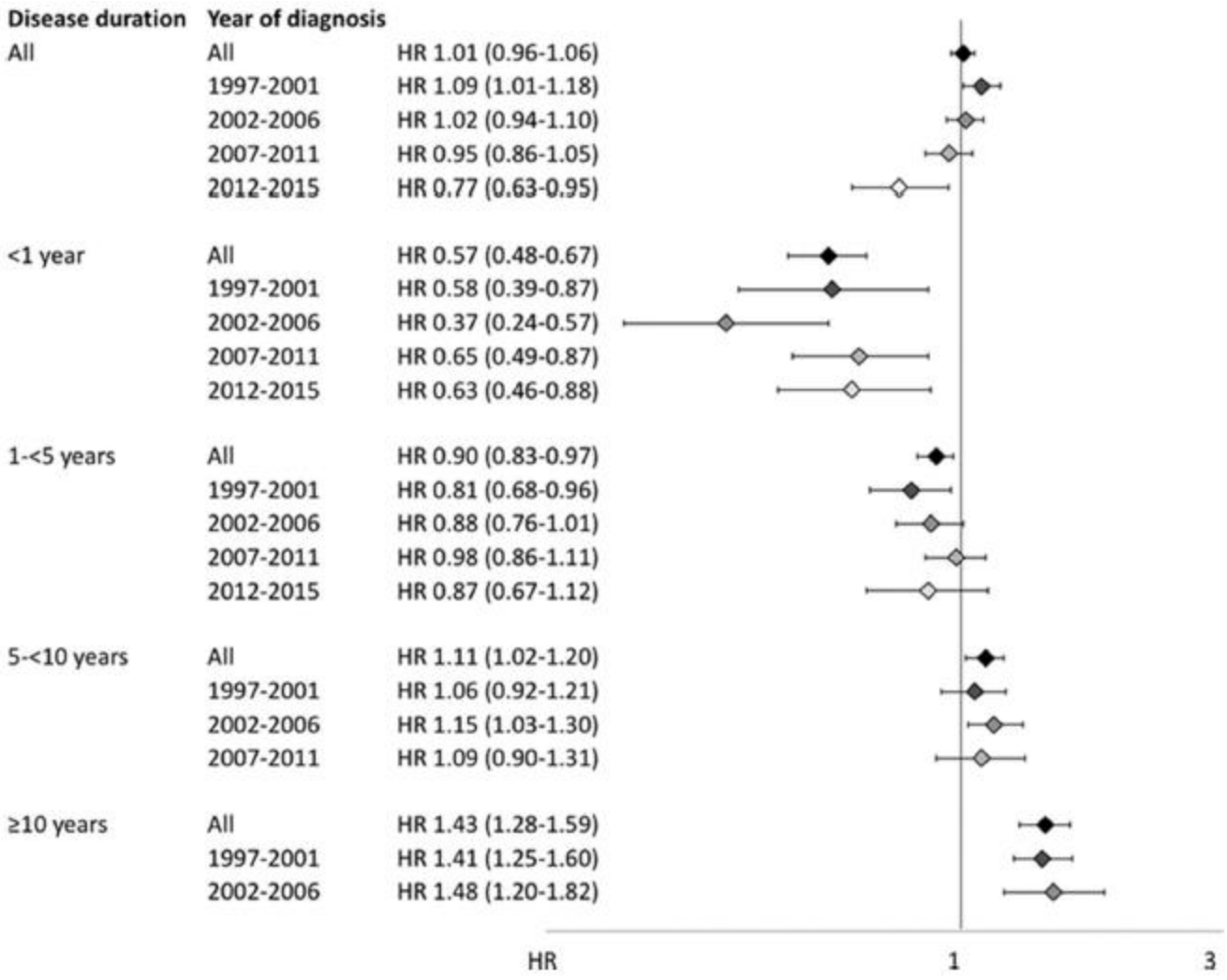
Ann Rheum Dis. 2018 Jan;77(1):85-91.

Παράγοντες κινδύνου

	Patients with new-onset RA			General population comparator subjects			
	n	PYR	Incidence rate	n	PYR	Incidence rate	HR (95% CI)
Overall	2386	123 360	19.3 (17.3 to 21.4)	9850	549 769	17.9 (17.0 to 18.9)	1.01 (0.96 to 1.06)
Women	1412	86 162	16.4 (14.1 to 18.7)	5607	381 574	14.7 (13.7 to 15.7)	1.06 (1.00 to 1.13)
Men	974	37 197	26.2 (21.9 to 30.4)	4243	168 194	25.2 (23.3 to 27.2)	0.93 (0.86 to 1.00)
Seropositive RA	1585	81 455	19.5 (16.9 to 22.0)	9850	549 769	17.9 (17.0 to 18.9)	1.20 (1.13 to 1.28)
Seronegative RA	801	41 904	19.1 (15.7 to 22.5)	9850	549 769	17.9 (17.0 to 18.9)	0.75 (0.70 to 0.82)
DAS28≤3.2 at diagnosis	162	11 777	13.8 (8.7 to 18.9)	9850	549 769	17.9 (17.0 to 18.9)	0.77 (0.64 to 0.92)
DAS28>3.2 at diagnosis	1981	100 723	19.7 (17.3 to 22.0)	9850	549 769	17.9 (17.0 to 18.9)	1.02 (0.97 to 1.07)
Age at diagnosis (years)							
<53	104	44 010	2.4 (1.1 to 3.6)	397	201 205	2.0 (1.4 to 2.5)	1.15 (0.92 to 1.44)
53 to <63	355	34 028	10.4 (7.4 to 13.5)	1306	152 182	8.6 (7.3 to 9.9)	1.20 (1.06 to 1.35)
63 to <72	663	25 622	25.9 (20.9 to 30.8)	2418	113 358	21.3 (19.2 to 23.5)	1.20 (1.10 to 1.32)
≥72	1264	19 697	64.2 (55.8 to 72.5)	5729	83 022	69.0 (64.9 to 73.1)	0.86 (0.80 to 0.92)
Calendar period							
1997–2001	924	38 553	24.0 (18.2 to 29.7)	3613	172 746	20.9 (18.4 to 23.5)	1.09 (1.01 to 1.18)
2002–2006	815	40 849	20.0 (15.6 to 24.4)	3242	180 754	17.9 (16.0 to 19.9)	1.02 (0.94 to 1.10)
2007–2011	535	33 580	15.9 (12.6 to 19.3)	2372	149 719	15.8 (14.3 to 17.4)	0.95 (0.86 to 1.05)
2012–2015	112	10 375	10.8 (8.0 to 13.6)	623	46 549	13.4 (11.9 to 14.9)	0.77 (0.63 to 0.95)

DAS28, Disease Activity Score 28-joint counts; PYR, person-years at risk; RA, rheumatoid arthritis; RR, relative risk.

Ann Rheum Dis. 2018 Jan;77(1):85-91.



Ann Rheum Dis. 2018 Jan;77(1):85-91.

OPEN ACCESS

CONCISE REPORT

Exposure to passive smoking and rheumatoid arthritis risk: results from the Swedish EIRA study

Anna Karin Hedström,[1,2] Lars Klareskog,[3] Lars Alfredsson[2,4]

Results No association was observed between exposure to passive smoking and RA risk (OR 1.0, 95% CI 0.8 to 1.2 for ACPA-positive RA, and OR 0.9, 95% CI 0.7 to 1.2, for ACPA-negative RA). No suggestion of a trend between duration of passive smoking and RA risk was observed.

Environmental Research 157 (2017) 60–63

Contents lists available at ScienceDirect

Environmental Research

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Industrial air emissions, and proximity to major industrial emitters, are associated with anti-citrullinated protein antibodies

Sasha Bernatsky[a,*], Audrey Smargiassi[b,c], Lawrence Joseph[a], Phillip Awadalla[d], Ines Colmegna[e], Marie Hudson[a,f], Marvin J. Fritzler[g]

ARTHRITIS & RHEUMATOLOGY
Vol. 69, No. 6, June 2017, pp 1165–1175
DOI 10.1002/art.40066

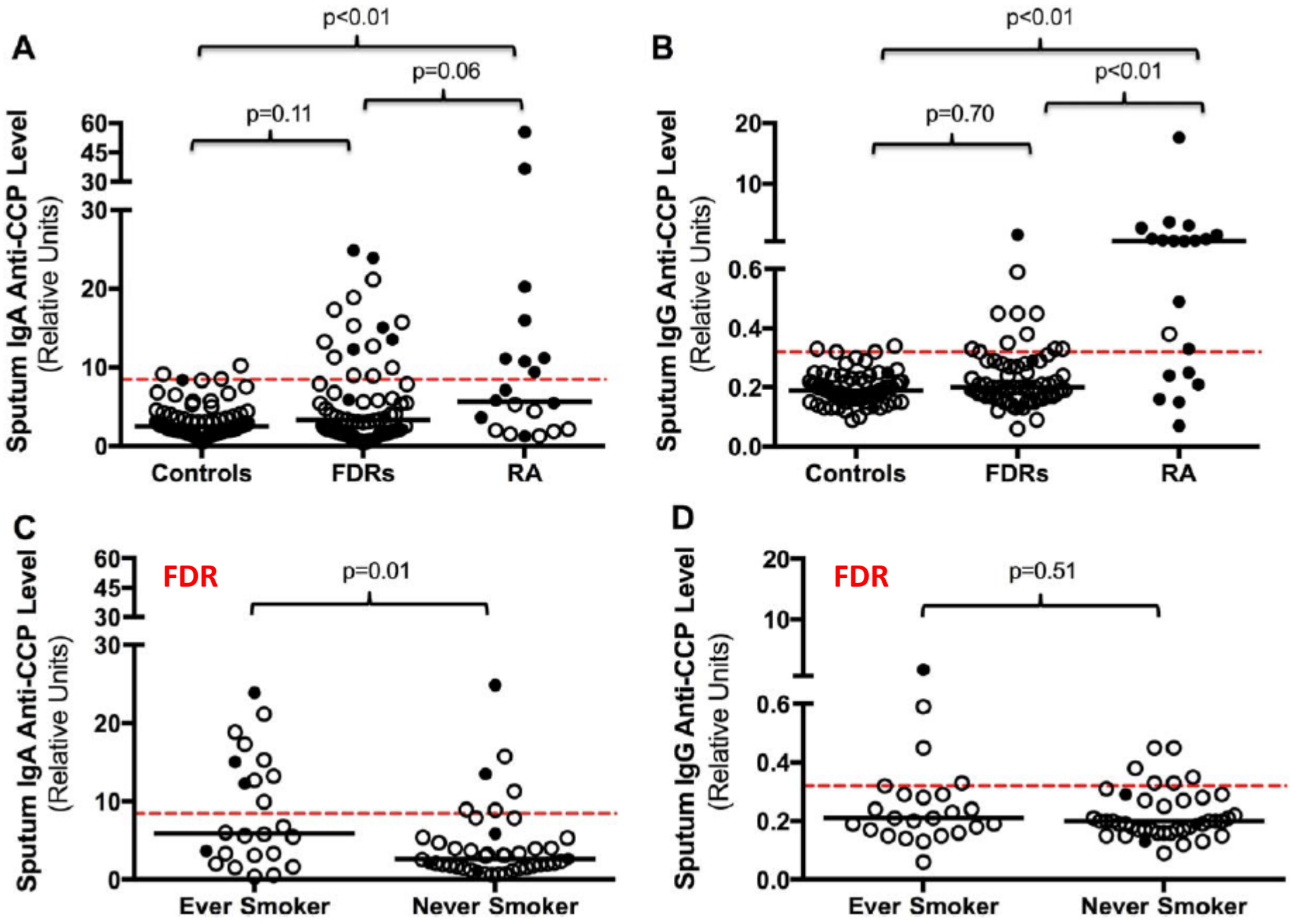
Anti–Citrullinated Protein Antibodies Are Associated With Neutrophil Extracellular Traps in the Sputum in Relatives of Rheumatoid Arthritis Patients

