Τα δεδομένα του Tofacitinib στις οροθετικές κι οροαρνητικές φλεγμονώδεις αρθρίτιδες

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Διευθύντρια ΕΣΥ
ΓΝΑ 'Γ. Γεννηματάς'

Σύγκρουση συμφερόντων

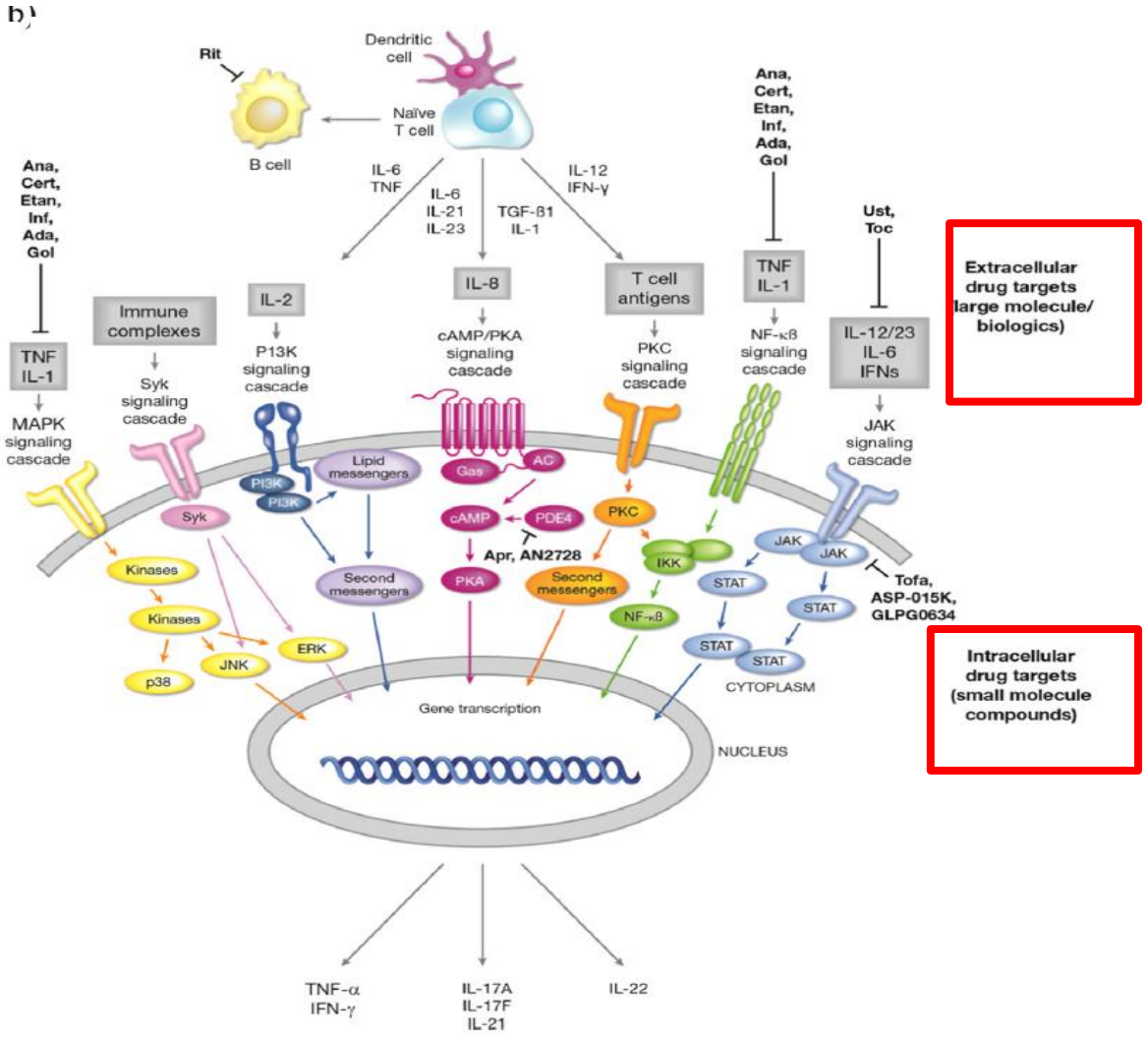
Τιμητικές αμοιβές από τις εταιρείες Lilly, MSD, Abbvie, Pfizer, Aenorasis, Novartis, Amgen, Genesis

Τιμητική αμοιβή από την Pfizer για τη συγκεκριμένη ομιλία
«Η Pfizer έχει ελέγξει το περιεχόμενο ώστε να ανταποκρίνεται στις ειδικές προδιαγραφές της αλλά δεν έχει επιβεβαιώσει ότι οι βιβλιογραφικές παραπομπές έχουν παρατεθεί ορθά».
«Για όλα τα φαρμακευτικά προϊόντα που αναφέρονται παρακαλείσθε να συμβουλεύεστε/συμβουλευτείτε τις εγκεκριμένες Περιλήψεις Χαρακτηριστικών των Προϊόντων»

Περίγραμμα ομιλίας

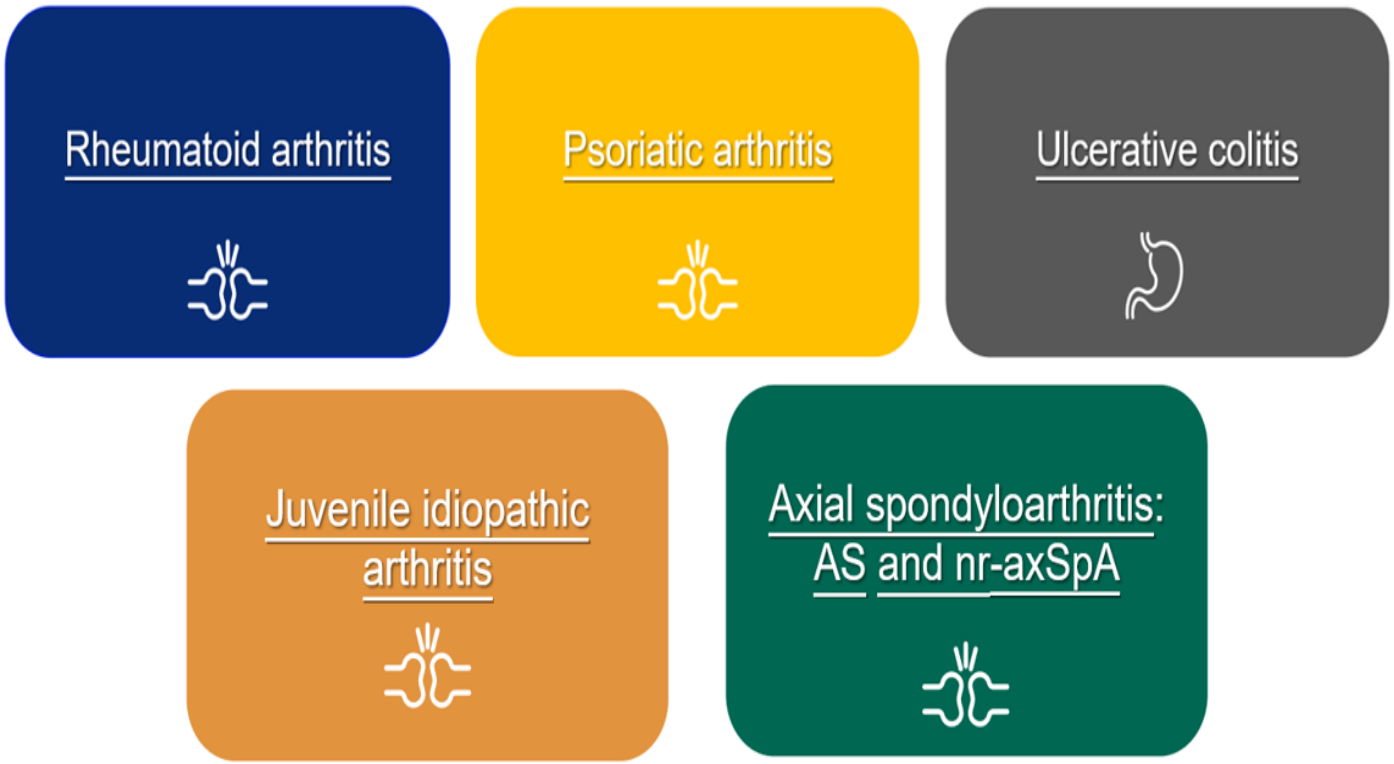
- Ενδείξεις του tofacitinib
- Αποτελεσματικότητα στη ΡΑ
- Αποτελεσματικότητα στις σπονδυλαρθρίτιδες
- Ασφάλεια

Tofacitinib



Coates L, et al. *Semin Arth Rheum 2016;* 46: 291–304

Tofacitinib



1η έγκριση Tofacitinib: ΗΠΑ 2012 (FDA)

Ευρώπη → Ελβετία: 2013

Ευρωπαϊκή Ένωση : 2017 (EMA)

Ελλάδα: 2018 (αποζημίωση από ΕΟΠΥΥ - PA)

2024 (αποζημίωση από ΕΟΠΥΥ- ΑΣ, ΝΙΑ)

Tofacitinib παρατεταμένης αποδέσμευσης 11mg

Φαρμακοκινητική ισοδυναμία

- Το TOFACITINIB 11 mg μια φορά την ημέρα είναι φαρμακοκινητικά ισοδύναμο με το TOFACITINIB 5 mg BID[1]
- Η ημίσεια ζωή του TOFACITINIB 11 mg μια φορά την ημέρα είναι ~6 ώρες και του TOFACITINIB 5 mg BID ~3 ώρες[1]

Πώς να λαμβάνετε το TOFACITINIB 5mg/TOFACITINIB 11mg

- Χορηγείται από το στόμα, με ή χωρίς τροφή. Τα δισκία λαμβάνονται ολόκληρα και ακέραια. Τα δισκία δεν θα πρέπει να συνθλίβονται, να κόβονται, ή να μασώνται.[1]
- Φύλαξη σε θερμοκρασία δωματίου[1]

Συνιστώμενη δοσολογία

- Οι ασθενείς που λαμβάνουν TOFACITINIB 5 mg BID μπορούν να μεταβούν σε TOFACITINIB 11 mg μια φορά την ημέρα, την επόμενη ημέρα από τη λήψη της τελευταίας δόσης του TOFACITINIB 5 mg[1]
- Τόσο το TOFACITINIB 5 mg όσο και το TOFACITINIB 11mg μπορούν να λαμβάνονται με ή χωρίς MTX. Δεν απαιτείται προσαρμογή της δόσης της MTX όταν συνδυάζεται με TOFACITINIB 5mg/11mg[1]

TOFACITINIB 5mg δυο φορές την ημέρα

TOFACITINIB 11mg μια φορά την ημέρα

Τα δισκία δεν απεικονίζονται σε πραγματικό μέγεθος.

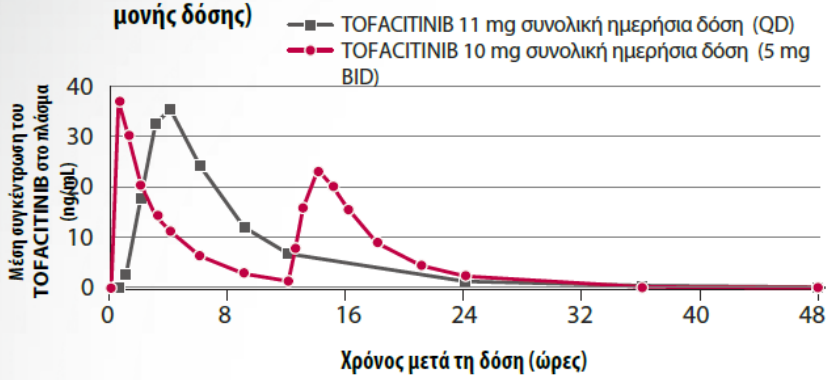
Νέο δισκίο παρατεταμένης αποδέσμευσης, με δοσολογία ΜΙΑ ΦΟΡΑ ΤΗΝ ΗΜΕΡΑ[1]

1. Περίληψη Χαρακτηριστικών Προϊόντος Xeljanz 07/2024

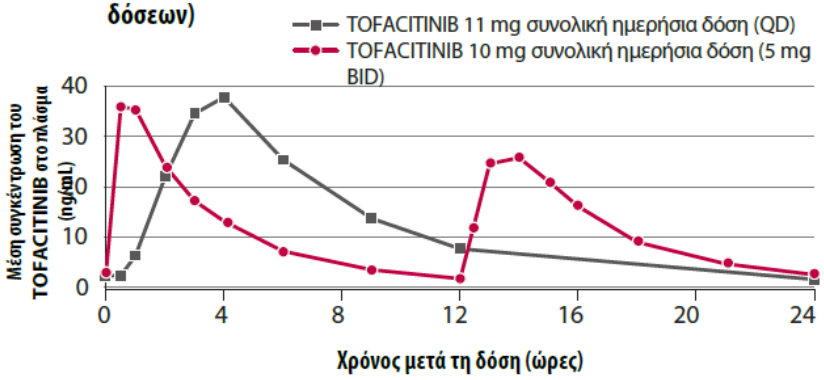
ΜΕΛΕΤΗ ΒΙΟΪΣΟΔΥΝΑΜΙΑΣ

Το TOFACITINIB 11 mg μια φορά την ημέρα και το TOFACITINIB 5 mg BID παρουσίασαν φαρμακοκινητική ισοδυναμία (AUC και C_{max}) σε μελέτες μιας δόσης και πολλαπλών δόσεων[1]

Προφίλ μέσης συγκέντρωσης του TOFACITINIB στο πλάσμα σε σχέση με το χρόνο την Ημέρα 1 (συνθήκες μονής δόσης)



Προφίλ μέσης συγκέντρωσης του TOFACITINIB στο πλάσμα σε σχέση με το χρόνο την Ημέρα 5 (συνθήκες πολλαπλών δόσεων)



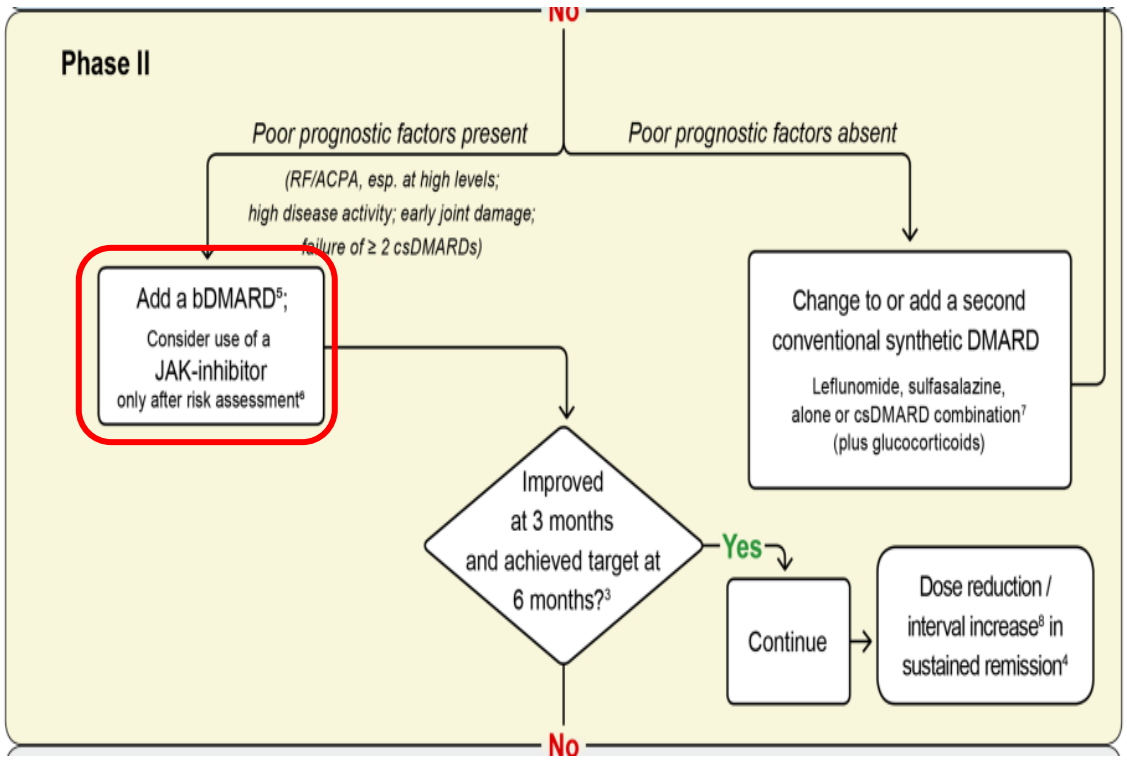
Προσαρμογή από Lamba et al. 2016.

