ΣΠΟΝΔΥΛΟΑΡΘΡΟΠΑΘΕΙΑ ΚΑΙ JAK INHIBITORS

ΑΛΕΞΑΝΔΡΑ ΦΙΛΙΠΠΟΠΟΥΛΟΥ, MD,PHD

ΕΙΔΙΚΟς ΡΕΥΜΑΤΟΛΟΓΟς

ΤΕΩς ΕΠΙΜΕΛΗΤΡΙΑ ΕςΥ, ΙΔΙΩΤΗς

Σύγκρουση συμφερόντων

- Καμία για την συγκεκριμένη ομιλία

Παρουσίαση κλινικής περίπτωσης

Δημογραφικά στοιχεία

Φύλο: Άρρεν

Ηλικία: 27 ετών

Βάρος: 175 cm

Ύψος: 74 kg

Κάπνισμα: περιστασιακά (1 packyear)

Αλκοόλ: κοινωνικά

Επάγγελμα: Δάσκαλος, ΜΗ χειρώνακτας

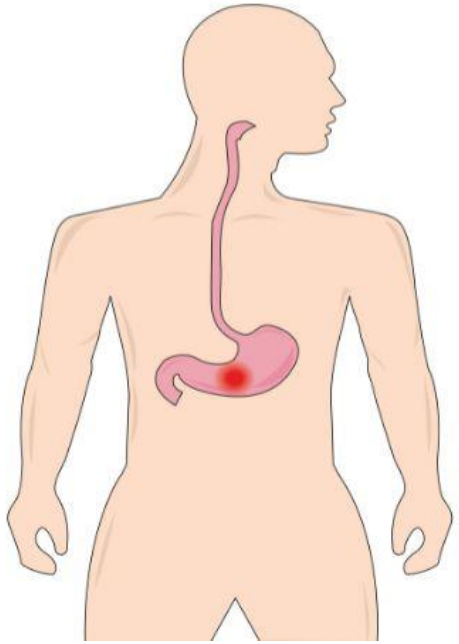
Κ.Κ.

Ατομικό ιστορικό

- Γαστρορραγία προ 2ετίας

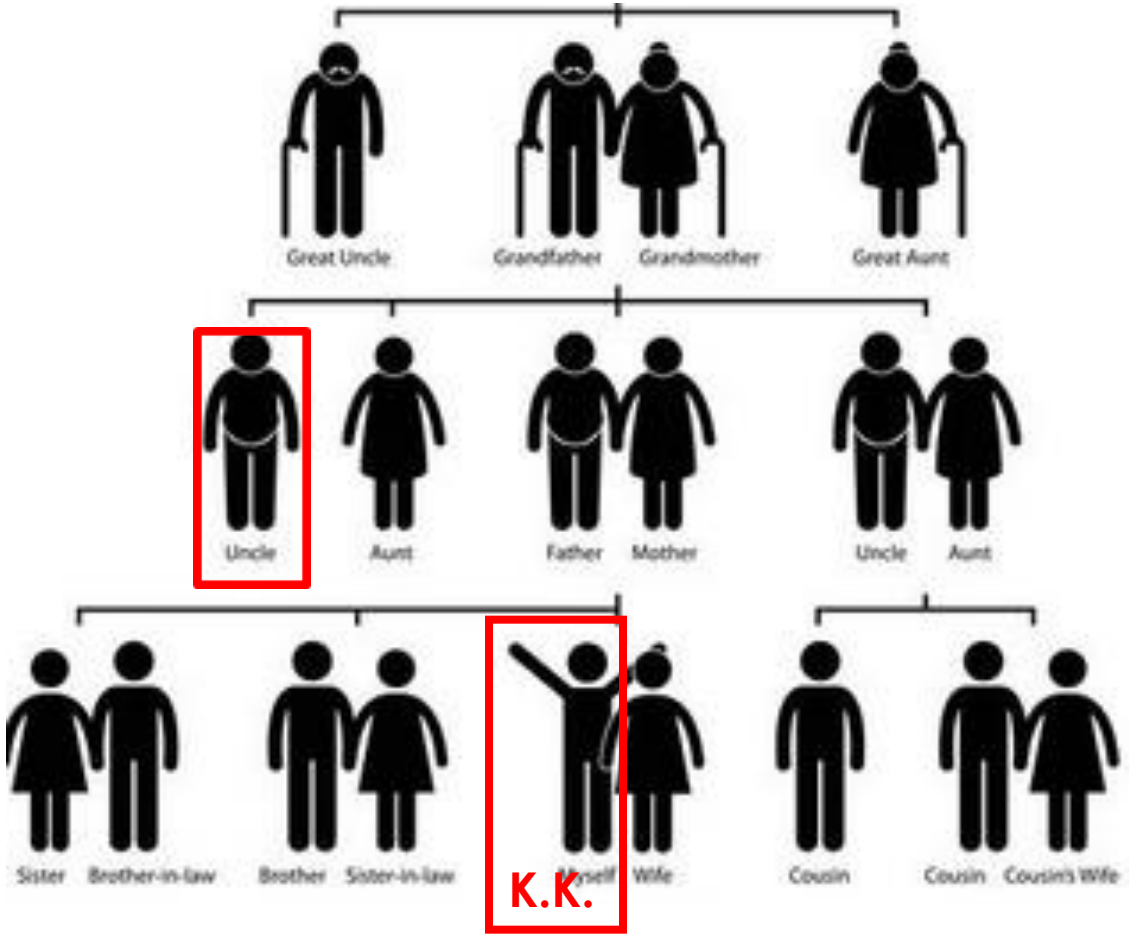
(επεισόδιο αιματέμεσης → έλκος δωδεκαδακτύλου)

- Χρήση ΜΣΑΦ λόγω οσφυαλγίας (όχι υπέρχρηση)



Οικογενειακό Ιστορικό

Πατρικός θείος : Αγκυλοποιητική Σπονδυλίτιδα (ΑΣ)
παρακολουθείται από Ρευματολόγο



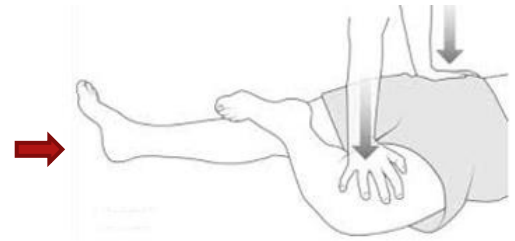
1η επίσκεψη (12/2023)

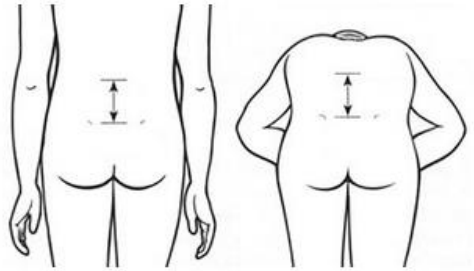
Αιτία προσέλευσης:

- **χαμηλή οσφυαλγία**
- **φλεγμονώδες** πρότυπο (πρωινή δυσκαμψία > 1 ώρα)
- από **2ετίας** περίπου

Κλινική εξέταση:

- Χωρίς περιφερική αρθρίτιδα
- Faber test: (+) ΑΡ
- Ήπια ευαισθησία σε πέλματα άμφω
- Schöber Test : 10 → 14cm
- Δέρμα: οκ , οφθαλμός: οκ, έντερο: οκ

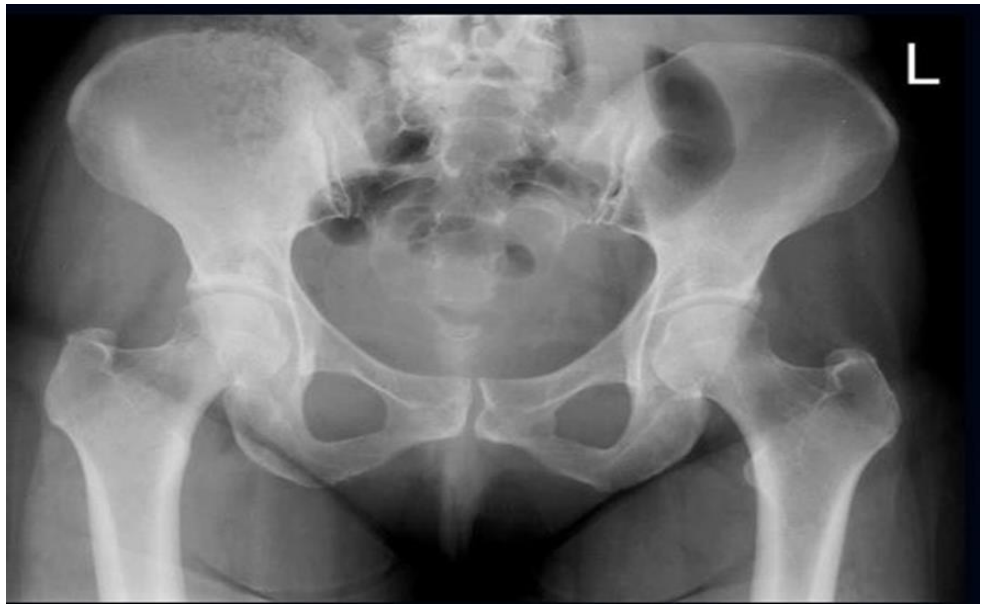




1η επίσκεψη (12/2023)

Εξέταση εκλογής???

- Ακτινογραφία Ιερολαγονίων (ferguson)



Χωρίς παθολογικά ευρήματα
Υποψία σκλήρυνσης ΔΕ;

1η επίσκεψη (12/2023)

- Διάγνωση εργασίας:

  Πιθανή Σπονδυλοαρθρίτιδα

  σε νεαρό **άντρα** με **(+) οικογενειακό ιστορικό για ΣπΑ**

  BASDAI 5,9 **BASFI** 1

- Οδηγίες – συστάσεις

1. Αποφυγή ΜΣΑΦ (ιστορικό γαστρορραγίας)
2. MRI ιερολαγονίων (STIR)
3. Εργαστηριακός Έλεγχος

(Βασικός έλεγχος, δείκτες φλεγμονής, HLA – B27,
quantiferon, HbsAg, AntiHbc, AntiHbs, AntiHCV, Ακτινογραφία θώρακος)

4. Άμεση επανεκτίμηση

2η επίσκεψη (01/2024)

- Εργαστηριακός έλεγχος

ΤΚΕ: 20mm/h CRP: 8 (<6mg/dl)

Hgb: 13,5 g/dl Hct: 41 % MCV: 71 fl MCH: 24 pg

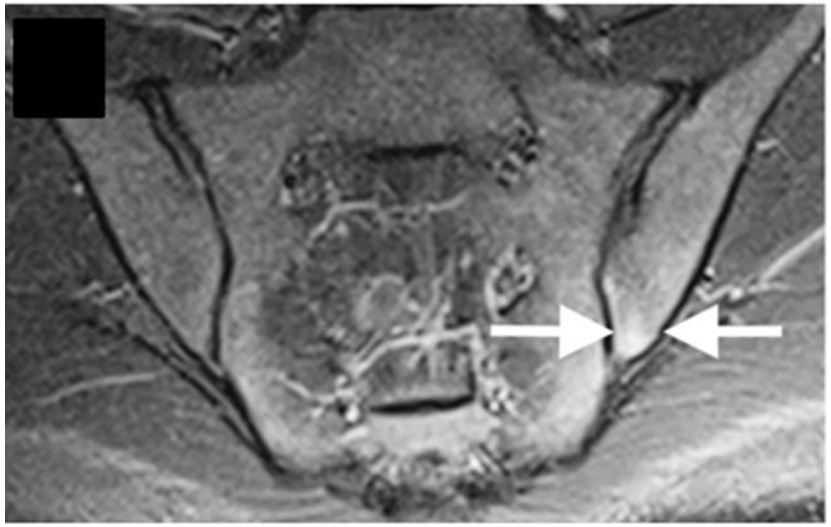
HLA B27: (+)

Quantiferon: (-)

AntiHbs (+) HbsAg (-) AntiHBc(-) Anti HCV (-)

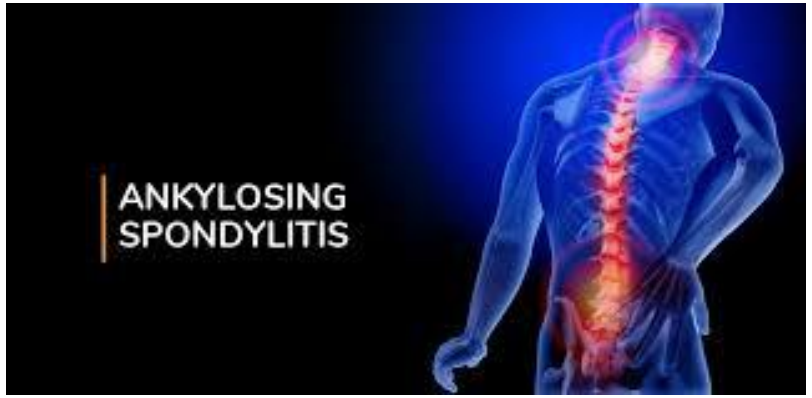
Ακτινογραφία Θώρακος: Χωρίς παθολογικά ευρήματα

- MRI ιερολαγονίων (STIR) 3T : εικόνα ιερολαγονίτιδας ΑΡ



Διάγνωση εργασίας

- Σπονδυλοαρθροπάθεια (ΣπΑ) ΜΗ ακτινολογικά επιβεβαιωμένη
- ενθεσίτιδα ΑΡ
- Χωρίς εξωαρθρικές εκδηλώσεις