M. Kristen Demoruelle,[1] Kylie K. Harrall,[1] Linh Ho,[1] Monica M. Purmalek,[2] Nickie L. Seto,[2] Heather M. Rothfuss,[3] Michael H. Weisman,[4] Joshua J. Solomon,[5] Aryeh Fischer,[1] Yuko Okamoto,[1] Lindsay B. Kelmenson,[1] Mark C. Parish,[1] Marie Feser,[1] Chelsie Fleischer,[1] Courtney Anderson,[1] Michael Mahler,[6] Jill M. Norris,[1] Mariana J. Kaplan,[2] Brian D. Cherrington,[3] V. Michael Holers,[1] and Kevin D. Deane[1]

Table 2. Sputum and serum anti-CCP positivity in RA patients and FDRs

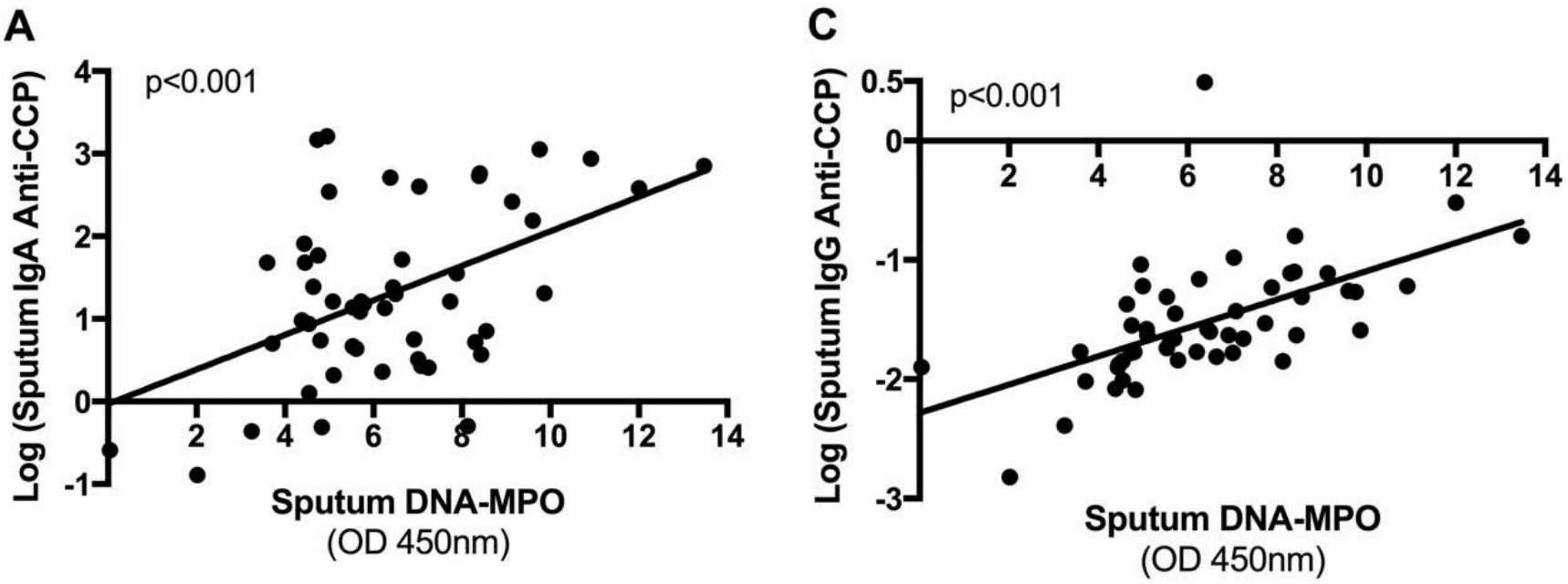
	FDRs of RA patients (n = 67)	RA patients (n = 20)
Sputum anti-CCP isotype, no. (%)		
IgA+ and/or IgG+*	17 (25)	14 (70)†
IgA+/IgG+	10 (15)	8 (40)‡
IgA+/IgG–	6 (9)	0 (0)
IgA–/IgG+	1 (1)	6 (30)†
IgA–/IgG–	50 (75)	6 (30)†
Serum anti-CCP isotype, no. (%)		
IgA+ and/or IgG+§	12 (18)	20 (100)†
IgA+/IgG+	2 (3)	12 (60)†
IgA+/IgG–	8 (12)	1 (5)
IgA–/IgG+	2 (3)	7 (35)†
IgA–/IgG–	55 (82)	0 (0)†

†,‡ $p<0.05$ vs FDR



Arthritis Rheumatol. 2017 Jun;69(6):1165-1175

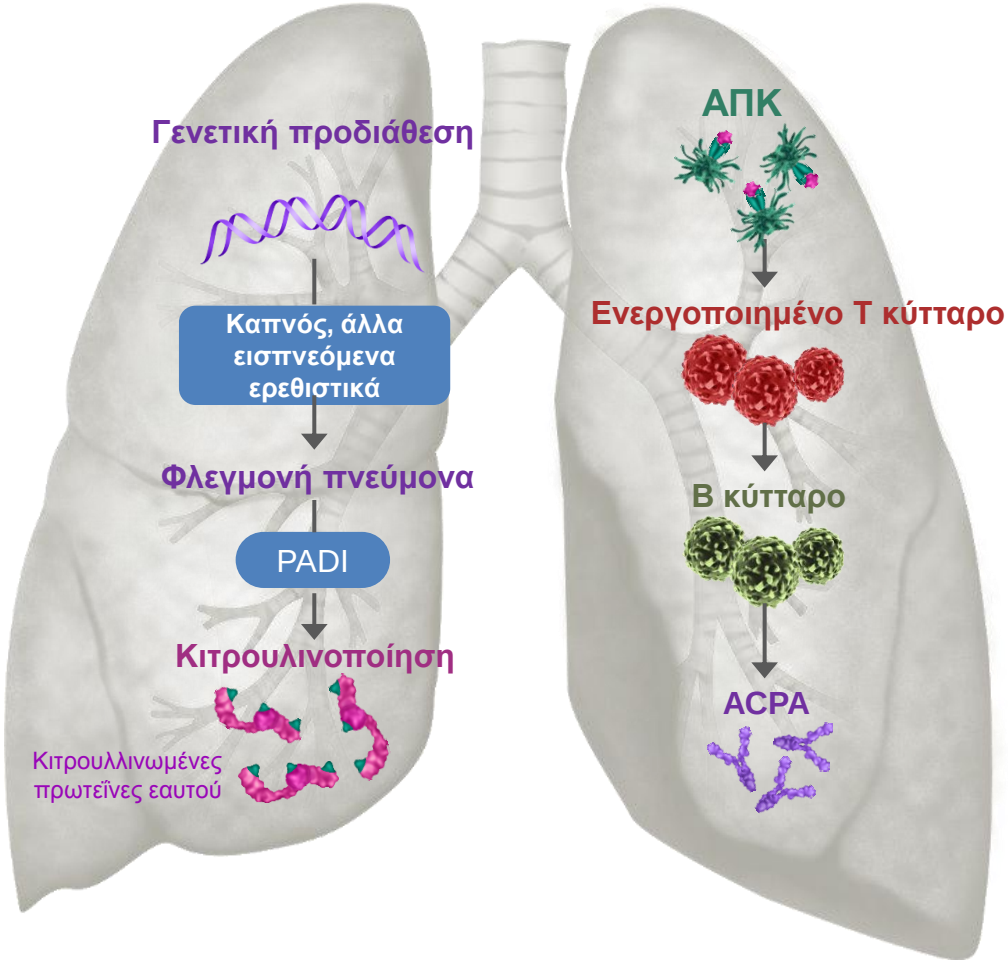
Sputum anti-CCP and NETs in FDR



No significant associations between sputum IgA or IgG anti-CCP levels and NET levels were found in RA patients

Arthritis Rheumatol. 2017 Jun;69(6):1165-1175

Η φλεγμονή του πνεύμονα (και άλλων βλεννογόνων;) πυροδοτεί ΝΕΤωση και παραγωγή IgA ACPA



Η εναλλαγή σε IgG ACPA αναγκαίο βήμα προς την κλινική ΡΑ;

Adapted from Catrina AE, et al. *Nat Rev Rheumatol*. 2014;10(11):645-653; Hajishengallis G. *Nature Rev Immunol*. 2015;15(1):30-44.

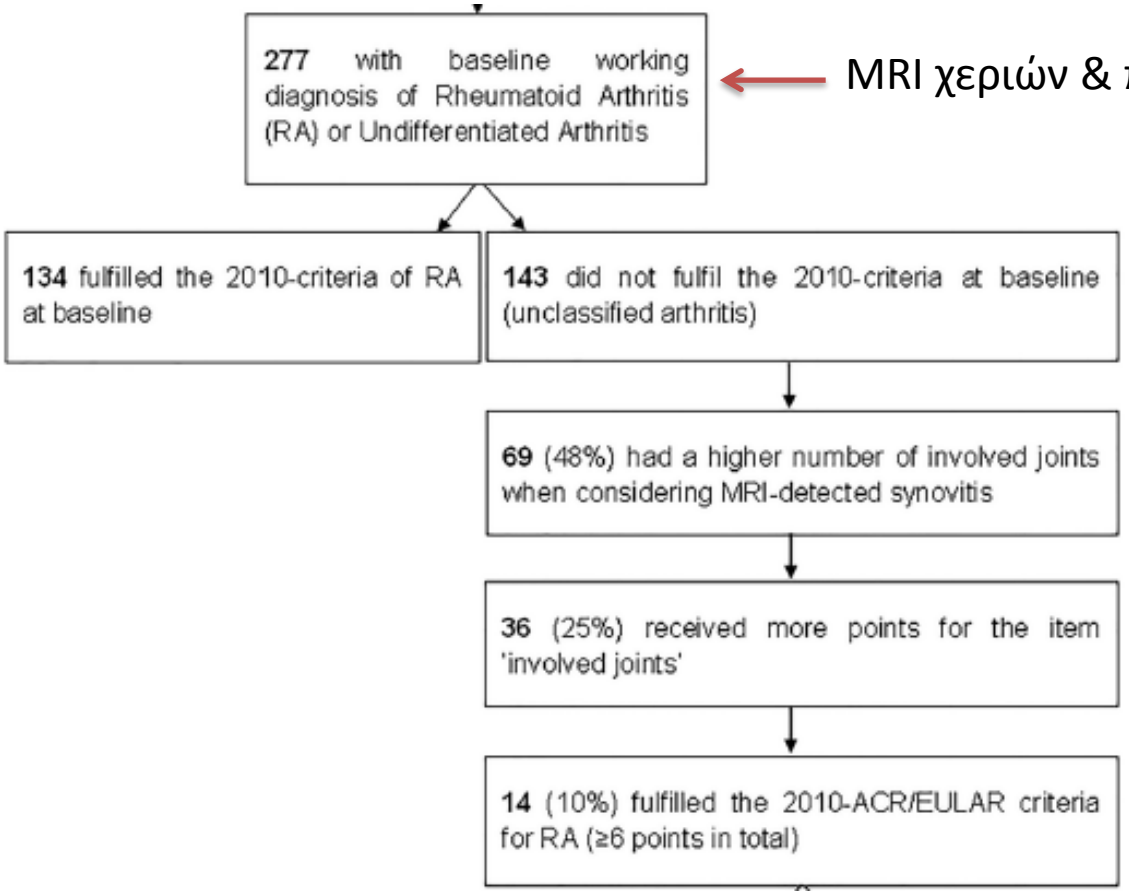
CONCISE REPORT

The use of MRI-detected synovitis to determine the number of involved joints for the 2010 ACR/EULAR classification criteria for Rheumatoid Arthritis – is it of additional benefit?

