«Εξατομικεύοντας την επιλογή θεραπείας στον ασθενή με ΡΑ:

Τί έχει αλλάξει στην καθημερινή κλινική πρακτική με τα JAKis»

Μιχαήλ. Δ. Αγγελάκος
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Ρευματολογική Κλινική
ΓΝΑ ΄΄ Ο ΕΥΑΓΓΕΛΙΣΜΟΣ΄΄, Αθήνα

ΣΥΓΚΡΟΥΣΗ ΣΥΜΦΕΡΟΝΤΩΝ

Τιμητική αμοιβή από LILLY

Περίγραμμα Ομιλίας

- Αποτελεσματικότητα
  - ✓ Naive
  - ✓ (cs/b) DMARDS IR
- Παραμονή στην θεραπεία
- Ασφάλεια
- Τιτλοποίηση της δόσης

ΠΕΡΙΣΤΑΤΙΚΟ

Θήλυ 42 ετών ,Καθηγήτρια μουσικής, μητέρα δύο παιδιών.

<u>Ελεύθερο ατομικό ιστορικό</u>

Από έτους άλγος σε μικρές και μεγάλες αρθρώσεις

ΠΔ:30min, Νυχτερινά άλγη:+

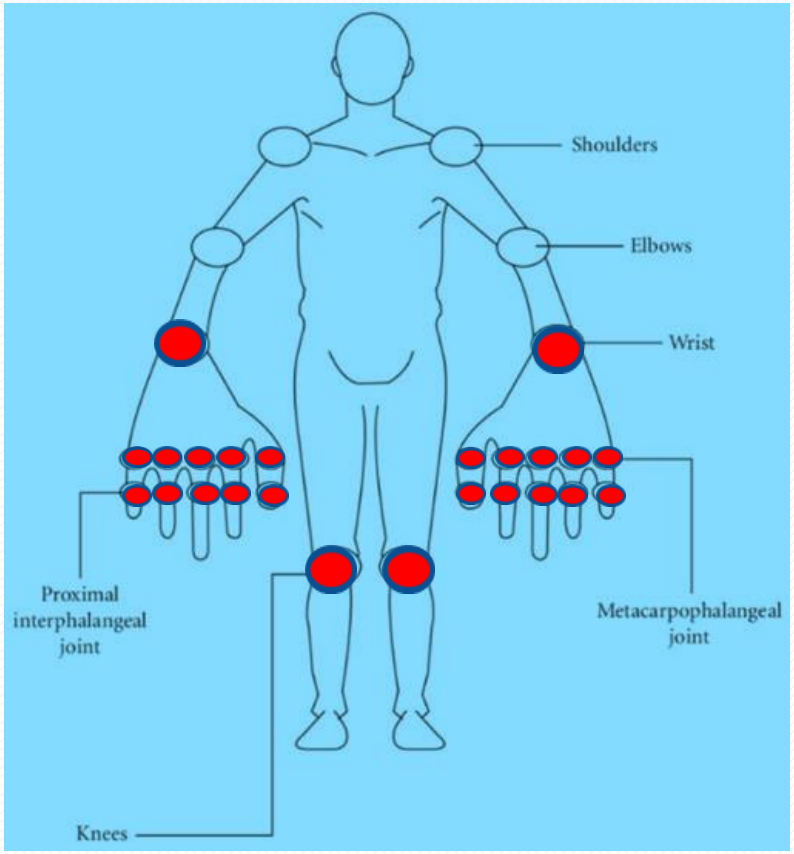
ΜΣΑΦ , ΠΑΥΣΙΠΟΝΑ , ΦΥΣΙΚΟΘΕΡΑΠΕΙΕΣ

ΠΕΡΙΣΤΑΤΙΚΟ

- Συμμετρική πολυαρθρίτιδα μικρών και μεγάλων αρθρώσεων (καρποί ,ΜΚΦ , ΕΦ, γόνατα)
- Τ:24, S: 24, VAS: 80/100

- ΤΚΕ :60mgrHg, CRP : 50mgr/l
- RF, CCP: αρνητικά
- Παρακέντηση δεξιού γόνατος : 25cc φλεγμονώδους υγρού (18000 κύτταρα)

- DAS28 ΤΚΕ : 8,41, DAS28 CRP: 7,61



- Ακτινογραφίες άκρων χειρών και γονάτων: Περιαρθρική οστεοπενία και διόγκωση ,μαλακών μορίων
- Γυναικολογικός έλεγχος : αρνητικός
- Ακτινογραφία θώρακος και υπερηχογράφημα ΑΚΚ: κφ
- Καλπροτρεκτίνη : αρνητική

Θεραπεία:

Tbs prednisolone 10mgr/d

SC Methotrexate 20mgr/w

3 μήνες μετά:

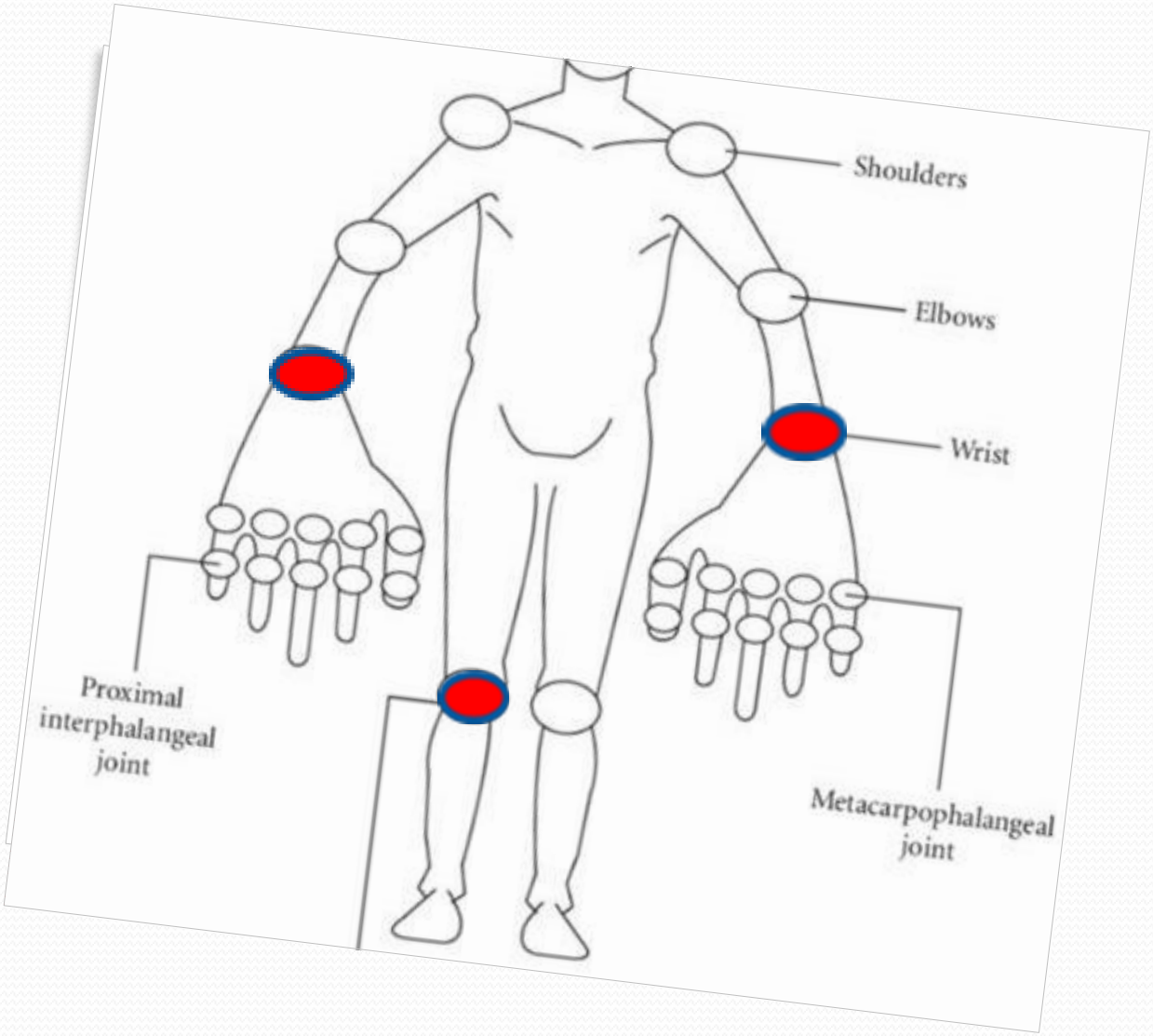
T,S: καρποί , δεξιό γόνατο

T: αριστερό γόνατο

TKE : 35mmgHg, CRP : 20mgr/l, VAS: 40/100

DAS28, CRP: 4,22, DAS28, TKE : 4,65

Δεξιό γόνατο: 10cc υγρού (7000 κύτταρα)



Το κλινικό μας πρόβλημα

ΣΥΝΟΨΗ

- Νέα μητέρα , με αυξημένες υποχρεώσεις
- Μέτρια ανταπόκριση στην θεραπεία (MDA)
- Εμμένον ύδραρθρο γόνατος (εγχύσεις κορτιζόνης)
- Μέγιστη δόση μεθοτρεξάτης
- 5-7,5 mgr/d predisolone

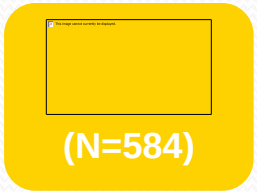
ΕΠΙΛΟΓΕΣ:

1. *anti-TnF-a*
2. *Tocilizumab*
3. *jak-inhibitors*
4. *Abatacept*
5. *Anakinra*
6. *rituximab*

θα λάβουμε υπόψη την ταχύτητα δράσης στην θεραπευτική μας απόφαση;

Και εάν δώσουμε baricitinib?