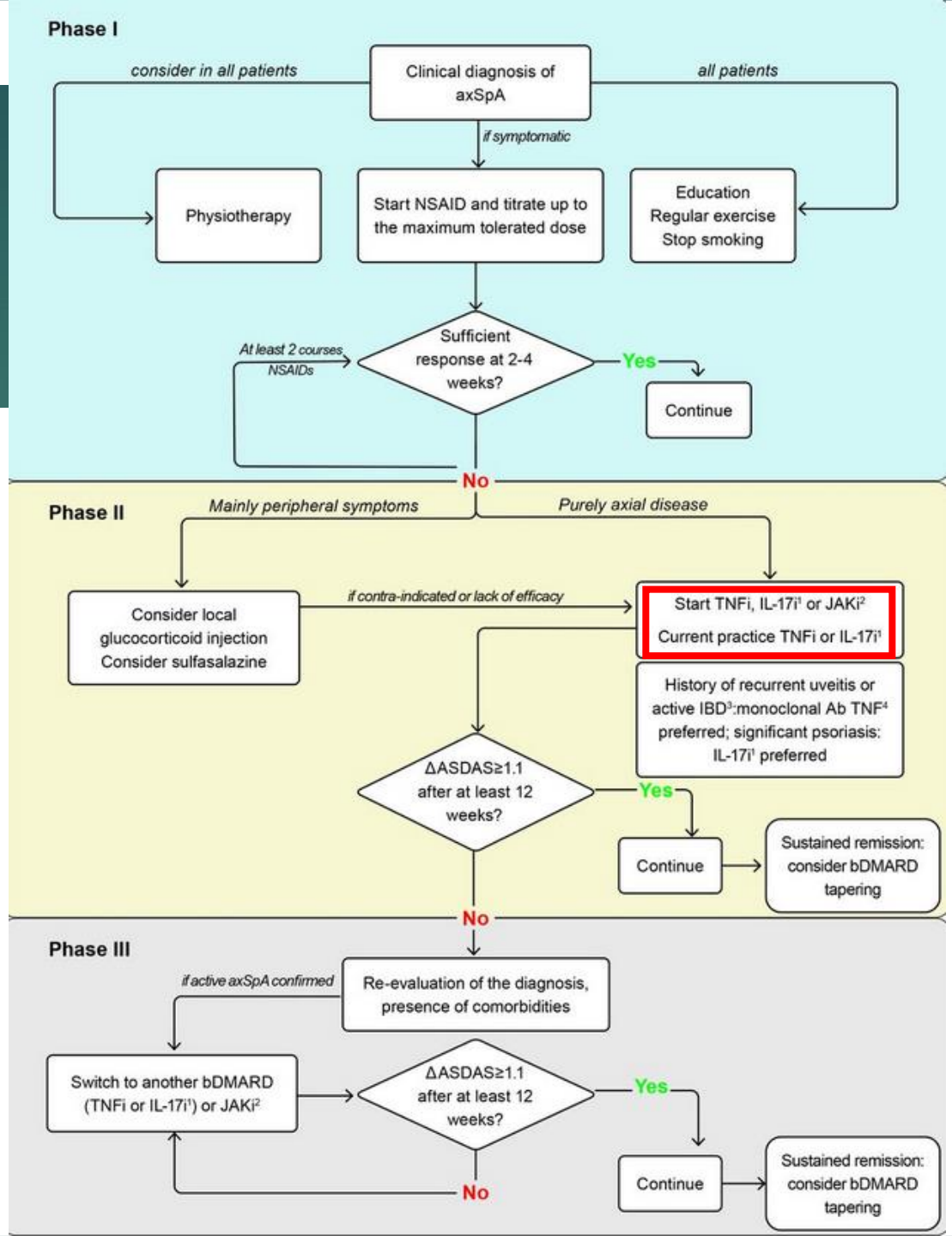


Axial SpA (AxSpA)

Θεραπευτική επιλογή;

ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update

Sofia Ramiro [1,2] Elena Nikiphorou [1,3] Alexandre Sepriano [1,4] Augusta Ortolan [5] Casper Webers [6] Xenofon Baraliakos,[7] Robert B M Landewé [8,9] Filip E Van den Bosch [10,11] Boryana Boteva,[12] Ann Bremander,[13,14] Philippe Carron [10,11] Adrian Ciurea [15] Floris A van Gaalen [1] Pál Géher,[16] Lianne Gensler,[17] Josef Hermann,[18] Manouk de Hooge [10] Marketa Husakova,[19] Uta Kiltz [7] Clementina López-Medina [20,21] Pedro M Machado [22,23,24] Helena Marzo-Ortega,[25] Anna Molto [26] Victoria Navarro-Compán [27] Michael J Nissen [28] Fernando M Pimentel-Santos,[4] Denis Poddubnyy [29] Fabian Proft [29] Martin Rudwaleit [30] Mark Telkman,[31] Sizheng Steven Zhao [32] Nelly Ziade [33,34] Désirée van der Heijde [1]



Θεραπευτική επιλογή;
Δεδομένα για συγκεκριμένο ασθενή

- Αποφυγή ΜΣΑΦ (ιστορικό γαστρορραγίας…)
- Βιολογική θεραπεία (Bdmard) – screening αρνητικό για λανθάνουσα ΤΒ
  ενεργό/παλιά HBV, HCV
- Συζήτηση με ασθενή

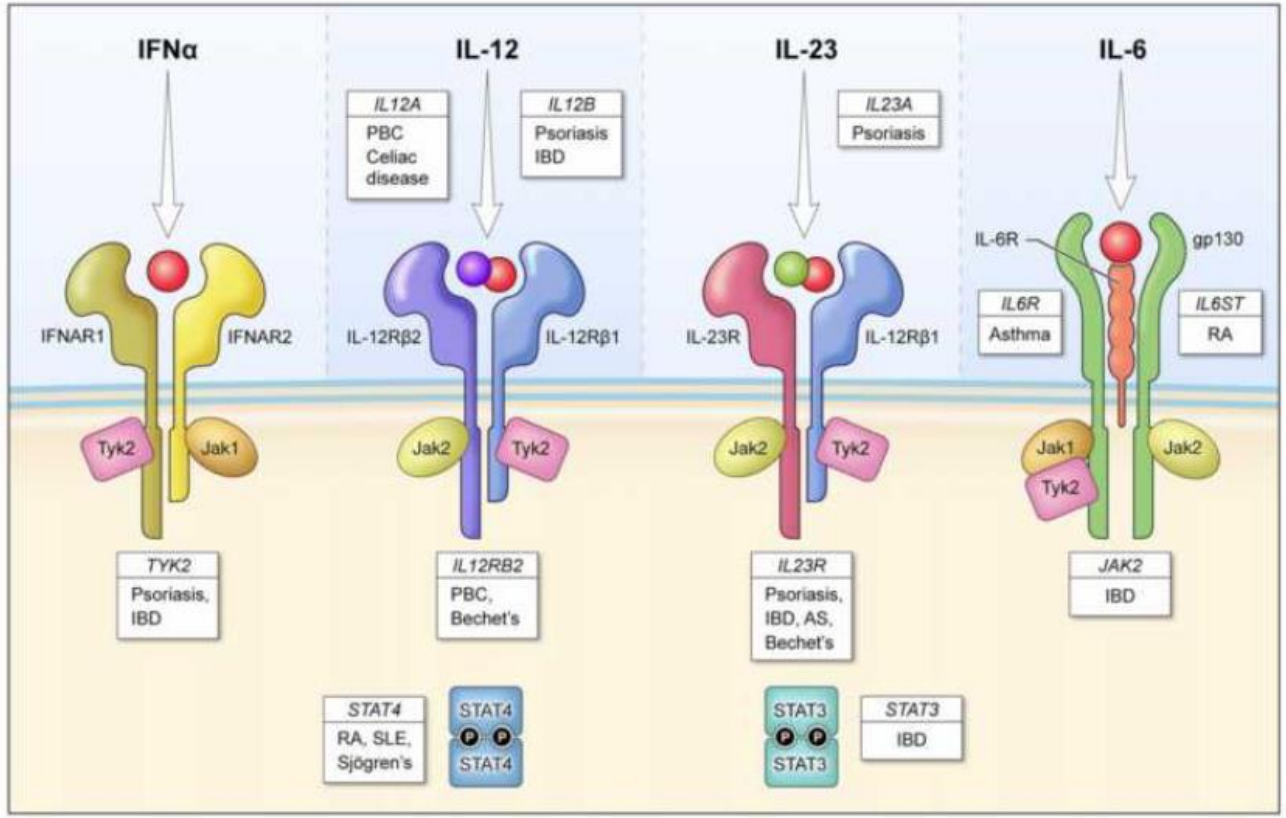
Θεραπευτική επιλογή

Έναρξη jak αναστολέα. ΓΙΑΤΙ;;;;

- pos αγωγή (καλύτερη συμμόρφωση ασθενή)
- ΗΔΗ Καλή εμπειρία από την Ρευματοειδή αρθρίτιδα
  - Αποτελεσματικότητα
  - **ταχεία** έναρξη δράσης
  - ασφάλεια *σε επιλεγμένες περιπτώσεις ασθενών*

ποιος jak αναστολέας;

Jak αναστολείς



Pos αγωγή
Πρώτα αποτελέσματα από ασθενείς σε PA

O'Shea JJ, et al. *Immunity*. 2012; 36: 542-50; Okada Y, et al. *Ann Rheum Dis*. 2019; 78: 446-453; Brown MA, et al. *Best Pract Res Clin Rheumatol*. 2017; 31: 763-776; Capon F. *Int J Mol Sci*. 2017; 18(12). pii: E2526

ΑΠΟΤΕΛΕΣΜΑΤΙΚΟΤΗΤΑ TOFACITINIB ΣΕ ΑΣ

Tofacitinib σε ΑΣ;

Spondyloarthritis

OPEN ACCESS

CLINICAL SCIENCE

Tofacitinib for the treatment of ankylosing spondylitis: a phase III, randomised, double-blind, placebo-controlled study

Atul Deodhar [1], Paula Sliwinska-Stanczyk [2], Huji Xu [3], Xenofon Baraliakos [4], Lianne S Gensler [5], Dona Fleishaker [6], Lisy Wang [6], Joseph Wu [6], Sujatha Menon [6], Cunshan Wang [6], Oluwaseyi Dina [7], Lara Fallon [8], Keith S Kanik [6], Désirée van der Heijde [9]

Received 26 November 2020
Revised 11 March 2021
Accepted 16 March 2021
Published Online First
27 April 2021

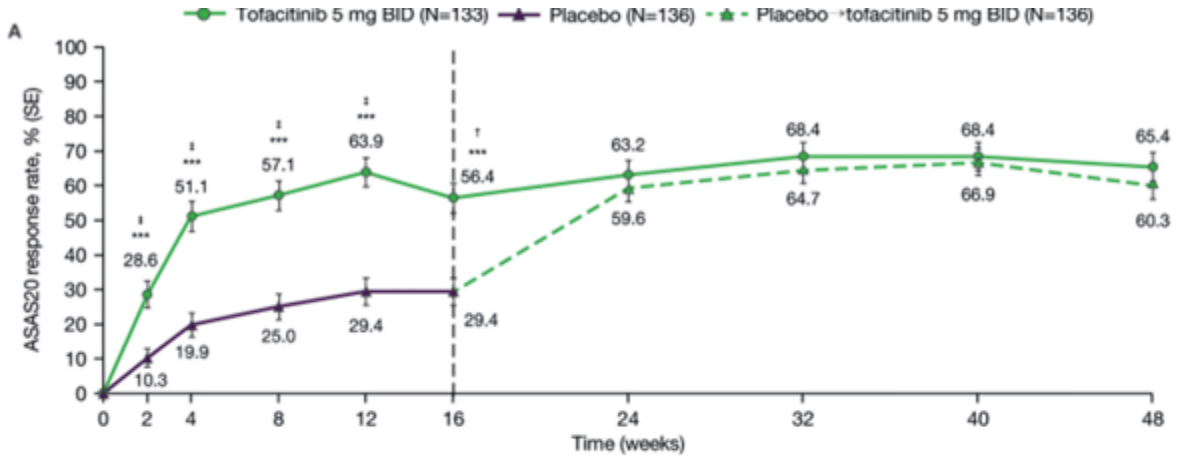
269 patients

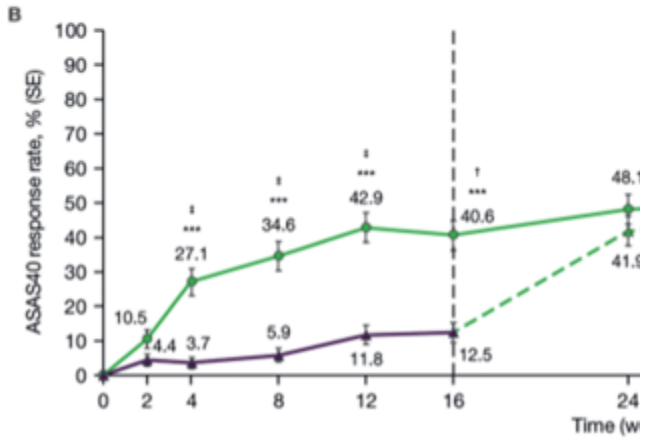
Tofacitinib(N=133) vs placebo (N=136)

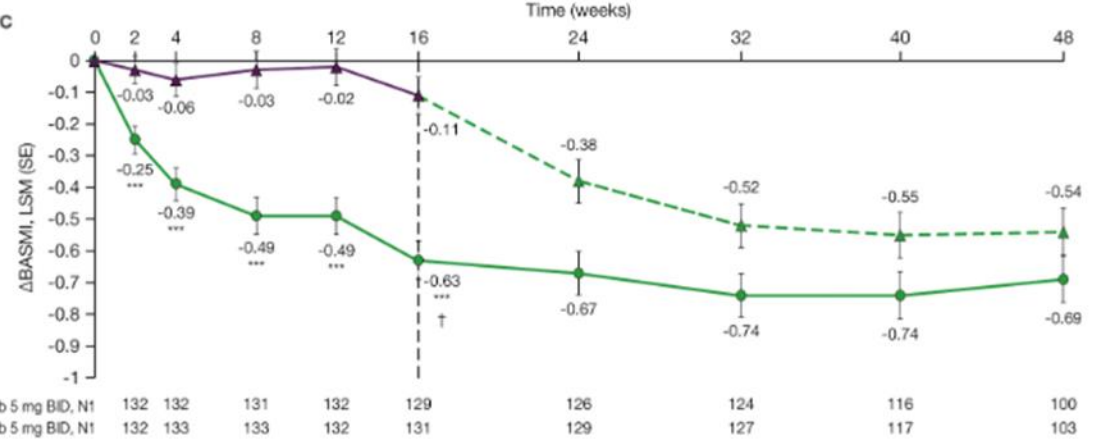
Tofacitinib σε ΑΣ;