Aleid C Boer,[1] Debbie M Boeters,[1] Annette H M van der Helm-van Mil[1,2]

- Κριτήρια ACR/EULAR 2010 για PA: Joint involvement refers to any swollen or tender joint on examination, which may be **confirmed** by imaging evidence of synovitis

Ann Rheum Dis. 2018 Apr 20



Αν στις μετρήσεις των αρθρώσεων για τα κριτήρια προστεθούν και οι προσβεβλημένες μόνο βάσει του MRI (Gold standard: DMARD initiation)

Ευαισθησία: 62%→ 67%

Ειδικότητα: 90 % → 84%

Boer AC et al. Ann Rheum Dis. 2018 Apr 20

EXTENDED REPORT

Risk of losing remission, low disease activity or radiographic progression in case of bDMARD discontinuation or tapering in rheumatoid arthritis: systematic analysis of the literature and meta-analysis

Sophie Henaux,[1,2] Adeline Ruyssen-Witrand,[1,2,3] Alain Cantagrel,[1,2,4] Thomas Barnetche,[5] Bruno Fautrel,[6] Nathalie Filippi,[7] Cédric Lukas,[7] Bernd Raffeiner,[8] Maurizio Rossini,[9] Yannick Degboé,[1,2,4] Arnaud Constantin[1,2,4]

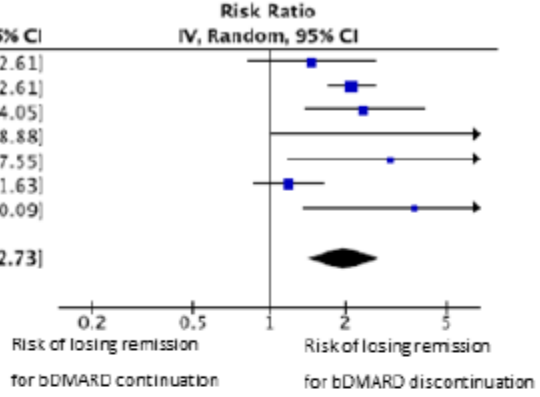
Ann Rheum Dis. 2018 Apr;77(4):515-522

Διακοπή βιολογικού

A

Study or Subgroup	bDMARD withdrawal Events	Total	bDMARD continuation Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Chatzidionysiou etal.2016	11	15	8	16	15.3%	1.47 [0.82, 2.61]
Smolen et al. 2013	142	200	68	202	26.4%	2.11 [1.70, 2.61]
Smolen et al. 2014	34	101	15	105	16.2%	2.36 [1.37, 4.05]
Takeuchi et al. 2014	14	34	1	17	2.5%	7.00 [1.00, 48.88]
Tanaka et al. 2015	27	52	4	23	8.6%	2.99 [1.18, 7.55]
Weinblatt et al. 2017	34	51	28	50	23.3%	1.19 [0.87, 1.63]
Yamaka et al. 2016	13	28	4	32	7.7%	3.71 [1.37, 10.09]
Total (95% CI)		**481**		**445**	**100.0%**	**1.97 [1.43, 2.73]**
Total events	275		128			

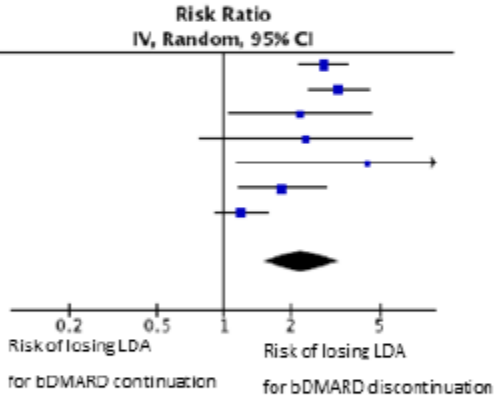
Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 15.15$, df = 6 (P = 0.02); $I^2 = 60\%$
Test for overall effect: Z = 4.12 (P < 0.0001)



B

Study or Subgroup	bDMARD withdrawal Events	Total	bDMARD continuation Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Ghiti Moghadam et al. 2016	272	531	52	286	19.6%	2.82 [2.17, 3.65]
Smolen et al. 2013	116	200	36	202	18.7%	3.25 [2.37, 4.48]
Smolen et al. 2014	19	101	9	105	12.0%	2.19 [1.04, 4.62]
Takeuchi et al. 2014	14	34	3	17	7.9%	2.33 [0.77, 7.03]
Tanaka et al. 2015	20	52	2	23	5.9%	4.42 [1.13, 17.37]
vanVollenhoven et al.2016	20	23	11	23	16.6%	1.82 [1.15, 2.87]
Weinblatt et al. 2017	48	79	43	84	19.4%	1.19 [0.90, 1.56]
Total (95% CI)		**1020**		**740**	**100.0%**	**2.24 [1.52, 3.30]**
Total events	509		156			

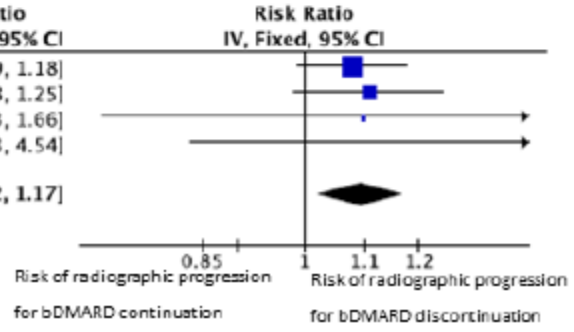
Heterogeneity: $Tau^2 = 0.18$; $Chi^2 = 30.35$, df = 6 (P < 0.0001); $I^2 = 80\%$
Test for overall effect: Z = 4.06 (P < 0.0001)



C

Study or Subgroup	bDMARD withdrawal Events	Total	bDMARD continuation Events	Total	Weight	Risk Ratio IV, Fixed, 95% CI
Smolen et al. 2013	164	184	138	167	63.1%	1.08 [0.99, 1.18]
Smolen et al. 2014	92	103	79	98	33.5%	1.11 [0.98, 1.25]
Takeuchi et al. 2014	12	17	18	28	2.7%	1.10 [0.73, 1.66]
Weinblatt et al. 2017	14	74	7	72	0.6%	1.95 [0.83, 4.54]
Total (95% CI)		**378**		**365**	**100.0%**	**1.09 [1.02, 1.17]**
Total events	282		242			

Heterogeneity: $Chi^2 = 1.92$, df = 3 (P = 0.59); $I^2 = 0\%$
Test for overall effect: Z = 2.56 (P = 0.01)



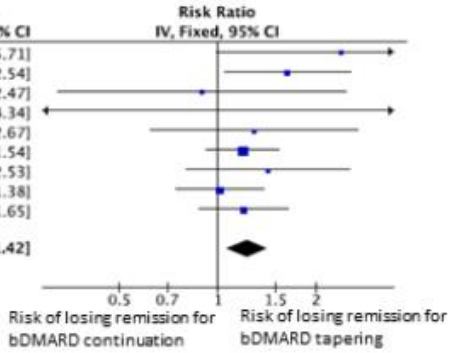
Ann Rheum Dis. 2018 Apr;77(4):515-522

Μείωση βιολογικού

A

Study or Subgroup	bDMARD tapering Events	Total	bDMARD continuation Events	Total	Weight	Risk Ratio IV, Fixed, 95% CI
Botsios et al. 2007	14	52	6	53	2.7%	2.38 [0.99, 5.71]
Fautrel et al. 2016	30	64	21	73	10.5%	1.63 [1.04, 2.54]
Galloway et al. 2015	6	48	7	50	2.0%	0.89 [0.32, 2.47]
Giollo et al. 2015	2	12	0	12	0.2%	5.00 [0.27, 94.34]
Raffeiner et al. 2015	15	159	12	164	4.0%	1.29 [0.62, 2.67]
Smolen et al. 2013	81	202	68	202	31.7%	1.19 [0.92, 1.54]
vanHerwaarden et al. 2015	35	121	12	59	6.3%	1.42 [0.80, 2.53]
Weinblatt et al. 2017	47	83	28	50	21.8%	1.01 [0.74, 1.38]
Westhovens et al. 2015	32	50	31	58	20.7%	1.20 [0.87, 1.65]
Total (95% CI)		**791**		**721**	**100.0%**	**1.23 [1.06, 1.42]**
Total events	262		185			

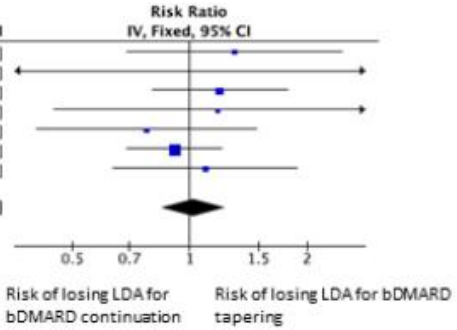
Heterogeneity: $Chi^2 = 6.85$, $df = 8$ ($P = 0.55$); $I^2 = 0\%$
Test for overall effect: $Z = 2.77$ ($P = 0.006$)



B

Study or Subgroup	bDMARD tapering Events	Total	bDMARD continuation Events	Total	Weight	Risk Ratio IV, Fixed, 95% CI
Fautrel et al. 2016	16	64	14	73	8.7%	1.30 [0.69, 2.46]
Okano et al. 2015	1	13	0	16	0.4%	3.64 [0.16, 82.62]
Smolen et al. 2013	43	202	36	202	22.2%	1.19 [0.80, 1.78]
vanHerwaarden et al. 2015	14	119	5	50	3.8%	1.18 [0.45, 3.09]
vanVollenhoven et al.2016	10	27	11	23	8.3%	0.77 [0.40, 1.49]
Weinblatt et al. 2017	59	126	43	84	44.8%	0.91 [0.69, 1.21]
Westhovens et al. 2015	17	50	18	58	11.8%	1.10 [0.64, 1.89]
Total (95% CI)		**601**		**506**	**100.0%**	**1.02 [0.85, 1.23]**
Total events	160		127			

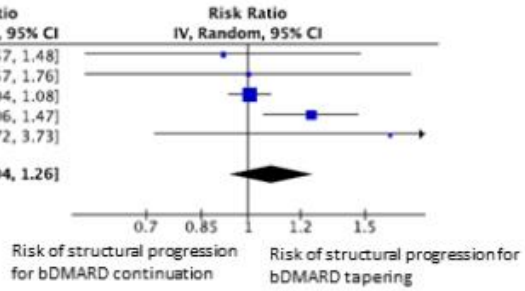
Heterogeneity: $Chi^2 = 3.24$, $df = 6$ ($P = 0.78$); $I^2 = 0\%$
Test for overall effect: $Z = 0.24$ ($P = 0.81$)



C

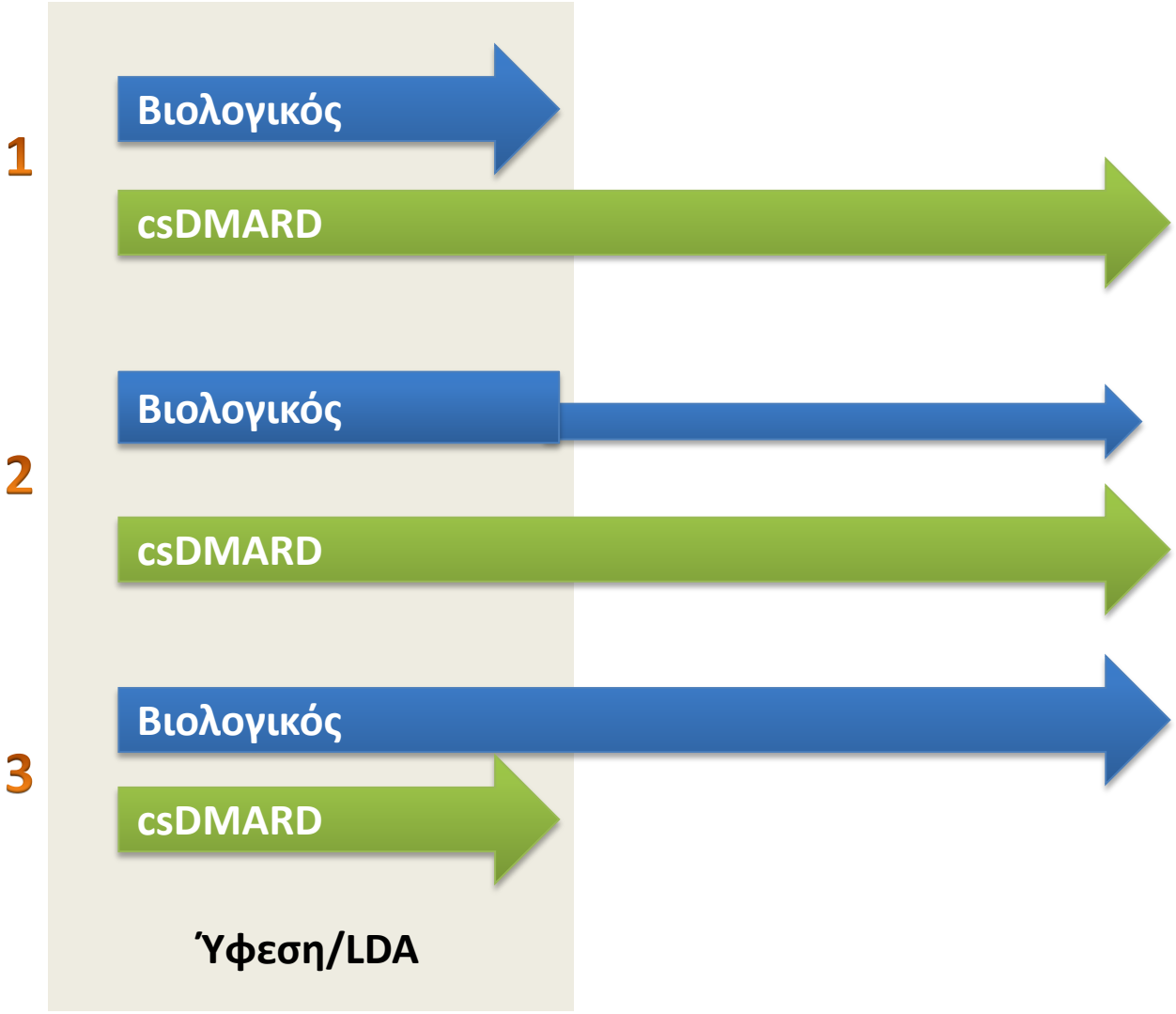
Study or Subgroup	bDMARD tapering Events	Total	bDMARD continuation Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Fautrel et al. 2016	23	73	22	64	7.9%	0.92 [0.57, 1.48]
Okano et al. 2015	8	12	8	12	5.9%	1.00 [0.57, 1.76]
Smolen et al. 2013	164	184	163	184	50.3%	1.01 [0.94, 1.08]
vanHerwaarden et al. 2015	50	59	79	116	32.9%	1.24 [1.06, 1.47]
Weinblatt et al. 2017	18	113	7	72	3.0%	1.64 [0.72, 3.73]
Total (95% CI)		**441**		**448**	**100.0%**	**1.09 [0.94, 1.26]**
Total events	263		279			