- **Η AUC και η C_{max} μετά από μονή δόση και πολλαπλές δόσεις ήταν ισοδύναμες μεταξύ του TOFACITINIB 11 mg άπαξ ημερησίως και του TOFACITINIB 5 mg BID[1]**
  - Η μέγιστη συγκέντρωση στο πλάσμα (C_{max}) επιτυγχάνεται στις 4 ώρες με το TOFACITINIB 11mg και σε 0,5 έως 1 ώρα με το TOFACITINIB 5mg BID
- **Η ημίσεια ζωή είναι ~6 ώρες με το TOFACITINIB 11 mg κ αι ~3 ώρες με το TOFACITINIB 5mg BID[1]**
  - Οι συγκεντρώσεις στη σταθερή κατάσταση του TOFACITINIB επιτυγχάνονται σε 24-48 ώρες, με αμελητέα συσσώρευση μετά από χορήγηση δ ύο φορές ημερησίως. Οι συγκεντρώσεις στη σταθερή κατάσταση του TOFACITINIB 11mg επιτυγχάνονται σε 48 ώρες, με αμελητέα συσσώρευση μ ετά από χορήγηση μια φορά την ημέρα[1]

1. Περίληψη Χαρακτηριστικών Προϊόντος Xeljanz 07/2024

Αποτελεσματικότητα στη PA

JAKi in the 2022 EULAR RA guidelines

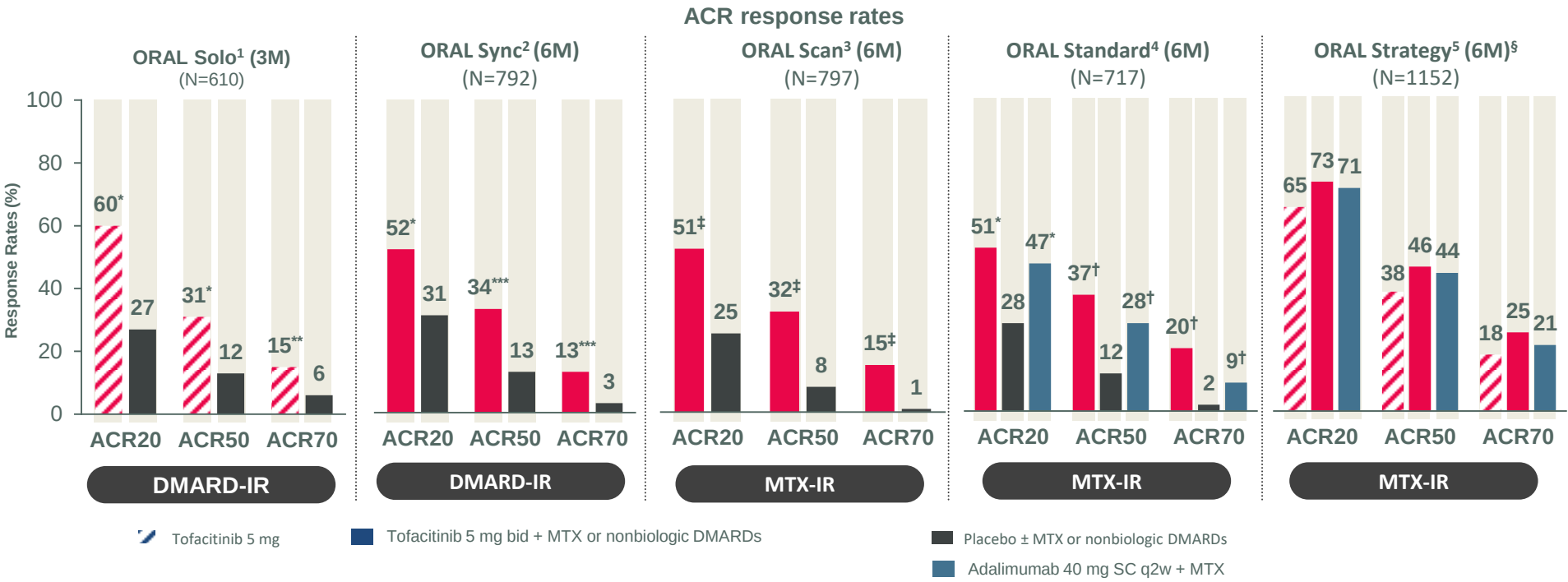


Risk assessment

- Age > 65yrs
- History of current or past smoking
- Other CVD factors (DM, obesity, HTN)
- Other risk factors for malignancy (current or history)
- Risk for thromboembolic events (history of MI or heart failure, cancer, inherited blood clotting disorder, HRT, major surgery, immobility)

Smolen JS, et al. Ann Rheum Dis 2023;82:3–18

Η *συνδυαστική θεραπεία* με TOFA αλλά και η *μονοθεραπεία* κατέδειξαν σημαντικές και σταθερές βελτιώσεις στα σημεία και τα συμπτώματα της νόσου



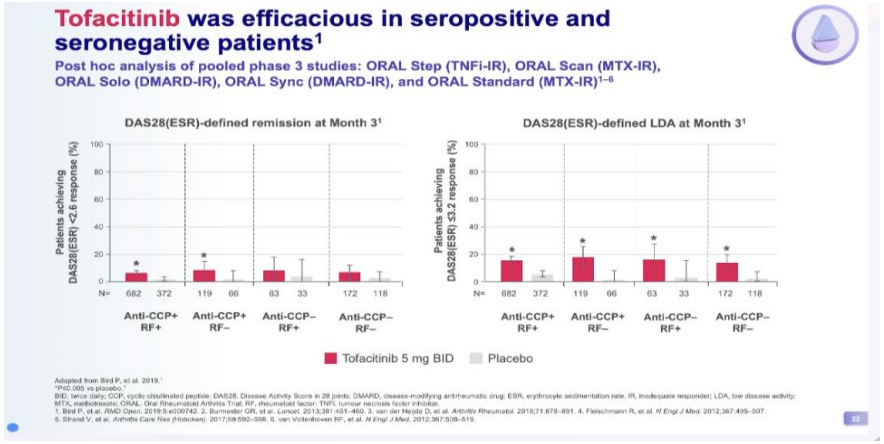
ORAL Standard was not powered to be a head-to-head trial with adalimumab.

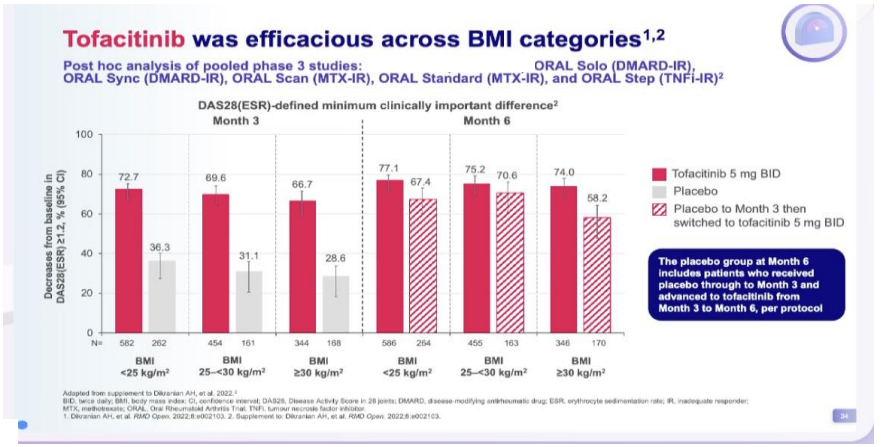
*P<0.001 **P=0.003 ***P≤0.001 vs baseline †P≤0.05 ‡P<0.0001 §All patients receiving active treatment, no advancement penalty applied

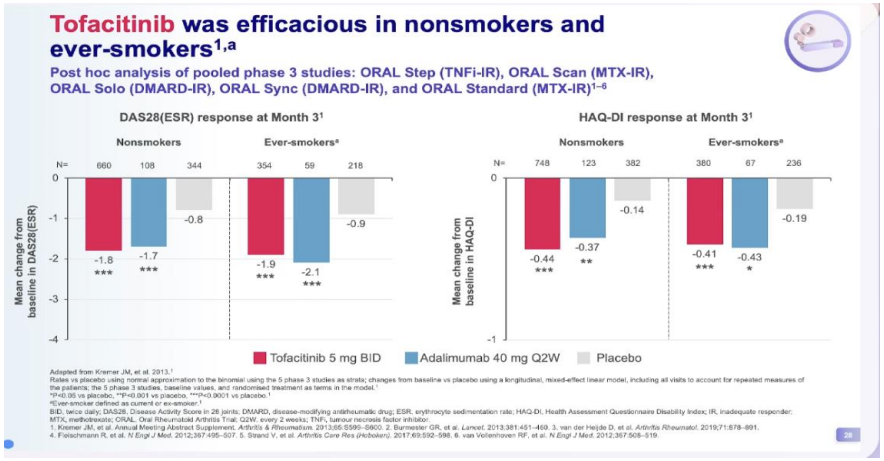
ACR20 at month 6 was a primary endpoint in ORAL Sync, ORAL Standard, and ORAL Scan. ACR20 was a primary endpoint at month 3 and a secondary endpoint at month 6 in ORAL Step.

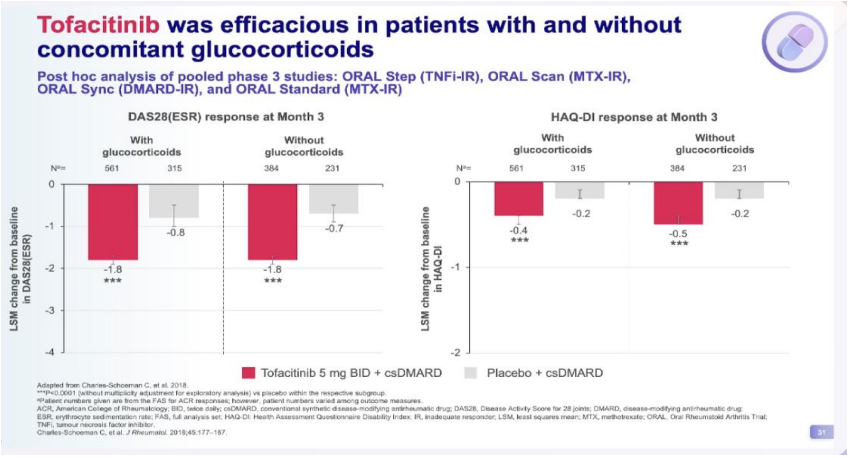
1. Fleischmann et al. *N Engl J Med* 2012;367:495–507.
2. Kremer et al. *Ann Intern Med* 2013;159:253–61.
3. van der Heijde et al. *Arth Rheum* 2013;65:559–70.
4. van Vollenhoven et al. *N Engl J Med* 2012;367:508–19.
5. Fleischmann R et al. *Lancet* 2017; S0140-6736(17)31618-5.

Tofacitinib σε συγκεκριμένους πληθυσμούς ασθενών της PA





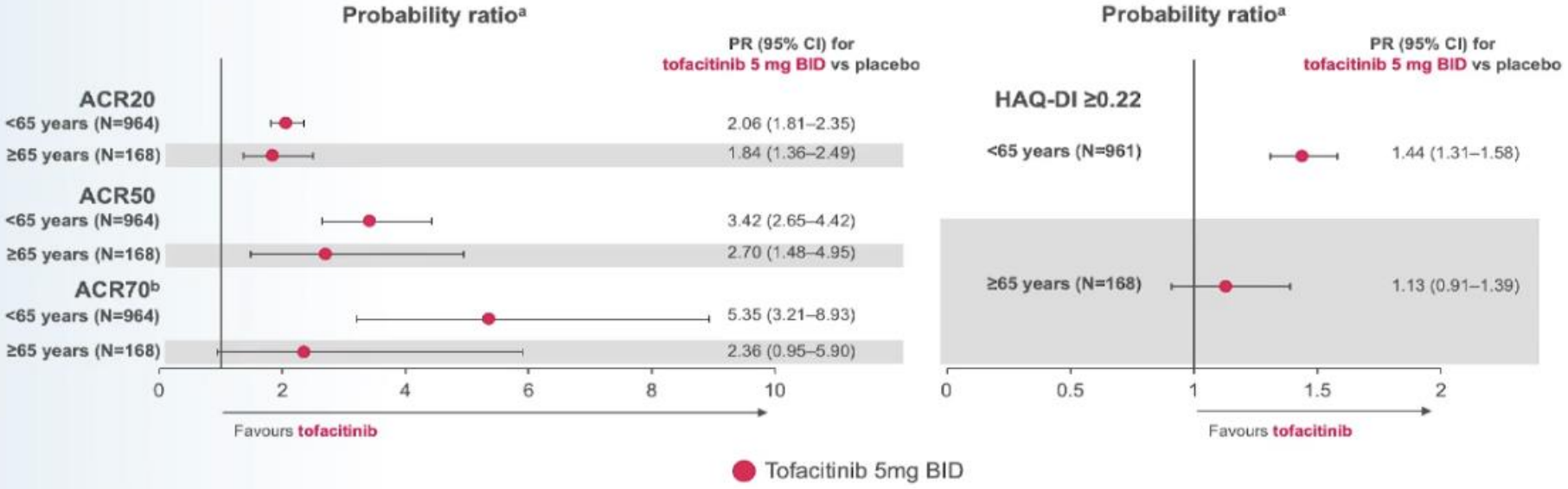




Tofacitinib σε συγκεκριμένους πληθυσμούς ασθενών της PA

Tofacitinib was efficacious in patients aged <65 and ≥65 years[1]

Post hoc analysis of pooled phase 3 studies at Month 3: ORAL Step (TNFi-IR), ORAL Scan (MTX-IR), ORAL Solo (DMARD-IR), ORAL Sync (DMARD-IR), ORAL Standard (MTX-IR)[1–6]



Adapted from Curtis JR, et al. 2017.[1]

[a]Probability ratio is the proportion of responders in the tofacitinib group divided by the proportion of responders in the placebo group at Month 3. A PR >1 favours tofacitinib.[1] [b]Comparisons of ACR70 rates should be interpreted with caution because of the limited number of patients achieving this response.[1]

ACR20/50/70, ≥20%/50%/70% improvement in American College of Rheumatology score; BID, twice daily; CI, confidence interval; DMARD, disease-modifying antirheumatic drug; HAQ-DI, Health Assessment Questionnaire Disability Index; IR, inadequate responder; MTX, methotrexate; ORAL, Oral Rheumatoid Arthritis Trial; PR, probability ratio; TNFi, tumour necrosis factor inhibitor.

1. Curtis JR, et al. *Clin Exp Rheumatol*. 2017;35:390–400. 2. Burmester GR, et al. *Lancet*. 2013;381:451–460. 3. van der Heijde D, et al. *Arthritis Rheumatol*. 2019;71:878–891. 4. Fleischmann R, et al. *N Engl J Med*. 2012;367:495–507. 5. Strand V, et al. *Arthritis Care Res (Hoboken)*. 2017;69:592–598. 6. van Vollenhoven RF, et al. *N Engl J Med*. 2012;367:508–519.

Αποτελεσματικότητα Tofacitinib στην καθημερινή κλινική πρακτική

Clinical Rheumatology
https://doi.org/10.1007/s10067-020-05021-7

ORIGINAL ARTICLE

The OPAL study dataset ~2000 RA patients

Real-world evaluation of effectiveness, persistence, and usage patterns of tofacitinib in treatment of rheumatoid arthritis in Australia

- Αναδρομική, μη παρεμβατική μελέτη
  - Κλινική αποτελεσματικότητα
  - Παραμονή στη Θεραπεία
  - Μοτίβο Θεραπείας
- Δεδομένα από OPAL dataset (από 42 Ρευματολ. κλινικές σε όλη την Αυστραλία)

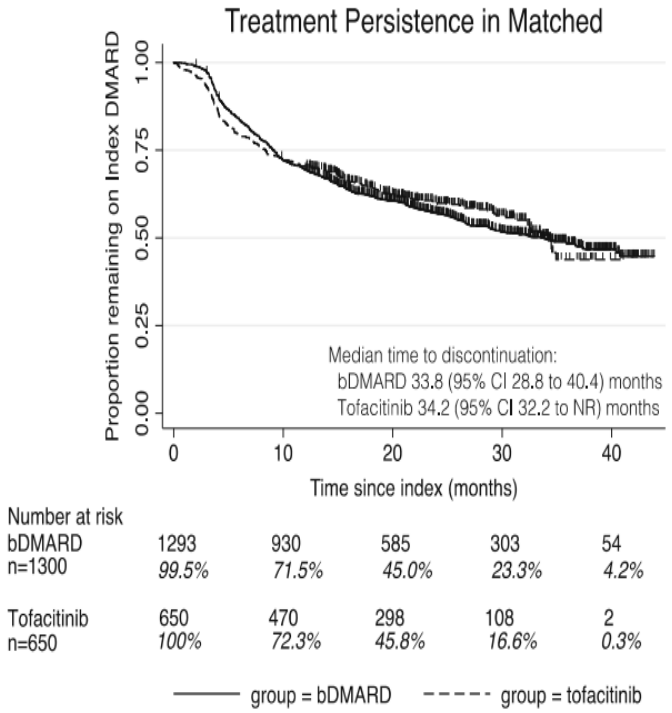


Fig. 3 Treatment persistence in the propensity score matched population for bDMARD and tofacitinib

- *Διαστρωμάτωση ασθενών 2:1*
- *Περίοδος: 2015 → 2018*

- ***57.8%** των ασθενών ήταν μεταξύ 55 και 74 ετών*
- *Οι ασθενείς που ξεκίνησαν με TOFA **είχαν πιο μακροχρόνια νόσο, είχαν λάβει περισσότερα DMARDs***
- *Οι ασθενείς που ξεκίνησαν με TOFA **έλαβαν μονοθεραπεία σε μεγαλύτερο ποσοστό (43,4% vs 33,4%)***