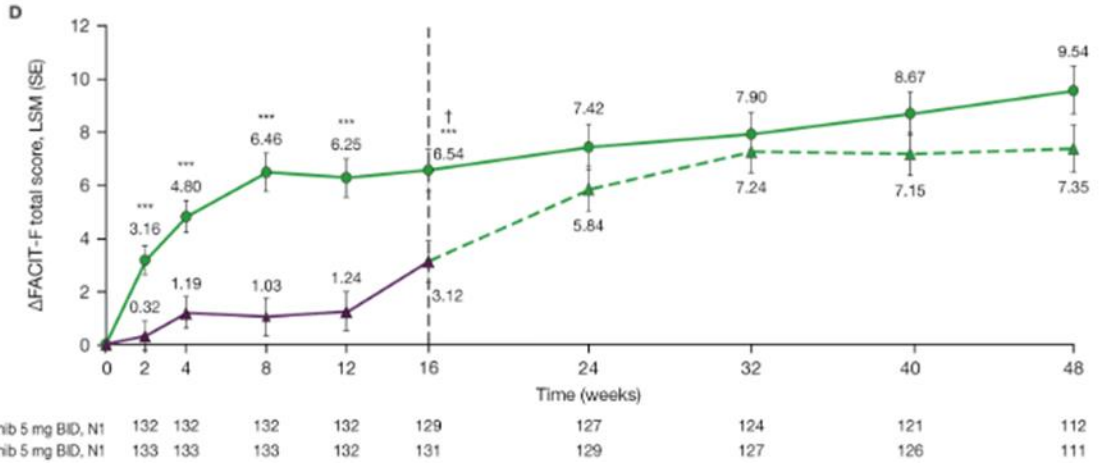
Table 2 Efficacy of tofacitinib 5 mg two times per day versus placebo at week 16: type I error-controlled primary and secondary endpoints†

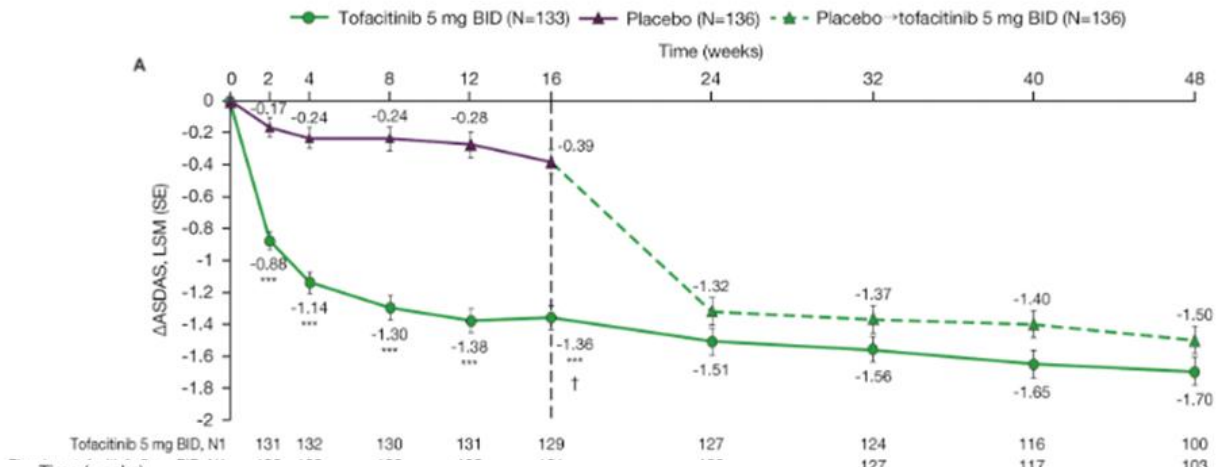
	Tofacitinib 5 mg two times per day (N=133)	Placebo (N=136)	p value
Global type I error-controlled endpoints at week 16, tested in the sequence below			
ASAS20 response,‡ n (%)	75 (56.4)	40 (29.4)	<0.0001***§
ASAS40 response,‡ n (%)	54 (40.6)	17 (12.5)	<0.0001***§
ΔASDAS,¶ LSM (SE) (N1)	−1.36 (0.07) (129)	−0.39 (0.07) (131)	<0.0001***§
ΔhsCRP (mg/dL),¶ LSM (SE) (N1)	−1.05 (0.10) (129)	−0.09 (0.10) (131)	<0.0001***§
ΔASQoL,** LSM (SE) (N1)	−4.03 (0.40) (129)	−2.01 (0.41) (130)	0.0001***§
ΔSF-36v2 PCS score,** LSM (SE) (N1)	6.69 (0.59) (129)	3.14 (0.59) (130)	<0.0001***§
ΔBASMI,¶ LSM (SE) (N1)	−0.63 (0.06) (129)	−0.11 (0.06) (131)	<0.0001***§
ΔFACIT-F total score,¶ LSM (SE) (N1)	6.54 (0.80) (129)	3.12 (0.79) (131)	0.0008***§
Type I error-controlled ΔASAS components at week 16¶§§ tested in the sequence below			
ΔPtGA (NRS 0–10), LSM (SE) (N1)	−2.47 (0.20) (129)	−0.91 (0.20) (131)	<0.0001***††
ΔTotal back pain (NRS 0–10), LSM (SE) (N1)	−2.57 (0.19) (129)	−0.96 (0.19) (131)	<0.0001***††
ΔBASFI (NRS 0–10), LSM (SE) (N1)	−2.05 (0.17) (129)	−0.82 (0.17) (131)	<0.0001***††
ΔMorning stiffness (inflammation, NRS 0–10),‡‡ LSM (SE) (N1)	−2.69 (0.19) (129)	−0.97 (0.19) (131)	<0.0001***††


Tofacitinib 5 mg BID (N=133)
Placebo (N=136)
Placebo → tofacitinib 5 mg BID (N=136)
A
ASAS20 response rate, % (SE)
Time (weeks)


B
ASAS40 response rate, % (SE)
Time (w


C
ΔBASMI, LSM (SE)
Tofacitinib 5 mg BID, N1
Placebo → tofacitinib 5 mg BID, N1


D
ΔFACIT-F total score, LSM (SE)
Time (weeks)
Tofacitinib 5 mg BID, N1
Placebo → tofacitinib 5 mg BID, N1


Tofacitinib 5 mg BID (N=133)
Placebo (N=136)
Placebo → tofacitinib 5 mg BID (N=136)
A
ΔASDAS, LSM (SE)
Time (weeks)
Tofacitinib 5 mg BID, N1

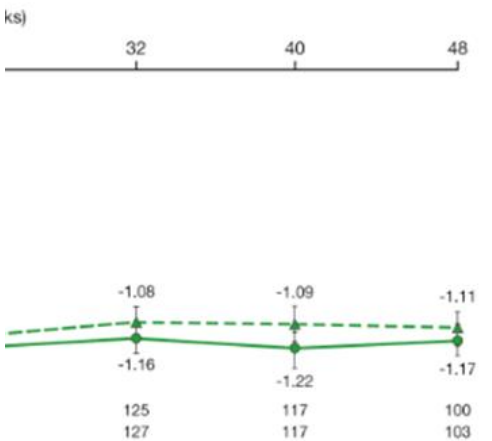

ks)

Table 4 Summary of safety up to week 16 and up to week 48

Patients with events, n (%)	Up to week 16 (double-blind phase)		Up to week 48 (double-blind and open-label phases)	
	Tofacitinib 5 mg two times per day (N=133)	Placebo (N=136)	Tofacitinib 5 mg two times per day (N=133)	Placebo→ tofacitinib 5 mg two times per d (N=136)
AEs	73 (54.9)	70 (51.5)	103 (77.4)	93 (68.4)
SAEs*	2 (1.5)	1 (0.7)	7 (5.3)	2 (1.5)
Severe AEs†	2 (1.5)	0	6 (4.5)	0
Discontinued study drug due to AEs	3 (2.3)	1 (0.7)	8 (6.0)	3 (2.2)
Reduced dose or temporarily discontinued study drug due to AEs	9 (6.8)	5 (3.7)	18 (13.5)	13 (9.6)
Deaths	0	0	0	0
Most common AEs by preferred term (>5% of any treatment group)				
Upper respiratory tract infection	14 (10.5)	10 (7.4)	21 (15.8)	18 (13.2)
Nasopharyngitis	9 (6.8)	10 (7.4)	11 (8.3)	17 (12.5)
Diarrhoea	6 (4.5)	5 (3.7)	10 (7.5)	8 (5.9)
Arthralgia	1 (0.8)	8 (5.9)	2 (1.5)	9 (6.6)
ALT increased	4 (3.0)	1 (0.7)	8 (6.0)	2 (1.5)
Protein urine present	5 (3.8)	2 (1.5)	8 (6.0)	4 (2.9)
Headache	2 (1.5)	3 (2.2)	5 (3.8)	7 (5.1)
Abdominal pain upper	0	4 (2.9)	2 (1.5)	7 (5.1)
AESIs				
Malignancies (including NMSC)‡	0	0	0	0
MACE‡	0	0	0	0
Thromboembolic events (DVT, PE or ATE)‡	0	0	0	0
GI perforation‡	0	0	0	0
Hepatic events‡	1 (0.8)§	0	3 (2.3)¶	0
DILI‡	0	0	0	0
HZ (serious and non-serious)	0	0	3 (2.3)**	2 (1.5)**
Opportunistic infections‡	0	0	0	0
Serious infections	1 (0.8)††	0	1 (0.8)††	0
ILD‡	0	0	0	0
Laboratory values meeting protocol criteria for monitoring‡‡	0	6 (4.4)	7 (5.3)	10 (7.4)
Haemoglobin drop >20 g/L below baseline	0	4 (2.9)	3 (2.3)	5 (3.7)
Platelet count <100×10^9/L	0	1 (0.7)	0	1 (0.7)
Serum creatinine increase >50% or increase 0.5 mg/dL over the average of screening and baseline values	0	0	4 (3.0)	3 (2.2)
Creatine kinase >5×ULN	0	1 (0.7)	0	1 (0.7)
Laboratory values meeting protocol criteria for discontinuation of study drug§§	1 (0.8)	0	2 (1.5)	0
Two sequential AST or ALT elevations >5×ULN	1 (0.8)	0	2 (1.5)	0

Tofacitinib σε ΑΣ;

- Η 1η τυχαιοποιημένη, διπλά τυφλή, φάσης 3, placebo-controlled μελέτη σε ασθενείς με ΕΝΕΡΓΟ ΑΣ:

Tofacitinib 5 mg S 1x2 ημερησίως vs placebo

- Στατιστικά υψηλότερη αποτελεσματικότητα την week 16
- ΜΕ ΓΡΗΓΟΡΗ και ΔΙΑΤΗΡΗΣΙΜΗ κλινική ανταπόκριση
- ΧΩΡΙΣ ΠΡΟΒΛΗΜΑ ΣΤΗΝ ΑΣΦΑΛΕΙΑ εως και την week 48 (end of study treatment)

Tofacitinib σε ΑΣ; Ακτινολογική βελτίωση (1)

RHEUMATOLOGY

Rheumatology 2018;57:1390–1399
doi:10.1093/rheumatology/key104
Advance Access publication 26 April 2018

Original article

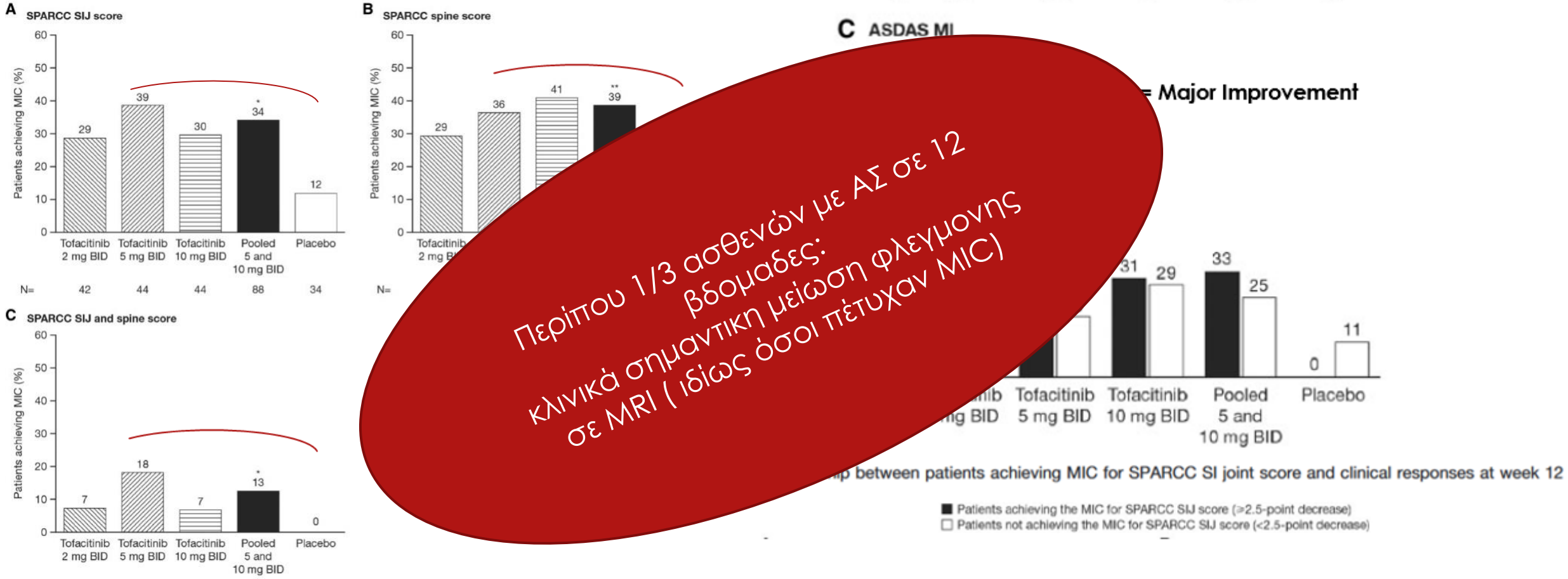
Tofacitinib is associated with attainment of the minimally important reduction in axial magnetic resonance imaging inflammation in ankylosing spondylitis patients