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 6.81$, $df = 4$ ($P = 0.15$); $I^2 = 41\%$
Test for overall effect: $Z = 1.12$ ($P = 0.26$)

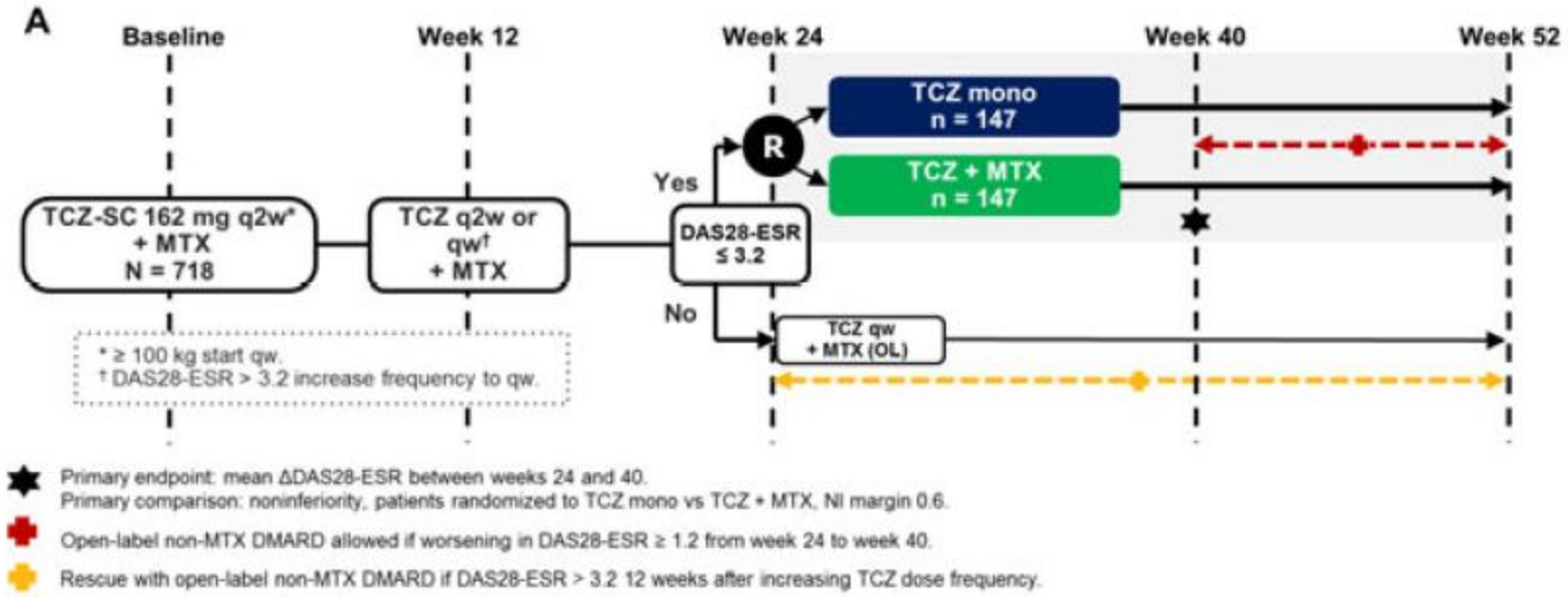


Ann Rheum Dis. 2018 Apr;77(4):515-522

Αποκλιμάκωση θεραπείας, όταν PA σε ύφεση ή LDA



Διακοπή MTX με συνέχιση TCZ σε ασθενείς με LDA
Η διπλά τυφλή τυχαιοποιημένη μελέτη COMP-ACT

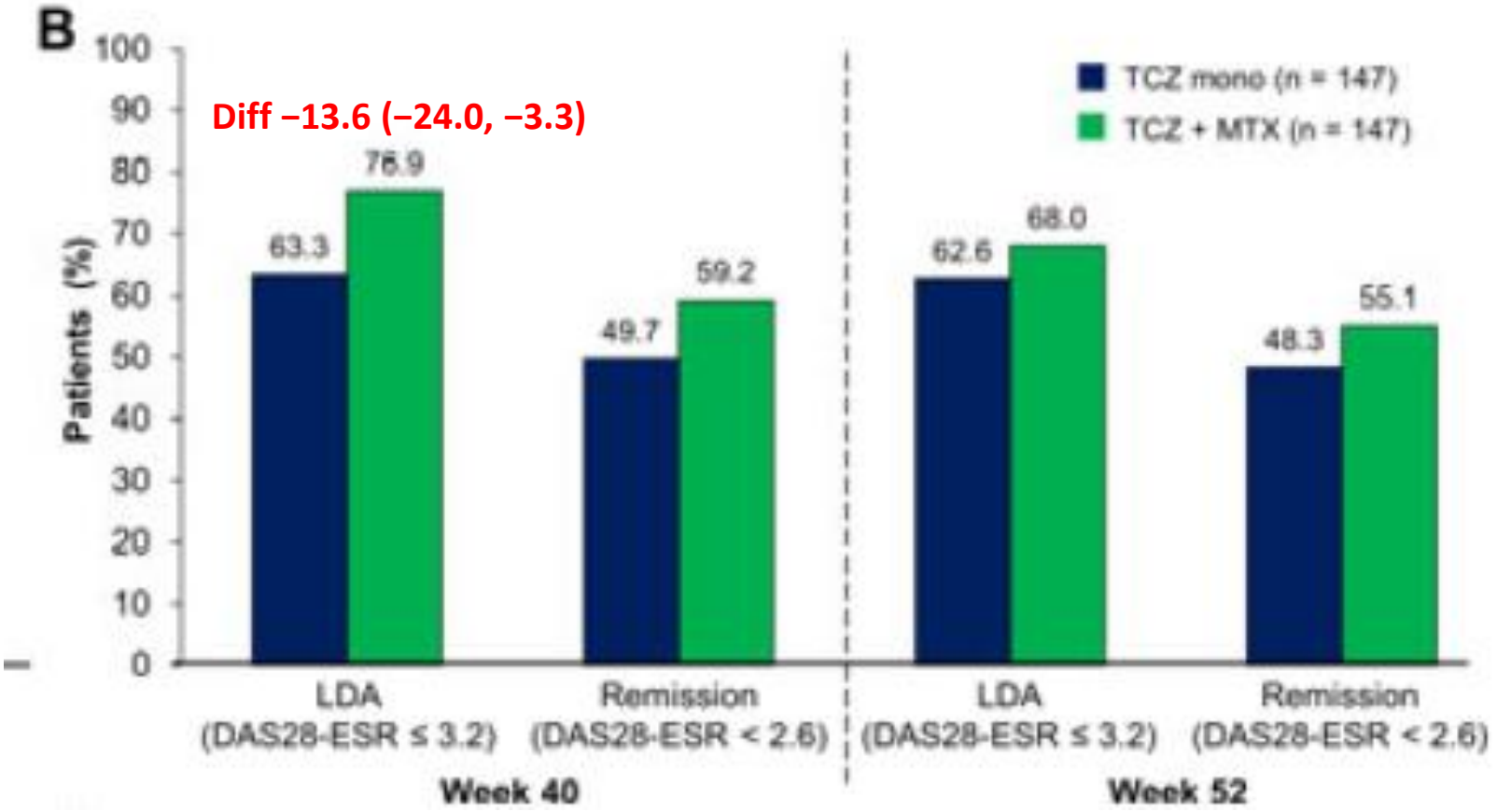


Arthritis Rheumatol. 2018 Mar 25

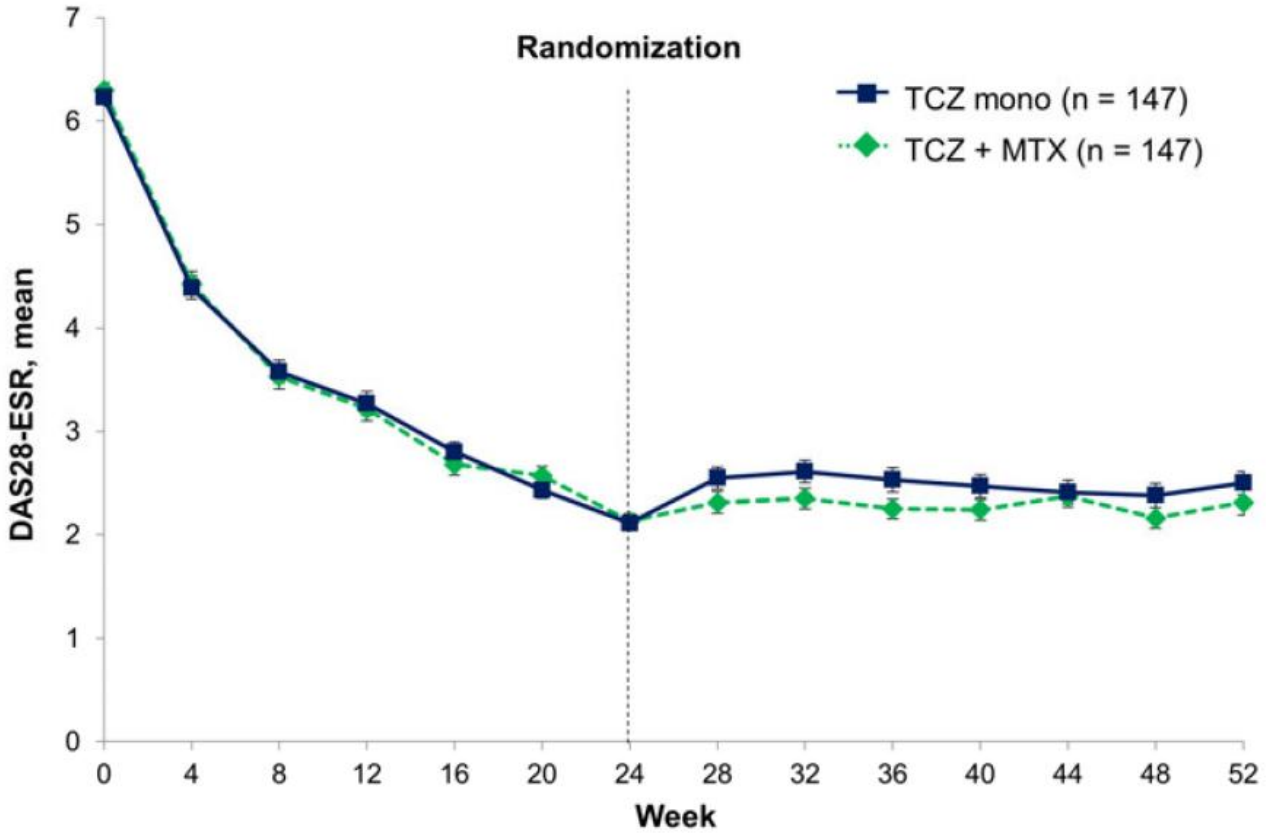
Μέση μεταβολή DAS28 W24→W40

- **TCZ monoTx 0.46 (95% CI 0.22, 0.70)** **Non-inferiority met**
- **TCZ+MTX 0.14 (95% CI −0.11, 0.39)**