Bird P. et al. Clin Rheumatology 2020:39 (9);2545-2551

Tofacitinib: δεδομένα επιβίωσης φαρμάκου στην καθημερινή κλινική πρακτική

Rheumatoid arthritis

RMD Open
Rheumatic & Musculoskeletal Diseases

ORIGINAL ARTICLE

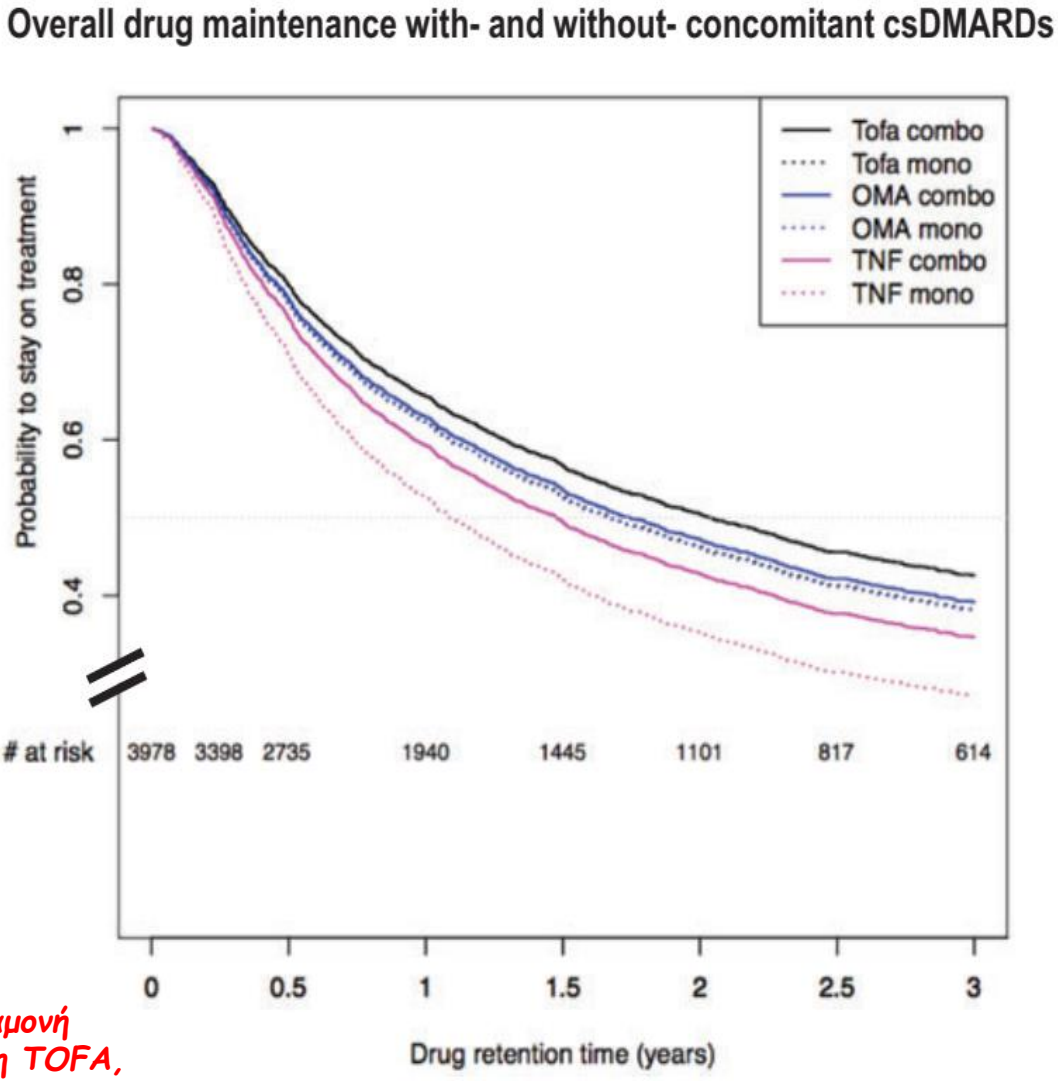
Comparative effectiveness of antitumour necrosis factor agents, biologics with ar alternative mode of action and tofacitinib in an observational cohort of patients with rheumatoid arthritis in Switzerland

(SCQM Registry ¬2600 RA patients)

- >50% Ασθενών από ιατρεία ιδιωτών
- Δεν υπάρχει περιορισμός στην συνταγογράφηση

• *Ίδια αποτελεσματικότητα και TNFi, OMA, JAKi (2013 -2019):*

- *Η διακοπή λόγω αναποτελεσματικότητας ήταν πιο συχνή στους TNFi σε σχέση με OMA και TOFA*
- *Η διακοπή λόγω ανεπιθύμητων ενεργειών συχνότερη σε IL6i και TOFA σε σχέση με TNFi*
- *Η συγχορήγηση MTX είχε αποτέλεσμα στην παραμονή των TNFi , αλλά ήταν ανεξάρτητη στην χορήγηση TOFA, IL6i*

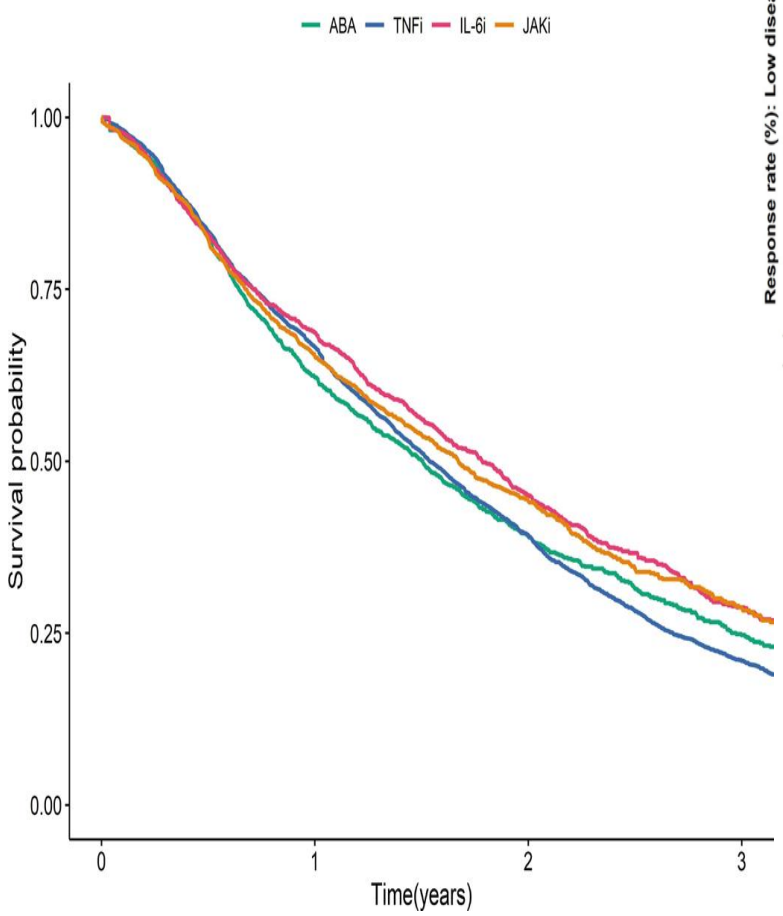


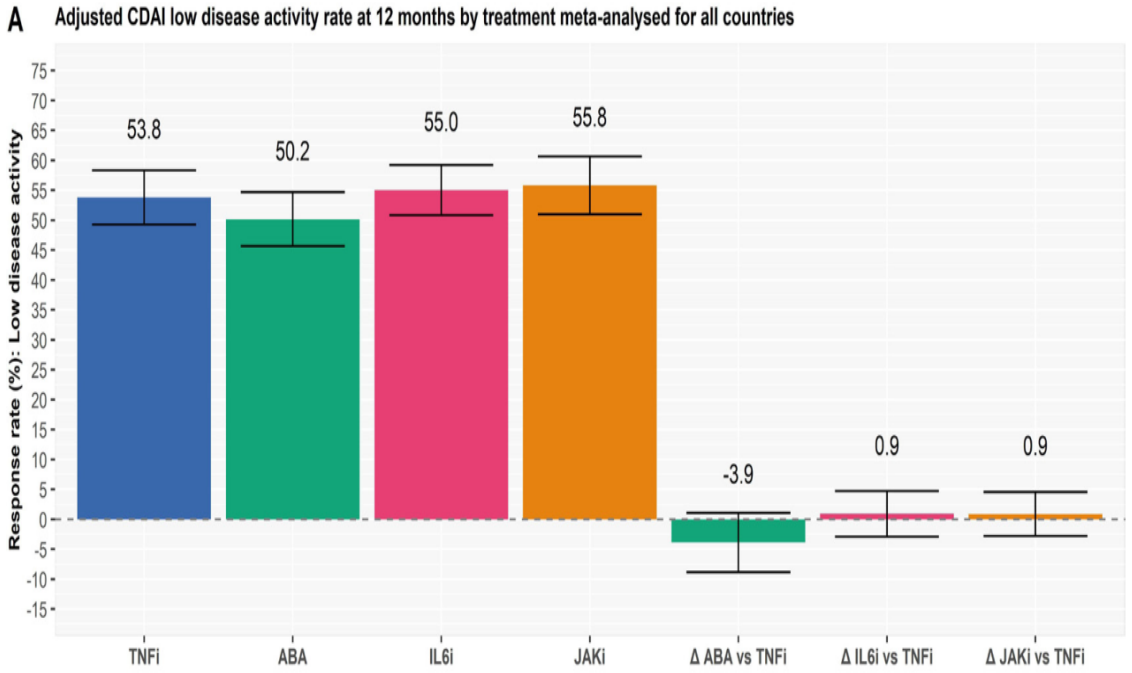
Finckh A, Tellenbach C, Herzog L, et al. RMD Open 2020;6:e001174

Tofacitinib: αποτελεσματικότητα καθημερινής κλινικής πρακτικής του φαρμάκου

EPIDEMIOLOGICAL SCIENCE

Effectiveness of TNF-inhibitors, abatacept, IL6-inhibitors and JAK-inhibitors in 31 846 patients with rheumatoid arthritis in 19 registers from the 'JAK-pot' collaboration





- ***Ίδια αποτελεσματικότητα με TNFi, IL6i, JAKi και ABA στον 1ο χρόνο…αλλά:***

- ***Οι ασθενείς που ξεκίνησαν με JAKi είχαν σχετικά βαρύτερη και πιο μακροχρόνια νόσο, είχαν λάβει περισσότερα DMARDs και πιο δυσμενείς προγνωστικούς παράγοντες και έλαβαν μονοθεραπεία***

- ***Η διακοπή λόγω αναποτελεσματικότητας ήταν πιο συχνή στους TNFi vs IL6i και JAKi***

- ***Η διακοπή λόγω ανεπιθύμητων ενεργειών συχνότερη σε IL6i και JAKi vs TNFi***

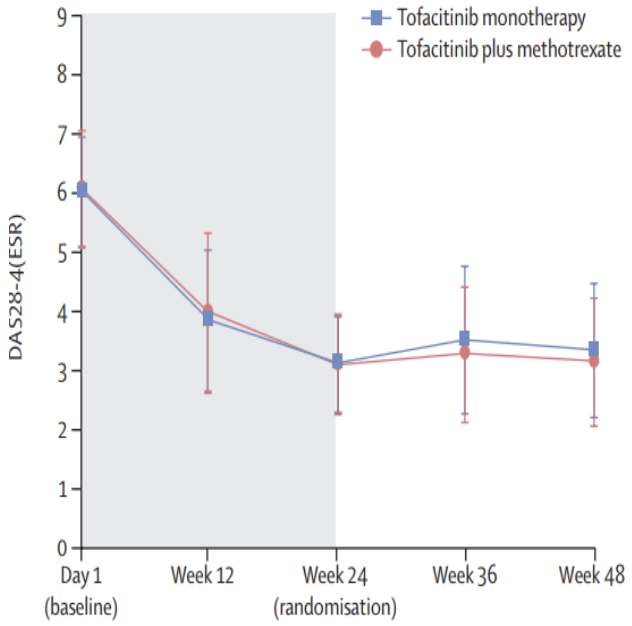
Lauper K, Iudici M, Mongin D, et al. Ann Rheum Dis 2022;**81**:1358–1366

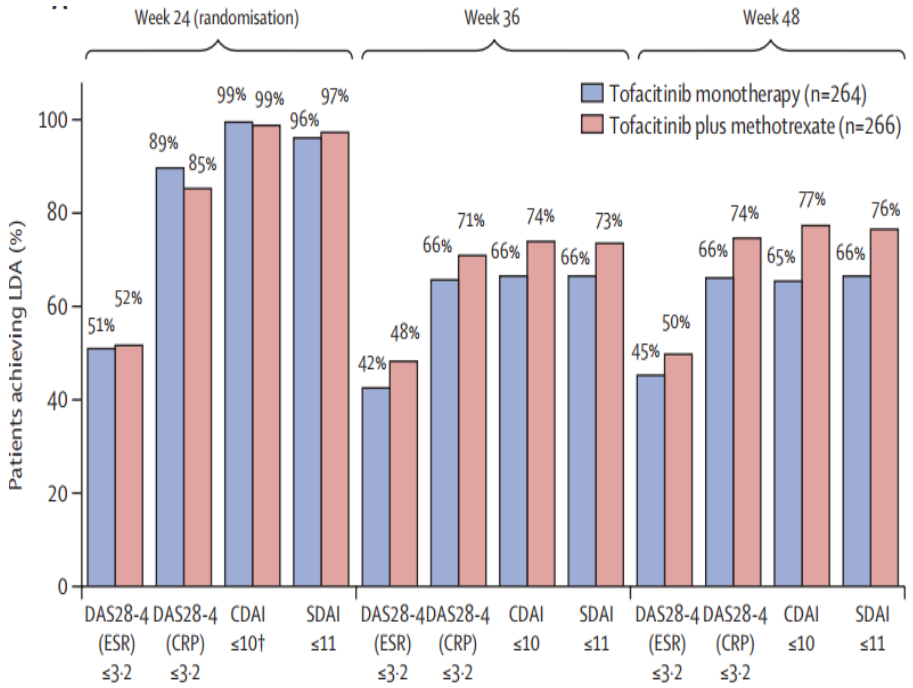
Δεδομένα μονοθεραπείας Tofacitinib από το κλινικό πρόγραμμα

Methotrexate withdrawal in patients with rheumatoid arthritis who achieve low disease activity with tofacitinib modified-release 11 mg once daily plus methotrexate (ORAL Shift): a randomised, phase 3b/4, non-inferiority trial

Ασθενείς σε ύφεση ή χαμηλή ενεργότητα νόσου διατηρούν το αποτέλεσμα μετά την απόσυρση της MTX

Stanley B Cohen, Janet Pope, Boulos Haraoui, Fedra Irazoque-Palazuelos, Mariusz Korkosz, Annette Diehl, Jose L Rivas, Tatjana Lukic, Shixue Liu, Lori Stockert, Noriko Iikuni, Edward C Keystone





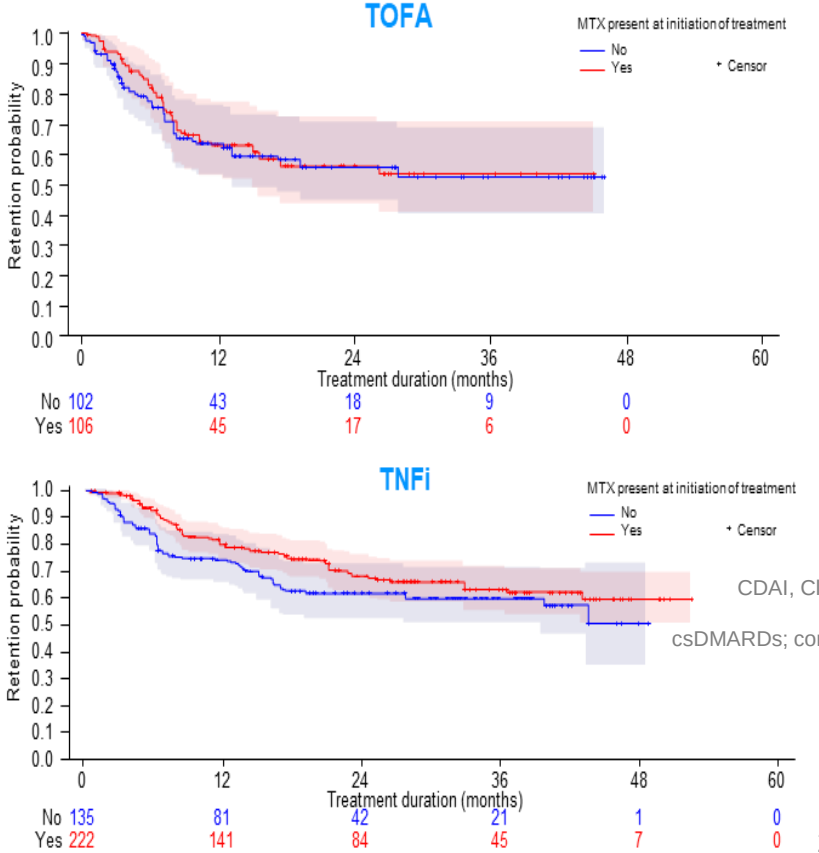
Lancet Rheumatol 2019; 1: e23–34

Δεδομένα μονοθεραπείας Tofacitinib στην καθημερινή κλινική πρακτική

Παραμονή στη θεραπεία με Tofacitinib με και χωρίς τη MTX
Δεδομένα από το μητρώο καταγραφής OBRI