Walter P. Maksymowych[1], Désirée van der Heijde[2], Xenofon Baraliakos[3], Atul Deodhar[4], Sarah P. Sherlock[5], David Li[6], Dona Fleishaker[7], Thijs Hendrikx[6] and Keith S. Kanik[7]

- Φάσης 2 τυχαιοποιημένη μελέτη, n = 207 ΑΣ ασθενείς, ΌΧΙ υπο BDMARD (μόνο ΜΣΑΦ)
- Μελέτη MRI (week 0, week 12)
- 1: 1: 1: 1 to tofacitinib 2, 5 ή 10 mg x2 qday ή placebo
- Διάρκεια 12 βδομάδες

Tofacitinib σε ΑΣ; Ακτινολογική Βελτίωση (1)

Fig. 1 Proportion of patients achieving the MIC at week 12



Περίπου 1/3 ασθενών με ΑΣ σε 12 βδομαδες:
κλινικά σημαντικη μείωση φλεγμονης σε MRI (ιδίως όσοι πέτυχαν MIC)

Tofacitinib σε ΑΣ; Ακτινολογική Βελτίωση (2)

Rheumatol Ther (2023) 10:1001–1020
https://doi.org/10.1007/s40744-023-00564-y

Check for updates

ORIGINAL RESEARCH

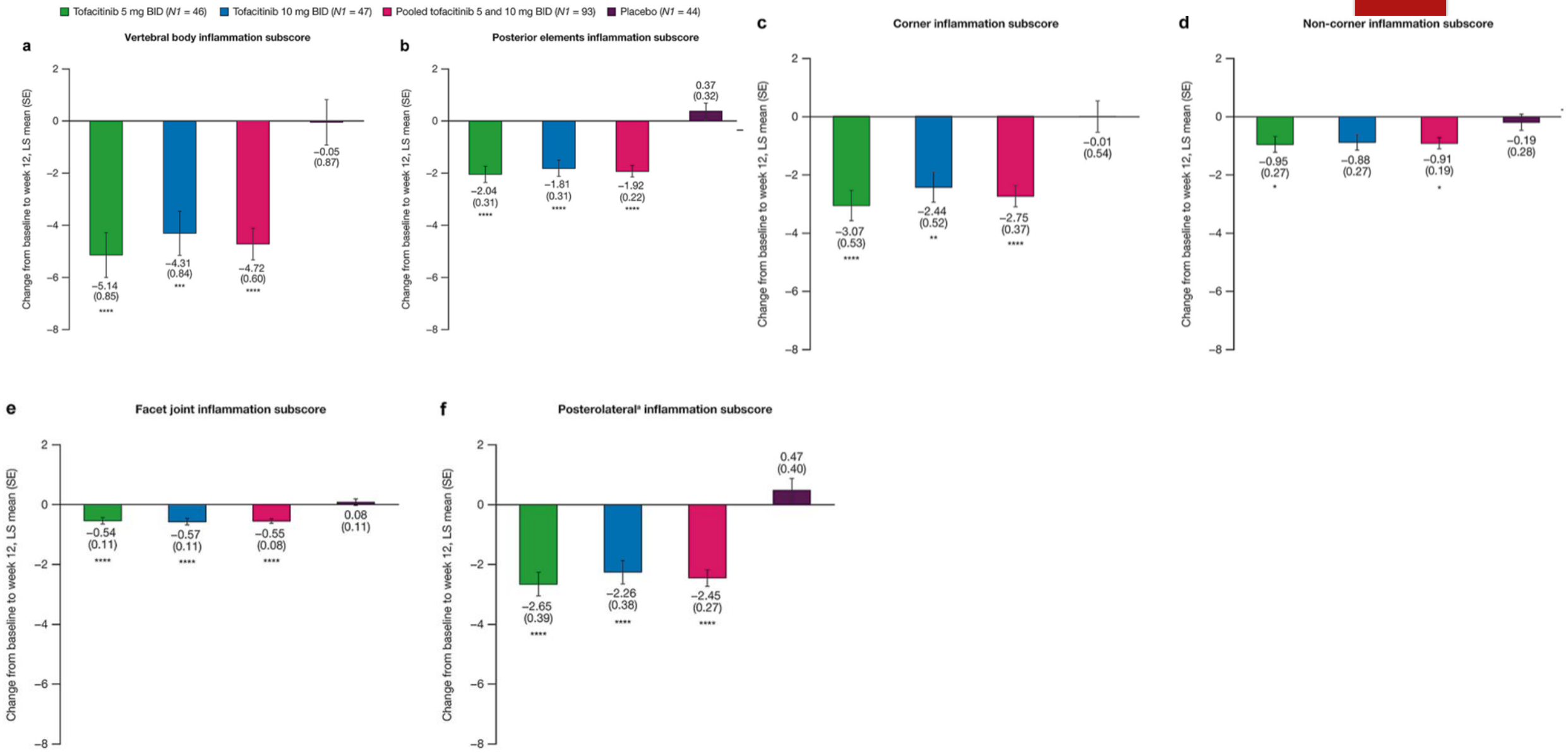
Tofacitinib Reduces Spinal Inflammation in Vertebral Bodies and Posterolateral Elements in Ankylosing Spondylitis: Results from a Phase 2 Trial

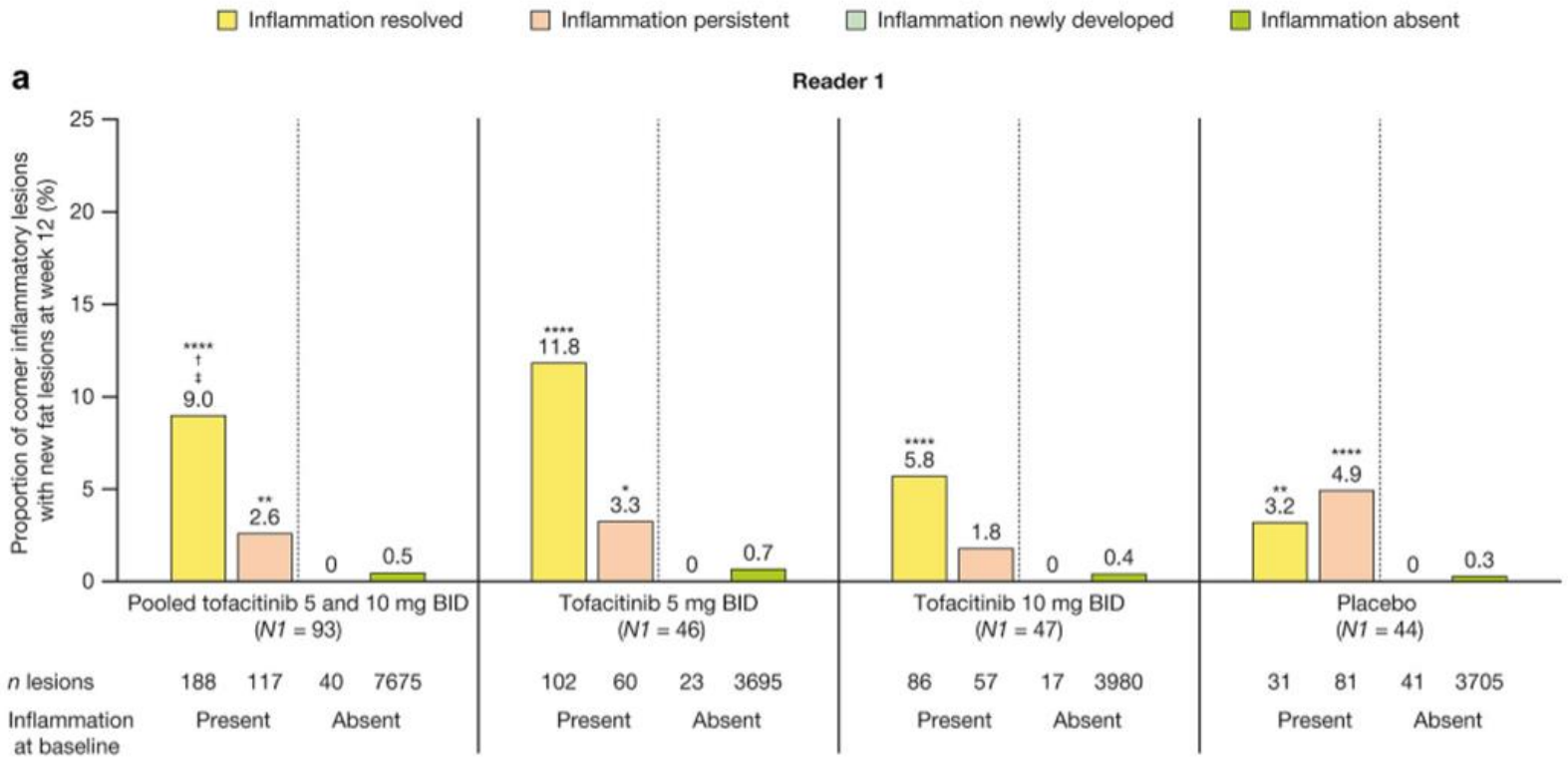
Mikkel Østergaard · Joseph Wu · Lara Fallon · Sarah P. Sherlock · Cunshan Wang · Dona Fleishaker · Keith S. Kanik · Walter P. Maksymowych

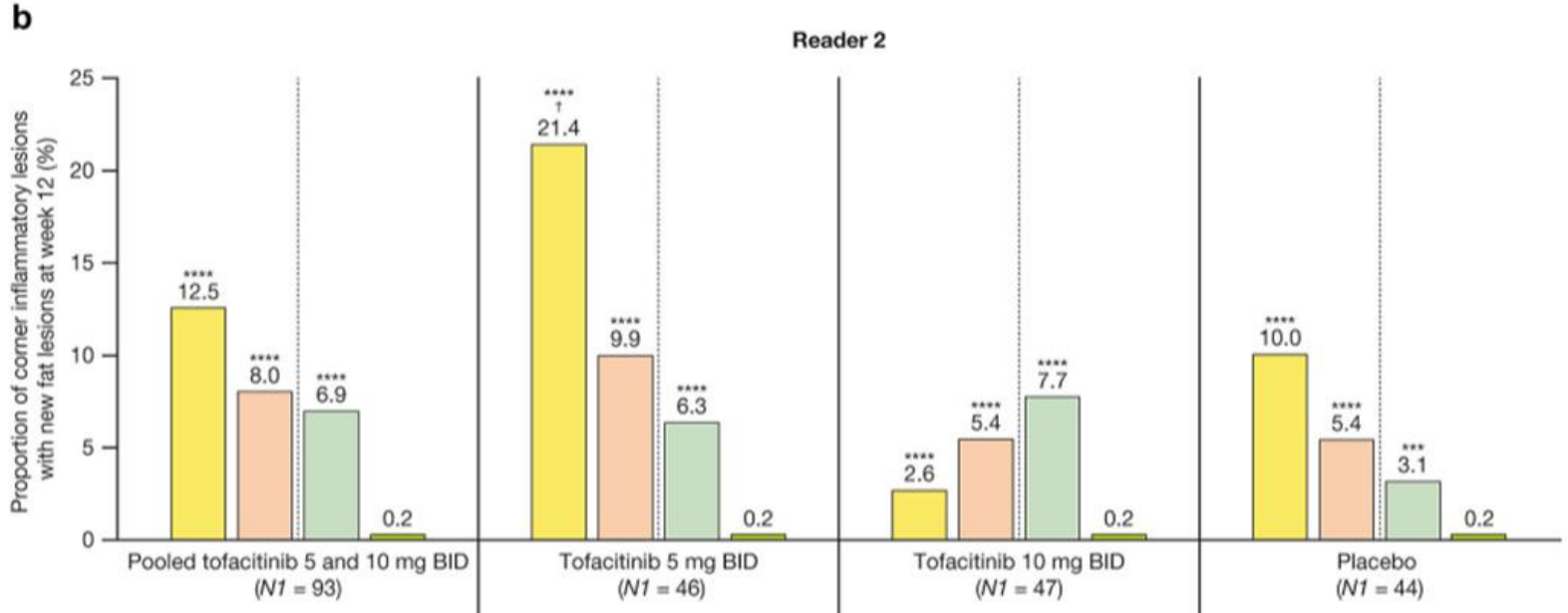
Post hoc analysis της προηγούμενης μελέτης Επανεκτίμηση MRI ασθενών από 2 ακτινολόγους σύμφωνα με το

Canada–Denmark (CANDEN) MRI scoring system

Assessment of inflammatory and structural changes in all spinal areas that can be affected in AS


Tofacitinib 5 mg BID (N1 = 46)
Tofacitinib 10 mg BID (N1 = 47)
Pooled tofacitinib 5 and 10 mg BID (N1 = 93)
Placebo (N1 = 44)
a
Vertebral body inflammation subscore
b
Posterior elements inflammation subscore
c
Corner inflammation subscore
d
Non-corner inflammation subscore
e
Facet joint inflammation subscore
f
Posterolateral[a] inflammation subscore
Change from baseline to week 12, LS mean (SE)
2
0
−2
−4
−6
−8
−5.14 (0.85) ****
−4.31 (0.84) ***
−4.72 (0.60) ****
−0.05 (0.87)
−2.04 (0.31) ****
−1.81 (0.31) ****
−1.92 (0.22) ****
0.37 (0.32)
−3.07 (0.53) ****
−2.44 (0.52) **
−2.75 (0.37) ****
−0.01 (0.54)
−0.95 (0.27) *
−0.88 (0.27)
−0.91 (0.19) *
−0.19 (0.28)
−0.54 (0.11) ****
−0.57 (0.11) ****
−0.55 (0.08) ****
0.08 (0.11)
−2.65 (0.39) ****
−2.26 (0.38) ****
−2.45 (0.27) ****
0.47 (0.40)