Adjusted difference between the groups: 0.318 (95% CI 0.045, 0.592)



Arthritis Rheumatol. 2018 Mar 25



Επίπτωση AEs per 100 patient-years

TCZ + MTX : **308.1** [95% CI 273.0, 346.4]

TCZ mono : **238.0** [95% CI 207.6, 271.6]

Επίπτωση SAEs per 100 patient-years

TCZ + MTX: **14.35** [7.64, 24.55)]

TCZ mono : **8.65** [3.74, 17.05]

Arthritis Rheumatol. 2018 Mar 25

Clinical and epidemiological research

EXTENDED REPORT

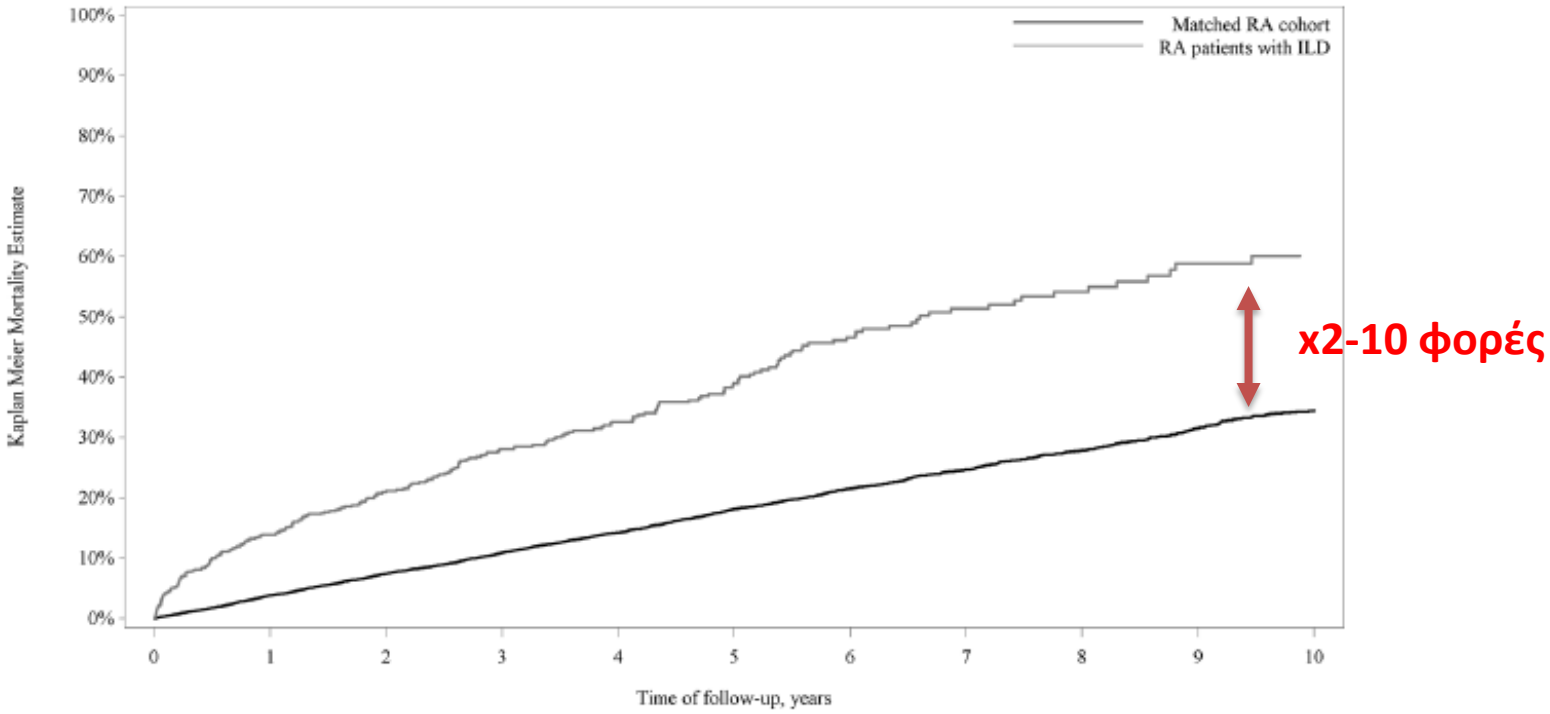
A population-based cohort study of rheumatoid arthritis-associated interstitial lung disease: comorbidity and mortality

Charlotte Hyldgaard,[1] Ole Hilberg,[2] Alma Becic Pedersen,[3] Sinna Pilgaard Ulrichsen,[3] Anders Løkke,[1] Elisabeth Bendstrup,[1] Torkell Ellingsen[4,5]

- Διάγνωση PA 2004-2016
- 679 ασθενείς με RA-ILD
- 11722 ασθενείς με PA αντίστοιχης χρονολογίας γέννησης, φύλου και ηλικίας διάγνωσης της PA
- Επιπολασμός RA-ILD: 2.2% επί της RA
- 34% των περιπτώσεων RA-ILD διαγνώστηκαν ±1 έτος από τη διάγνωση της RA

Ann Rheum Dis. 2017 Oct;76(10):1700-1706

Θνητότητα RA-ILD vs RA



Stratified analysis showed that HRR for death was higher in patients who were diagnosed with RA prior to ILD

Ann Rheum Dis. 2017 Oct;76(10):1700-1706

Clinical and epidemiological research

EXTENDED REPORT

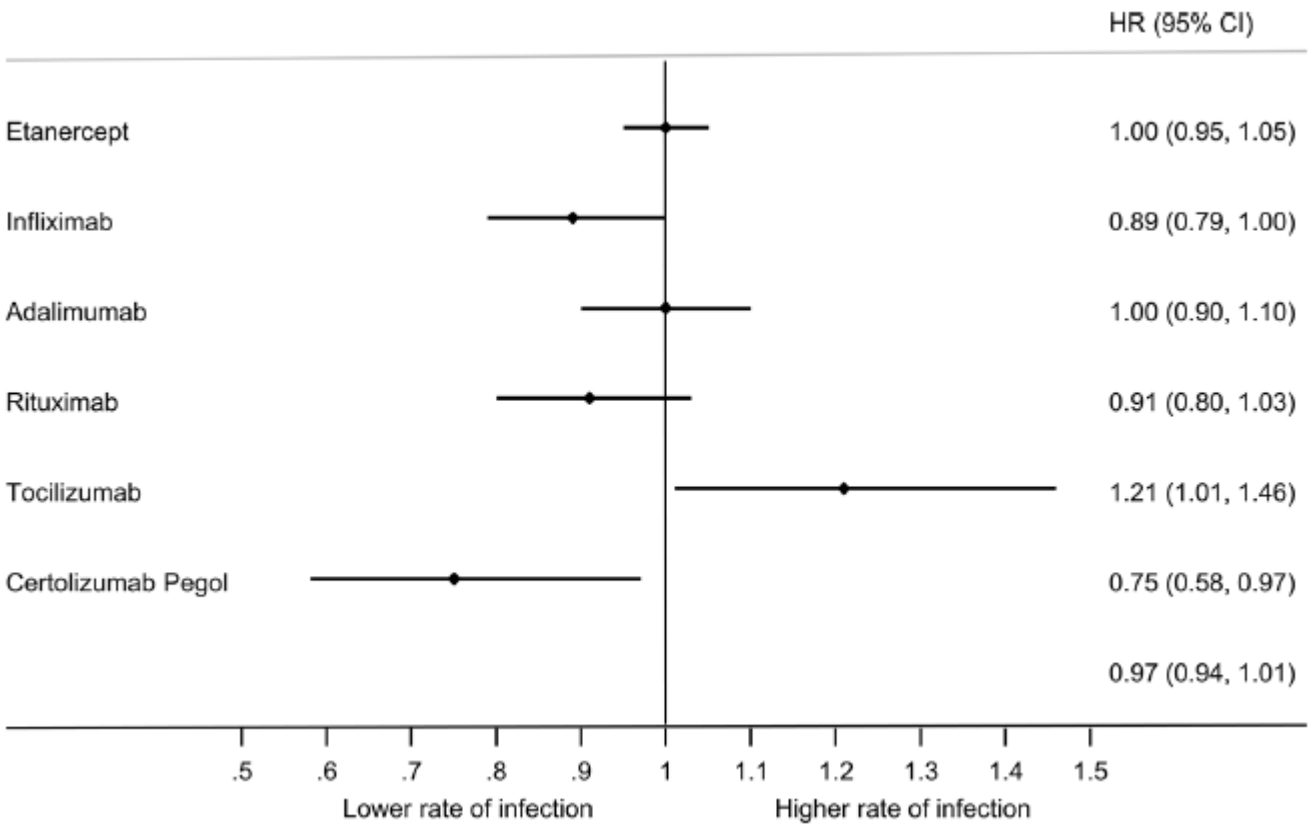
Serious infection across biologic-treated patients with rheumatoid arthritis: results from the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis

Andrew I Rutherford,[1,2] Sujith Subesinghe,[1] Kimme L Hyrich,[3,4] James B Galloway[1,2]

- 19 282 ασθενείς με 46 771p-y παρακολούθησης
- Έκβαση: λοίμωξη που οδήγησε σε εισαγωγή σε Νοσοκομείο, θεραπεία με iv αντιβιοτικά ή θάνατο

Ann Rheum Dis. 2018 Jun;77(6):905-910

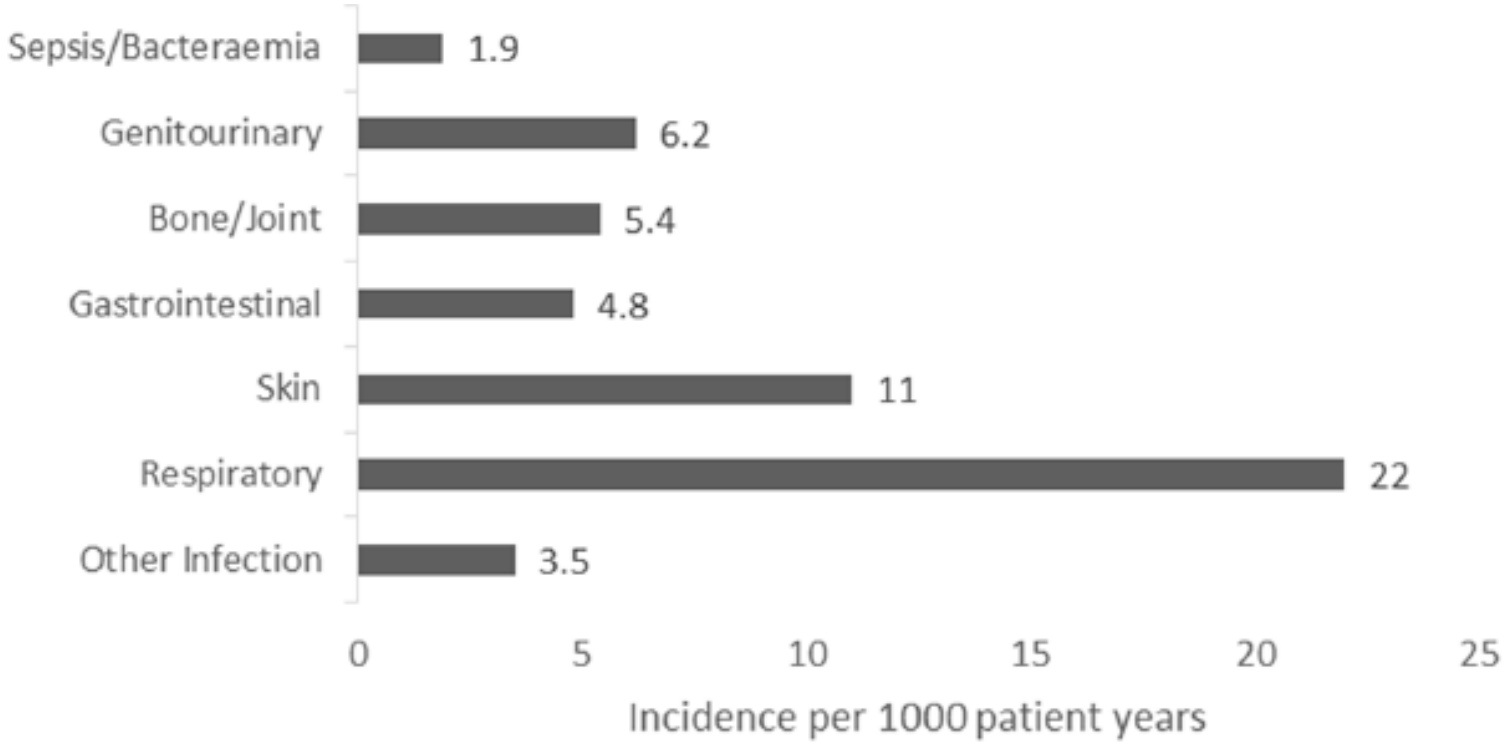
Προσαρμοσμένος σχετικός κίνδυνος ανά βιολογικό φάρμακο