Tofa n=208[1]

Propensity score weighted KM survival curves for time to discontinuation of tofacitinib or TNFi with MTX and without MTX[1]



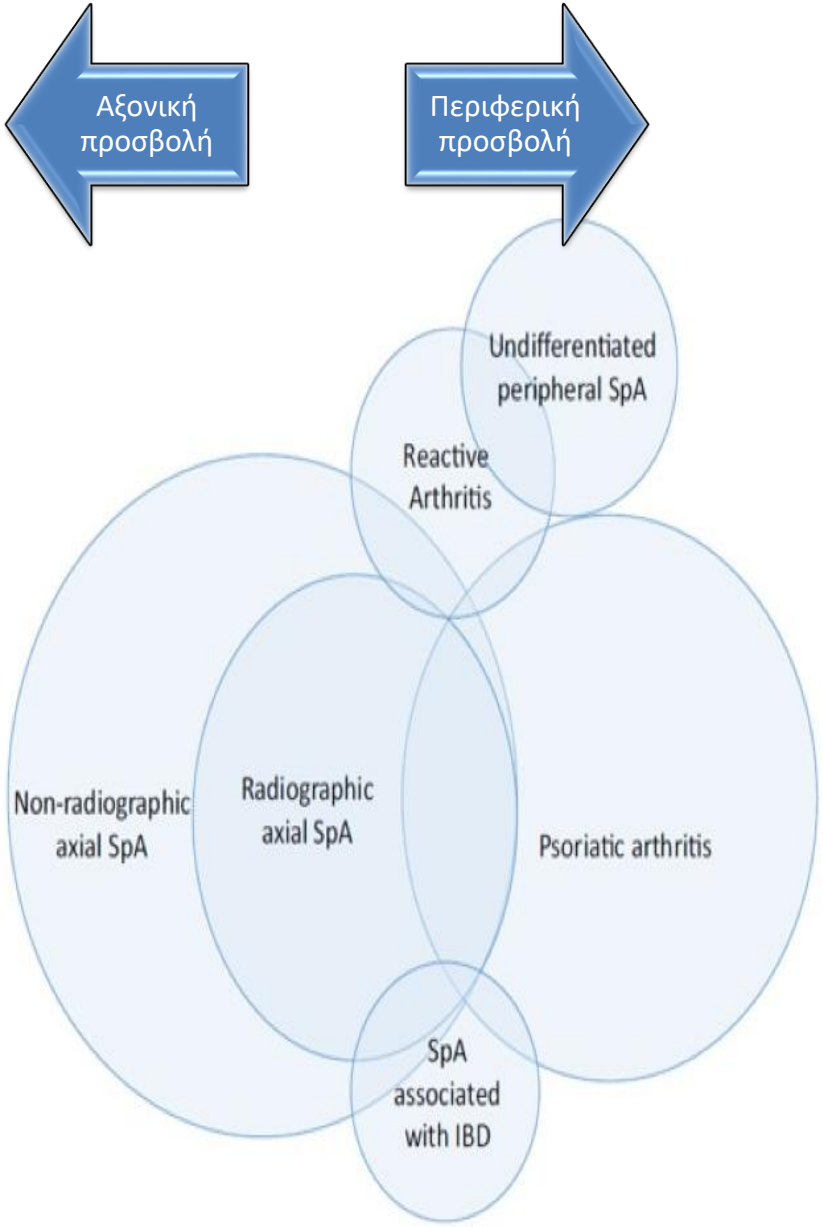
Η παραμονή στη θεραπεία με tofacitinib είναι παρόμοια με τη χρήση csDMARDs ή χωρίς

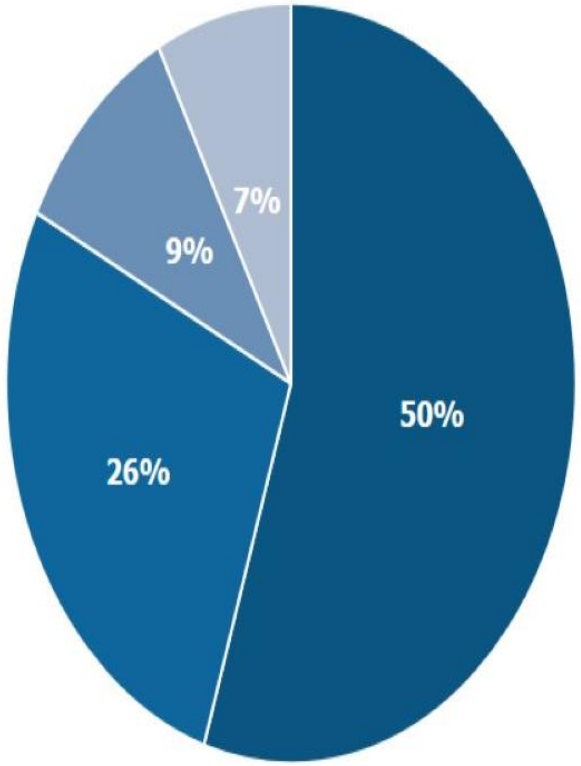
CDAI, Clinical Disease Activity Index; JAKi, Janus Kinase inhibitor; KM, Kaplan-Meier; MTX, methotrexate; OBRI, Ontario Best Practices Research Initiative; csDMARDs; conventional synthetic disease modifying antirheumatic drugs, TNFi, tumour necrosis factor inhibitor.

Movahedi M, *et al*. *BMJ Open* 2023;13:e063198. doi:10.1136/bmjopen-2022-063198

Αποτελεσματικότητα στις σπονδυλαρθροπάθειες

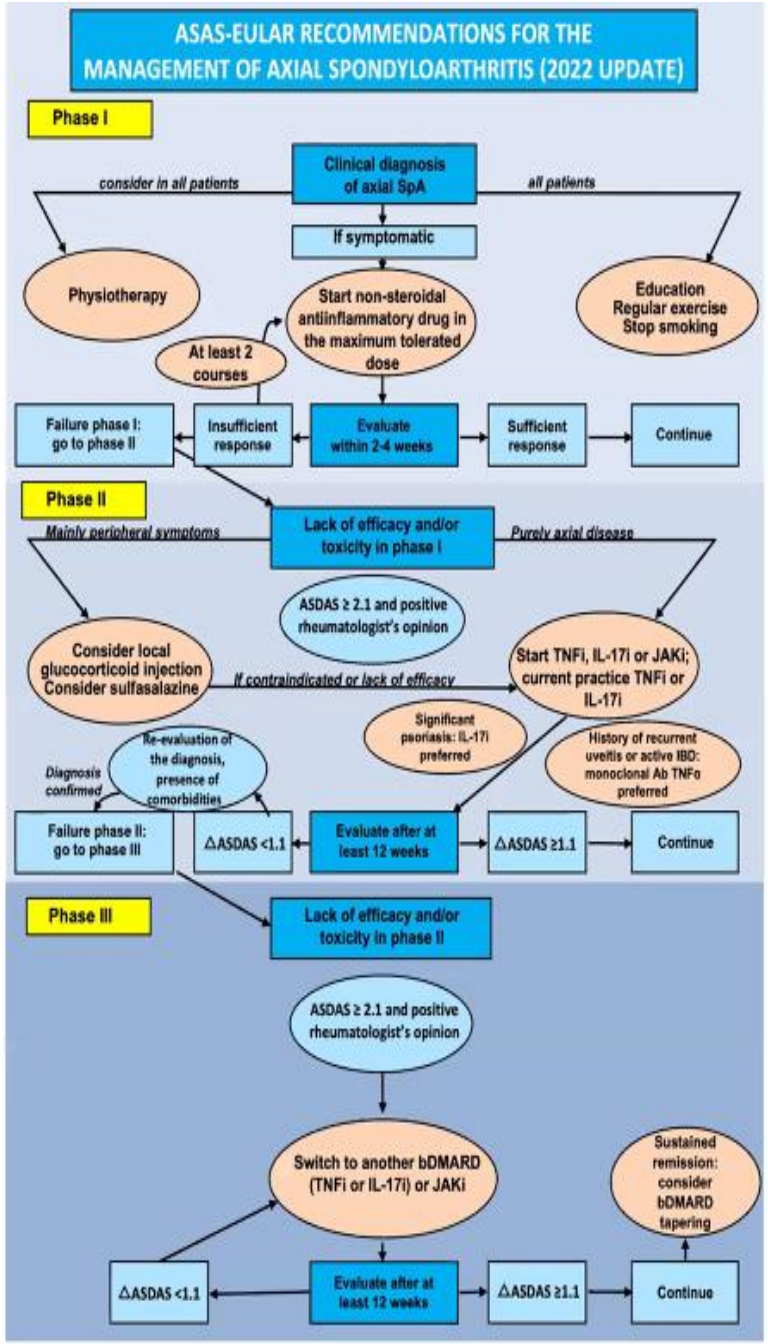
Το φάσμα μίας "ευρύτερης" νόσου





- Περιφερική αρθρίτιδα
- Οξεία πρόσθια ραγοειδίτιδα
- Ψωρίαση
- ΙΦΝΕ

er V, Schachna L. Aust Fam Physician. 2013;42:780-784; b. Stolwijk C, et al. Ann Rheum Dis. 2015;74:65-73; Tubergen A. Nat Rev Rheumatol. 2015;11:110-118.



ASAS Assessment of SpondyloArthritis International Society

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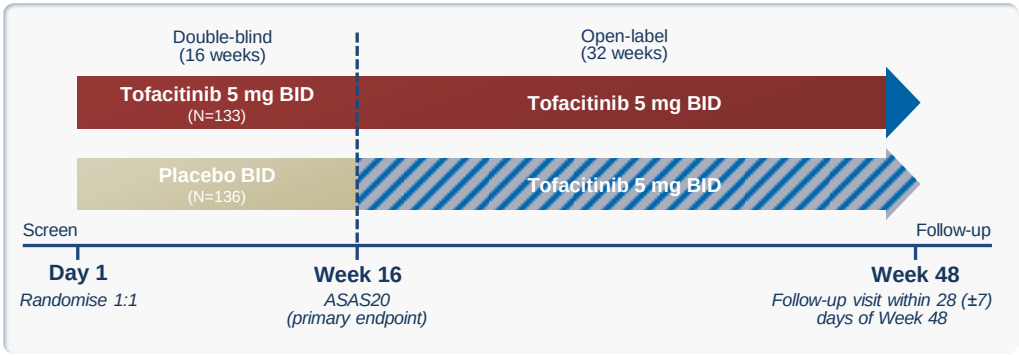
Ramiro S, et al. Ann Rheum Dis 2022;0:1–16. doi:10.1136/ard-2022-223296

TOFA AS Study

Study Design and Selected Eligibility Criteria



Stratification by Prior Treatment History

bDMARD-naïve	TNFi-IR or bDMARD use (non-IR)
102 (76.7%) tofacitinib	31 (23.3%) tofacitinib
105 (77.2%) placebo	31 (22.8%) placebo

Selected Inclusion Criteria

- Age ≥18 years
- Diagnosis of AS
- Fulfill modified New York criteria for AS*
- Inadequate response or intolerance to ≥2 NSAIDs
- Active disease at screening and baseline (BASDAI score ≥4, back pain score ≥4)

*Sacroiliitis (grade ≥2 bilaterally or grade 3–4 unilaterally) plus at least 1 of the following: low back pain and stiffness for more than 3 months that improves with exercise, but is not relieved by rest; limitation of motion of the lumbar spine in the sagittal and frontal planes; or limitation of chest expansion relative to normal values correlated for age and sex

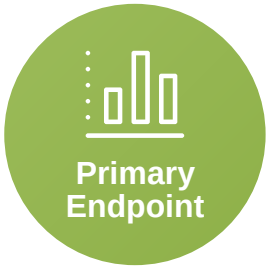
Selected Exclusion Criteria

- History of known or suspected complete ankylosis of the spine
- Currently receiving bDMARDs
- Previously or currently receiving tsDMARDs

TNFi-IR: inadequate response to tumour necrosis factor inhibitor (inadequate response to at least 1 but not more than 2 approved TNFi); bDMARD: biologic disease-modifying antirheumatic drug

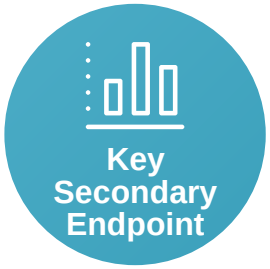
1. Deodhar A, et al. *Ann Rheum Dis.* 2021;80:1004–1013.

TOFA AS Study



ASAS20 response at Week 16

- ≥20% and ≥1 unit improvement from baseline in ≥3 of 4 components **AND**
- No worsening of ≥20% and ≥1 unit in the remaining component



ASAS40 response at Week 16

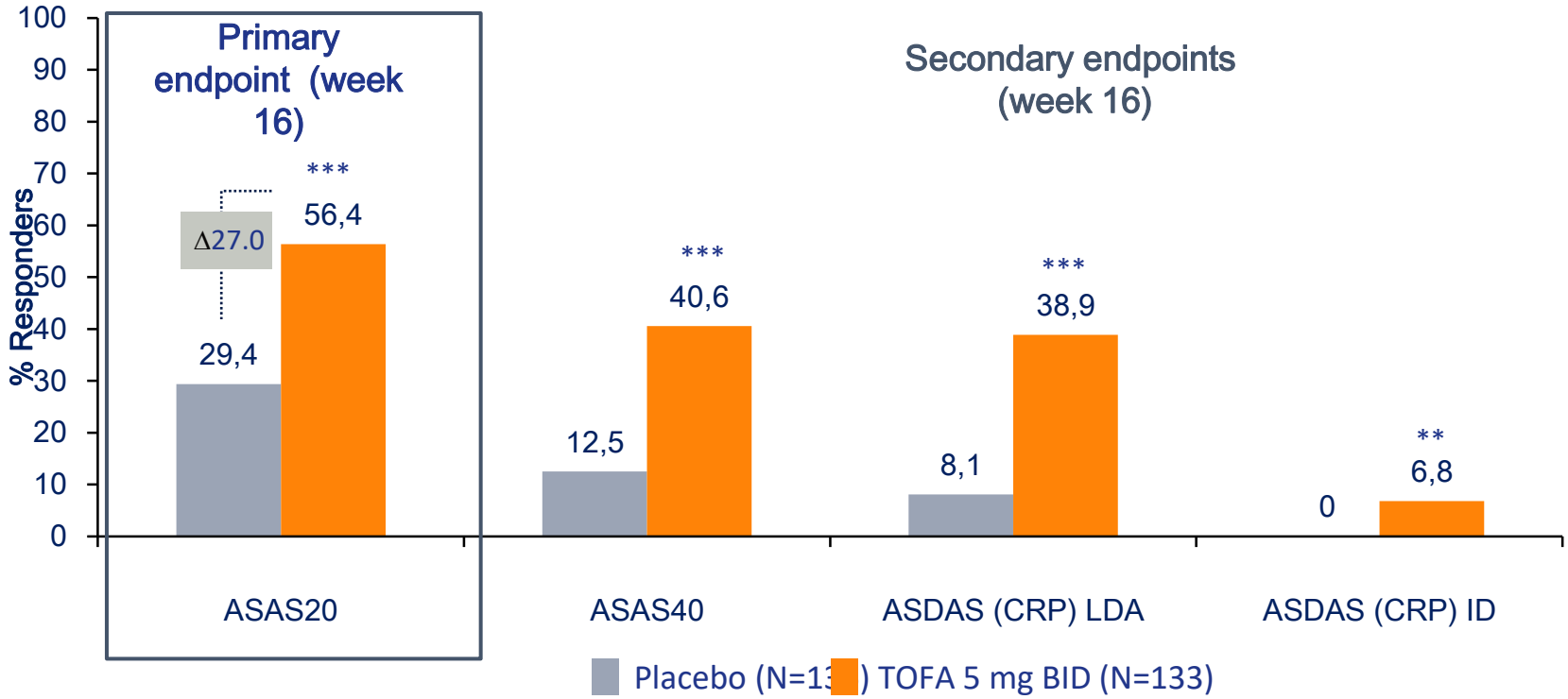
- ≥40% and ≥2 units improvement from baseline in ≥3 of 4 components **AND**
- No worsening in the remaining component

1. Deodhar A, et al. *Ann Rheum Dis.* 2021;80:1004–1013.

Tofacitinib vs. Placebo στην ΑΣ (16 εβδ.)