Γενική Θεώρηση Δοκιμών PA



(N=584)

RA BEGIN

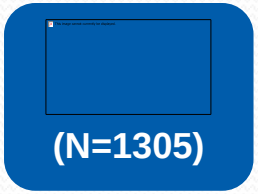
Δεν είχαν λάβει MTX στο παρελθόν

ΣΚΕΛΗ ΔΟΚΙΜΗΣ

- MTX
- Bari 4 mg μονοθεραπεία
- Bari 4 mg + MTX

ΔΙΑΡΚΕΙΑ ΔΟΚΙΜΗΣ

52 εβδομάδες



(N=1305)

RA BEAM

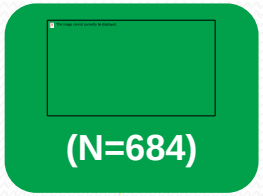
MTX-IR

ΣΚΕΛΗ ΔΟΚΙΜΗΣ

- Εικ. φάρμακο
- Ada + MTX
- Bari 4 mg + MTX

ΔΙΑΡΚΕΙΑ ΔΟΚΙΜΗΣ

52 εβδομάδες



(N=684)

RA BUILD

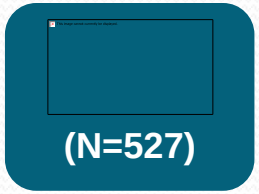
csDMARD-IR

ΣΚΕΛΗ ΔΟΚΙΜΗΣ

- Εικ. φάρμακο
- Bari 2 mg
- Bari 4 mg

ΔΙΑΡΚΕΙΑ ΔΟΚΙΜΗΣ

24 εβδομάδες



(N=527)

RA BEACON

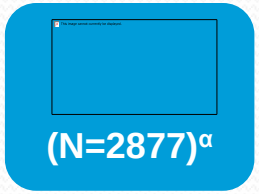
bDMARD-IR

ΣΚΕΛΗ ΔΟΚΙΜΗΣ

- Εικ. φάρμακο
- Bari 2 mg
- Bari 4 mg

ΔΙΑΡΚΕΙΑ ΔΟΚΙΜΗΣ

24 εβδομάδες



(N=2877)[α]

RA BEYOND

Μακροχρόνια

ΣΚΕΛΗ ΔΟΚΙΜΗΣ

- Bari 2 mg
- Bari 4 mg

ΔΙΑΡΚΕΙΑ ΔΟΚΙΜΗΣ

7 έτη

ΜΗ ΕΓΚΕΚΡΙΜΕΝΗ ΕΝΔΕΙΞΗ

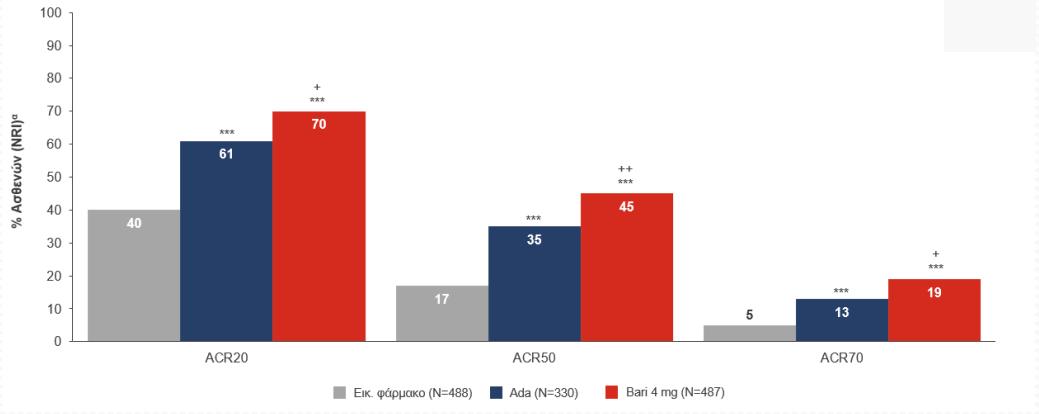
1. Fleischmann R, et al. Arthritis Rheumatol. 2017;69(3):506-517. 2. Taylor PC, et al. N Engl J Med. 2017;376(7):652-662. 3. Dougados M, et al. Ann Rheum Dis. 2017;76(1):88-95. 4. Genovese MC, et al. N Engl J Med. 2016;374(13):1243-1252. 5. Li Z, et al. Ann Rheum Dis. 2018;77(Suppl 2):969. 6. Keystone EC, et al. Ann Rheum Dis. 2015;74(2):333-340.

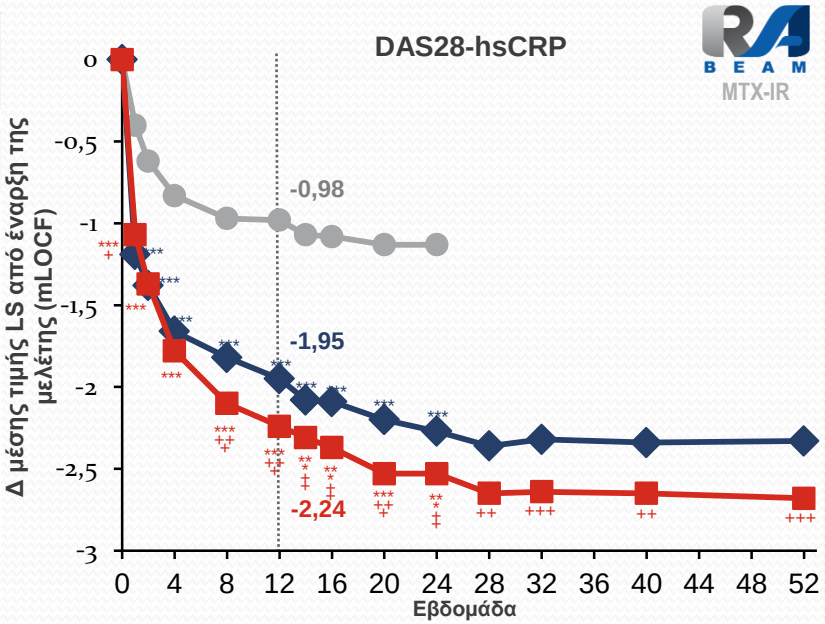
Ανωτερότητα Baricitinib vs. Adalimumab σε MTX-IR Ασθενείς

Ανταπόκριση ACR20 και Μέση Μεταβολή DAS28-hsCRP (week12)

Η Μπαρισιτινίμπη Επιδεικνύει Στατιστικά Σημαντικά Υψηλότερα Ποσοστά Ανταπόκρισης ACR Έναντι της Αδαλιμουμάμπης σε Ασθενείς που Έχουν Εμφανίσει MTX-IR

Ανταπόκριση ACR20/50/70 την Εβδομάδα 12

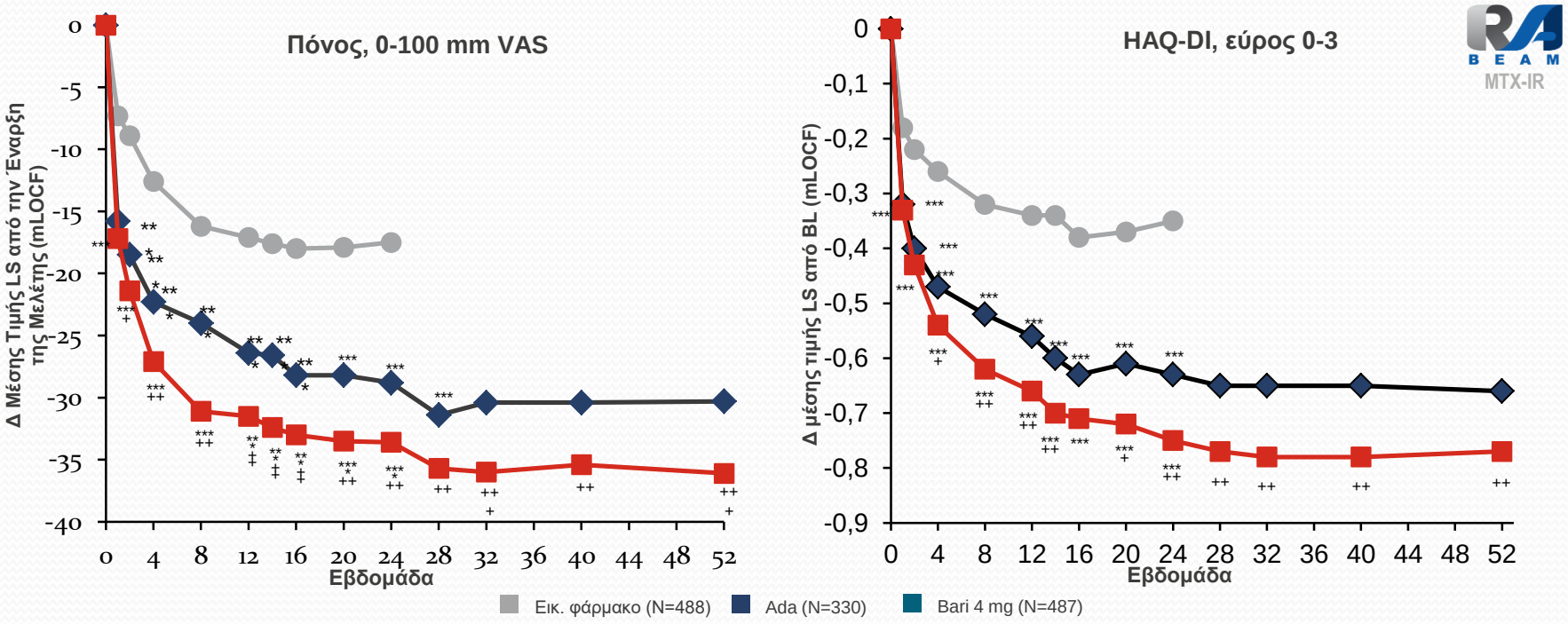




Εικ. φάρμακο (N=488) Ada (N=330) Bari 4 mg (N=487)

Taylor PC, et al. N Engl J Med. 2017;376(7):652-662.