MRI
βασικό εργαλείο διάγνωσης ΑΣ
Υποκειμενική η ανάγνωση MRI

Εν προκειμένω
ΣΥΜΦΩΝΙΑ ΚΑΙ 2 ΑΚΤΙΝΟΛΟΓΩΝ
Tofacitinib > placebo
Ως προς μείωση φλεγμονής σε MRI

Με το CANDEN score
(πιο αναλυτικό συγκριτικά
με άλλα scores)

Νεότερα δεδομένα για tofacitinib σε ΑΣ

Chang and Wang *BMC Rheumatology* (2024) 8:3
https://doi.org/10.1186/s41927-024-00373-y

BMC Rheumatology

RESEARCH Open Access

The efficacy of tofacitinib combined with bDMARDs in the treatment of ankylosing spondylitis patients with inadequate response to bDMARDs: a retrospective study

Jie Chang[1] and Gang Wang[1*]

15 ΑΣ ασθενεις
με **υψηλή** ενεργότητα νόσου

Bdmard + tofa

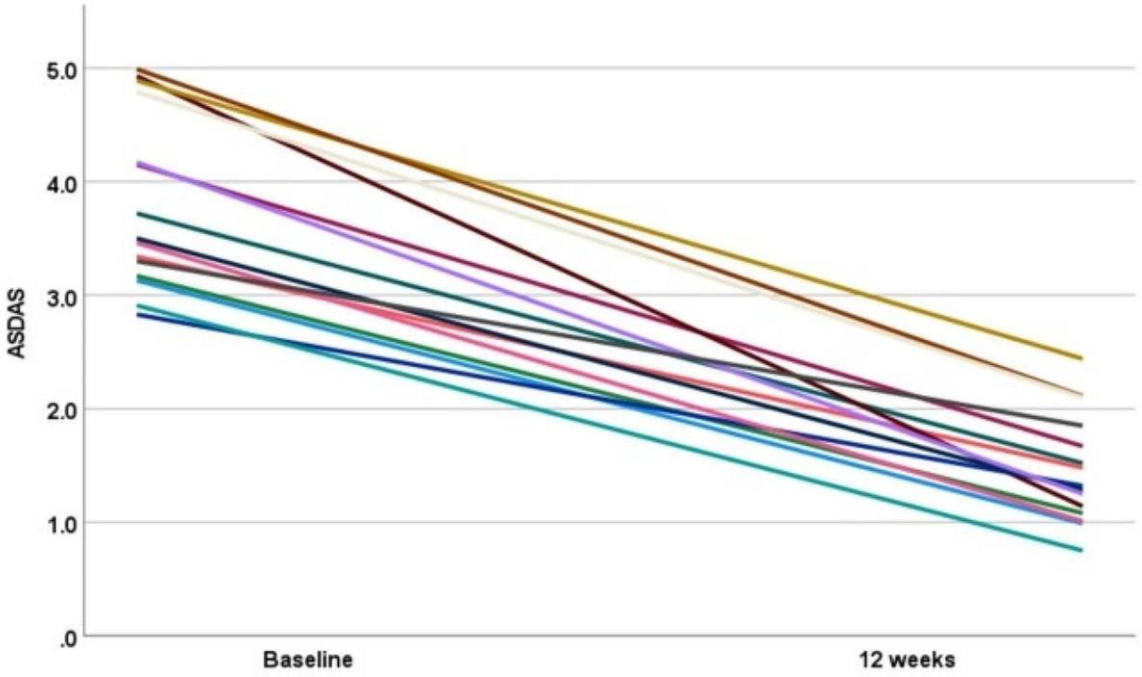
ΓΙΑ ***12 ΒΔΟΜΑΔΕΣ***

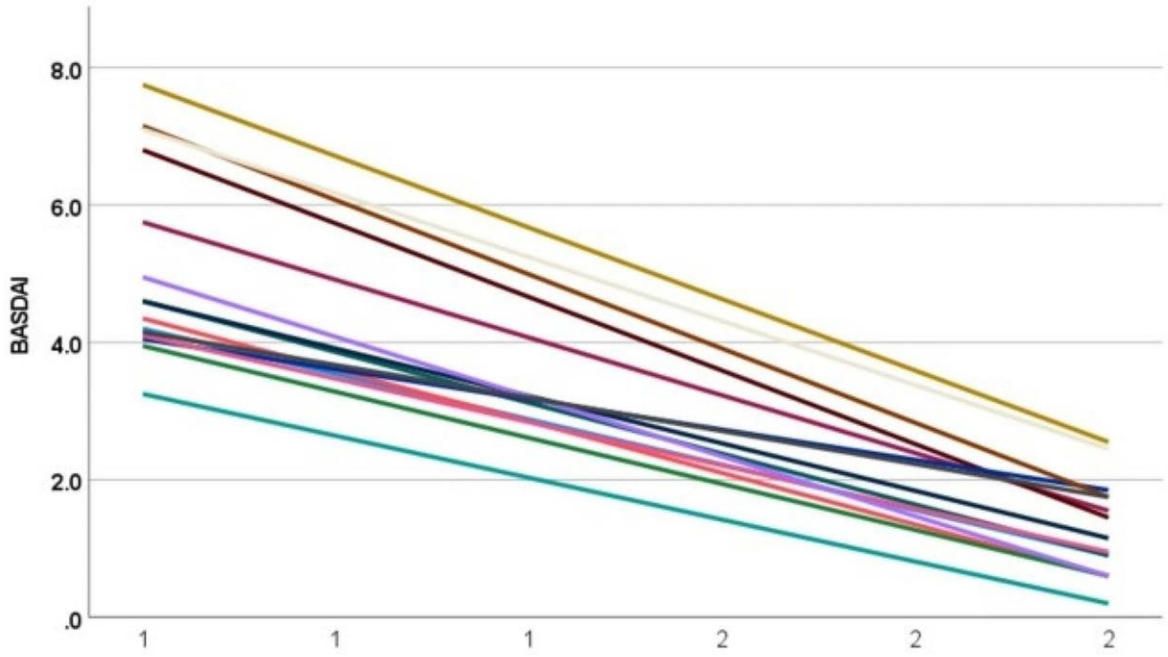
Bdmard + tofacitinib
ΕΠΙΛΟΓΗ ΑΣΘΕΝΩΝ

Table 1 Baseline information of patients. ETN: etanercept; ADA: adalimumab; INF: infliximab; SEC: secukinumab

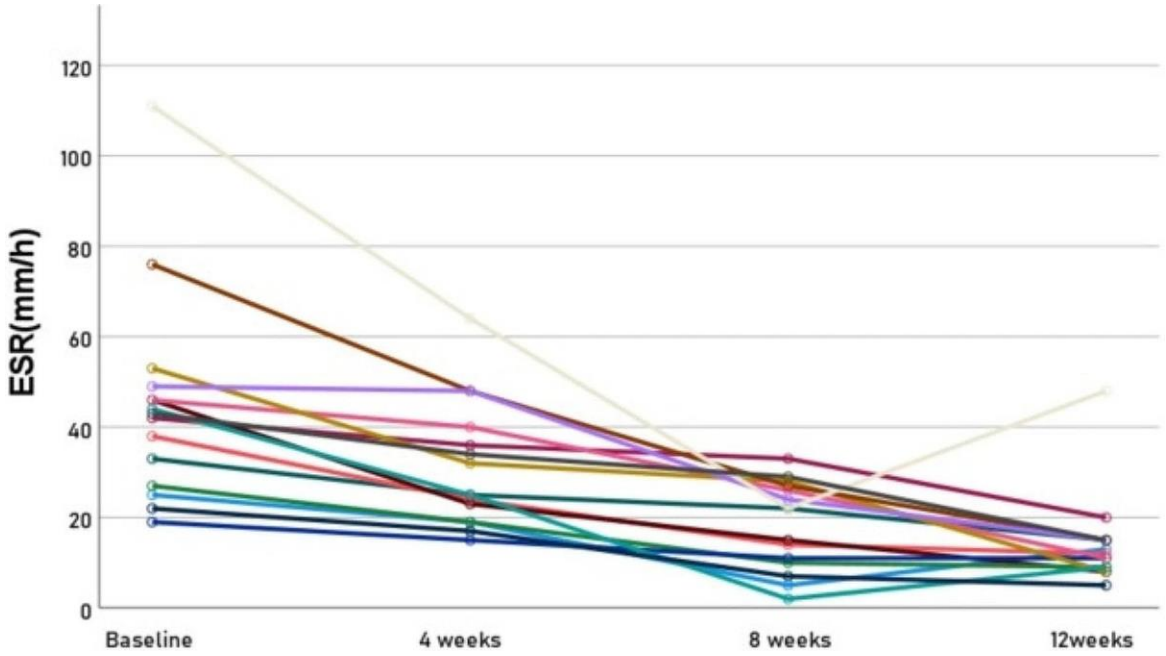
Patient number	Sex	Age	Baseline bDMARD	Baseline ESR(mm/h)	Baseline CRP(mg/L)	Baseline BASDAI	Baseline ASDAS-CRP
1	Female	31	ETN	25	13.3	4.20	3.13
2	Male	25	ETN	33	36.1	4.60	3.72
3	Female	28	ADA	42	33.0	5.75	4.15
4	Female	22	ADA	38	22.2	4.35	3.34
5	Male	21	INF	46	64.8	6.80	4.93
6	Male	37	SEC	27	18.8	3.95	3.17
7	Male	30	INF	19	10.6	4.05	2.83
8	Male	42	ETN	46	28.0	4.10	3.46
9	Male	28	INF	53	31.1	7.75	4.89
10	Female	33	SEC	44	20.2	3.25	2.91
11	Male	26	SEC	22	22.7	4.60	3.50
12	Male	44	ADA	76	56.4	7.15	4.99
13	Male	33	ADA	49	34.3	4.95	4.17
14	Male	23	ETN	111	44.9	7.10	4.79
15	Male	26	ADA	43	20.6	4.15	3.30