Η χορήγηση Tofacitinib βελτίωσε σημαντικά τους δείκτες ενεργότητας στις 16 εβδομάδες

77% χωρις προηγούμενη λήψη bDMARD



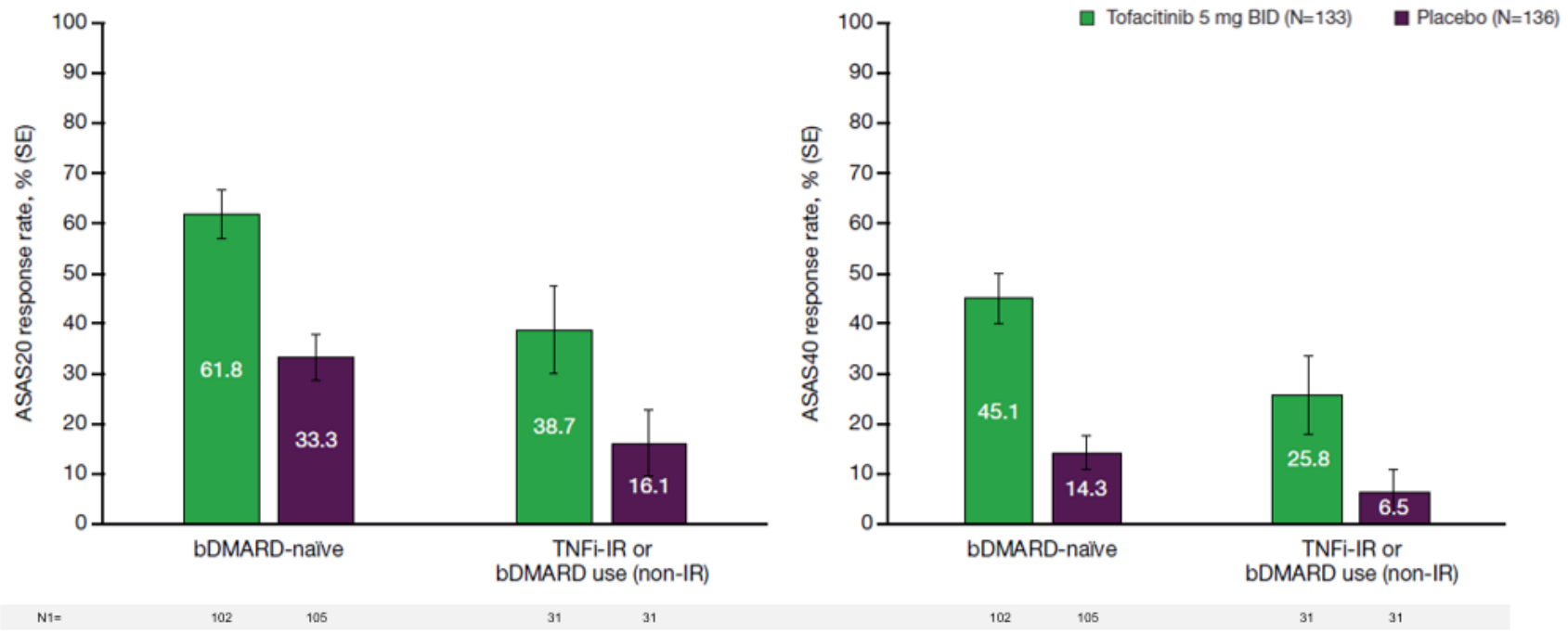
**p<0.0

ASAS20, 20% improvement in Assessment in Ankylosing Spondylitis response criteria; BID, twice a day; bMARD, biologic disease-modifying antirheumatic drug; CRP, c-reactive protein; ID, inactive disease (<1.3); IR, inadequate response; LDA, low disease activity (<2.1); TOFA, tofacitinib; TNFi, tumor necrosis factor inhibitor.

Adapted from: Deodhar A, et al. Ann Rheum Dis. 2021; 80(8):1004-1013.

TOFA AS Study

ASAS20 and ASAS40 Response Rates[a] at Week 16 Stratified by bDMARD Treatment History[b]

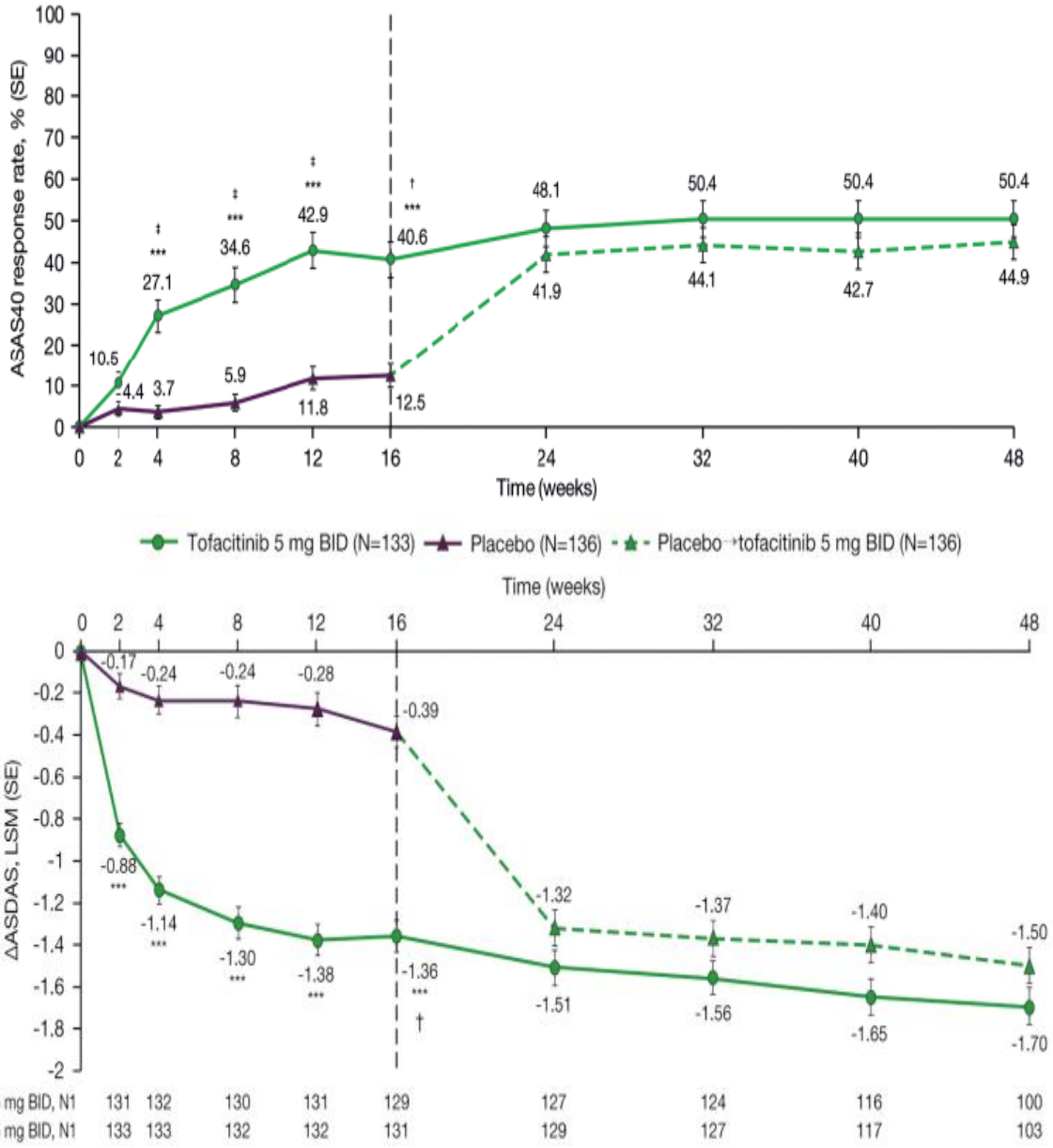


Data are from the Week 16 analysis: data cutoff 19 December 2019; data snapshot 29 January 2020. [a]Normal approximation was used. Missing response was considered as non-response. [b]bDMARD treatment history was derived from the clinical database. ASAS=Assessment of SpondyloArthritis International Society; bDMARD=biologic disease-modifying antirheumatic drug; BID=twice daily; BL=baseline; IR=inadequate response or intolerance; N=number of patients in full analysis set; N1=number of patients in full analysis set, stratified by bDMARD treatment history; SE=standard error; TNFi=tumor necrosis factor inhibitor.

Deodhar A, et al. *Ann Rheum Dis.* 2021;0:1-10. doi:10.1136/annrheumdis-2020-219601.

TOFA AS Study

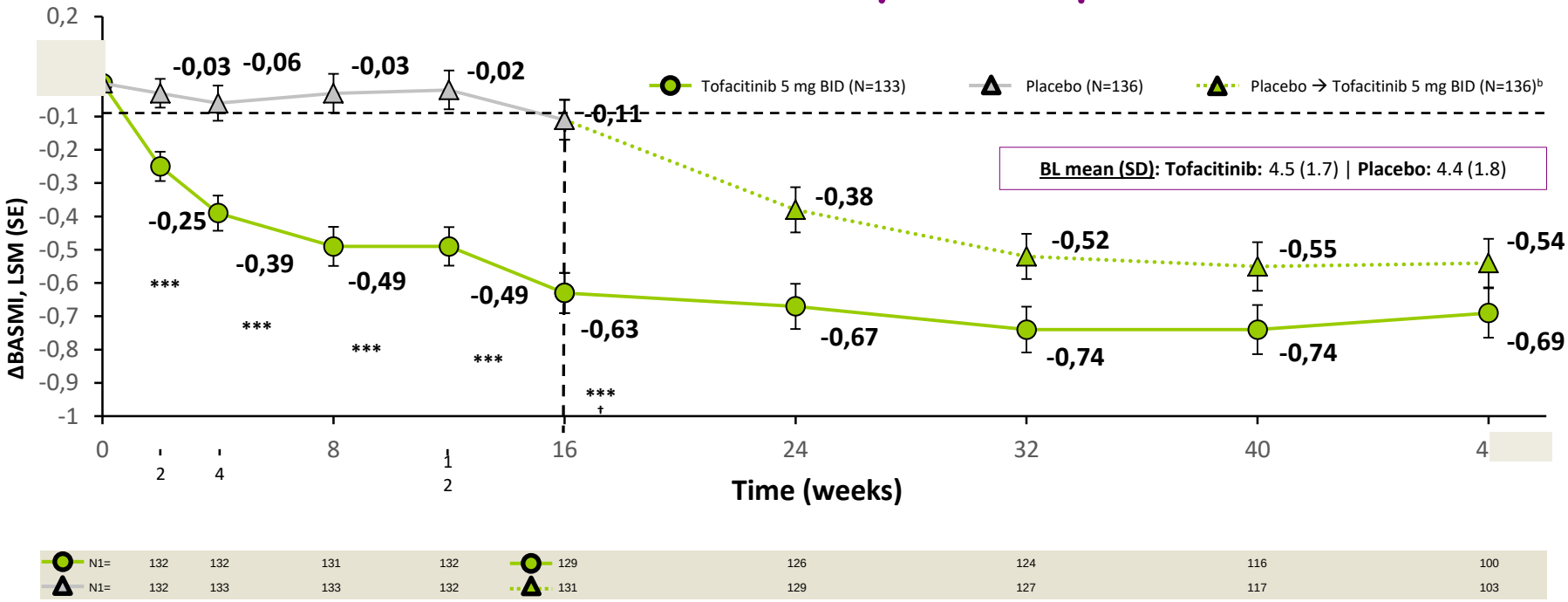
- Ταχεία έναρξη δράσης
- 40% ASAS40 και ASDAS-LDA στην 16η εβδομάδα
- Παρόμοια αποτελεσματικότητα την 40η εβδομάδα στους ασθενείς που αρχικά έλαβαν PBO



Deodhar A, et al. Ann Rheum Dis. 2021; 80(8):1004-1013.

TOFA AS Study

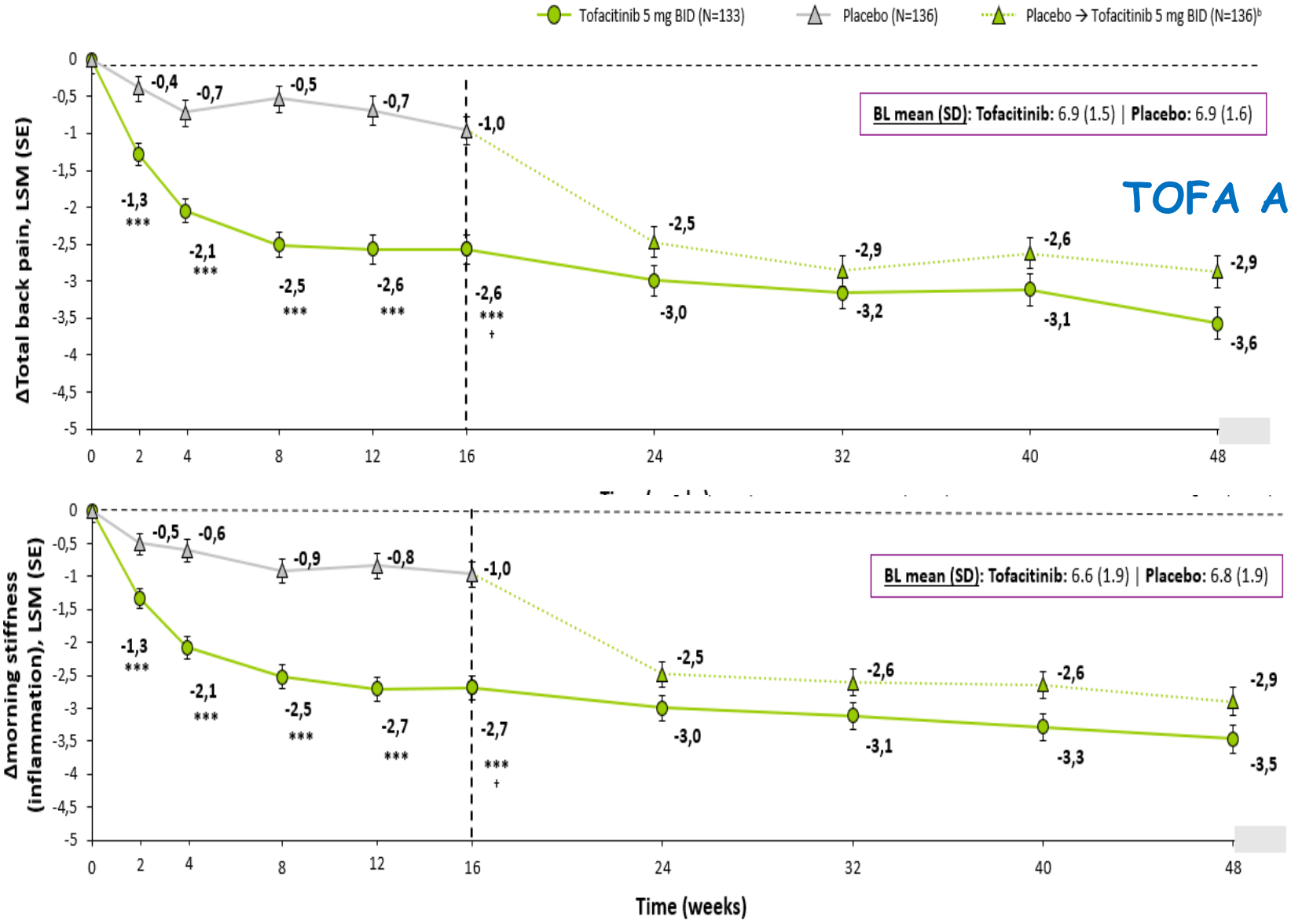
LS Mean ΔBASMI[a] at Week 16 and by Visit Up to Week 48



Data up to Week 16 are from the Week 16 analysis: data cutoff 19 December 2019; data snapshot 29 January 2020. Data for Weeks 24-48 are from the Week 48 final analysis. ***P<0.001 for comparing tofacitinib 5 mg BID vs placebo. †P≤0.05 for comparing tofacitinib 5 mg BID vs placebo, according to the prespecified step-down testing procedure for global type I error control. [a]Mixed model for repeated measures included fixed effects of treatment group, visit, treatment-group-by-visit interaction, stratification factor (bDMARD treatment history: bDMARD naïve vs TNFi-IR or prior bDMARD use without IR) derived from the clinical database, stratification-factor-by-visit interaction, BL value, and BL-value-by-visit interaction. The model used a common unstructured variance-covariance matrix, without imputation for missing values. Two separate models were used. In the analyses of results through the first 16 weeks, the data cutoff of 19 December 2019 was used; the results through Week 16 are from this model. In the analyses of the results through Week 48 (including all post-BL data through Week 48), the Week 48 final data were used; the results from Week 24 through Week 48 are from this model. [b]Patients receiving placebo advanced to tofacitinib 5 mg BID at Week 16 (dashed line). Δ=change from BL; BASMI=Bath Ankylosing Spondylitis Metrology Index; bDMARD=biologic disease-modifying antirheumatic drug; BID=twice daily; BL=baseline; IR=inadequate response or intolerance; LS=least squares; LSM=least squares mean; N=number of patients in full analysis set; N1=number of patients with observation at visit; SE=standard error; TNFi=tumor necrosis factor inhibitor.

Deodhar A, et al. *Ann Rheum Dis.* 2021;0:1-10. doi:10.1136/annrheumdis-2020-219601.