Adjustment for age, gender, DAS25-ESR, HAQ, disease duration, smoking, seropositivity, polypharmacy and baseline steroid usage

Ann Rheum Dis. 2018 Jun;77(6):905-910

Επίπτωση σοβαρών λοιμώξεων ανά σύστημα



The 30-day mortality following SI was 10.4% (95% CI 9.2% to 11.6%)

Ann Rheum Dis. 2018 Jun;77(6):905-910

CORRONA Registry

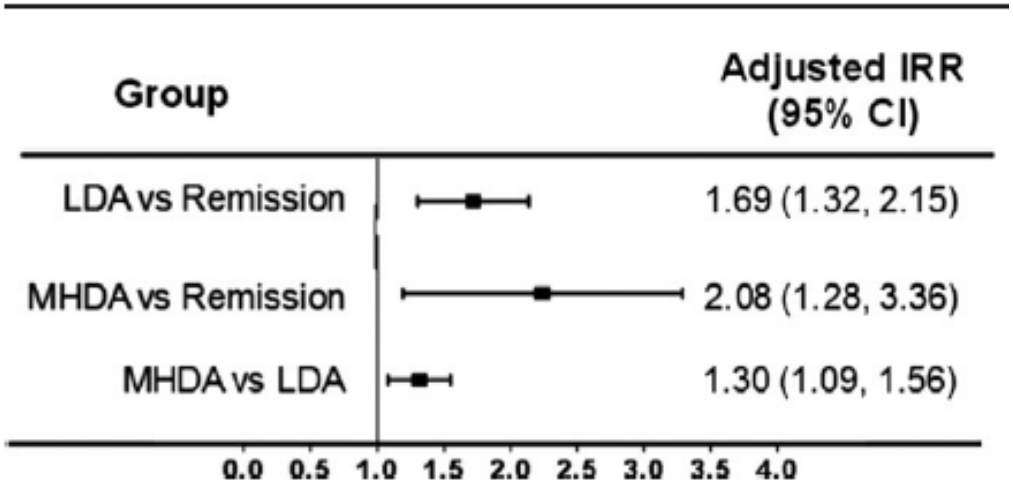
Arthritis Care & Research
Vol. 70, No. 5, May 2018, pp 679–684
DOI 10.1002/acr.23426

ORIGINAL ARTICLE

Impact of Sustained Remission on the Risk of Serious Infection in Patients With Rheumatoid Arthritis

NEIL A. ACCORTT,[1] TAMARA LESPERANCE,[2] MEI LIU,[3] SABRINA REBELLO,[3] MONA TRIVEDI,[1] YOUFU LI,[4] AND JEFFREY R. CURTIS[5]

Κατηγορία	N	Διάμεση παρακολούθηση (έτη)
Ύφεση	3355	2.4
LDA	3912	2.5
MHDA	5062	1.7



Adjusted for age, sex, and prednisone dose

The goal of attaining the lowest possible RA disease activity may lead to reduced risk for serious infections

Σοβαρές λοιμώξεις σε τέκνα γυναικών με ΡΑ που είχαν λάβει TNFi

Κατηγορία	N	Επίπτωση ΣΛ/100p-y
Non-RA	14596	**2.4** (2.1, 2.7)
RA-nonTNFi	2476	**2.5** (1.9, 3.3)
RA-preconception TNFi	133	**1.9** (0.5, 7.6)
RA-pregnancy TNFi	380	**4.2** (2.4, 7.4)
RA- 3rd trimester TNFi	156	**4.2** (1.8, 10.2)

Unadjusted and adjusted odds ratios for the risk of serious infections comparing different exposure categories in PAROUS Comparison		
	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)
TNFi pregnancy vs non-RA	1.7 (0.9, 3.0)	1.7 (0.8, 3.7)
TNFi preconception vs non-RA offspring	0.8 (0.2, 3.2)	0.9 (0.2, 3.9)
TNFi pregnancy vs unexposed RA offspring	1.6 (0.9, 3.1)	1.4 (0.7, 2.8)
TNFi 3rd trimester vs unex-posed RA offspring	1.6 (0.6, 4.2)	1.4 (0.5, 3.6)
**Adjusted for maternal age, pre-gestational diabetes, gestational diabetes, preterm birth, and medications*		

Vinet E et al. Arthritis Rheumatol. 2018 May 17

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OPEN ACCESS

EXTENDED REPORT

Spectrum of lymphomas across different drug treatment groups in rheumatoid arthritis: a European registries collaborative project

Louise K Mercer,[1] Anne C Regierer,[2] Xavier Mariette,[3] William G Dixon,[1] Eva Baecklund,[4] Karin Hellgren,[5] Lene Dreyer,[6,7] Merete Lund Hetland,[8,9] René Cordtz,[6,7] Kimme Hyrich,[1,10] Anja Strangfeld,[2] Angela Zink,[2,11] Helena Canhao,[12] M Victoria Hernandez,[13] Florence Tubach,[14] Jacques-Eric Gottenberg,[15] Jacques Morel,[16] Jakub Zavada,[17] Florenzo Iannone,[18] Johan Askling,[5] Joachim Listing[2]

Table 1 Baseline characteristics and crude incidence rate of lymphomas among biologic-naïve, TNFi, rituximab, tocilizumab or abatacept-treated patients with RA

	Bionaïve	TNFi	Rituximab	Tocilizumab	Abatacept	Total
No. of patients	71 088	47 864*	9094	2029	1708*	124 997*
Follow-up time (pyrs)	322 167	242 260*	29 810	2827	3352*	584 236*
Female (%)	72.1	74.8	79.0	80.1	78.0	73.7
Age mean (mean range)	61.1 (57–62)	55.0 (50–57)	57.9 (58–58)	55.9 (55–57)	57.5 (56–58)	58.5 (50–62)
No. of lymphomas	288	230	6	6	3	533
Incidence per 100 000 pyrs (95% CI)	89 (79–100)	81 (70–94)	20 (7–44)	177 (57–413)	60 (7–216)	85 (77–92)

Μετά προτύπωση για την ηλικία	**PA**	**Γ. Πληθυσμός**
N. Hodgkin	**9.5%**	**10.1%**
B-NHL	**83.8%**	**82.6%**
T-NHL	**6.8%**	**7.3%**

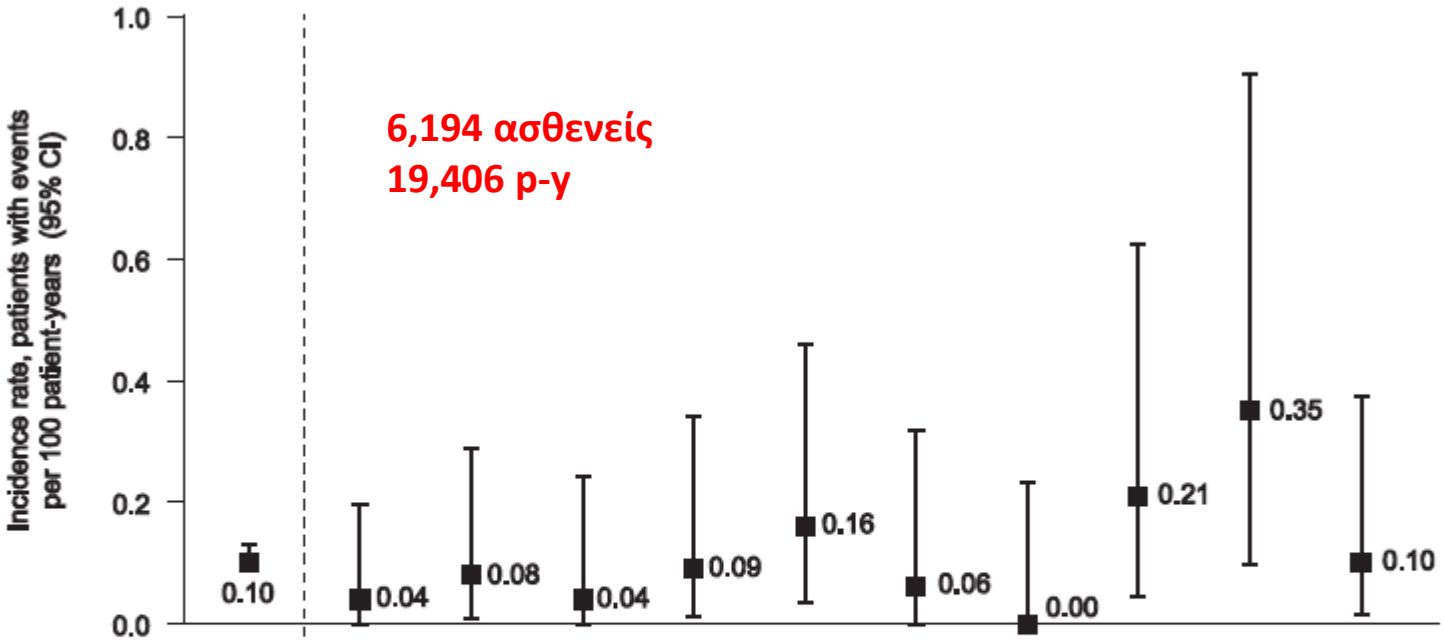
Ann Rheum Dis. 2017 Dec;76(12):2025-2030

Arthritis Care & Research
Vol. 70, No. 5, May 2018, pp 685–694
DOI 10.1002/acr.23421