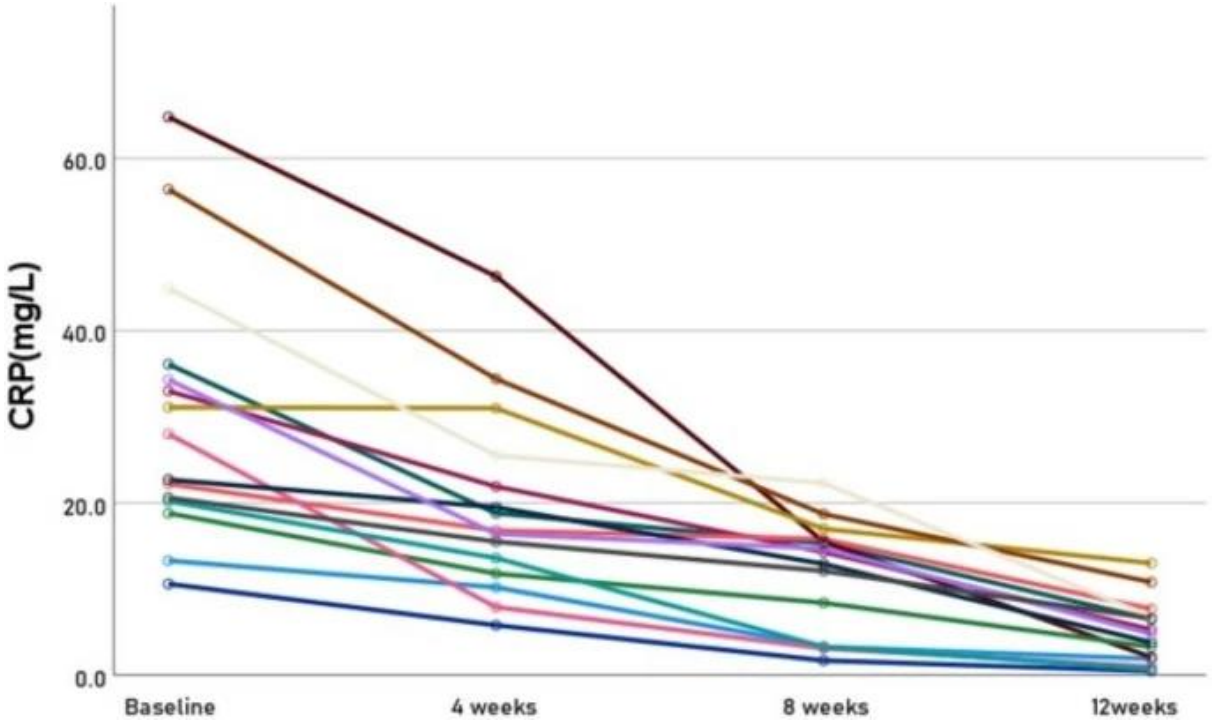
Bdmard+ tofactinib ΑΠΟΤΕΛΕΣΜΑΤΙΚΟΤΗΤΑ





Bdmard+ tofactinib ΑΠΟΤΕΛΕΣΜΑΤΙΚΟΤΗΤΑ





Bdmard+ tofactinib
ΑΠΟΤΕΛΕΣΜΑΤΙΚΟΤΗΤΑ + ΑΣΦΑΛΕΙΑ

Table 2 Changes of BASDAI, ASDAS-CRP, ESR and CRP

		BASDAI	ASDAS-CRP	ESR(mm/h)	CRP(mg/L)
All patients	**Baseline**	5.11 ± 1.42(3.25 ~ 7.75)	3.82 ± 1.47(2.83 ~ 4.99)	44.93 ± 23.20(19 ~ 111)	30.47 ± 15.30(10.6 ~ 64.8)
	Week 4			31.27 ± 13.91(15 ~ 64)	19.69 ± 10.86(5.8 ~ 46.3)
	Week 8			18.33 ± 9.79(2 ~ 33)	11.89 ± 6.42(1.7 ~ 22.3)
	Week 12	1.28 ± 0.70(0.20 ~ 2.55)	1.47 ± 0.48(0.75 ~ 2.44)	14.27 ± 10.07(5 ~ 48)	4.99 ± 3.69(0.5 ~ 13.0)
	P(week 4, 8, 12 vs. Baseline)	**< 0.001**	**< 0.001**	0.060, **< 0.001, < 0.001**	**0.034, < 0.001, < 0.001**
Etanercept group	**Baseline**	5.00 ± 1.42(4.10 ~ 7.10)	3.78 ± 0.72(3.13 ~ 4.79)	53.75 ± 39.14(25 ~ 111)	30.58 ± 13.43(13.3 ~ 44.9)
	Week 4			37.00 ± 20.05(19 ~ 64)	15.60 ± 8.10(7.9 ~ 25.5)
	Week 8			18.75 ± 9.36(5 ~ 26)	11.00 ± 9.45(3.1 ~ 22.3)
	Week 12	1.30 ± 0.77(0.90 ~ 2.45)	1.41 ± 0.52(0.99 ~ 2.10)	21.75 ± 17.58(11 ~ 48)	4.05 ± 3.03(1.0 ~ 6.8)
	P(week 4, 8, 12 vs. Baseline)	**0.007**	**0.002**	0.475, 0.133, 0.186	0.105, 0.054, **0.008**
Infliximab group	**Baseline**	6.20 ± 1.92(4.05 ~ 7.75)	4.22 ± 1.20(2.83 ~ 4.93)	39.33 ± 17.95(19 ~ 53)	35.50 ± 27.37(10.6 ~ 64.8)
	Week 4			23.33 ± 8.50(15 ~ 32)	27.70 ± 20.45(5.8 ~ 46.3)
	Week 8			18.00 ± 8.89(11 ~ 28)	11.40 ± 8.43(1.7 ~ 17.0)
	Week 12	1.95 ± 0.56(1.45 ~ 2.55)	1.63 ± 0.70(1.14 ~ 2.44)	9.00 ± 1.73(8 ~ 11)	5.20 ± 6.80(0.5 ~ 13.0)
	P(week 4, 8, 12 vs. Baseline)	**0.021**	**0.032**	0.235,0.139, 0.098	0.713, 0.219, 0.136
Adalimum-ab group	**Baseline**	5.27 ± 1.22(4.15 ~ 7.15)	3.99 ± 0.70(3.30 ~ 4.99)	49.60 ± 15.27(38 ~ 76)	33.30 ± 14.31(20.6 ~ 56.4)
	Week 4			38.00 ± 10.20(24 ~ 48)	21.00 ± 7.90(15.5 ~ 34.4)
	Week 8			25.40 ± 7.16(14 ~ 33)	15.12 ± 2.41(12.1 ~ 18.7)
	Week 12	1.25 ± 0.60(0.60 ~ 1.75)	1.67 ± 0.33(1.25 ~ 2.11)	15.40 ± 2.88(12 ~ 20)	7.04 ± 2.39(4.8 ~ 10.8)
	P(week 4, 8, 12 vs. Baseline)	**< 0.001**	**< 0.001**	0.196, **0.012, 0.001**	0.131, **0.023**, **0.004**
Secukinum-ab group	**Baseline**	3.93 ± 0.68(3.25 ~ 4.60)	3.19 ± 0.30(2.91 ~ 3.50)	31.00 ± 11.53(22 ~ 44)	20.57 ± 1.98(18.8 ~ 22.7)
	Week 4			20.33 ± 4.16(17 ~ 25)	14.97 ± 4.03(11.8 ~ 19.5)
	Week 8			6.33 ± 4.04(2 ~ 10)	8.20 ± 4.80(3.3 ~ 12.9)
	Week 12	0.65 ± 0.48(0.20 ~ 1.15)	1.04 ± 0.27(0.75 ~ 1.28)	7.67 ± 2.31(5 ~ 9)	2.60 ± 1.66(0.7 ~ 3.8)
	P(week 4, 8, 12 vs. Baseline)	**0.002**	**< 0.001**	**0.206, 0.025, 0.026**	0.097, **0.015**, **< 0.001**

<u>Στις 12 βδομάδες: (συνδυαστική θεραπεία)</u>

- ΔΕΝ αναφέρονται ανεπιθύμητες ενέργειες

Tofacitinib σε ΨΑ

Mease *et al. Arthritis Research & Therapy* (2023) 25:153
https://doi.org/10.1186/s13075-023-03108-5

Arthritis Research & Therapy

RESEARCH Open Access

Efficacy of tofacitinib on enthesitis in patients with active psoriatic arthritis: analysis of pooled data from two phase 3 studies

Philip J. Mease[1*], Ana-Maria Orbai[2], Oliver FitzGerald[3], Mohamed Bedaiwi[4], Dona L. Fleishaker[5], Rajiv Mundayat[6], Pamela Young[7] and Philip S. Helliwell[8]

post hoc analysis (Opal Broaden, Opal beyond)

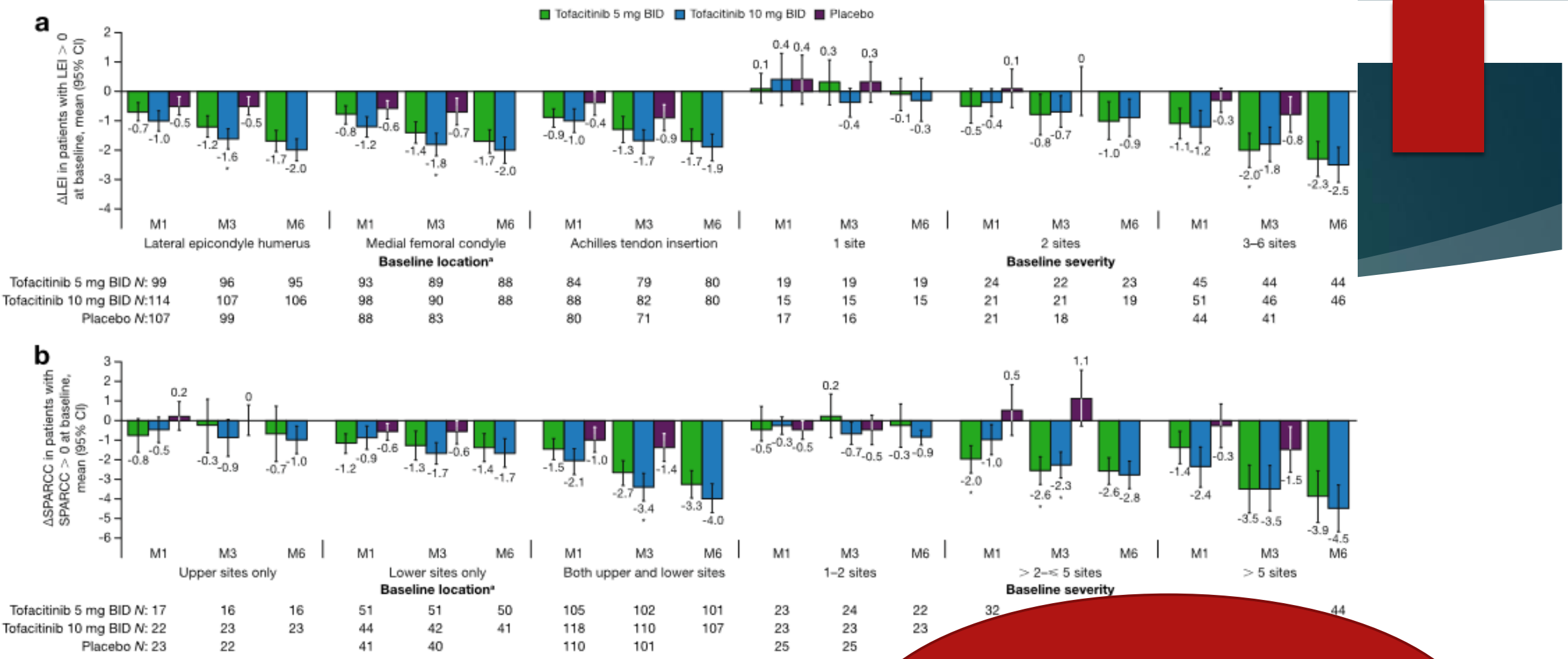


Fig. 2 Change from baseline in LEI/SPARCC (patients with LEI > 0/SPARCC > 0 at baseline). *Indic
does not overlap with the 95% CI for placebo. [a]Each site was assessed bilaterally, and results w
daily; CI, confidence interval; LEI, Leeds Enthesitis Index; M, month; *N*, total number of patient
or number of affected sites at baseline; SPARCC, Spondyloarthritis Research Consortium of Ca

Tofacitinib >>> placebo
ως προς λύση ενθεσίτιδας

Tofacitinib σε ΨΑ

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

N Engl J Med 2017;377:1537-50.
DOI: 10.1056/NEJMoa1615975

Tofacitinib or Adalimumab versus Placebo for Psoriatic Arthritis

P. Mease, S. Hall, O. FitzGerald, D. van der Heijde, J.F. Merola, F. Avila-Zapata, D. Cieślak, D. Graham, C. Wang, S. Menon, T. Hendrikx, and K.S. Kanik

OPAL Broaden

PsA κατά τα CASPAR κριτηρια
Αποτυχία σε τουλ 1 DMARD
(όχι προηγούμενη έκθεση σε bdamrd)

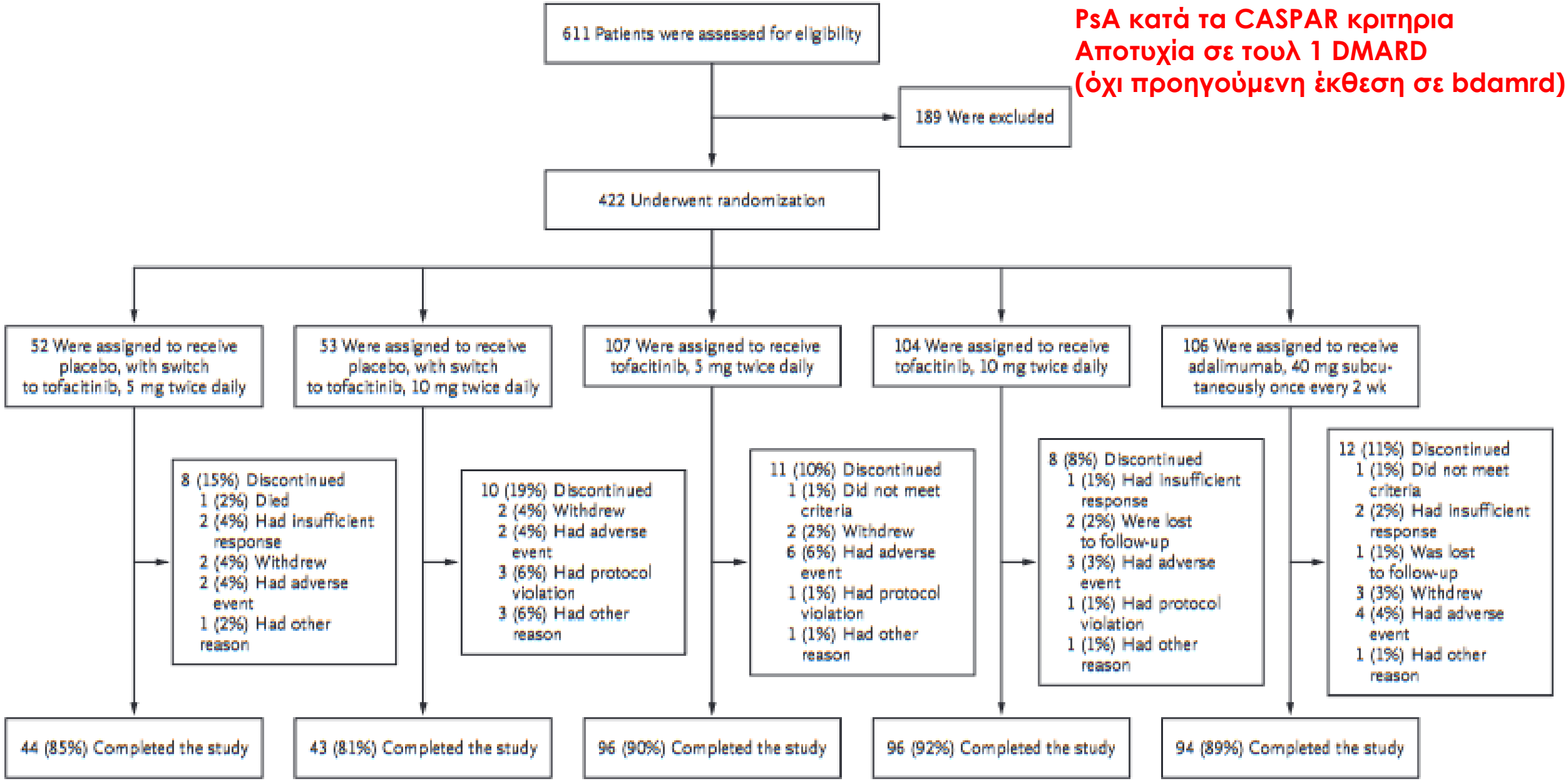
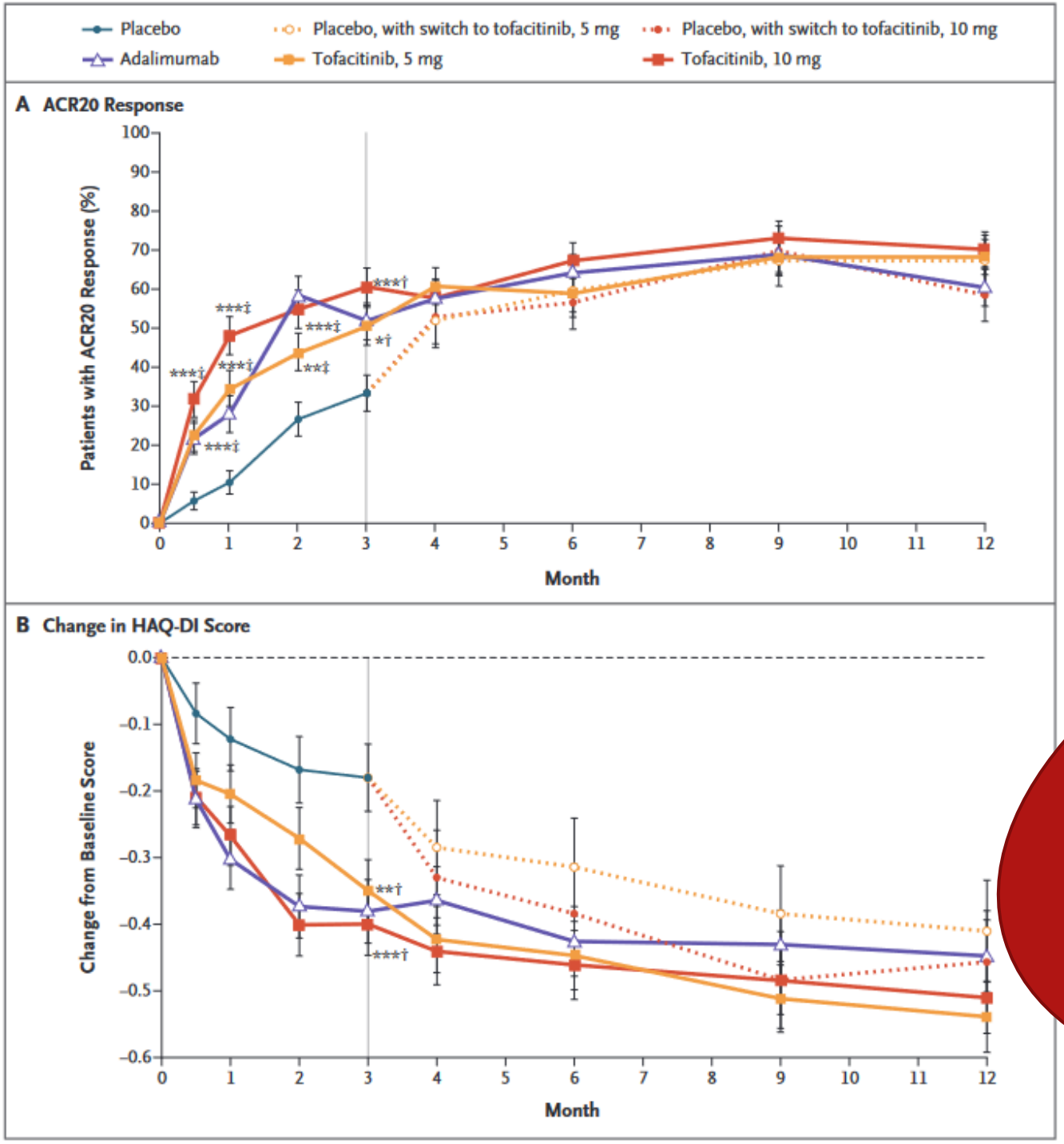