LS Mean ΔTotal Back Pain[a] at Week 16 and by Visit Up to Week



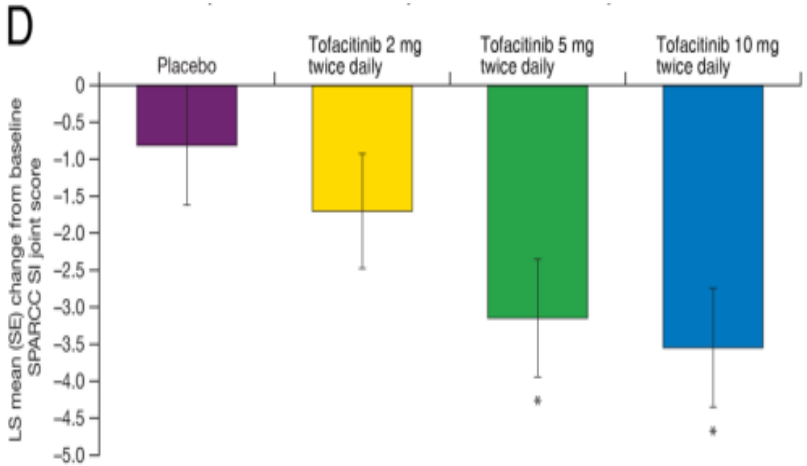
TOFA AS Study

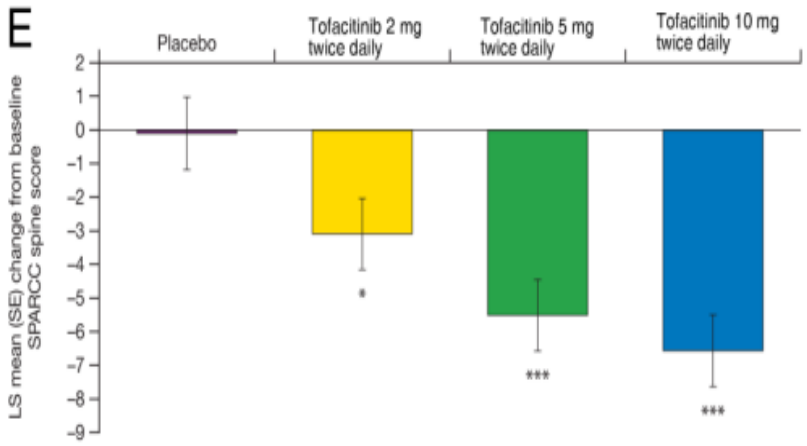
N1=	132	132	132	132	129	127	124	121	113
N1=	133	132	133	132	131	129	127	126	112

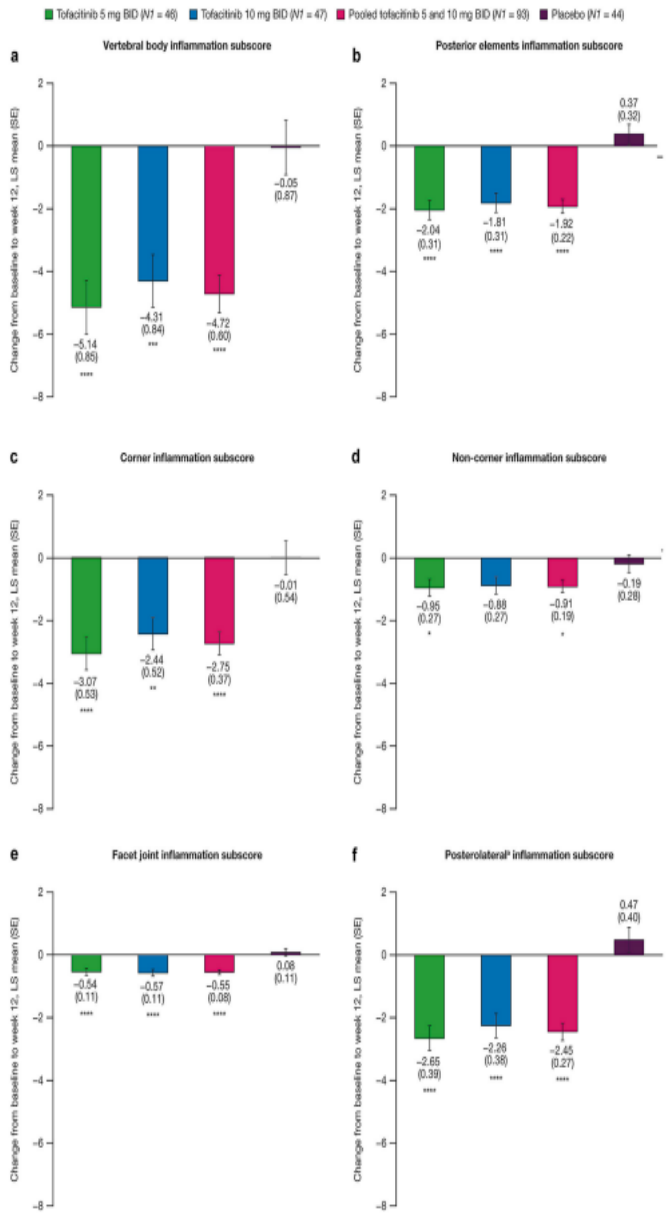
Deodhar A, et al. *Ann Rheum Dis*. 2021;0:1-10. doi:10.1136/annrheumdis-2020-219601

TOFA AS Study

- Στατιστικα σημαντική υποχώρηση της οξείας φλεγμονής στην ΣΣ και στις ιερολαγόνιες αρθρώσεις μετά από 16 εβδομάδες αγωγής με Tofacitinib (vs. PBO)



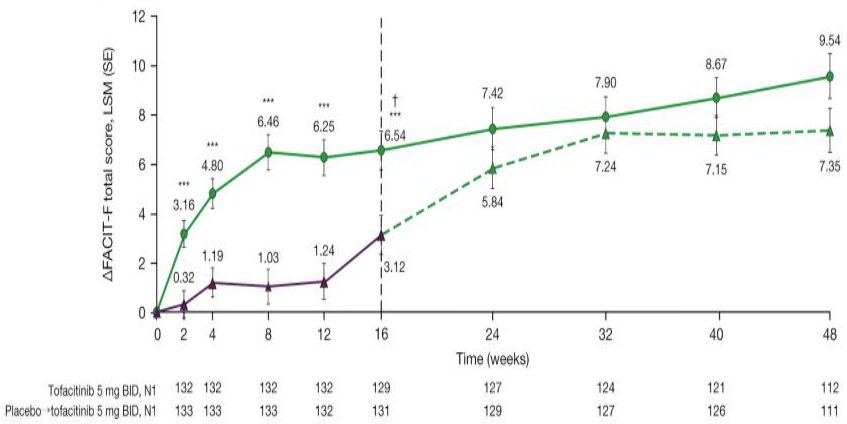




Van der Heijde. Ann Rheum Dis. 2017;76:1340-1347
Ostergaard et al. Rheumatol Ther. 2023 Aug;10(4):1001-1020

TOFA Study

Σημαντική βελτίωση στους δείκτες ποιότητας ζωής και στην παραγωγικότητα



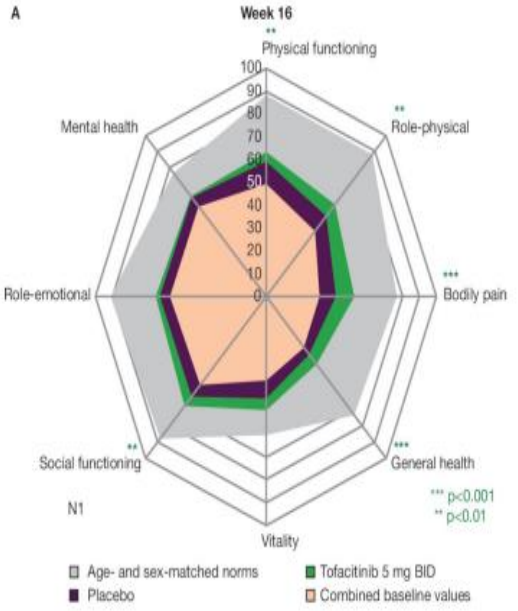


Table 1 Continued

PRO	Baseline, mean (SD) [N1] (range)		Week 16, LS mean Δ (SE) [N1]		Week 48, LS mean Δ (SE) [N1]	
	Tofacitinib 5 mg twice daily (N=133)	Placebo (N=136)	Tofacitinib 5 mg twice daily (N=133)	Placebo (N=136)	Tofacitinib 5 mg twice daily (N=133)	Placebo→ tofacitinib 5 mg twice daily (N=136)
EQ-VAS (0–100 mm)††	46.9 (18.6) (10.0–95.0)	47.4 (21.9) [135] (5.0–95.0)	13.0 (1.84)*** [128]	2.89 (1.84) [130]	20.64 (1.88) [112]	18.00 (1.86) [111]
Work productivity						
WPAI††						
Activity impairment, %	56.5 (23.4) (0–90)	56.0 (21.4) (0–100)	−19.03 (1.97)*** [129]	−5.63 (1.97) [131]	−27.37 (2.34)** [112]	−19.77 (2.31) [112]
Absenteeism (work time missed), %	9.9 (22.4) [81] (0–100)	11.5 (24.6) [88] (0–100)	−3.65 (2.66) [74]	0.88 (2.62) [81]	−8.10 (2.14) [61]	−5.79 (2.05) [70]
Presenteeism (impairment while working), %	48.4 (26.3) [79] (0–100)	49.6 (22.2) [85] (0–90)	−19.83 (2.27)*** [71]	−6.94 (2.30) [77]	−25.35 (2.77) [58]	−23.00 (2.66) [70]
Overall work impairment, %	50.8 (27.4) [79] (0–100)	53.5 (23.1) [85] (0–100)	−21.49 (2.51)*** [71]	−7.64 (2.56) [76]	−27.63 (3.01) [58]	−23.22 (2.90) [69]

Deodhar A, et al. Ann Rheum Dis. 2021; 80(8):1004-1013.

60% των ασθενών με SpA έχουν ενεργό φλεγμονώδη κολίτιδα ή υποκλινική φλεγμονή

Subclinical gut inflammation in axSpA is associated with[2–4]:

- Male sex
- High disease activity[a]
- Restricted spinal mobility[b]
- Younger age
- Early disease onset
- Radiographic sacroiliitis
- Bone marrow oedema of the SIJs[c]

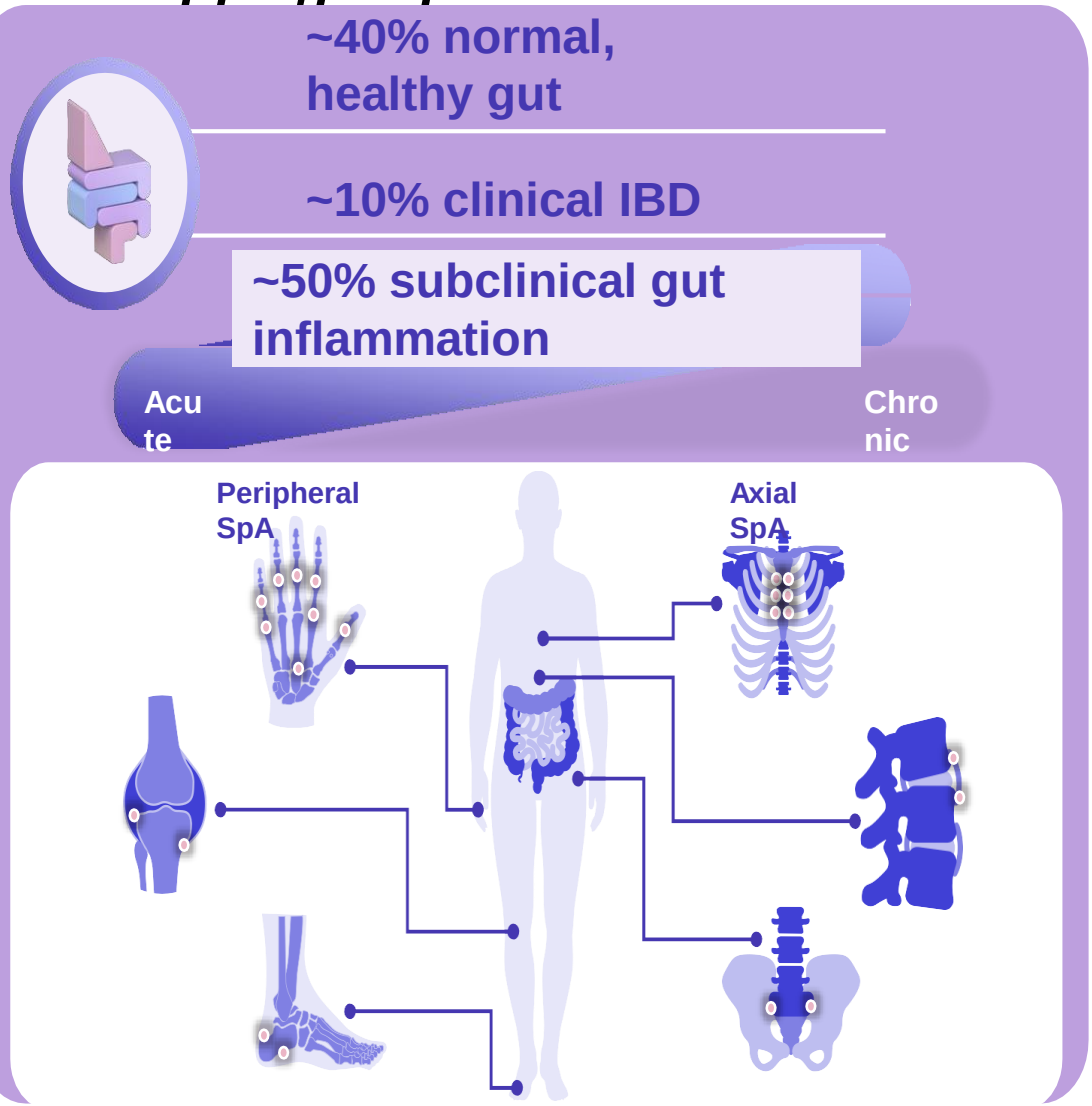


Figure adapted from Gracey E, et al. 2020.[1]
[a]Assessed by the Bath Ankylosing Spondylitis Disease Activity Index.[2] [b]Measured by the Bath Ankylosing Spondylitis Metrology Index.[2] [c]Measured by MRI; data show correlation between chronic gut inflammation and bone marrow oedema of SIJs.[4]
axSpA, axial spondyloarthritis; IBD, inflammatory bowel disease; MRI, magnetic resonance imaging; SIJ, sacroiliac joint; SpA, spondyloarthritis.

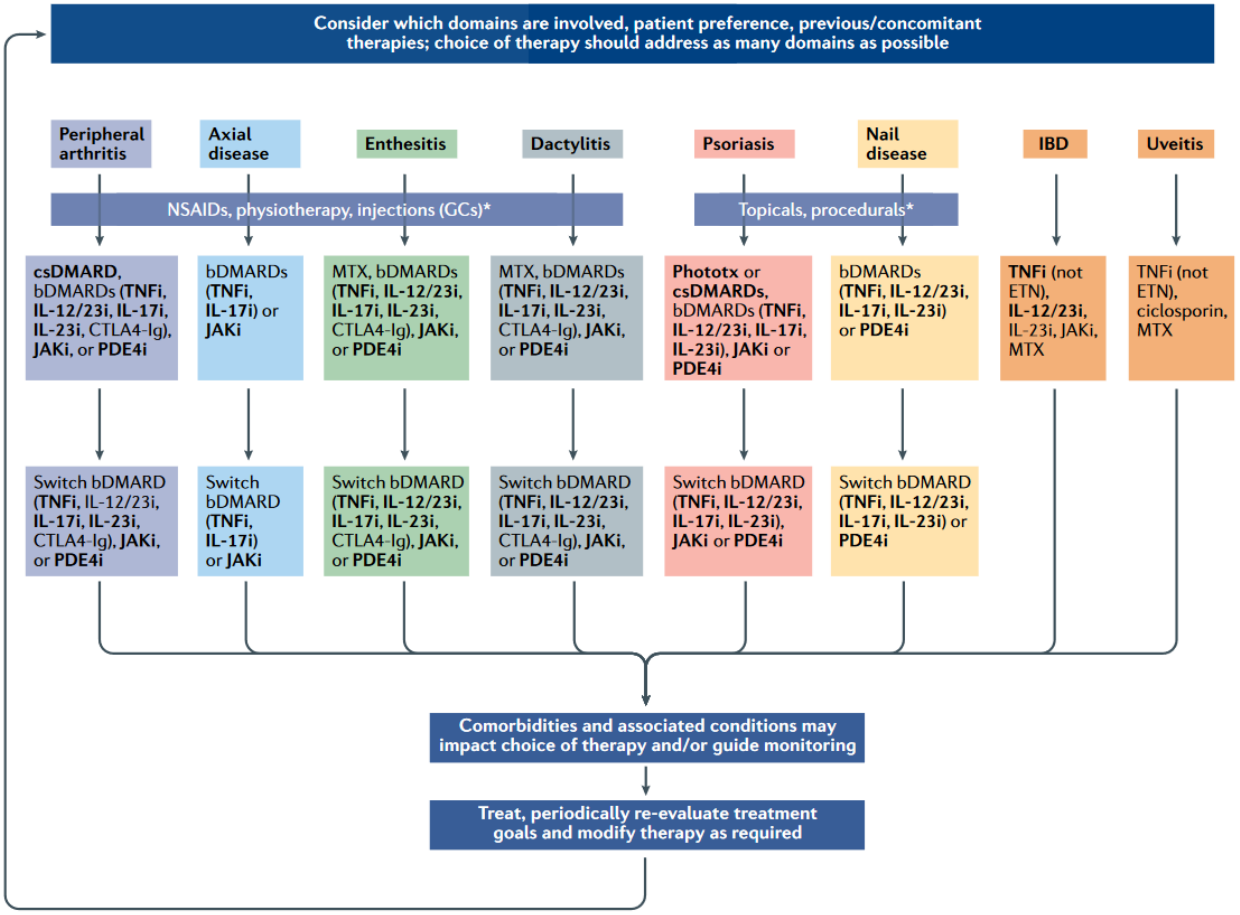
1. Gracey E, et al. *Nat Rev Rheumatol.* 2020;16:415–433. 2. Fragoulis G, et al. *World J Gastroenterol.* 2019;25:2162–2176. 3. Van Praet L, et al. *Ann Rheum Dis.* 2013;72:414–417. 4. Van Praet L, et al. *Ann Rheum Dis.* 2014;73:1186–1189.