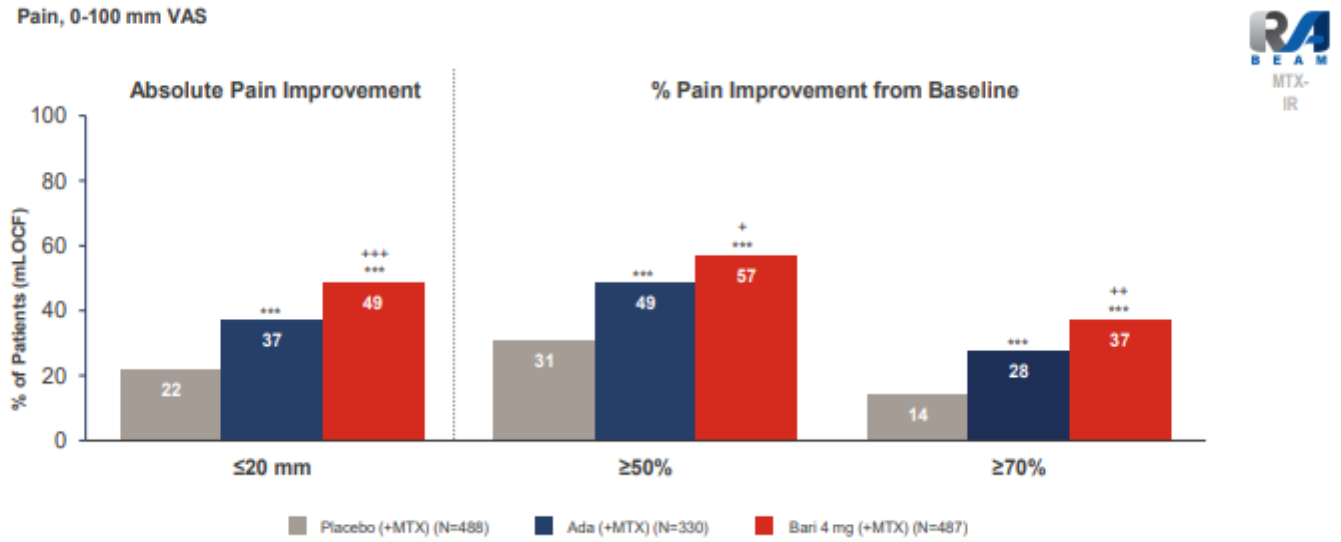
Ταχεία Βελτίωση σε Πόνο και Σωματική Λειτουργικότητα σε MTX-IR Ασθενείς



Taylor PC, et al. N Engl J Med. 2017;376(7):652-662.

More Patients Treated with Baricitinib Achieve High Levels of Pain Improvement Compared with Adalimumab-Treated Patients

Pain Improvement at Week 24 in MTX-IR Patients



RA BEAM MTX-IR

P-value vs Placebo: *** p≤0.001 ** p≤0.01 * p≤0.05 | P-value vs Ada: + p≤0.001

Mean baseline Pain VAS:
Placebo: 60 mm; ADA: 61 mm; Bari 4 mg: 62 mm.[2]

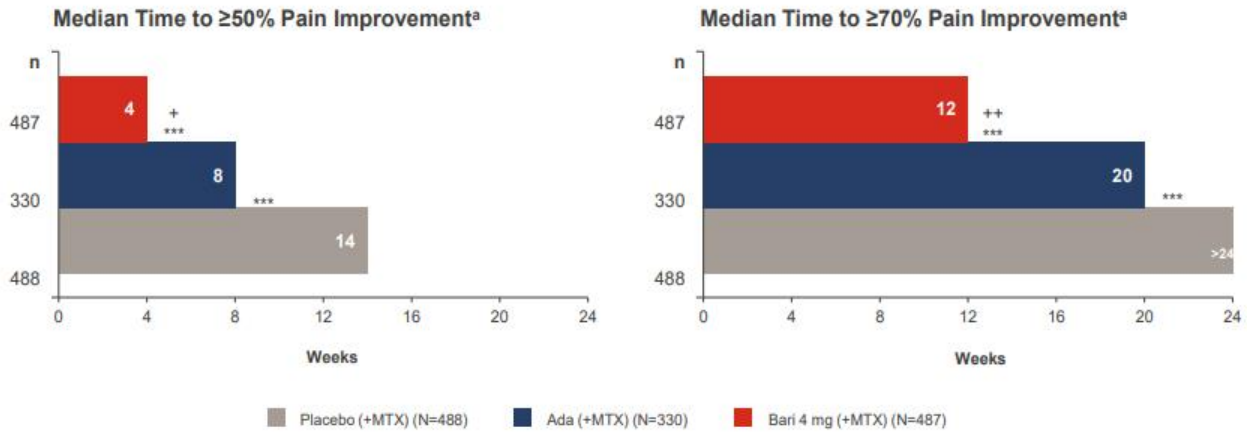
*At Week 1 only: Placebo (n=481), Ada (N=325).
Ada: adalimumab; Bari: baricitinib; IR: inadequate responder; mLOCF: modified last observation carried forward; MTX: methotrexate; VAS: visual analog scale.
1. Taylor PC, et al. *J Clin Med*. 2019;8(6):831. 2. Taylor PC, et al. *N Engl J Med*. 2017;376(7):652-662.

Significantly Faster Median Time to Achieve 50% and 70% Pain Improvement with Baricitinib Compared with Adalimumab or Placebo

Time to Pain Improvement in MTX-IR Patients

RA BEAM

MTX-IR



P-value vs Placebo: *** p≤0.001 ** p≤0.01 * p≤0.05 | P-value vs Ada: + p≤0.05

[a]Median time when 50% of patients achieved ≥50 and ≥70% improvement from baseline; [b]At Week 1 only: Placebo (n=481), Ada (N=325).
Ada: adalimumab; Bari: baricitinib; IR: inadequate responder; MTX: methotrexate.

1. Taylor PC, et al. *J Clin Med*. 2019;8(6):831.

PERFECT-RA: **A Pragmatic, Multicenter, Real-Life Study** Comparing Treat-To-Target Strategies with Baricitinib Versus TNF Inhibitors in Patients with Active Rheumatoid Arthritis After Failure of csDMARDs

Celine J van de Laar, Martijn AH Oude Voshaar, Peter ten Klooster, Danyta I Tedjo, Reinhard Bos, Tim Jansen, Annemiek Willemze, Grada A Versteeg, Yvonne PM Goekoop-Ruiterman, Eric-Jan Kroot, Mart van de Laar
RMD Open. 2024;10(2):e004291

Study Objectives

Primary Outcome

- To establish the non-inferiority of BARI to TNFi in terms of ACR 50 response[a] at 12 weeks
- If non-inferiority is confirmed, to assess the superiority of BARI strategy at 12 weeks

Secondary Outcomes

- The proportion of patients achieving DAS28-CRP remission (DAS28-CRP <2.6) at Week 12
- Changes in DAS28-CRP and CDAI scores, and PROMs over 48 weeks
- Radiological progression over 48 weeks

[a]Defined as a reduction of at least 50% in both the TJC and SJC and a reduction of at least 50% in three of the five core measures: physician global assessment of disease severity, patient global assessment of well-being, patient-reported pain, patient-reported disability and CRP.

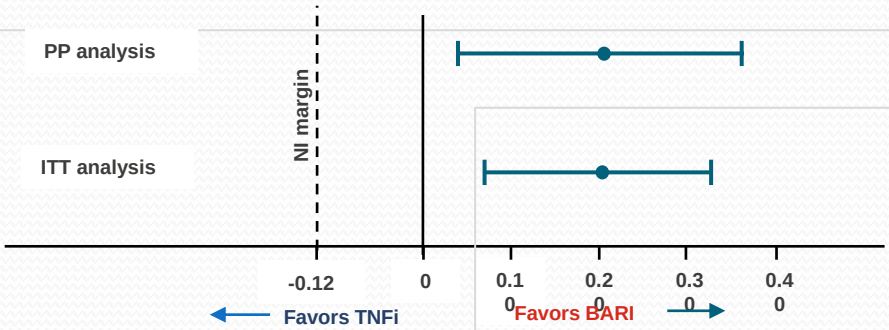
ACR 50=American College of Rheumatology 50% Response; BARI=Baricitinib; CDAI=Clinical Disease Activity Index; CRP=C-Reactive Protein; DAS28-CRP=Disease Activity Score 28 for Rheumatoid Arthritis with CRP; PROMs=Patient-Reported Outcome Measures; SJC=Swollen Joint Count; TJC=Tender Joint Count; TNFi=Tumor Necrosis Factor Inhibitor.

van de Laar CJ, et al. RMD Open. 2024;10(2):e004291 (incl. Suppl.).

Το BARI ήταν μη κατώτερο και στατιστικά ανώτερο από τους **TNFi** με βάση το **ACR 50 την εβδομάδα 12**[1]

Αναλύσεις πρωτογενούς αποτελεσματικότητας

Διαφορά στο ποσοστό των ασθενών που επιτυγχάνουν ACR 50 την Εβδομάδα12[a]



Διαφορά μεταξύ αναλογιών (BARI – TNFi)

ITT population
Comprised all subjects who correctly enrolled in the study

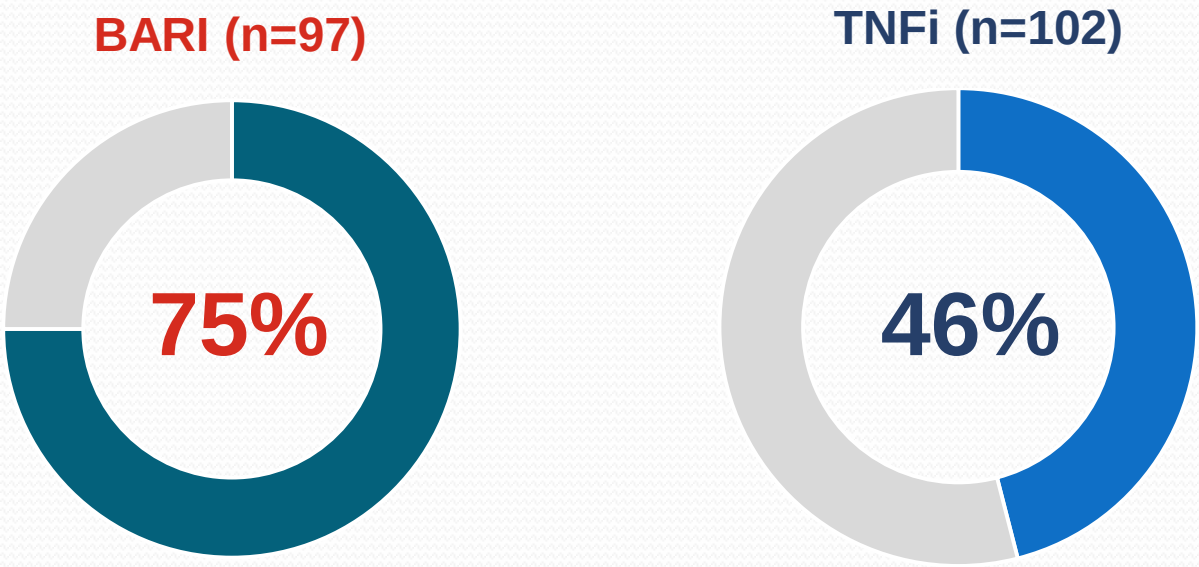
PP population
Excluded all subjects who met any of the following criteria:
- Discontinued the study
- Had missing data for ≥1 assessment of the primary outcome (ACR 50) at baseline or 12 weeks

[a]The NI margin of 12% was based on previous studies in the RA population, including the RA-BEAM study.[1,2]

ACR 50=American College of Rheumatology 50% Response; BARI=Baricitinib; CI=Confidence Interval; ITT=Intention-to-Treat; NI=Non-Inferiority; PP=Per-Protocol; RA=Rheumatoid Arthritis; TNFi=Tumor Necrosis Factor Inhibitor.