Figure 1. Screening, Randomization, and Follow-up of the Patients.

A total of five patients in the pooled placebo group, six in the 5-mg tofacitinib group, one in the 10-mg tofacitinib group, and four in the adalimumab group discontinued the trial in



Σε ΨΑ
(τον 3ο μήνα θεραπείας)
με μη καλή ανταπόκριση σε
DMARD :
tofacitinib>> placebo

ΑΕ πιο συχνές υπό tofacitinib

Tofacitinib σε ΙΦΝΕ

Ther Adv Gastroenterol

2019, Vol. 12: 1–10

DOI: 10.1177/1756284819848631

Table 1. Efficacy data on tofacitinib in patients with ulcerative colitis.

Study	Population	Primary endpoint	
Phase II trial, Sandborn *et al.*[10]		Clinical response at 8 weeks	
	TFB 0.5 mg b.i.d. (31 pts)	32% ($p = 0.39$)	
	TFB 3 mg b.i.d. (33 pts)	48% ($p = 0.55$)	
	TFB 10 mg b.i.d. (33 pts)	61% ($p = 0.10$)	
	TFB 15 mg b.i.d. (49 pts)	78% ($p < 0.001$)	
	PBO (48 pts)	42%	
OCTAVE 1[11]		Remission at 8 weeks	
	TFB 10 mg b.i.d. (476 pts)	18.5% ($p = 0.007$)	
	PBO (122 pts)	8.2%	
OCTAVE 2[11]		Remission at 8 weeks	
	TFB 10 mg b.i.d. (429 pts)	16.6% ($p < 0.001$)	
	PBO (112 pts)	3.6%	
OCTAVE Sustain[11]		Remission at 52 weeks	
	TFB 5 mg b.i.d. (198 pts)	34.3% ($p < 0.001$)	
	TFB 10 mg b.i.d. (197 pts)	40.6% ($p < 0.001$)	
	PBO (198 pts)	11.1%	
Real-world experience, Weisshof *et al.*[15]	TFB 5/10 mg b.i.d (58 pts)	Clinical response at 8 weeks 36%	Clinical remission at 8 weeks 33%

TFB, tofacitinib; PBO, placebo; b.i.d., twice daily; pts, patients.

Tofacitinib σε ΙΦΝΕ

Table 2. Safety data on tofacitinib in patients with ulcerative colitis.

	OCTAVE 1[11]		OCTAVE 2[11]		OCTAVE Sustain[11]		
AEs, *n* (%)	PBO (*n* = 122)	TFB (*n* = 476)	PBO (*n* = 112)	TFB (*n* = 429)	PBO (*n* = 198)	TFB 5 mg b.i.d. (*n* = 198)	TFB 10 mg b.i.d. (*n* = 198)
Pts with AEs	73 (59.8%)	269 (56.5%)	59 (52.7 %)	232 (54.1%)	149 (75.3%)	143 (72.2%)	156 (79.6%)
Pts with SAEs	5 (4.1%)	16 (3.4%)	9 (8.0%)	18 (4.2%)	13 (6.6%)	10 (5.1%)	11 (5.6%)

AEs, adverse events; SAEs, severe adverse events; PBO, placebo; TFB, tofacitinib; b.i.d., twice daily; Pts, patients.

D'Amico et al, Ther Adv Gastroenterol 2019

Table 3. Tofacitinib dose adjustments in special conditions.

Condition	Value	Recommendation
Low absolute lymphocyte count (ALC)	ALC ⩾ 750 ALC 500–750 ALC < 500	Maintain Reduce to 5 mg twice daily Discontinue
Low absolute neutrophil count (ANC)	ANC ⩾ 1000 ANC 500–1000 ANC < 500	Maintain Reduce to 5 mg twice daily Discontinue
Low hemoglobin value	Decrease ⩽ 2 g/dl and Hb ⩾ 9.0 g/dl Decrease > 2 g/dl or Hb < 8.0 g/dl	Maintain Interrupt until Hb normalizes
Hepatic impairment	Child Pugh A	No dose adjustment
	Child Pugh B	Reduce to 5 mg once daily if 5 mg twice daily is the indicated dose in the absence of hepatic impairment Reduce to 5 mg twice daily if 10 mg twice daily is the indicated dose in the absence of hepatic impairment
	Child Pugh C	Contraindicated
Renal impairment	Mild: Cr. clearance 50–80 ml/min	No dose adjustment
	Moderate: Cr. clearance 30–49 ml/min	No dose adjustment
	Severe: Cr. clearance < 30 ml/min	Reduce to 5 mg once daily when the indicated dose in the presence of normal renal function is 5 mg twice daily Reduce to 5 mg twice daily when the indicated dose in the presence of normal renal function is 10 mg twice daily Patients with severe renal impairment should remain on a reduced dose even after hemodialysis

D'Amico et al, Ther Adv Gastroenterol 2019

Tofacitinib σε ΙΦΝΕ

Table 4. Tofacitinib dose adjustments in case of drug co-administration.

Co-administered drug	Recommendation
Ketoconazol (*CYP3A* inhibitor)	Reduce tofacitinib dose*
Fluconazol (*CYP3A* and *CYP2C19* inhibitor)	Reduce tofacitinib dose*
Rifampicin (CYP inducer)	May decrease efficacy
Methotrexate	No dose adjustme
Tacrolimus	Combined use s
Cyclosporine	Combined use sh
Co-administration of tofacitinib did not have an effect on the pharmacokinetics of ora levonorgestrel and ethinyl estradiol, in healthy female volunteers	

*Tofacitinib dose should be reduced to 5 mg twice daily in patients receiving 10 mg twice daily and reduced to daily in patients receiving 5 mg twice daily.

Η χρήση tofacitinib
για την θεραπεία
Ελκώδους Κολίτιδας
είναι μια νέα θεραπευτική
στρατηγική
και αυξάνει την πιθανότητα
αντιμετώπισης της

D'Amico et al, Ther Adv Gastroenterol 2019

2ος Jak αναστολέας σε SpA

- Upadacitinib

Upadacitinib:
1. σε όλο το Φάσμα της axSpA
2. διαφορετικούς πληθυσμούς ασθενών

	SELECT-AXIS 1[1]	Placebo-Controlled Efficacy and Safety of Upadacitinib Through One Year in Patients With Non-Radiographic Axial Spondyloarthritis	SELECT-AXIS 2 Study 2[3]
	SELECT-AXIS 1 Upadacitinib	Filip Van den Bosch,[1] Atul Deodhar,[2] Denis Poddubnyy,[3] Walter P. Maksymowych,[4] Désirée van der Heijde,[5] Tae-Hwan Kim,[6] Mitsumasa Kishimoto,[7] Xenofon Baraliakos,[8] Yuanyuan Duan,[9] Kristin D'Silva,[9] Peter Wung,[9] In-Ho Song[9]	SELECT-AXIS 2 Upadacitinib
Patients	bDMARD-naïve AS	bDMARD-IR AS	nr-axSpA (bDMARD-naïve and bDMARD-IR)
Treatment arms	• UPA 15 mg QD for 104 weeks • PBO for 14 weeks followed by UPA 15 mg QD for 90 weeks	• UPA 15 mg QD for 104 weeks • PBO for 14 weeks followed by UPA 15 mg QD for 90 weeks	• UPA 15 mg QD for 104 weeks • PBO for 52 weeks followed by UPA 15 mg QD for 52 weeks
Sample size, N	187	420	314
Primary endpoint	ASAS40 at Week 14 ✓	ASAS40 at Week 14 ✓	ASAS40 at Week 14 ✓

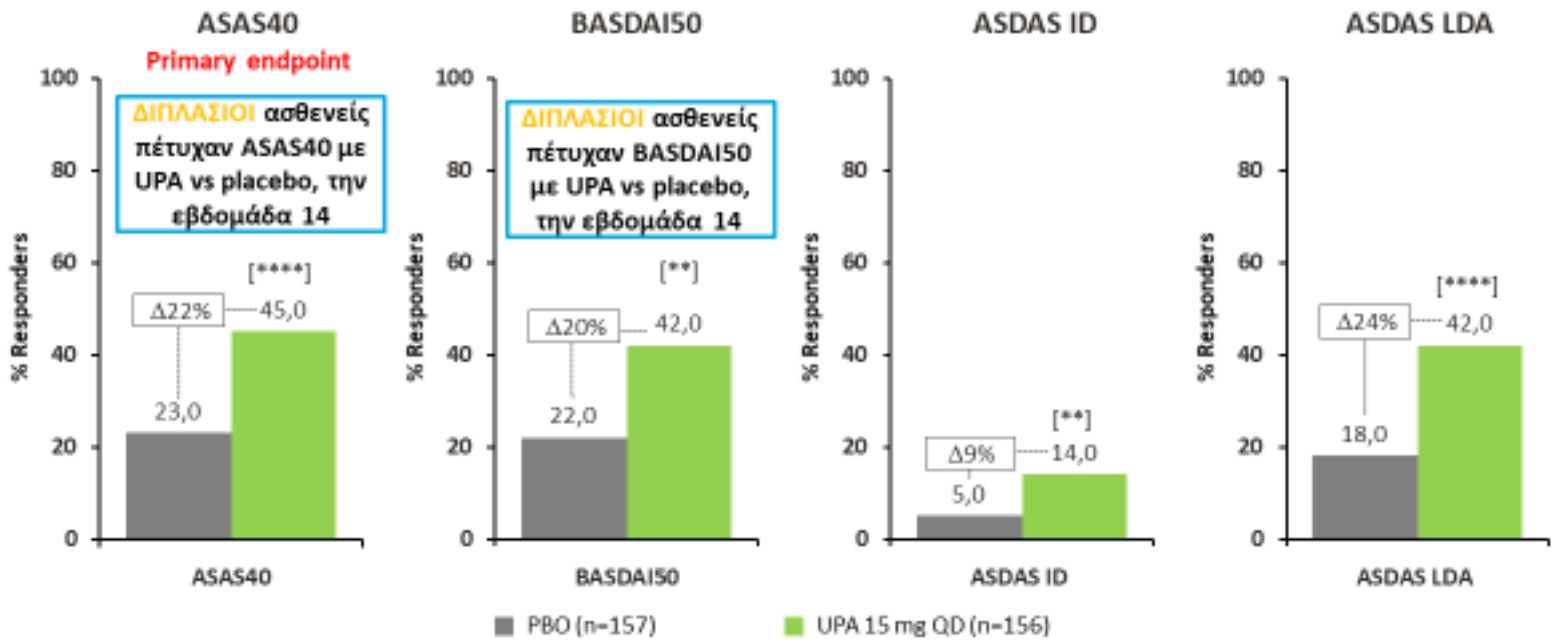
AS, ankylosing spondylitis; ASAS40, ≥40% improvement in Assessment of SpondyloArthritis International Society; axSpA, axial spondyloarthritis; b, biologic; DMARD, disease-modifying anti-rheumatic drug; IR, inadequate response; nr, non-radiographic; NSAID, non-steroidal anti-inflammatory drug; PBO, placebo; QD, once daily; UPA, upadacitinib.