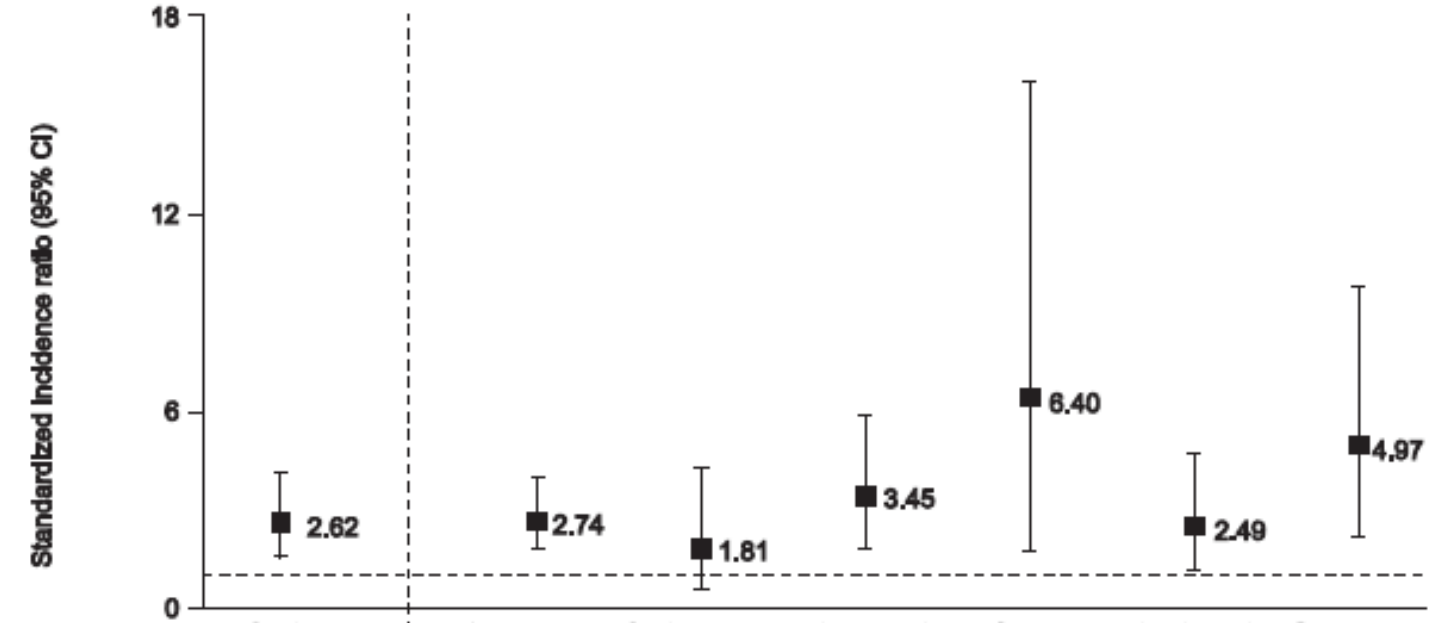
ORIGINAL ARTICLE

Lymphoma in the Tofacitinib Rheumatoid Arthritis Clinical Development Program

XAVIER MARIETTE,[1] CONNIE CHEN,[2] PINAKI BISWAS,[2] KENNETH KWOK,[2] AND MARY G. BOY[3]



Patients	6,194	6,194	5,309	4,852	4,454	4,145	3,684	3,415	3,035	2,643	2,003
Total patient-years	19,404	2,811	2,498	2,276	2,120	1,905	1,742	1,587	1,399	1,129	1,937
Patients with events	19	1	2	1	2	3	1	0	3	4	2



Arthritis Care Res (Hoboken). 2018 May;70(5):685-694

EXTENDED REPORT

Risk of second malignant neoplasm and mortality in patients with rheumatoid arthritis treated with biological DMARDs: a Danish population-based cohort study

Lene Dreyer,[1,2] René L Cordtz,[1,2] Inger Marie J Hansen,[3,4] Lars Erik Kristensen,[2] Merete L Hetland,[5,6,7] Lene Mellemkjaer[8]

Table 2 Observed numbers (Obs) and HRs of a SMN in patients with rheumatoid arthritis according to bDMARD treatment

Treatment	SMN, Obs	Person-years	HR* (95% CI)
Non-use of bDMARDs	70†	2461	1 (Ref)
Ever bDMARDs	38	1225	1.11 (0.74 to 1.67)
bDMARDs before first cancer	11‡	272	1.06 (0.52 to 2.14)
bDMARDs after first cancer	27	953	1.13 (0.71 to 1.80)
bDMARDs only after first cancer	21§	760	1.15 (0.68 to 1.95)
bDMARDs both before and after first cancer	6¶	193	1.09 (0.46 to 2.57)
Type of bDMARD after first cancer**			
TNF-I	21	723	1.21 (0.73 to 2.03)
Rituximab	7	235	1.05 (0.47 to 2.34)

*Adjusted for age, gender, calendar time and cancer site.

Ann Rheum Dis. 2018 Apr;77(4):510-514

Table 3 Observed number (Obs) of deaths and overall mortality in patients with rheumatoid arthritis with cancer according to bDMARD treatment

	All n=1678			Extent of disease recorded n=1326			
Treatment	Deaths Obs	Person-years	Adjusted* HR (95% CI)	Deaths Obs	Person-years	Adjusted* HR (95% CI)	Further adjusted† HR (95% CI)
Non-user of bDMARDs	207	2461	1 (Ref)	150	2022	1 (Ref)	1 (Ref)
Ever bDMARDs	135	1225	1.25 (0.99 to 1.57)	110	982	1.35 (1.04 to 1.76)	1.23 (0.94 to 1.60)
bDMARDs before first cancer	93	272	1.50 (1.15 to 1.97)	75	214	1.53 (1.13 to 2.09)	1.20 (0.88 to 1.63)
bDMARDs after first cancer	42	953	0.92 (0.64 to 1.31)	35	767	1.08 (0.73 to 1.61)	1.29 (0.86 to 1.94)
bDMARDs only after first cancer	23	760	1.01 (0.62 to 1.65)	20	640	1.19 (0.69 to 2.04)	1.36 (0.78 to 2.39)
bDMARDs both before and after first cancer	19	193	0.85 (0.52 to 1.38)	15	128	0.99 (0.57 to 1.73)	1.22 (0.70 to 2.13)
Type of bDMARD after first cancer‡							
TNF-I	35	723	0.96 (0.66 to 1.41)	29	568	1.13 (0.73 to 1.74)	1.42 (0.91 to 2.20)
Rituximab	9	235	0.86 (0.43 to 1.72)	8	205	1.13 (0.54 to 2.40)	1.11 (0.53 to 2.35)

*Adjusted for age, gender, calendar time, cancer site.
†Further adjusted for extent of disease.
‡If a patient is treated with both TNF-I and rituximab after first cancer, the patient will contribute person-years to both types of bDMARD.

Ann Rheum Dis. 2018 Apr;77(4):510-514

EXTENDED REPORT

Comparative effectiveness of tocilizumab versus TNF inhibitors as monotherapy or in combination with conventional synthetic disease-modifying antirheumatic drugs in patients with rheumatoid arthritis after the use of at least one biologic disease-modifying antirheumatic drug: analyses from the pan-European TOCERRA register collaboration

Kim Lauper,[1,2] Dan C Nordström,[3] Karel Pavelka,[4] Maria Victoria Hernández,[5] Tore K Kvien,[6] Eirik Klami Kristianslund,[6] Maria Jose Santos,[7] Žiga Rotar,[8] Florenzo Iannone,[9] Catalin Codreanu,[10] Galina Lukina,[11] Sara L Gale,[12] Khaled Sarsour,[12] Yves Luder,[13] Delphine Sophie Courvoisier,[1] Cem Gabay[1,2]

- 86806 ασθενείς που είχαν αποτύχει σε **≥1 βιολογικό**
  - Ακολούθως έλαβαν TCZ mono (N=771), TCZ combo (N=1773), TNFi mono (N=1404), ή TNFi combo (N=4660)
- Εκβάσεις: επιβίωση βιολογικού, CDAI

Ann Rheum Dis. 2018 May 5

Επιβίωση TCZ (mono ή combo) vs TNFi (mono ή combo)

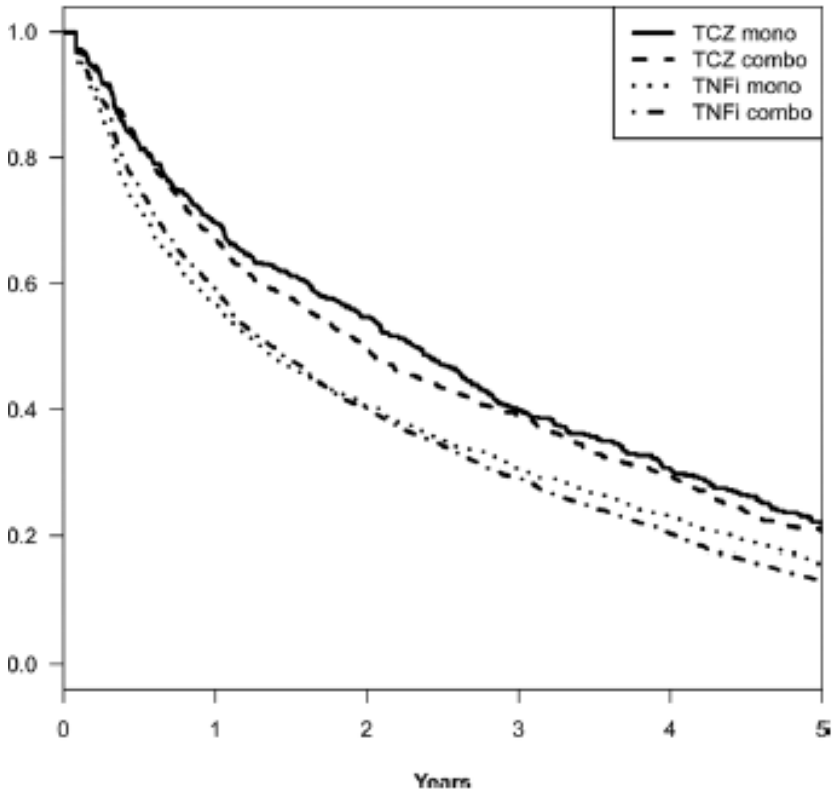


Table 2 Multivariable analysis of drug discontinuation.

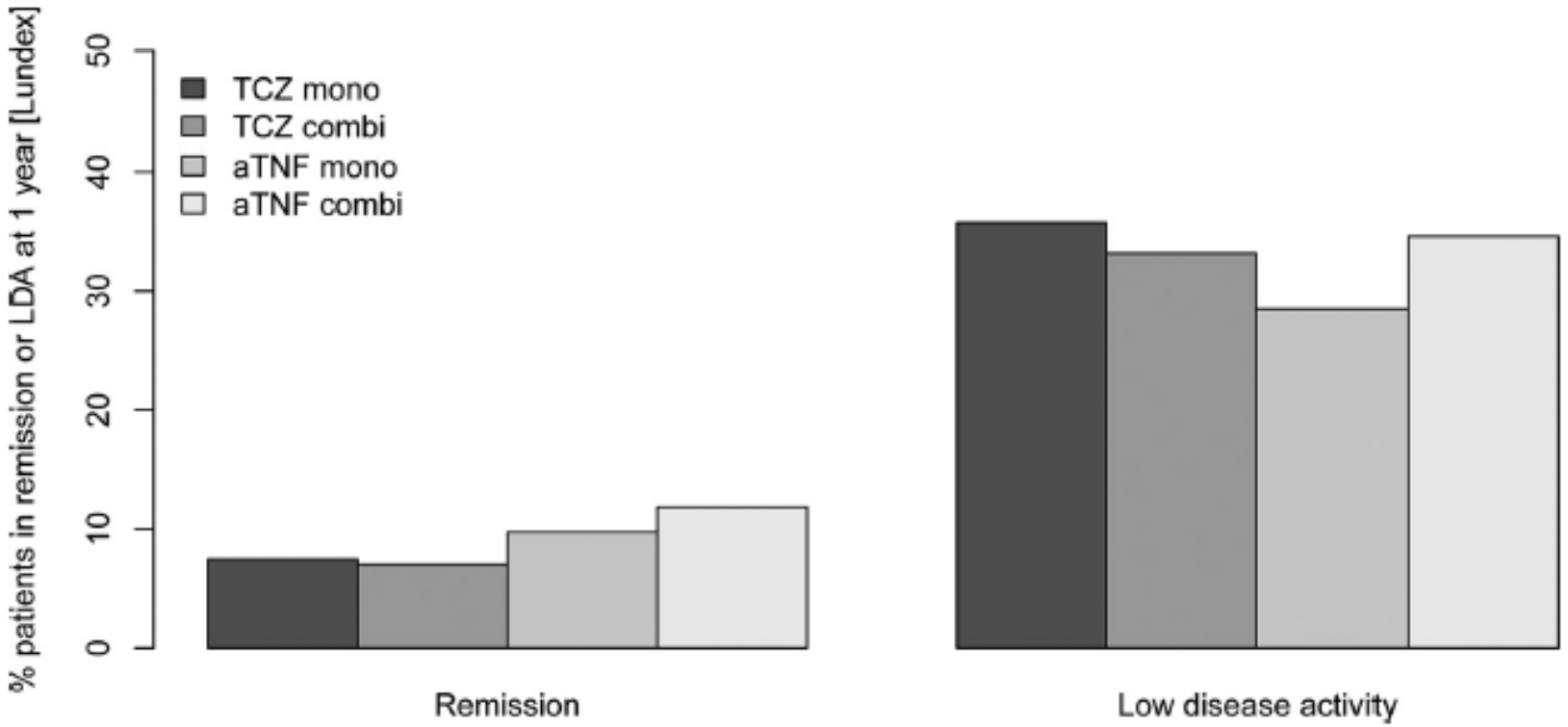
	HR	95% CI	P values
TCZ mono vs TNFi combo	0.78	0.70 to 0.86	<0.001
TNFi mono vs TNFi combo	1.15	1.06 to 1.23	<0.001
TCZ mono vs TCZ combo	0.96	0.86 to 1.08	0.53
TCZ mono vs TNFi mono	0.65	0.58 to 0.74	<0.001
TCZ combo vs TNFi combo	0.70	0.65 to 0.76	<0.001
TCZ combo vs TNFi mono	0.65	0.59 to 0.72	<0.001

Adjusted by age, gender, disease duration, seropositivity, number of previous biologic disease-modifying antirheumatic drugs, glucocorticoids at baseline, Disease Activity Score 28 at baseline, Clinical Disease Activity Index at baseline, Health Assessment Questionnaire at baseline.

combo, combination therapy; mono, monotherapy; TCZ, tocilizumab; TNFi, tumour necrosis factor inhibitor.