1. van de Laar CJ, et al. RMD Open. 2024;10(2):e004291 (incl. Suppl.). 2. Taylor PC, et al. N Engl J Med. 2017;376(7):652–62.

Ποσοστό ασθενών που πέτυχαν ύφεση κατά **DAS28-CRP την εβδομάδα 12**

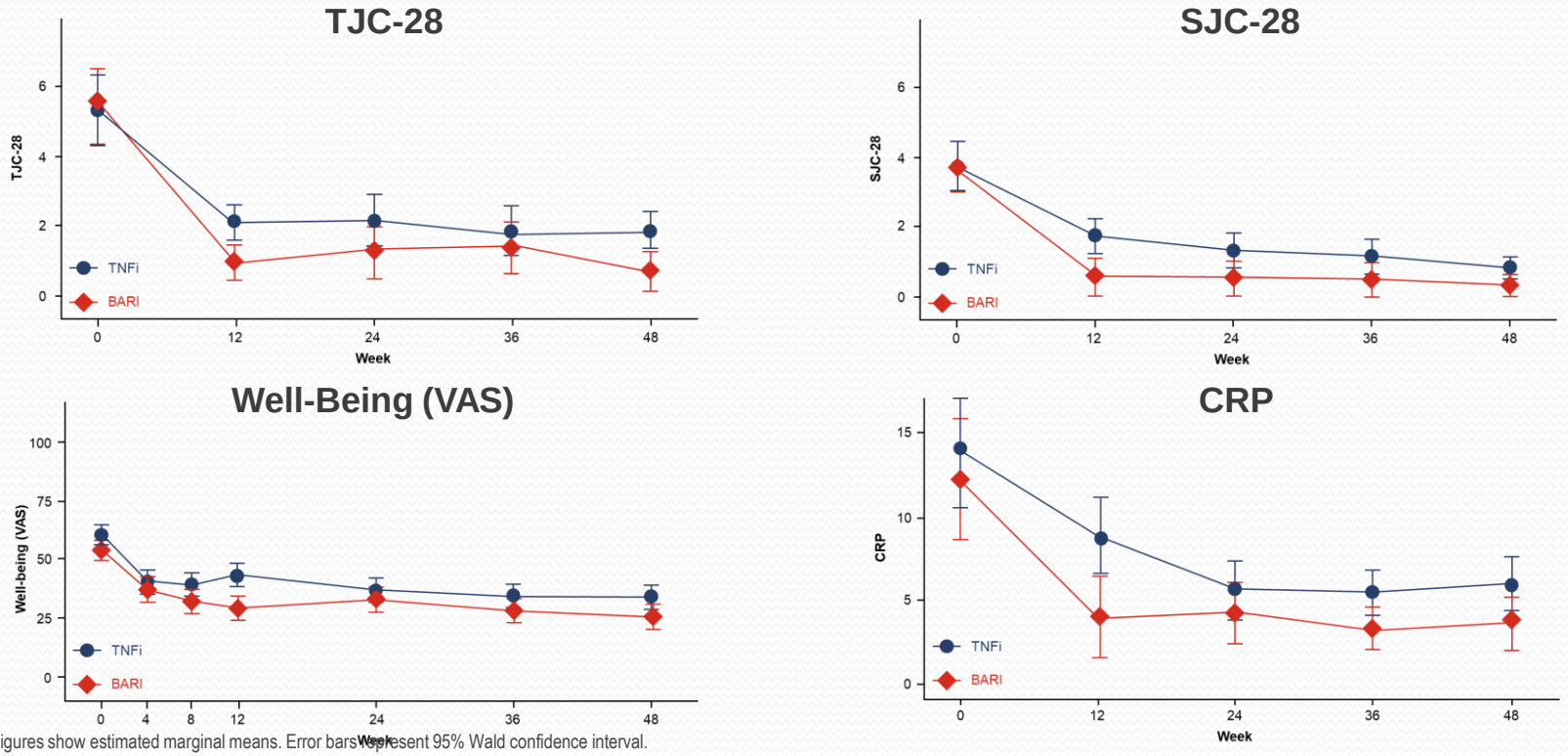


[a]DAS28-CRP <2.6.

BARI=Baricitinib; DAS28-CRP=Disease Activity Score 28 for Rheumatoid Arthritis with C-Reactive Protein; TNFi=Tumor Necrosis Factor Inhibitor.

van de Laar CJ, et al. RMD Open. 2024;10(2):e004291 (incl. Suppl.).

DAS28-CRP Components Over Time to Week 48

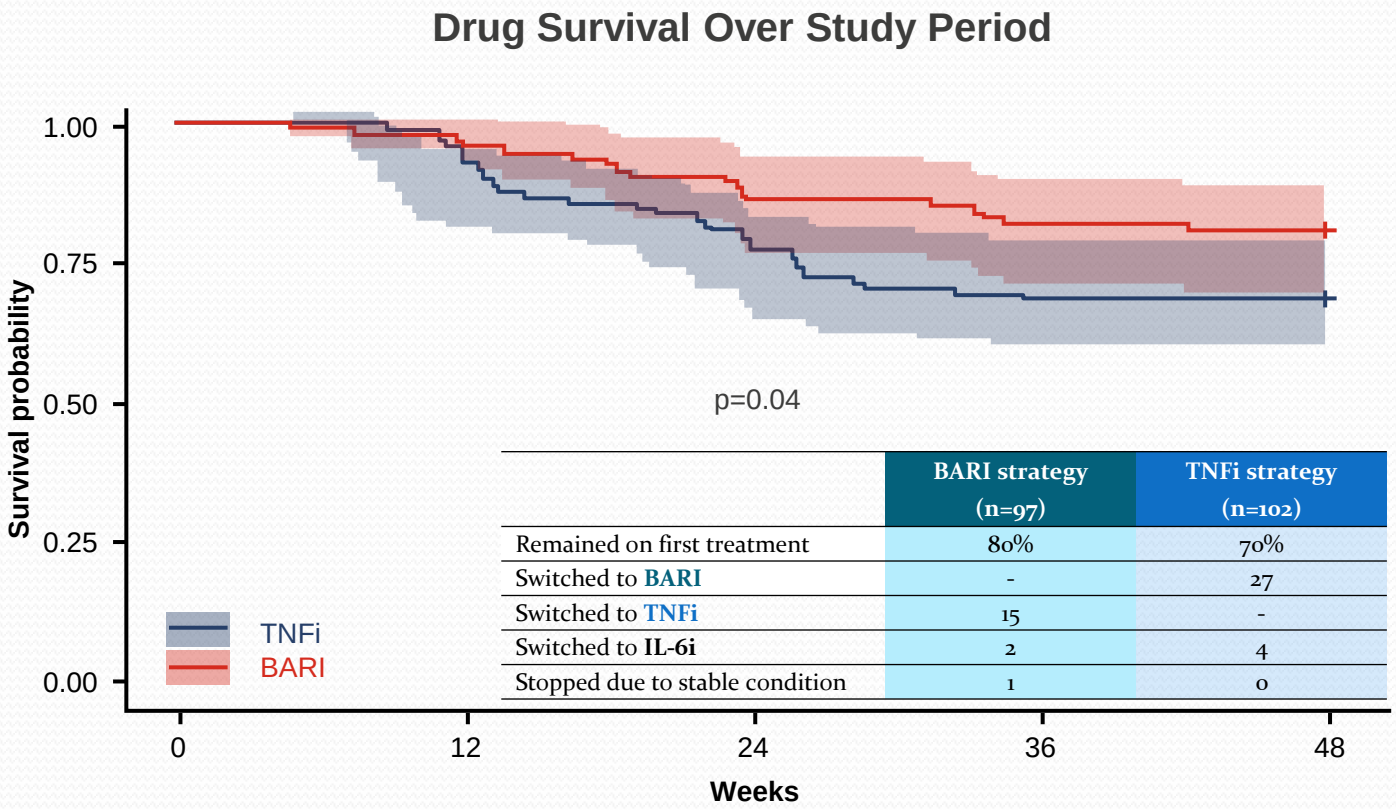


Figures show estimated marginal means. Error bars represent 95% Wald confidence interval.

BARI=Baricitinib; CRP=C-Reactive Protein; DAS28-CRP=Disease Activity Score 28 for Rheumatoid Arthritis with CRP; SJC-28=Swollen Joint Count 28; TJC-28=Tender Joint Count 28; TNFi=Tumor Necrosis Factor Inhibitor; VAS=Visual Analog Scale.

van de Laar CJ, et al. RMD Open. 2024;10(2):e004291 (incl. Suppl.).

Drug Survival for BARI Versus TNFi Strategies



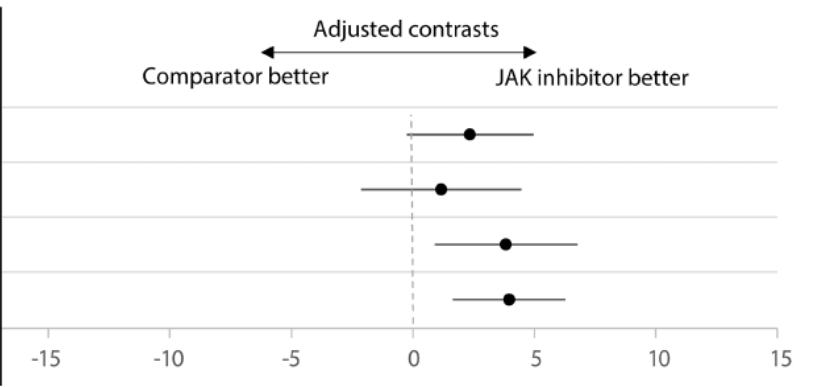
	BARI strategy (n=97)	TNFi strategy (n=102)
Remained on first treatment	80%	70%
Switched to **BARI**	-	27
Switched to **TNFi**	15	-
Switched to **IL-6i**	2	4
Stopped due to stable condition	1	0

BARI=Baricitinib; IL-6i=Interleukin-6 Inhibitor; TNFi=Tumor Necrosis Factor Inhibitor.

van de Laar CJ, et al. RMD Open. 2024;10(2):e004291 (incl. Suppl.).