2021 GRAPPA (Recs)

Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021

Laura C. Coates[1,2], Enrique R. Soriano[3], Nadia Corp[4], Heidi Bertheussen[4], Kristina Callis Duffin[5], Cristiano B. Campanholo[6], Jeffrey Chau[7], Lihi Eder[8], Daniel G. Fernández-Ávila[9], Oliver FitzGerald[10], Amit Garg[11], Dafna D. Gladman[12], Niti Goel[13], Philip S. Helliwell[14], M. Elaine Husni[15], Deepak R. Jadon[16], Arnon Katz[17], Dhruvkumar Laheru[18], John Latella[19], Ying-Ying Leung[20], Christine Lindsay[21], Ennio Lubrano[22], Luis Daniel Mazzuoccolo[23], Philip J. Mease[24], Denis O'Sullivan[25], Alexis Ogdie[26], Wendy Olsen[27], Penelope Esther Palominos[28], Lori Schick[29], Ingrid Steinkoenig[30], Maarten de Wit[31], D. A. van der Windt[5], Arthur Kavanaugh[32] and the GRAPPA Treatment Recommendations domain subcommittees* * *

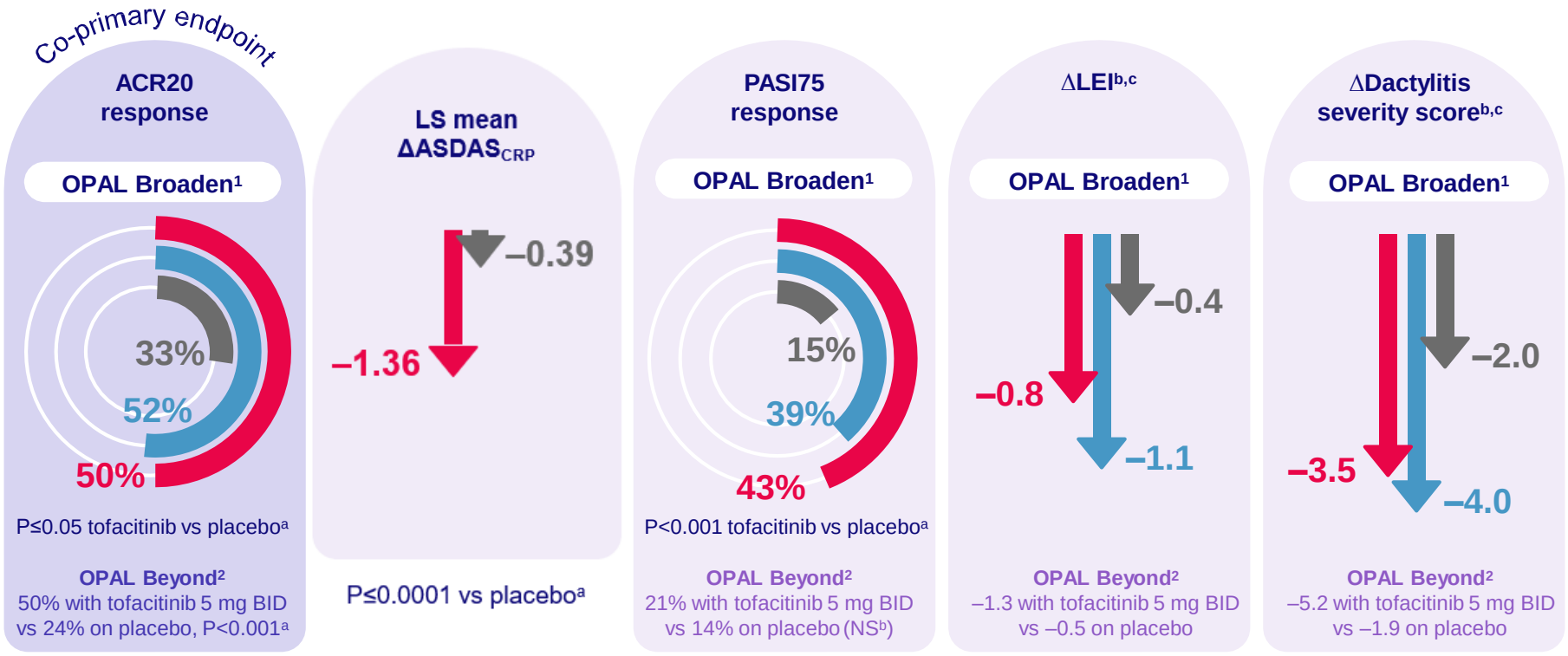
NATURE REVIEWS | RHEUMATOLOGY



Coates LC, et al. J Rheumatol. 2022 Jun;49(6 Suppl 1):52-54. doi: 10.3899/jrheum.211331. Epub 2022 Mar 15.

Tofacitinib is only recommended for RA, PsA, UC, AS, JIA

Βελτίωση σε πολλαπλούς δείκτες ενεργότητας της PsA στην εβδομάδα 12



Trials should not be compared owing to differences in trial design, populations, and methodology.

Tofacitinib 5 mg BID · Adalimumab 40 mg SC Q2W · Placebo

Graphs adapted from Mease P, et al. 2017.[1]

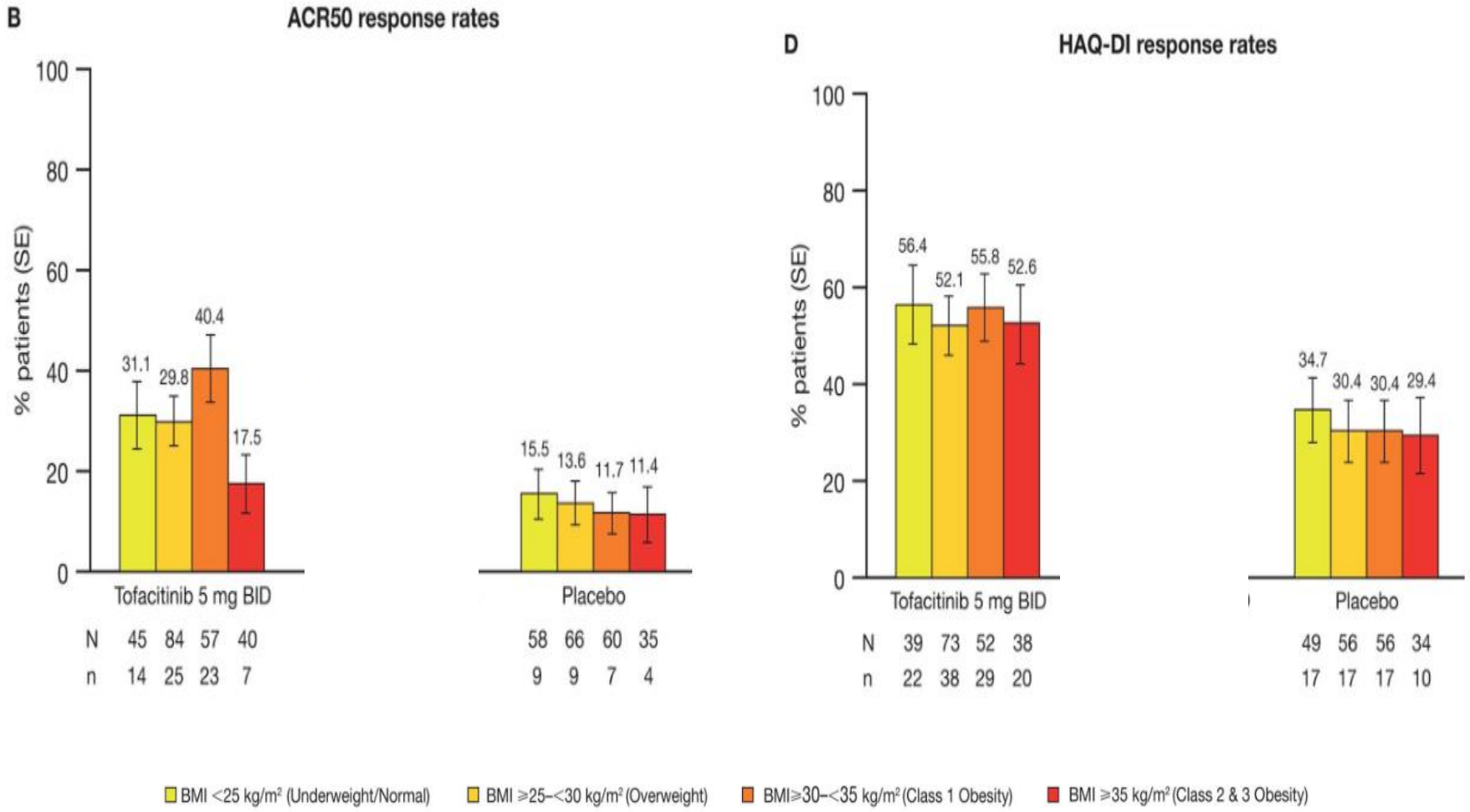
OPAL Broaden population at baseline and Month 3: placebo (n=105), tofacitinib (n=107), adalimumab (n=106)[1]; OPAL Beyond population at baseline: placebo (n=131), tofacitinib (n=131).[2]

[a]Unadjusted P values. The result was significant at a P value of 0.05 or less according to the prespecified step-down testing procedure for global type I error control.[1,2] [b]Prespecified in the original study protocols; hierarchical testing failed at the LEI endpoint in OPAL Broaden and at the PASI75 endpoint in OPAL Beyond.[1,2] [c]Results were assessed among patients who had a baseline score >0.[1,2]

Δ, change from baseline; ACR20, ≥20% improvement in American College of Rheumatology score; BID, twice daily; HAQ-DI, Health Assessment Questionnaire Disability Index; LEI, Leeds Enthesitis Index; NS, not significant; OPAL, Oral Psoriatic Arthritis trial; PASI75, 75% improvement in Psoriasis Area and Severity Index; PsA, psoriatic arthritis; Q2W, every 2 weeks; SC, subcutaneous.

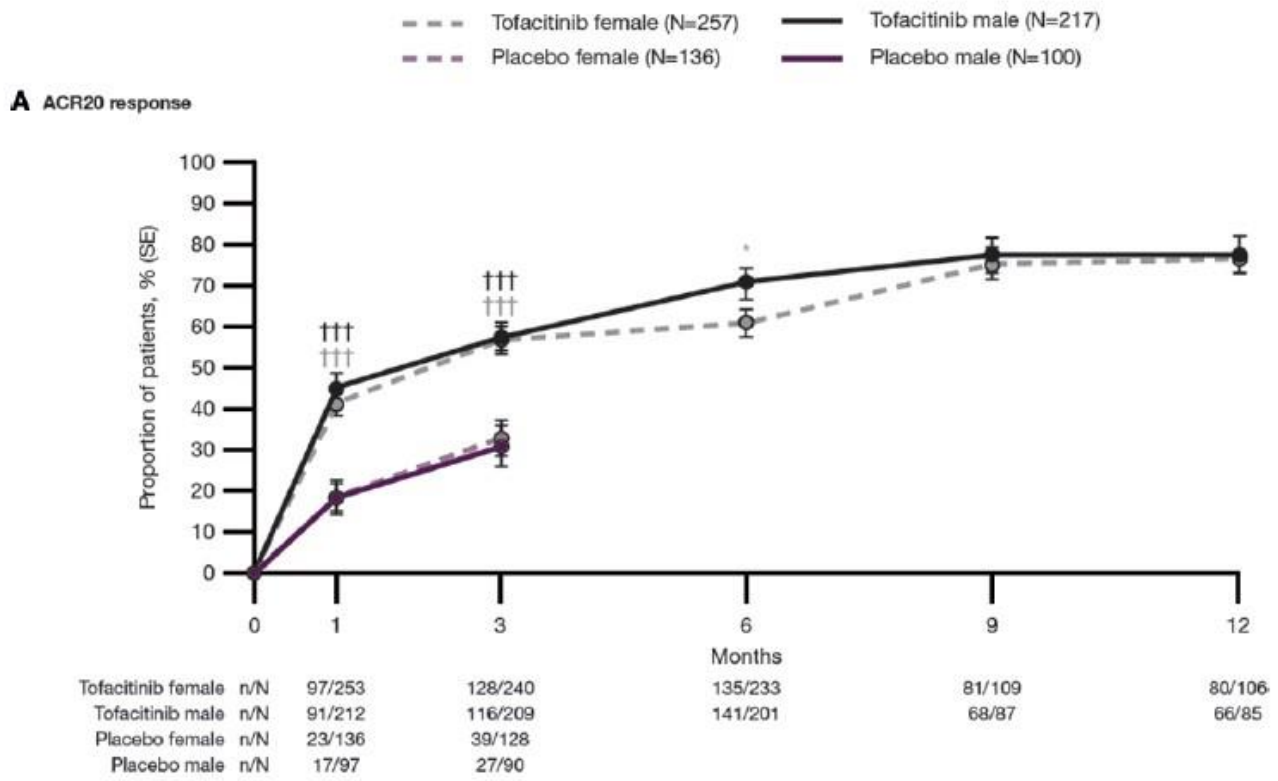
1. Mease P, et al. *N Engl J Med.* 2017;377:1537–1550 and supplementary appendix. 2. Gladman D, et al. *N Engl J Med.* 2017;377:1525–1536 and supplementary appendix.

Αποτελεσματικότητα σε ασθενείς με PsA και αυξημένο σωματικό βάρος



Giles et al.RMD Open. 2021 Jan;7(1):e001486.

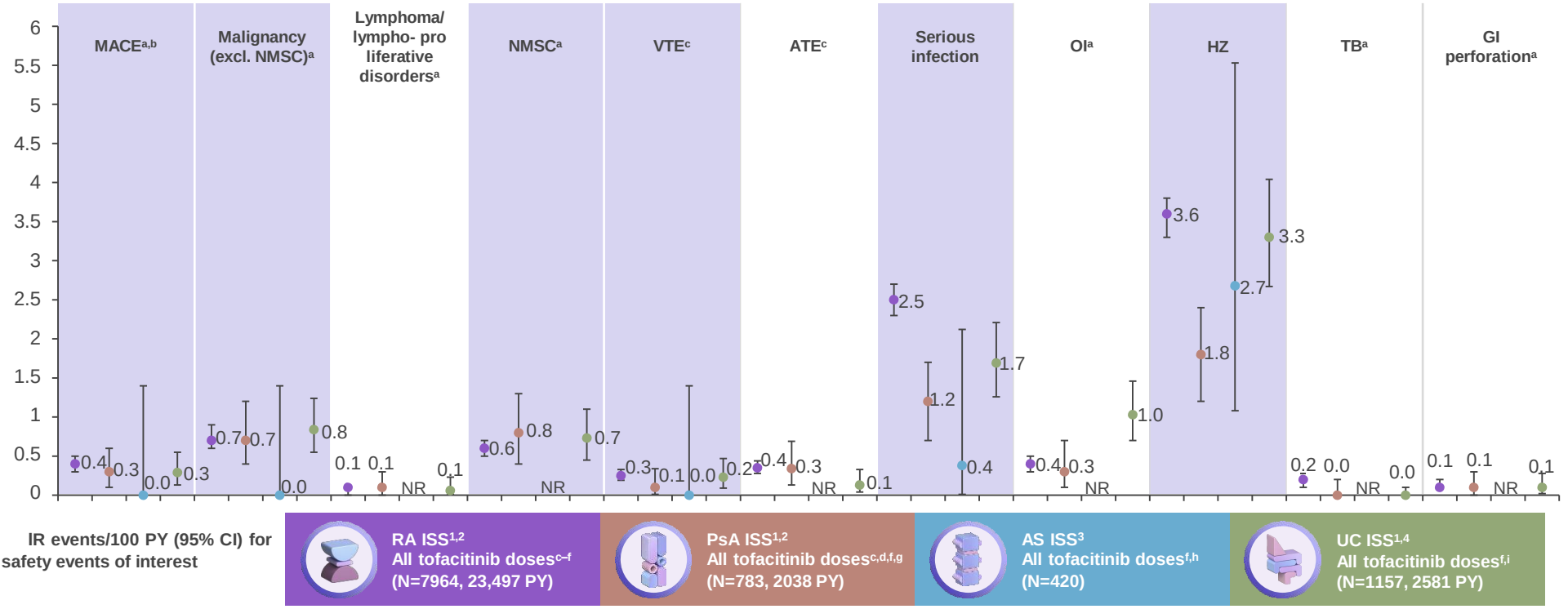
Διαφορές φύλου στην αποτελεσματικότητα, την ασφάλεια και την παραμονή των ασθενών με ψωριασική αρθρίτιδα που υποβλήθηκαν σε θεραπεία με tofacitinib: μια μετα-hoc ανάλυση



Eder L, *et al*. *RMD Open* 2023;9:e002718.