Ann Rheum Dis. 2018 May 5

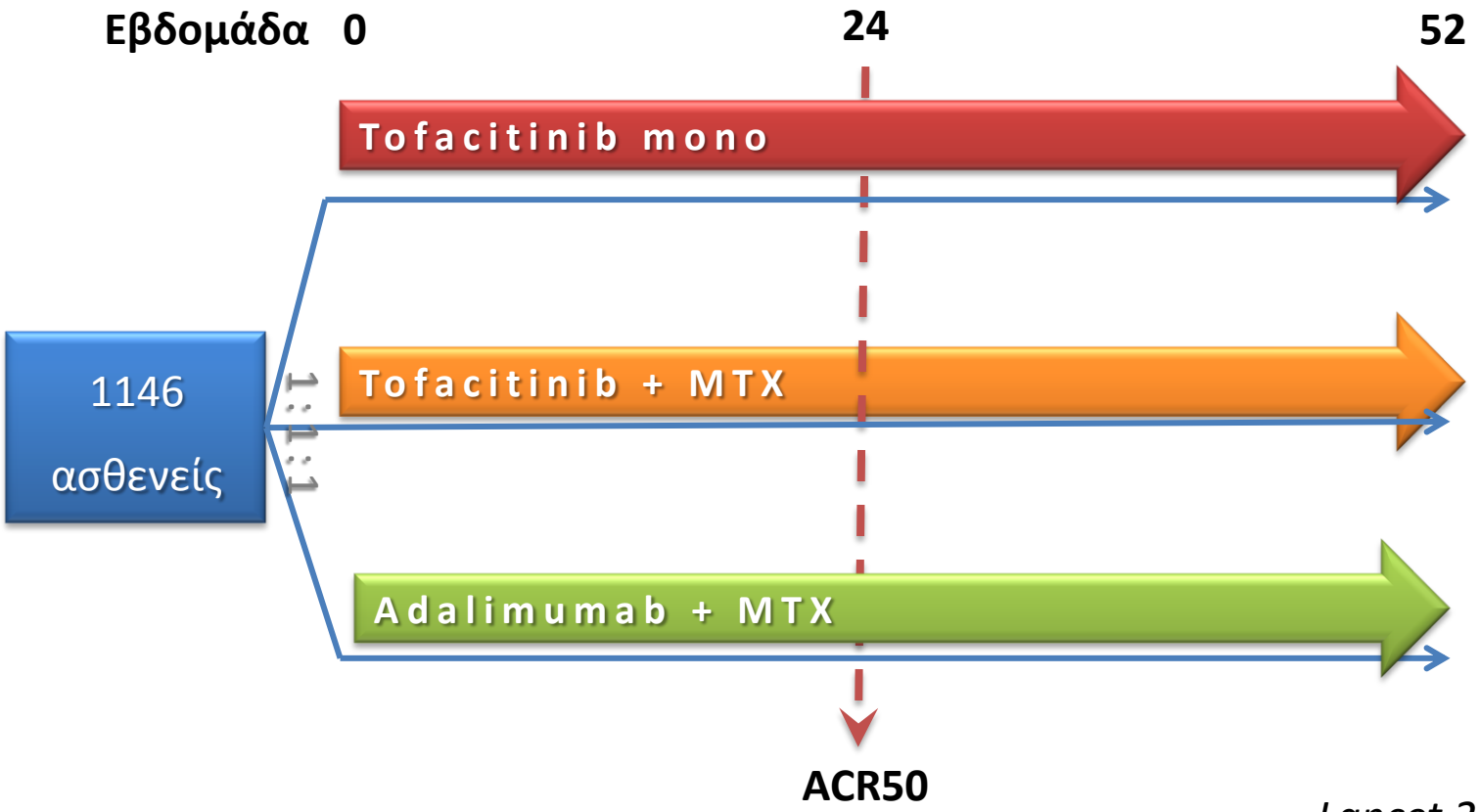
Αποτελεσματικότητα (mono ή combo) vs TNFi (mono ή combo)



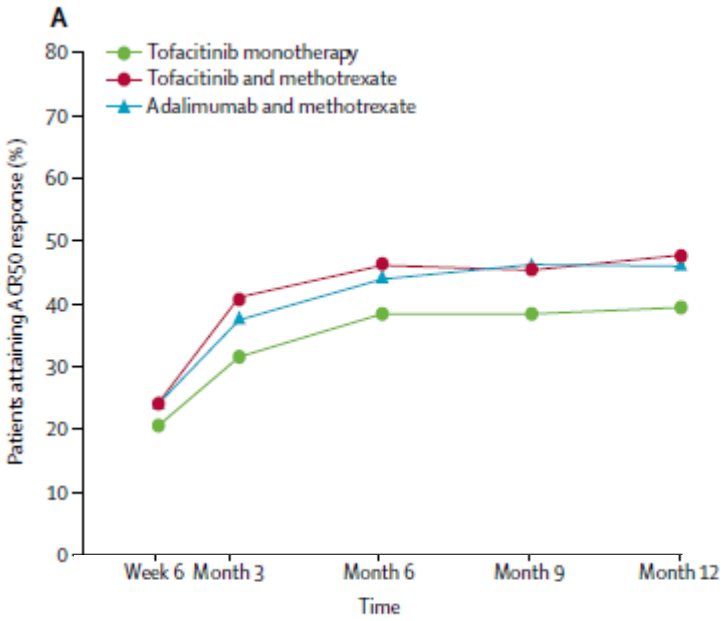
Ann Rheum Dis. 2018 May 5

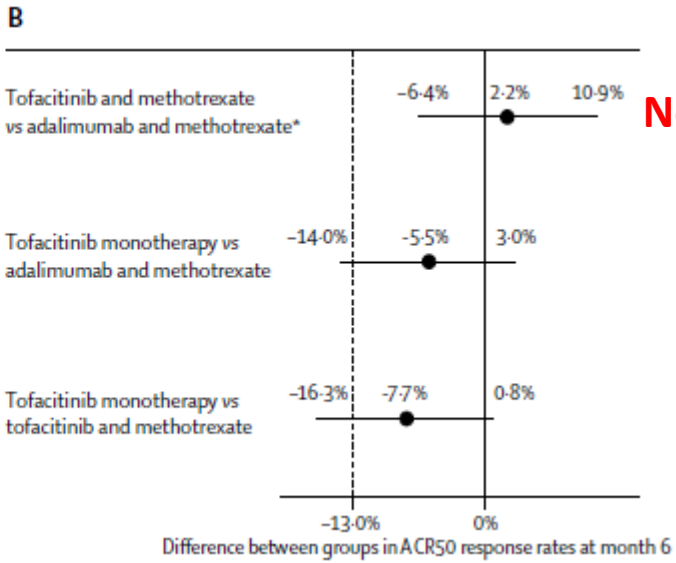
Efficacy and safety of tofacitinib monotherapy, tofacitinib with methotrexate, and adalimumab with methotrexate in patients with rheumatoid arthritis (ORAL Strategy): a phase 3b/4, double-blind, head-to-head, randomised controlled trial

Roy Fleischmann, Eduardo Mysler, Stephen Hall, Alan J Kivitz, Robert J Moots, Zhen Luo, Ryan DeMasi, Koshika Soma, Richard Zhang, Liza Takiya, Svitlana Tatulych, Christopher Mojcik, Sriram Krishnaswami, Sujatha Menon, Josef S Smolen, on behalf of the ORAL Strategy investigators*

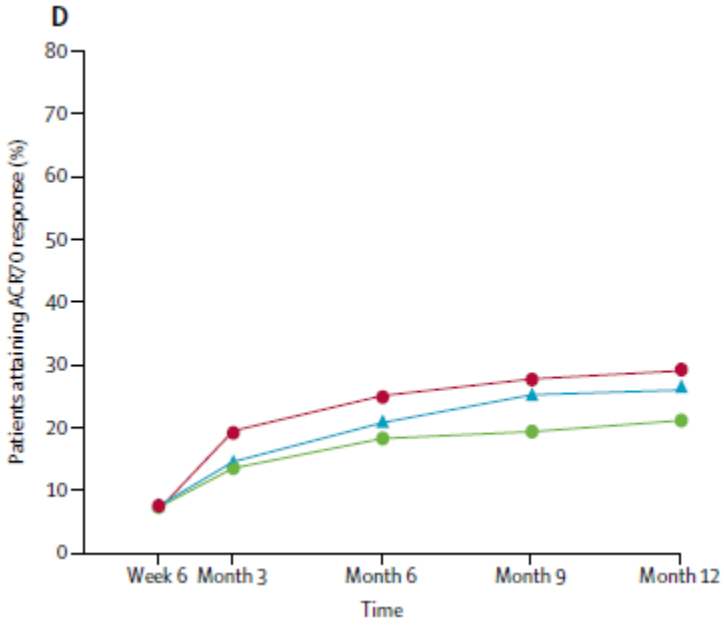


Lancet 2017; 390: 457–68





Non-inferiority



Lancet 2017; 390: 457–68

	Tofacitinib monotherapy (n=384)	Tofacitinib and methotrexate (n=376)	Adalimumab and methotrexate (n=386)
Total number of adverse events*	598	652	620
Patients with adverse events	226 (59%)	231 (61%)	253 (66%)
Patients with treatment-related adverse events	101 (26%)	111 (30%)	133 (35%)
Patients with serious adverse events	35 (9%)	27 (7%)	24 (6%)
Patients discontinuing due to adverse events	23 (6%)	26 (7%)	37 (10%)
Patients with severe adverse events (defined by the investigator)	24 (6%)	17 (5%)	23 (6%)
Deaths†	2 (1%)	0	0
Adverse events of special interest			
Serious infections	6 (2%)	10 (3%)	6 (2%)
Herpes zoster (serious and non-serious)	4 (1%)	8 (2%)	6 (2%)
Herpes zoster (serious and non-serious) in patients who were vaccinated	1/69 (1%)	2/75 (3%)	0/72 (0%)
Opportunistic infections (excluding tuberculosis)	2 (1%)	1 (<1%)	2 (1%)
Tuberculosis	0	2 (1%)	0
MACE (non-fatal)	0	0	2 (1%)
Malignancy (excluding non-melanoma skin cancer)	1 (<1%)	0	0
Non-melanoma skin cancer	2 (1%)	0	1 (<1%)

Lancet 2017; 390: 457–68

Συμπεράσματα

- Η θεραπεία της ΡΑ τις τελευταίες 10ετίες έχει βελτιώσει τις εκβάσεις των ασθενών, αλλά υπάρχουν ακόμη περιθώρια βελτίωσης
- Όσο χαμηλότερη η ενεργότητα της ΡΑ, τόσο μικρότερη η επίπτωση σοβαρών λοιμώξεων
- Η μείωση της δοσολογίας του βιολογικού φαίνεται ότι διατηρεί το θεραπευτικό αποτέλεσμα καλύτερα από την πλήρη διακοπή του
- Το tofacitinib φαίνεται ότι έχει μεγαλύτερο θεραπευτικό αποτέλεσμα, όταν συνδυάζεται με MTX, οπότε είναι συγκρίσιμο με το συνδυασμό Adalimumab+ MTX

Ευχαριστώ