Η επίδραση των JAKis στον πόνο στους 3 μήνες

Treatment initiation	N	Adj. change contrast
Abatacept	1040	2.4 (-0.3, 5.0)
IL-6 inhibitor	821	1.2 (-2.1, 4.5)
Rituximab	1101	3.8 (0.9, 6.8)
TNF inhibitor	6118	4.0 (1.6, 6.3)
JAK inhibitor	1699	Ref

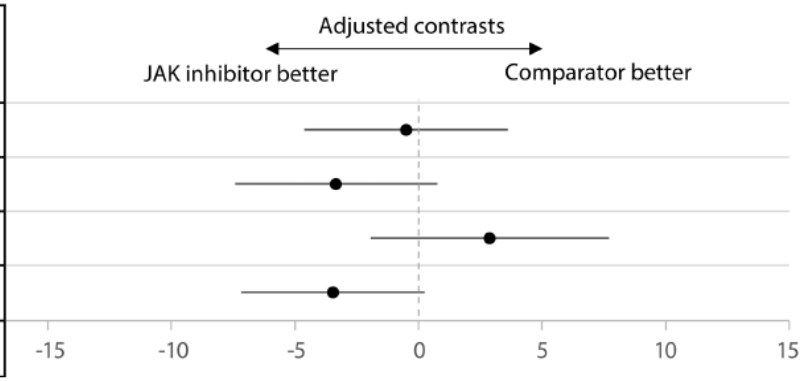


Fully adjusted differences in mean change in pain from baseline to 3-months follow-up. Multivariate linear regression with JAK inhibitor as reference

Eberhard A, et al Arthritis Rheumatol. 2024 Sep 22. doi: 10.1002/art.43014

Η επίδραση των JAKis στον πόνο στους 12 μήνες

Treatment initiation	N	Adj. change contrast
Abatacept	1102	-0.5 (-4.6, 3.6)
IL-6 inhibitor	887	-3.3 (-7.4, 0.8)
Rituximab	1149	2.9 (-1.9, 7.7)
TNF inhibitor	6422	-3.5 (-7.2, 0.3)
JAK inhibitor	1827	Ref

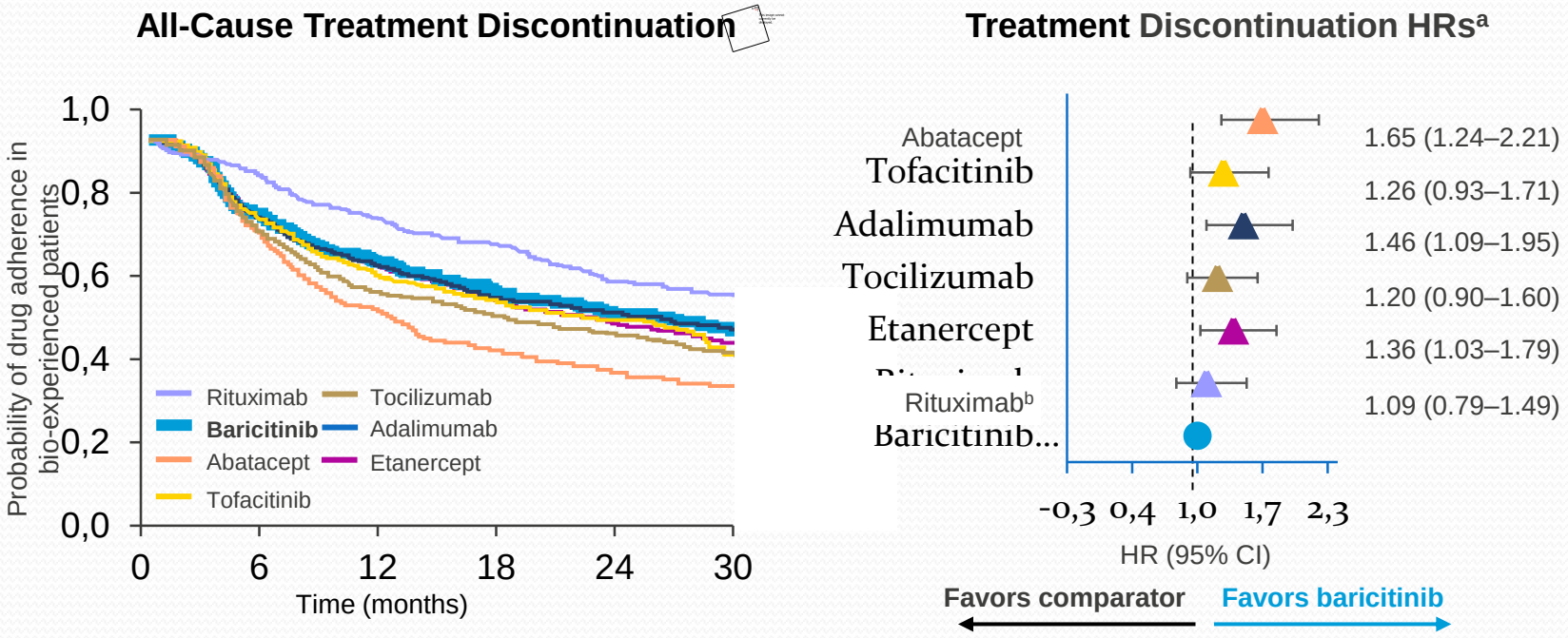


Fully adjusted differences in proportions attaining low pain score at 12 months.
Multivariate linear regression with JAK inhibitor as reference.

Eberhard A, et al Arthritis Rheumatol. 2024 Sep 22. doi: 10.1002/art.43014

Baricitinib Drug Adherence Was Higher Than Abatacept, Adalimumab, and Etanercept in Bio-Experienced Patients[1]

DANBIO/DERMBIO



[a]Adjusted for age, sex, MTX, number of previous treatment series, disease duration, calendar time, patient global assessment, smoking, CRP, pain, HAQ, and SJC.

[b]The frequency of administration of rituximab was 1–2 times per year. Efficacy can last for up to 2 years.

CI=Confidence Interval; CRP=C-reactive Protein; HAQ=Health Assessment Questionnaire; HR=Hazard Ratio; MTX=Methotrexate; Ref=Reference; SJC=Swollen Joint Count.

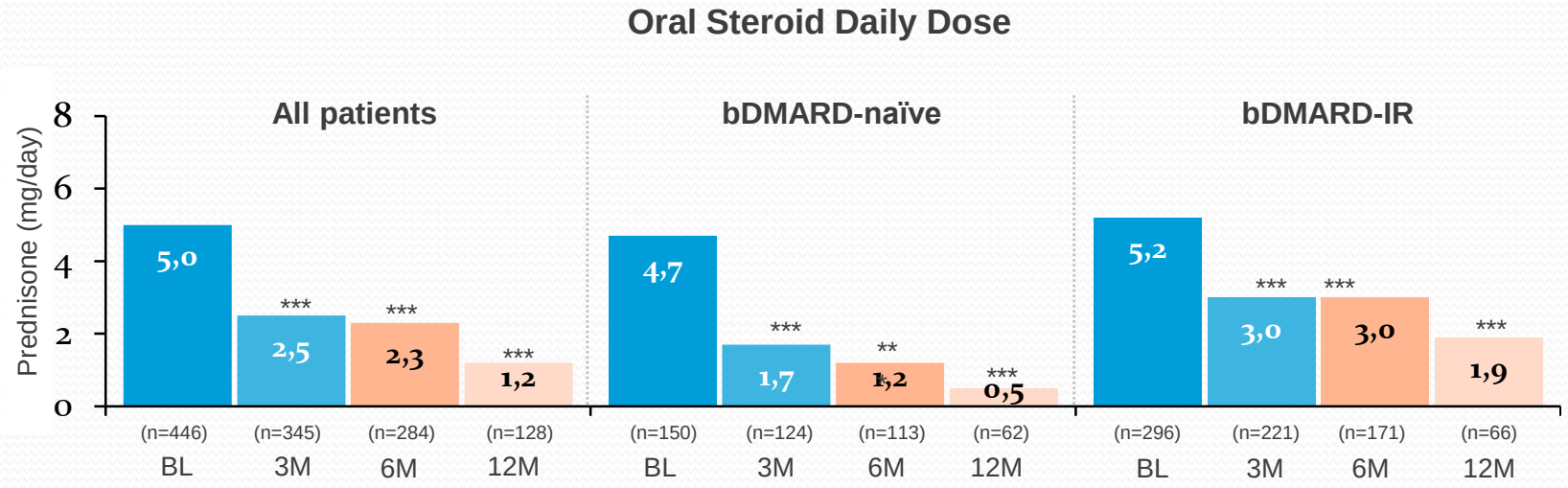
1. Egeberg A, et al. Semin Arthritis Rheum. 2022;53:151979 (incl. Suppl.).

Baricitinib Was Associated with a Reduction in Steroid Use in a Real-World Setting[1]

Italian Prospective Study

Treatment Response

- A significant reduction in oral steroid dose was observed as early as 3 months in patients receiving baricitinib, regardless of prior bDMARD experience, and with or without concomitant MTX



***p<0.0001 vs. baseline.

bDMARD=Biologic Disease-Modifying Anti-Rheumatic Drug; BL=Baseline; IR=Inadequate Responder; M=Month; MTX=Methotrexate; n=Number of Patients in the Specified Category.

1. Guidelli GM, et al. Clin Exp Rheumatol. 2021;39(4):868–73.

Έναρξη tbs baricitinib 4mgr/d

ΣΕ 2 ΜΗΝΕΣ:

- ✓ Τ: Δεξιό γόνατο
- ✓ ΤΚΕ , CRP : ΚΦ, VAS : 10/100
- ✓ Μείωση της κορτιζόνης στα 2,5mgr/d
- ✓ Μείωση της MTX σε 15mgr/w

2ο ΠΕΡΙΣΤΑΤΙΚΟ

Θήλυ 64 ετών, άνεργη .