Ασφάλεια

AEs στα κλινικά προγράμματα του tofacitinib στην RA, PsA, AS, UC

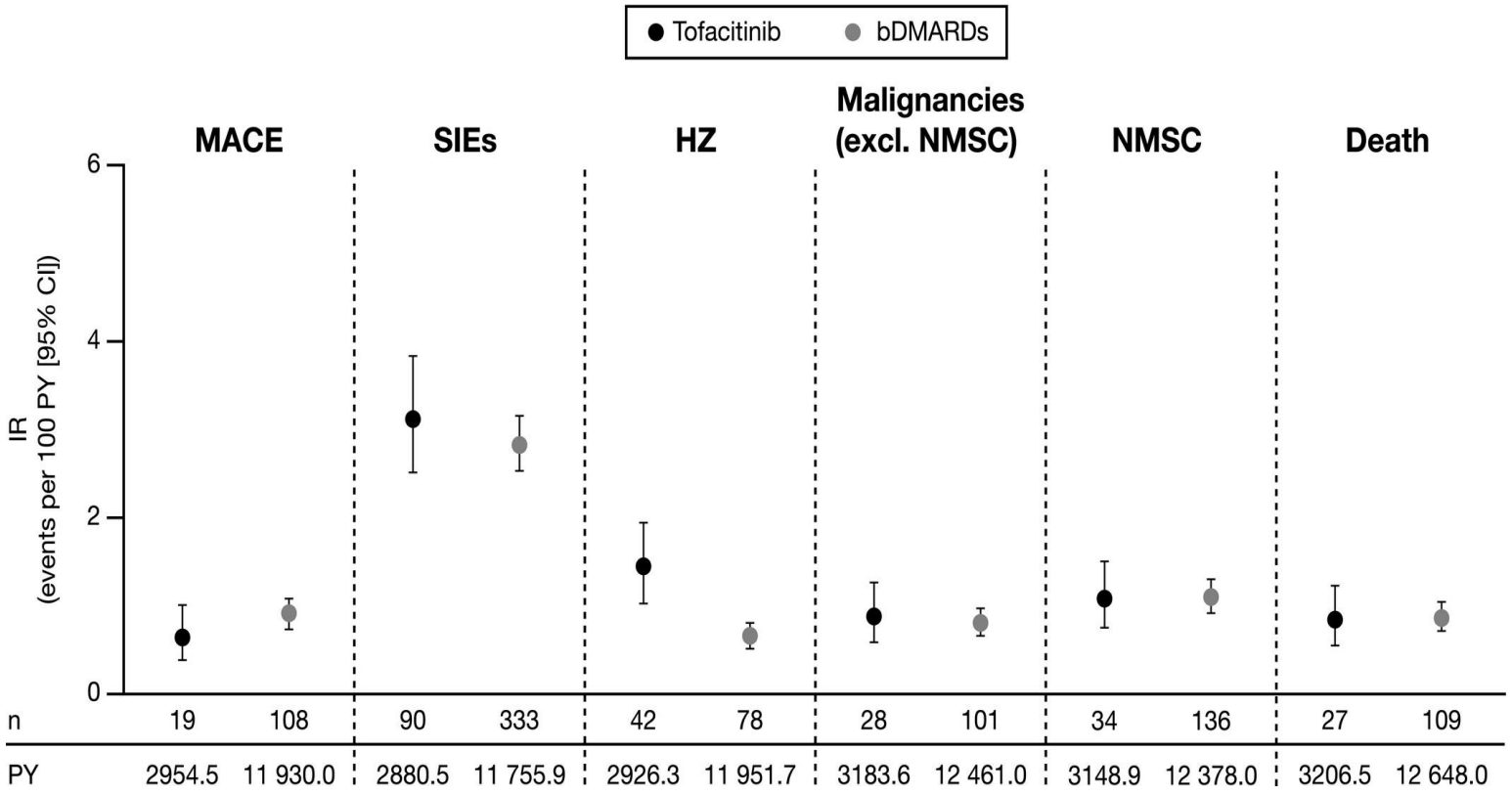


The approved dose of XELJANZ (tofacitinib citrate) for RA, AS, and PsA is 5 mg BID, and for UC is 10 mg BID for induction and 5 mg BID for maintenance.[5] Figure adapted from Burmester GR, et al. 2021,[1] Mease P, et al. 2020,[2] Deodhar A, et al. 2022,[3] and Sandborn WJ, et al. 2023.[4]
[a]Adjudicated events.[1,4] [b]MACE is defined as a composite of any myocardial infarction, stroke, or cardiovascular death.[1,3] [c]Drug exposures for RA and PsA were VTE: 24064.6 PY and 2098.4 PY, and ATE: 23957.1 PY and 2086.4 PY, respectively.[2] [d]Final data for the RA and PsA cohorts are from 18 April 2019 and 31 July 2019, respectively.[1,4] AESI, adverse event of special interest; AS, ankylosing spondylitis; ATE, arterial thromboembolism; BID, twice daily; CI, confidence interval; GI, gastrointestinal; HZ, herpes zoster; ISS, integrated safety summary; LTE, long-term extension; MACE, major adverse cardiovascular event;
MR, modified release; NMSC, nonmelanoma skin cancer; NR, not reported; OI, opportunistic infections; OLE, open-label extension; PsA, psoriatic arthritis; PY, patient-years; QD, once daily; RA, rheumatoid arthritis; TB, tuberculosis; UC, ulcerative colitis; VTE, venous thromboembolism.

1. Burmester GR, et al. *RMD Open*. 2021;7:e001595. 2. Mease P, et al. *Ann Rheum Dis*. 2020;79:1400–1413. 3. Deodhar A, et al. *Ann Rheum Dis*. 2022;81(S1):394–395. 4. Sandborn WJ, et al. *J Crohns Colitis*. 2023;17:338–351 and supplementary appendix.

5. XELJANZ (tofacitinib citrate) Summary of Product Characteristics. Pfizer Inc. March 2023. https://ec.europa.eu/health/documents/community-register/html/h1178.htm#mod_download (accessed May 9, 2023).

Postapproval Comparative Safety Study of Tofacitinib and Biological Disease-Modifying Antirheumatic Drugs: 5-Year Results from a United States–Based Rheumatoid Arthritis Registry



Incidence rates (IRs; number of first events/100 patient-years [PY]) of outcomes in the propensity score–trimmed population.
IRs were based on different definitions of the risk window for outcomes with acute onset (major cardiovascular adverse events [MACE], serious infection events [SIEs], and herpes zoster [HZ]) or latent onset (malignancies and death).
Tofacitinib initiators primarily received tofacitinib 5 mg twice daily. bDMARD, biological disease-modifying antirheumatic drug; CI, confidence interval; NMSC, nonmelanoma skin cancer.

Kremer jm, et al.ACR Open Rheumatology, Volume: 3, Issue: 3, Pages: 173-184, First published: 11 February 2021, DOI: (10.1002/acr2.11232)

Tofacitinib: τα περισσότερα δεδομένα σχετικά με την ασφάλεια

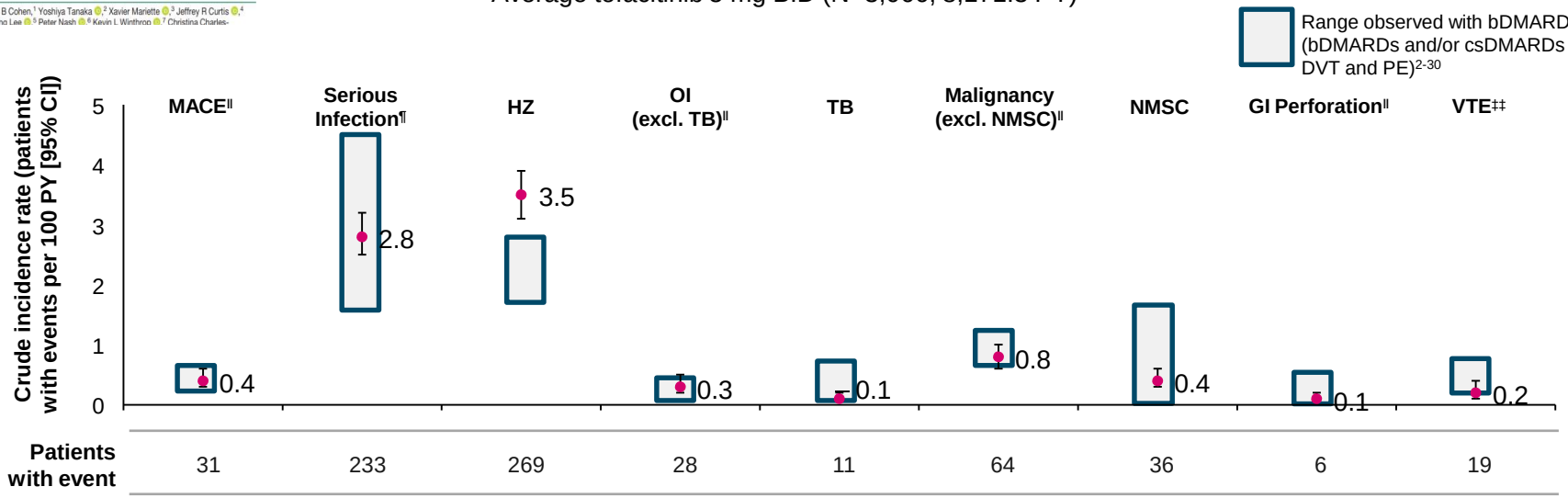
RMD Open
Rheumatic & Musculoskeletal Diseases
Original research

Long-term safety of tofacitinib up to 9.5 years: a comprehensive integrated analysis of the rheumatoid arthritis clinical development programme

Stanley B Cohen,[1] Yoshiya Tanaka,[2] Xavier Mariette,[3] Jeffrey R Curtis,[4] Eun Bong Lee,[5] Peter Nash,[6] Kevin L Winthrop,[7] Christina Charles-

Integrated safety data in overall tofacitinib population—Phase I, II, III, IIIb/IV, LTE;‡ excluding ORAL Surveillance[1]

Average tofacitinib 5 mg BID (N=3,066; 8,171.3 PY)§



Conclusions cannot be drawn from comparisons across different studies as populations and other factors may vary considerably.

Tofacitinib 5 mg twice daily is the approved dosage for the treatment of moderate to severe active rheumatoid arthritis in the EU, based on the EMA prescribing information. The prescribing information in other countries, including Switzerland, may be different. For details of licenced indications in your country of residence, please refer to the country- specific prescribing information. Adapted from Cohen S, et al. 2020.

‡The database lock for the integrated safety data was March 2017. Incidence rates were based on the number of patients with events during the time between the first and last tofacitinib dose plus 28 days. §Average dosing was based on average daily dose: patients receiving <15 mg/day were assigned to the tofacitinib 5 mg BID group. **All tofacitinib doses: N=7,061, 22,874.5 PY.**

‖Adjudicated events. ¶Defined as requiring hospitalisation or parenteral antimicrobial therapy, or otherwise meeting SAE criteria. ‡‡Patients with a DVT event, a PE event, or both DVT and PE events. A total of five patients experienced a DVT and a PE event (may not have occurred at the same time).

AE=adverse event; BID=twice daily; CI=confidence interval; DVT=deep vein thrombosis; GI=gastrointestinal; HZ=herpes zoster; LTE=long-term extension; MACE=major adverse cardiac event; NMSC=nonmelanoma skin cancer; OI=opportunistic infection; ORAL=Oral Rheumatoid Arthritis Trial; PE=pulmonary embolism; PY=patient-year; RA=rheumatoid arthritis; SAE=serious adverse event; TB=tuberculosis; VTE=venous thromboembolism.

1. Cohen SB, et al. Long-term safety of tofacitinib up to 9.5 years: a comprehensive integrated analysis of the rheumatoid arthritis clinical development programme. *RMD Open.* 2020;6:e001395. Full references for this slide available at the end of the presentation. References available on request

Tofacitinib: τα περισσότερα δεδομένα σχετικά με την ασφάλεια

Rheumatol Ther (2023) 10:1255–1276
https://doi.org/10.1007/s40744-023-00576-8

ORIGINAL RESEARCH

Post-Marketing Safety Surveillance of Tofacitinib over 9 Years in Patients with Psoriatic Arthritis and Rheumatoid Arthritis

Gerd R. Burmester · Laura C. Coates · Stanley B. Cohen · Yoshiya Tanaka · Ivana Vranic · Edward Nagy · Irina Lazariciu · All-shine Chen · Kenneth Kwok · Lara Fallon · Cassandra Kinch

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Table 3 Safety outcomes by tofacitinib formulation among patients with PsA and RA

PsA	Tofacitinib IR 14,000 PY			Tofacitinib MR 6706 PY			All tofacitinib 20,706 PY		
	N	%[a]	RR[b]	*N*	%[a]	RR[b]	*N*	%[a]	RR[b]
Case reports	2601			2425			5026		
AEs	8349		59.64	7602		113.36	15,951		77.04
SAEs	1136	13.61	8.11	912	12.00	13.60	2048	12.84	9.89
AESIs[c]									
Serious infections	239	2.86	1.71	200	2.63	2.98	439	2.75	2.12
HZ (serious and nonserious)	49	0.59	0.35	35	0.46	0.52	84	0.53	0.41
Cardiovascular events[d]	44	0.53	0.31	25	0.33	0.37	69	0.43	0.33
Malignancies (excluding NMSC)	30	0.36	0.21	27	0.36	0.40	57	0.36	0.28
NMSC	4	0.05	0.03	7	0.09	0.10	11	0.07	0.05
VTE[e]	27	0.32	0.19	12	0.16	0.18	39	0.24	0.19
Fatal cases	22	0.85[f]	0.16	19	0.78[f]	0.28	41	0.82[f]	0.20
RA	**Tofacitinib IR 312,632 PY**			**Tofacitinib MR 126,738 PY**			**All tofacitinib 439,370 PY**		
	N	%[a]	RR[b]	*N*	%[a]	RR[b]	*N*	%[a]	RR[b]
Case reports	39,744			24,148			63,892		
AEs	137,476		43.97	82,153		64.82	219,629		49.99
SAEs	24,966	18.16	7.99	11,978	14.58	9.45	36,944	16.82	8.41
AESIs[c]									
Serious infections	4944	3.60	1.58	2467	3.00	1.95	7411	3.37	1.69
HZ (serious and nonserious)	1194	0.87	0.38	529	0.64	0.42	1723	0.78	0.39
Cardiovascular events[d]	773	0.56	0.25	413	0.50	0.33	1186	0.54	0.27
Malignancies (excluding NMSC)	941	0.68	0.30	429	0.52	0.34	1370	0.62	0.31
NMSC	193	0.14	0.06	109	0.13	0.09	302	0.14	0.07
VTE[e]	318	0.23	0.10	150	0.18	0.12	468	0.21	0.11
Fatal cases	839	2.11[f]	0.27	279	1.16[f]	0.22	1118	1.75[f]	0.25

All cases reported at least one AE. Some cases reported > 1 AE; therefore, the number of AEs exceeds the number of cases
AE adverse event, *AESI* adverse event of special interest, *HZ* herpes zoster, *IR* immediate release, *MedDRA* Medical Dictionary for Regulatory Activities, *MR* modified release, *NMSC* nonmelanoma skin cancer, *PsA* psoriatic arthritis, *PT* Preferred Term, *PY* patient-years, *RA* rheumatoid arthritis, *RR* reporting rate, *SAE* serious adverse event, *VTE* venous thromboembolism
[a]Percentages are based on total AEs by formulation except where otherwise indicated
[b]Events/100 PY (exposure estimated from IQVIA's Multinational Integrated Data Analysis System and Prescriber Insights databases)
[c]Search criteria for AESI categories are described in the Supplementary Methods
[d]Includes the following Standardised MedDRA Queries: central nervous system vascular disorders, myocardial infarction and associated terms, ischemic heart disease and associated terms; and the following PTs: cardiac death, cardiac failure congestive, sudden cardiac death, and pulmonary embolism
[e]Pulmonary embolism events are captured in the cardiovascular events and VTE categories
[f]Percentages based on total case reports by formulation

Συμπερασματικά…

- Το tofacitinib βελτιώνει τα συμπτώματα και σημεία των φλεγμονωδών αρθριτίδων ταχέως και μακροπρόθεσμα
- Δρα το ίδιο καλά με και χωρίς προσθήκη ΜΤΧ
- Δρα σ' όλες τις εκφάνσεις των ΑξΣπΑ/ΨΑ, όπως και σε ειδικούς πληθυσμούς της ΡΑ
- Είναι ασφαλές
- Ικανοποιεί τις ανάγκες των ασθενών


Ευχαριστώ