Adapted from:
1. van der Heijde D, et al. Lancet 2019;394(10214):2108-2117.
2. van der Heijde et al. Ann Rheum Dis 2022;81(11):1515-1523.
3. Deodhar A., et al. Lancet 2022;400:369-379.

Upadacitinib
Απάντηση στην 14η βδομάδα

Significantly more patients achieved multiple stringent disease activity targets with UPA versus PBO at Week 14 (NRI)

ΕΠΙΤΕΥΞΗ ΕΛΕΓΧΟΥ ΤΗΣ ΝΟΣΟΥ

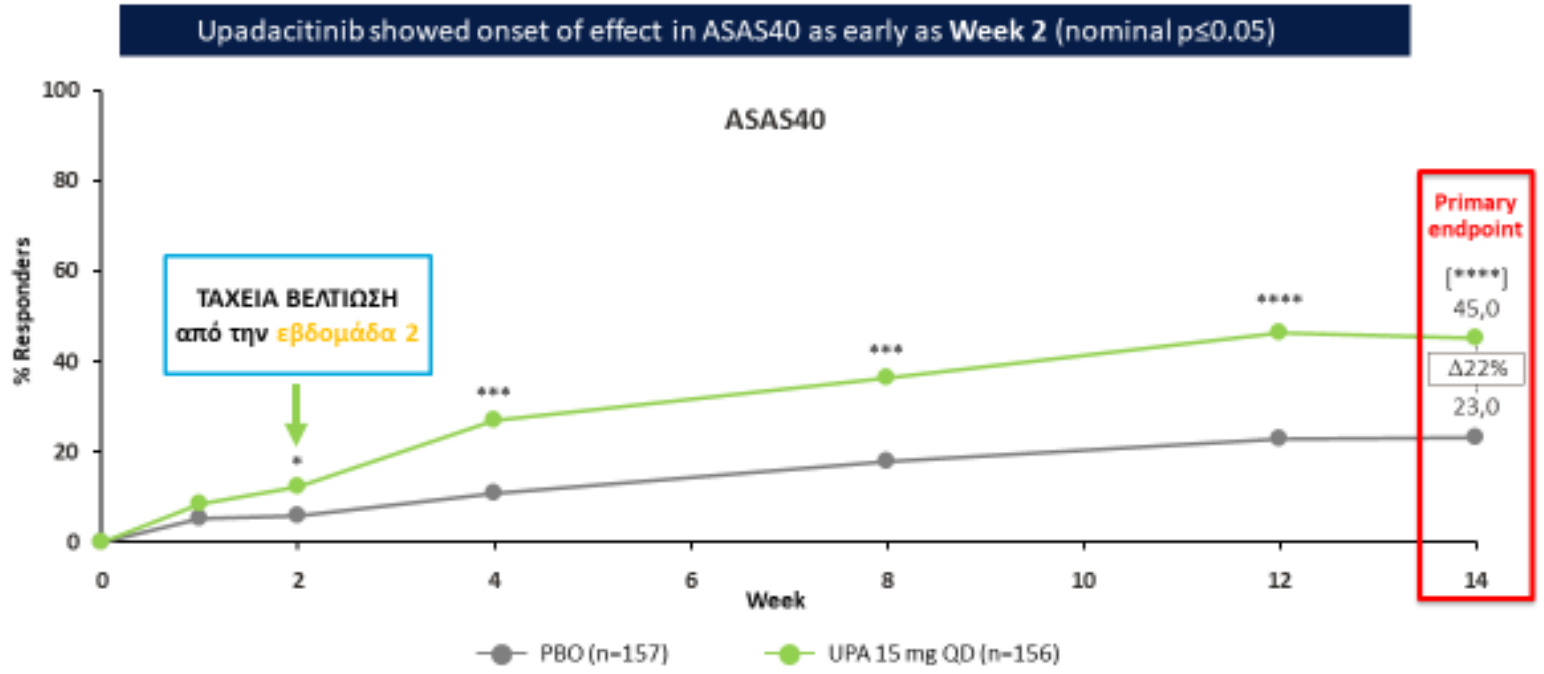


Deodhar A., et al. Lancet 2022;400:369-379.

Comparisons adjusted for multiplicity: [**] p<0.01, [****] p<0.0001 for UPA vs PBO. ASAS, Assessment of SpondyloArthritis International Society; ASAS40, 240% improvement in Assessment of SpondyloArthritis International Society; ASDAS, Ankylosing Spondylitis Disease Activity Score; axSpA, axial spondyloarthritis; ID, inactive disease; LDA, low disease activity; nr, non-radiographic; NRI, non-responder imputation; PBO, placebo; PR, partial remission; QD, once daily; UPA, upadacitinib.

Upadacitinib
Ταχεία έναρξη δράσης

UPA significantly improved signs and symptoms (ASAS40) through Week 14 with a **rapid onset of effect** (NRI) vs PBO

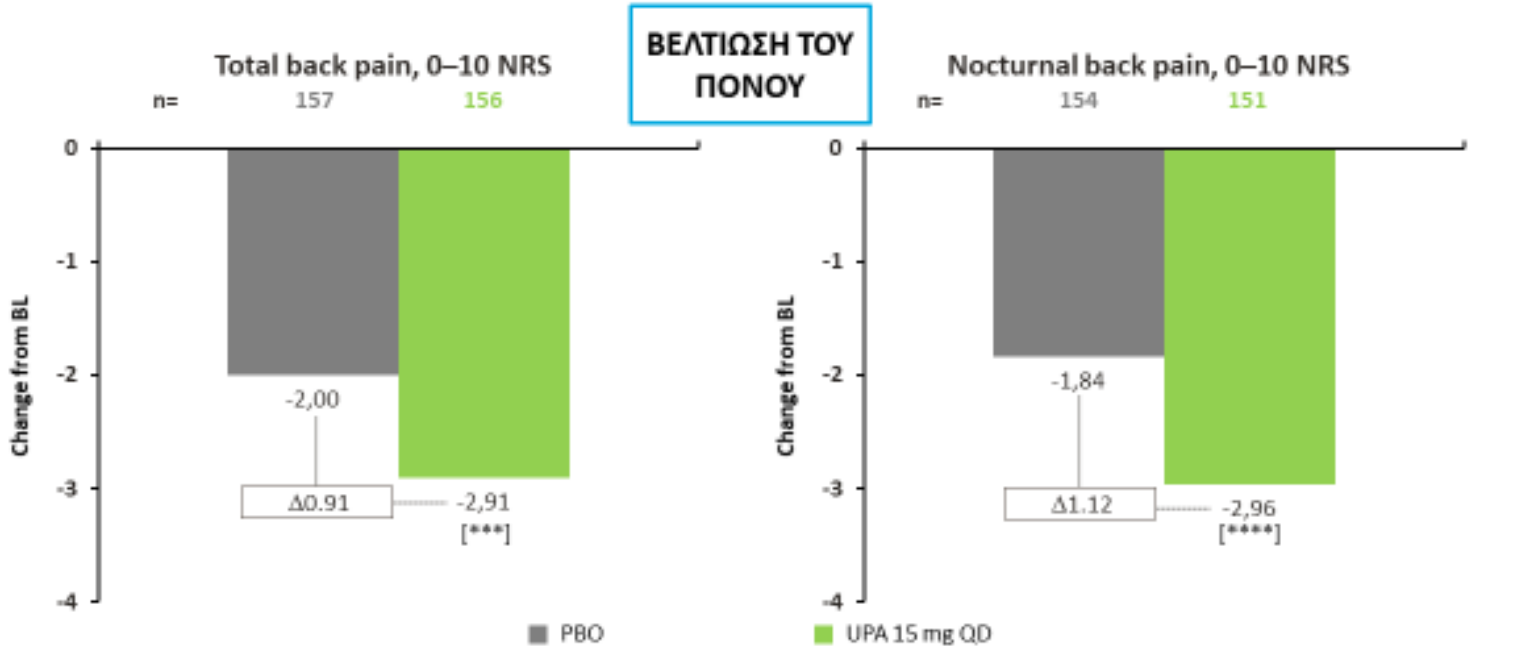


Comparison adjusted for multiplicity: [****] p<0.0001 for upadacitinib vs placebo. Comparisons not adjusted for multiplicity: *nominal p<0.05, ***nominal p<0.001, ****nominal p<0.0001 for upadacitinib vs placebo. ASAS40, 40% improvement in Assessment of SpondyloArthritis International Society; NRI, non-responder imputation; PBO, placebo; QD, once daily; UPA, upadacitinib.

Deodhar A., et al. Lancet 2022;400:369-379.

Upadacitinib: Βελτίωση πόνου

Statistically significant improvement in multiple types of pain with UPA vs PBO: change from BL in total and nocturnal back pain at Week 14 (MMRM)



Deodhar A., et al. Lancet 2022;400:369-379.

Analysis based on MMRM on AO data. Comparisons adjusted for multiplicity: [***] p<0.001, [****] p<0.0001 for upadacitinib vs placebo. AO, as observed; axSpA, axial spondyloarthritis; BL, baseline; MMRM, mixed-model repeated measures; nr, non-radiographic; NRS, numeric rating score; PBO, placebo; QD, once daily; UPA, upadacitinib.

Upadacitinib: καλό προφίλ ασφάλειας

Καλό προφίλ ασφάλειας με UPA την 14η εβδομάδα

Two AEs leading to discontinuation of the study drug in the PBO arm, and four in the UPA arm

No opportunistic infections, active tuberculosis, lymphopenia, renal dysfunction, gastrointestinal perforation, major adverse cardiovascular events, venous thromboembolic events, inflammatory bowel disease, psoriasis, or deaths were reported with UPA treatment

Patients, n (%)	PBO n=157	UPA 15 mg QD n=156
AEs	72 (46)	75 (48)
Serious AEs*	2 (1.3)	4 (2.6)
AE leading to discontinuation of study drug†	2 (1.3	4 (2.6)
Severe AEs	3 (1.9)	8 (5.1)
COVID-19-related AE	10 (6.4)	8 (5.1)
Infection	36 (23)	36 (23)
Serious infection‡	1 (0.6)	2 (1.3)
Herpes zoster§	1 (0.6)	2 (1.3)
Malignancy with NMSC#	1 (0.6)	0
Hepatic disorder¶	5 (3.2)	4 (2.6)
Anemia‖	0	1 (0.6
Neutropenia**	0	5 (3.2
Uveitis††	0	1 (0.6)

*PBO: hemorrhagic fever with renal syndrome (n=1) and pancreatitis (n=1); UPA: COVID-19 pneumonia (n=1), pyelonephritis (n=1), foot fracture (n=1), and knee osteoarthritis (n=1). †PBO: moderate axSpA (n=1) and mild vomiting (n=1); UPA: moderate axSpA (n=2), moderate headache/mild tremor/severe rash (n=1), and mild abdominal pain/nausea (n=1). ‡PBO: hemorrhagic fever with renal syndrome (n=1); UPA: COVID-19 pneumonia (n=1) and pyelonephritis (n=1). §All herpes zoster events were non-serious, mild or moderate, and limited to one dermatome. Both events on UPA resolved without study drug interruption. #Basal cell carcinoma (n=1). ¶All events of hepatic disorder were non-serious mild or moderate transaminase elevations. One event led to interruption of study drug; none led to study drug discontinuation. ‖Event of anemia was non-serious, transient, and did not lead to study drug discontinuation. **All neutropenia events were non-serious: four were mild or moderate in severity, and one was severe. The event of severe neutropenia occurred at baseline prior to study drug initiation. ††Event of uveitis occurred in a patient with a history of uveitis. AE, adverse event; axSpA, axial spondyloarthritis; GI, gastrointestinal; MACE, major adverse cardiac event; NMSC, non-melanoma skin cancer; nr, non-radiographic; PBO, placebo; QD, once daily; UPA, upadacitinib; VTE, venous thromboembolism.

Deodhar A., et al. Lancet 2022;400:369-379.

Ραγοειδίτιδα και jak αναστολείς;;;;

Meta-Analysis > Arthritis Rheumatol. 2024 May;76(5):704-714. doi: 10.1002/art.42788.
Epub 2024 Apr 13.

Ανάλυση **42** μελετών

Incidence of Uveitis in Patients With Axial Spondylarthritis Treated With Bi… Synthetics: A Systematic R… Analysis

Katie Bechman [1], Zijing Yang [1], Maryam …
Nicky Wilson [1], Sophia Steer [1], Sam Nort…

μονοκλωνικά Abs (Anti-TNF mAbs)
JAK αναστολείς
anti-IL-17

ΙΔΙΑ ΠΡΟΣΤΑΣΙΑ
ως προς εμφάνιση
πρόσθιας ραγοειδίτιδας
σε
AxSpA

Ο ασθενής μας

- Σε ΈΝΑ μήνα
- Καλή ανταπόκριση υπό tofacitinib 5 mg x2

(οσφυαλγία, ενθεσίτιδα)

- Basdai = 3 (από basdai 5,9)
- Εξετάσεις αίματος → χωρίς παθολογικά ευρήματα

  ομαλοποίηση δεικτών φλεγμονής

…Συνέχιση αγωγής

Tofacitinib σε SpA

- Αποτελεσματικό σε ΟΛΟ το φάσμα ΣπΑ
- Ασφαλές σχετικά φάρμακο

Πλέον συχνή η χρήση και upadacitinib

ΕΡΩΤΗΣΕΙΣ - ΣΧΟΛΙΑ ????