- Ατομικό ιστορικό:

α) ΑΥ (valsartan/hydrochlorothiazide 160/12,5mgr/tab)

β) ΥΠΟΘΥΡΟΕΔΙΣΜΟΣ (λεβοθυροξίνη 88μgr/d)

γ) ΚΑΤΑΘΛΙΨΗ (φλουοξετίνη 20mgr/d)

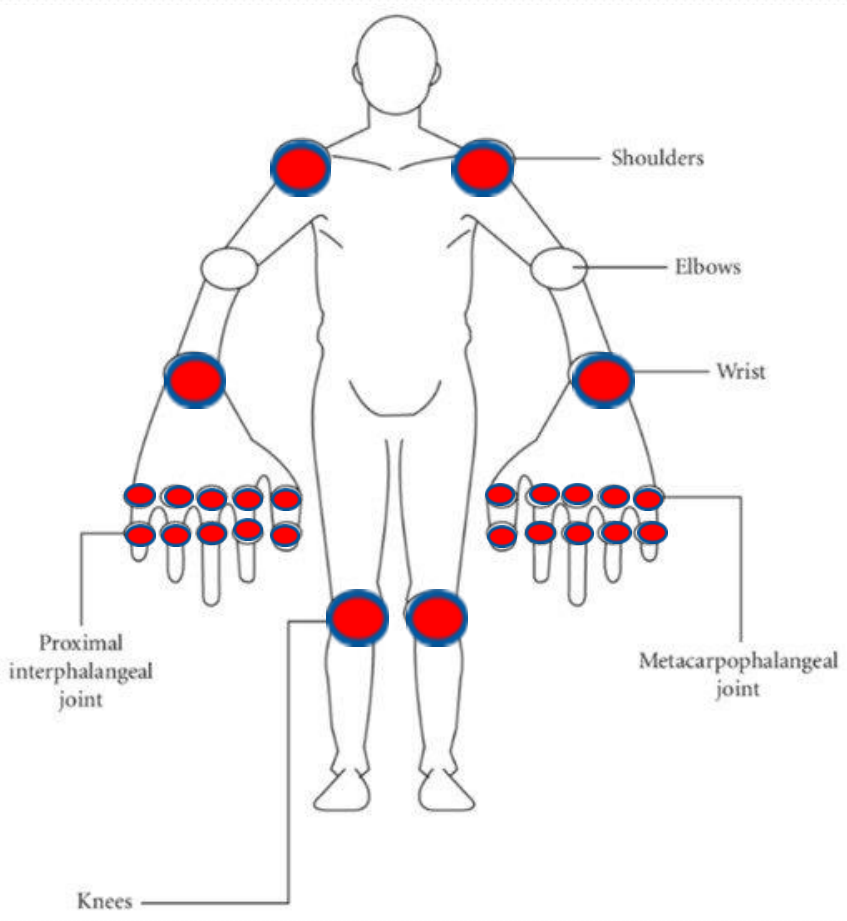
- Από 10 ετίας άλγος σε μικρές και μεγάλες αρθρώσεις

- ΠΔ: 1 ώρα, Νυχτερινά άλγη:+

- Σημαντικός περιορισμός της κινητικότητας

ΠΕΡΙΣΤΑΤΙΚΟ

- Συμμετρική πολυαρθρίτιδα (ώμων, καρπών, ΜΚΦ, ΕΦ, γονάτων , ΠΔΚ)
- Τ: 26, S: 24 VAS : 90/100
- ΤΚΕ: 80mmHg, CRP :75mgr/l,
- RF: 65, CCP>500
- DAS28 ΤΚΕ:8,57 , DAS28, CRP: 8,0



2ο ΠΕΡΙΣΤΑΤΙΚΟ

- Παρακέντηση γονάτων: 25-30 cc φλεγμονώδους υγρού(15000-25000 κύτταρα)
- Αξονική τομογραφία θώρακος: ήπια ινώδη στοιχεία βάσεων
- Σπιρομέτρηση: χωρίς παθολογικά ευρήματα

ΘΕΡΑΠΕΙΑ

1. tbs methyprednisolone 16mgr/d
2. sc methotexate 20mgr/w

3 μήνες μετά:

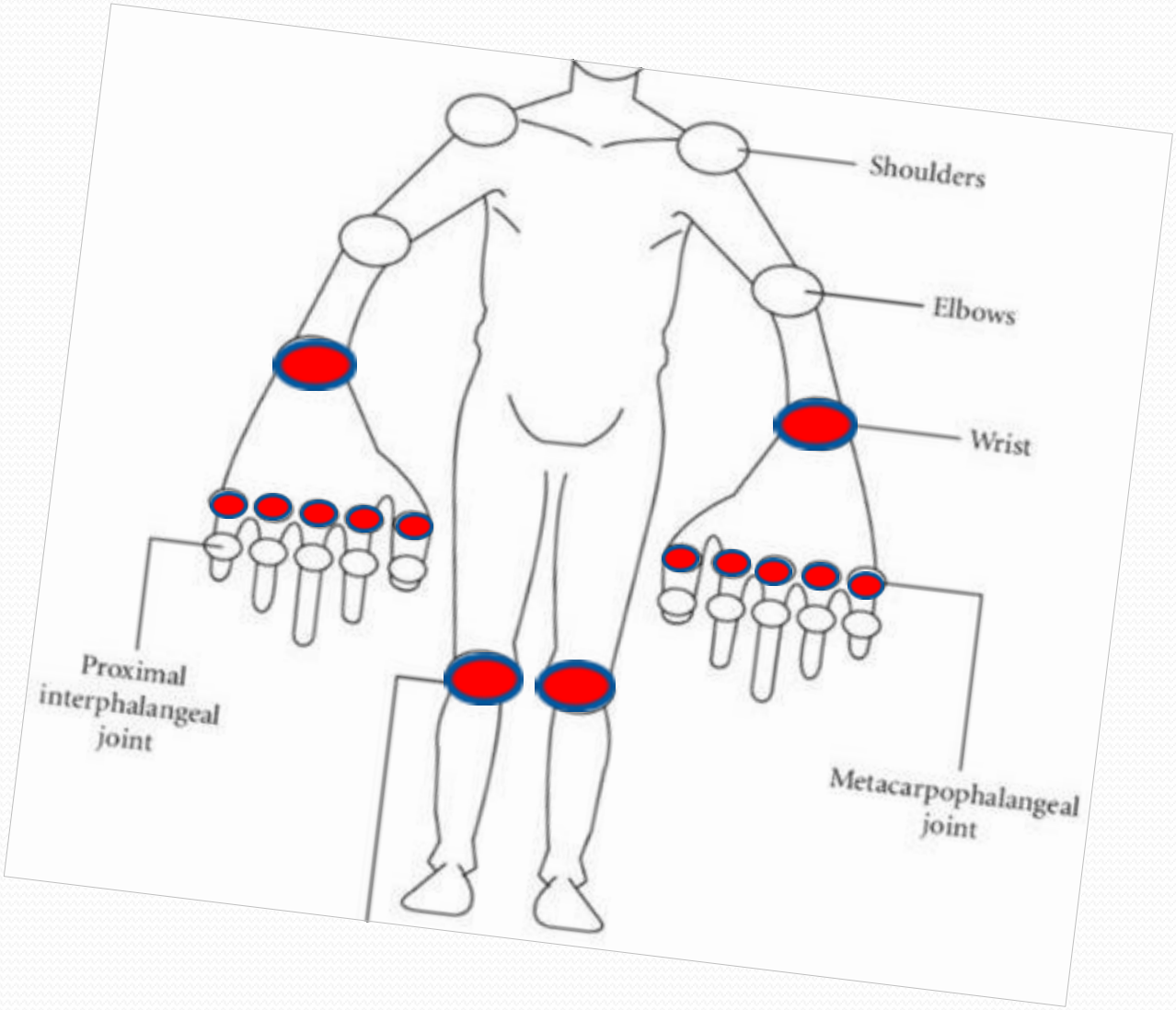
Αρθρίτιδα γονάτων και καρπών

Αρθρίτιδα ΜΚΦ

T:14 , S: 14, VAS: 60/100

TKE : 60mmHg, CRP: 50mgr/l

DAS 28 TKE:6,82,
DAS28,CRP:6,33



- Προσθήκη inj Etarnecept 50mgr/w
- sc MTX 20mgr/w
- tbs methyprednisolone 8mgr/d

3 μήνες

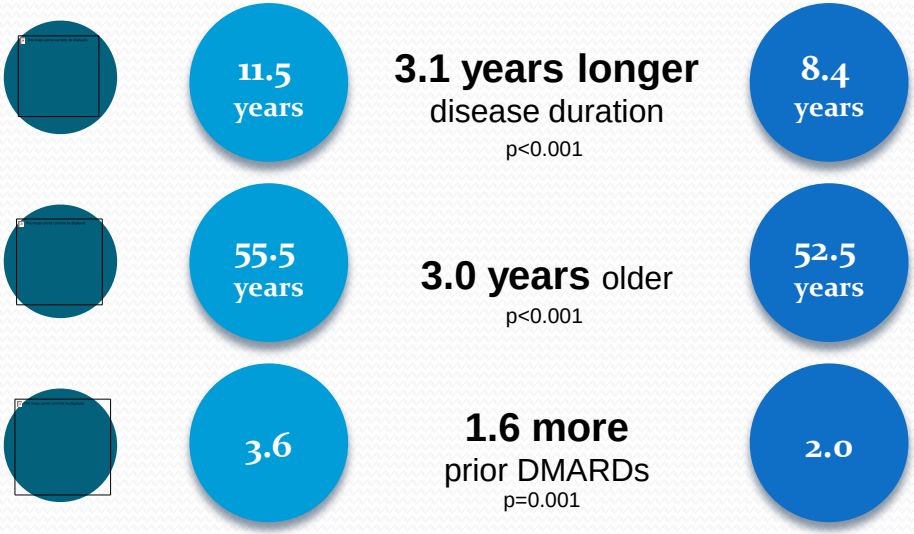
- T: 4, S: 10 , VAS : 40/100
- TKE : 35mmHg, CRP:25mgr/l,
- DAS 28 TKE: 4,96, DAS28 CRP: 4,6

ΣΥΝΟΨΗ

- Μακροχρόνιο νόσημα, με διαβρώσεις και στενώσεις
- Κακοί προγνωστικοί παράγοντες (γυναίκα, οροθετικότητα, υψηλή ενεργότητα, μόνιμες ακτινολογικές αλλοιώσεις)
- Αδυναμία επίτευξης LDA στους 6 μήνες
- Αύξηση ηπατικών ενζύμων x3
- Methylprednisolone 6 mgr/d

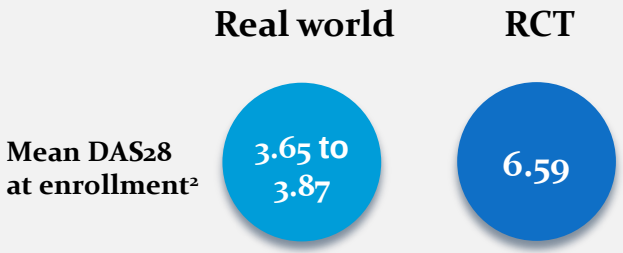
Real-World Studies in Rheumatoid Arthritis vs. RCTs

General Characteristics of Patients with RA in Observational Studies vs. RCTs[1]



>90%

of patients in observational clinical cohorts **do not meet inclusion criteria** for RCTs for targeted agents[2]



Data presented as mean.
DAS28=Disease Activity Score 28; DMARD=Disease-Modifying Anti-Rheumatic Drug; RA=Rheumatoid Arthritis; RCT=Randomized Controlled Trial.
1. Kilcher G, et al. Rheumatology (Oxford). 2018;57(2):354–69. 2. Vashisht P, et al. Arthritis Care Res (Hoboken). 2016;68(10):1478–88.

A Numerically Higher Proportion of Patients Achieved Remission with Baricitinib vs. b/tsDMARDs

RA-BE-REAL Study

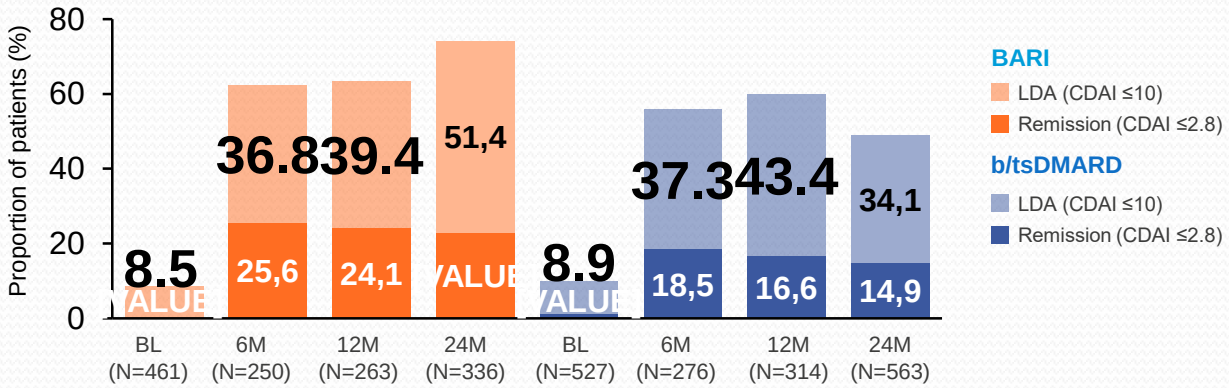
Treatment Response[1]

- Despite being older and having longer disease duration at baseline, a numerically higher percentage of patients treated with baricitinib achieved remission compared with b/tsDMARD-treated patients

Baseline characteristics[1]

	BARI	b/tsDMARD
Age, years	59	57
Disease duration, years	10	9
b/tsDMARD-naïve	48%	61%

CDAI Response Rates at 6, 12, and 24 Months[1–3]



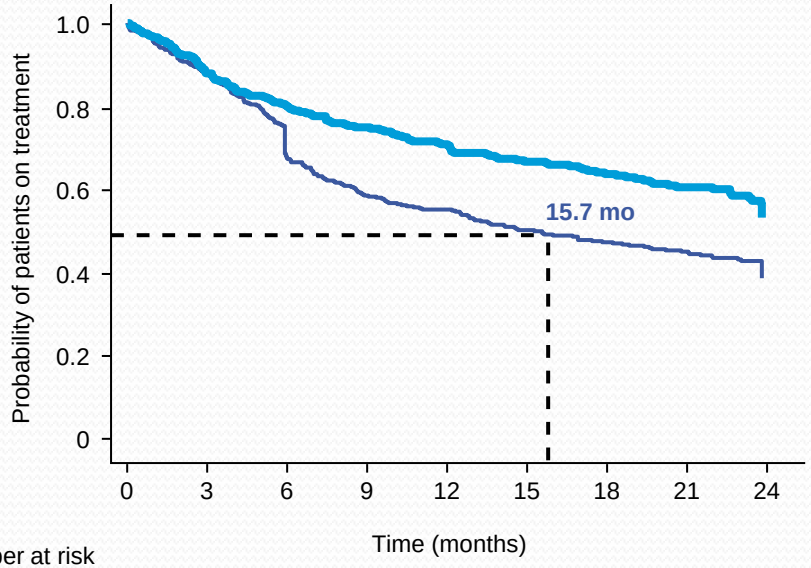
Missing values were imputed using non-responder imputation for binary variables LDA and remission. Missing values were imputed using modified Baseline Observation Carried Forward for continuous variable of CDAI.
BARI=Baricitinib; BL=Baseline; b/tsDMARD=Biologic or Targeted Synthetic DMARD; CDAI=Clinical Disease Activity Index; DMARD=Disease-Modifying Anti-Rheumatic Drug; LDA=Low Disease Activity; M=Month; N=Number of Patients in the Analysis Population.

1. Alten R, et al. Rheumatol Ther. 2023;10:1575–95. 2. Alten R, et al. Rheumatol Ther. 2023;10:73–93.
3. Alten R, et al. Poster presentation POS0666 at the American College of Rheumatology (ACR) Convergence, Nov 10–14, 2022, Philadelphia, PY, USA.

Drug Survival Rates Were Consistent in Both Age Subgroups[1]

RA-BE-REAL Study

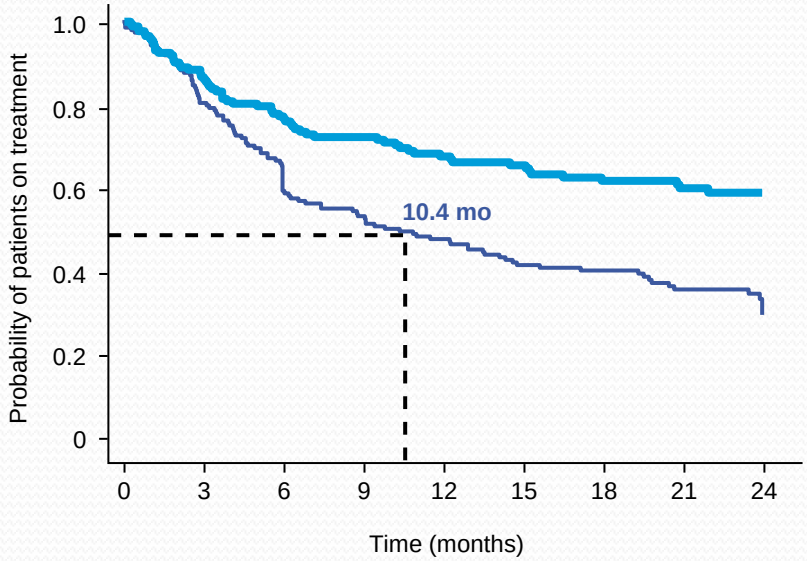
Population Aged <65 Years



Number at risk

Baricitinib	329	283	248	225	206	191	171	150	70
b/tsDMARD	391	344	267	229	215	195	177	154	84

Population Aged ≥65 Years



Baricitinib	180	151	127	113	100	92	80	69	27
b/tsDMARD	168	135	100	89	78	68	58	47	27

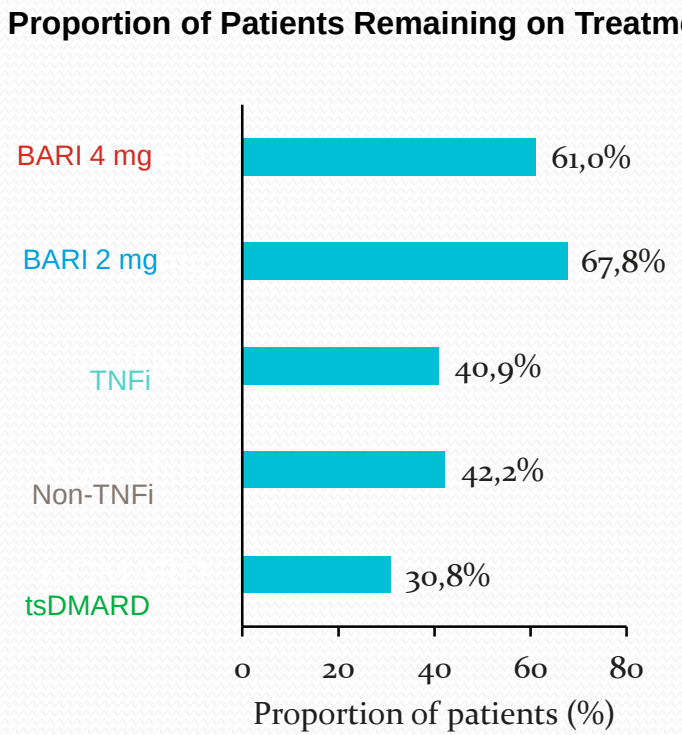
Instances where the median value was absent indicate the median was unable to be calculated as it did not reach the probability of 0.5.

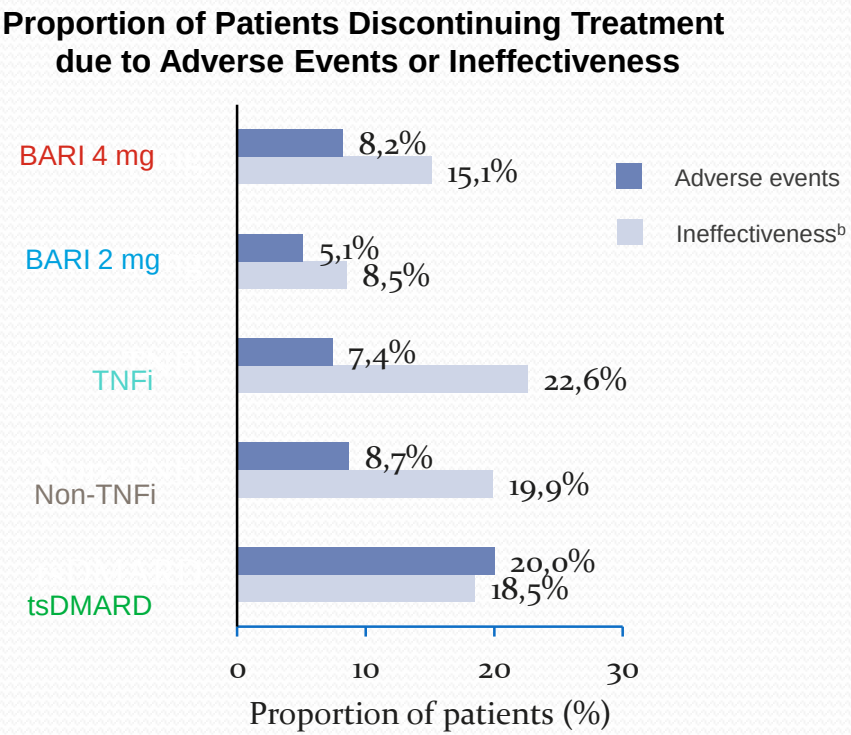
b/tsDMARD=Biologic or Targeted Synthetic Disease-Modifying Anti-Rheumatic Drug; Mo=Months.

1. Alten R, et al. Rheumatol Ther. 2023;10:1575–95 (incl. Suppl).

A Greater Proportion of Patients Remained on Baricitinib Compared with Those Receiving Comparator Treatments at 24 Months[a,1]

RA-BE-REAL Study





[a]In the overall population. [b]Includes primary non-response and secondary loss of response.

BARI=Baricitinib; TNFi=Tumor Necrosis Factor Inhibitor; tsDMARD=Targeted Synthetic Disease-Modifying Anti-Rheumatic Drug.

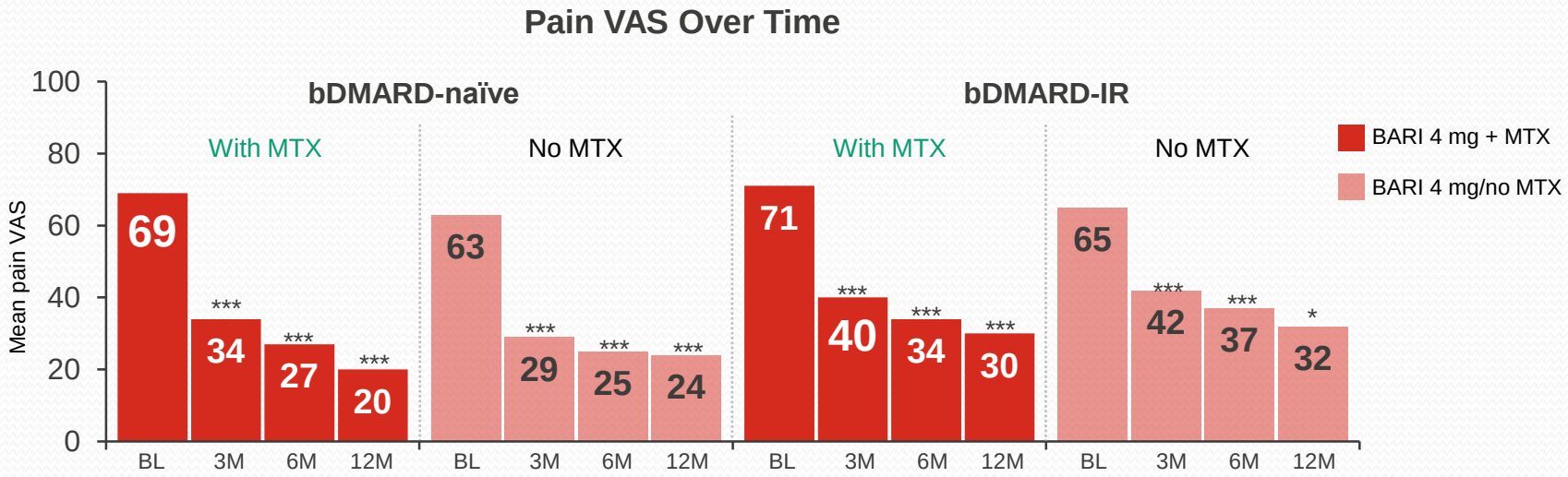
1. Alten R, et al. Rheumatol Ther. 2023;10:1575–95.

Baricitinib Significantly Reduced Pain in Real-World Patients[1] bDMARD-Naïve and bDMARD-IR Patients

Italian Prospective Study

Treatment Response

- Patients treated with baricitinib reported significant reductions in pain VAS at 12 months, regardless of prior bDMARD experience or concomitant MTX
- Most patients had a significant reduction in pain VAS as early as 3 months



*p<0.01; ***p<0.0001 vs. baseline.

BARI=Baricitinib; bDMARD=Biologic Disease-Modifying Anti-Rheumatic Drug; BL=Baseline; IR=Inadequate Responder; M=Month; MTX=Methotrexate; VAS=Visual Analog Scale.

1. Guidelli GM, et al. Clin Exp Rheumatol. 2021;39(4):868–73.

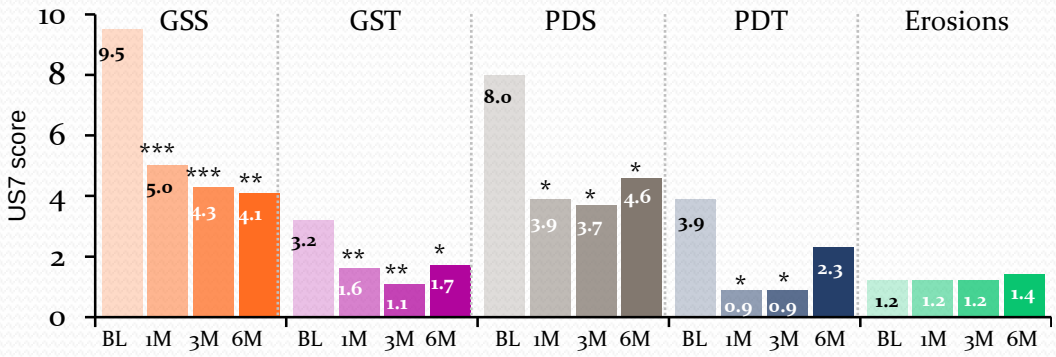
Real-World Improvements in Ultrasound-Detected Synovitis and Bone Erosion with Baricitinib[1]

Italian Single-Center Experience

Treatment Response

- Statistically significant improvements were **observed as early as the first month** in all domains of the US7 score

Ultrasound Parameters



Disease Activity Scores

Outcome	Baseline (N=43)	6 months
DAS28-ESR	5.27 ± 1.33	3.50 ± 1.30***
CDAI	27.68 ± 10.62	11.30 ± 9.63***
SDAI	25.01 ± 11.40	11.33 ± 10.74***

***p<0.0001 vs. baseline
Data presented as mean ± standard deviation

*p<0.05; **p<0.001; ***p<0.0001 vs. baseline.
BL=Baseline; CDAI=Clinical Disease Activity Index; DAS28-ESR=Disease Activity Score 28 for Rheumatoid Arthritis with Erythrocyte Sedimentation Rate; GSS=Gray-Scale Synovitis; GST=Gray-Scale Tenosynovitis; M=Month; N=Number of Patients in the Analysis Population; PDS=Power Doppler Synovitis; PDT=Power Doppler Tenosynovitis; SDAI=Simplified Disease Activity Index; US7=Ultrasound 7 Joints.

1. Tesei G, et al. Ther Adv Musculoskelet Dis. 2021;13:1759720X211014019.

ΠΕΡΙΣΤΑΤΙΚΟ

- 6 μήνες

Απουσία ενεργού αρθρίτιδας
(+ υπερηχογραφικά)

Μόνο διογκωμένες
(χωρίς ευαισθησία και doppler(-))

TKE: 10mmHg, CRP 5mgr/l, VAS 10/100

DAS28 TKE : 2,72, DAS 28 CRP:2,71

tbs methylprednisolone 2mgr/d

- 24 μήνες

Προοδευτική μείωση της Hb (12,1gr/dl σε 10,4 gr/dl)

Βελτίωση με την διακοπή

Επιδείνωση με την επαναχορήγηση

RA-BEACON

Baricitinib vs Placebo

BEACON

TNFi-IR

PRIMARY ENDPOINT

ACR20 response at Week 12
(Bari 4 mg vs Placebo)

DURATION OF TRIAL

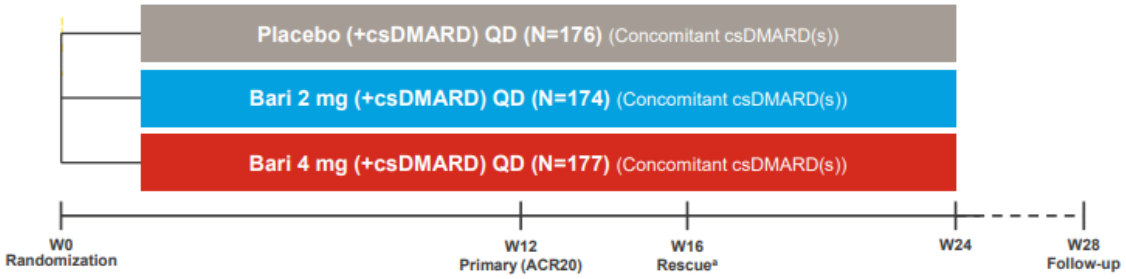
24 weeks

MEAN DURATION OF RA

10.7 years

PATIENT INCLUSION CRITERIA

- Inadequate response or intolerance to ≥1 prior TNFi
- ≥28 days since last bDMARD; 6 months for rituximab
- Stable background cDMARD(s)
- ≥6/68 tender joints
- ≥6/66 swollen joints
- hsCRP ≥3 mg/L

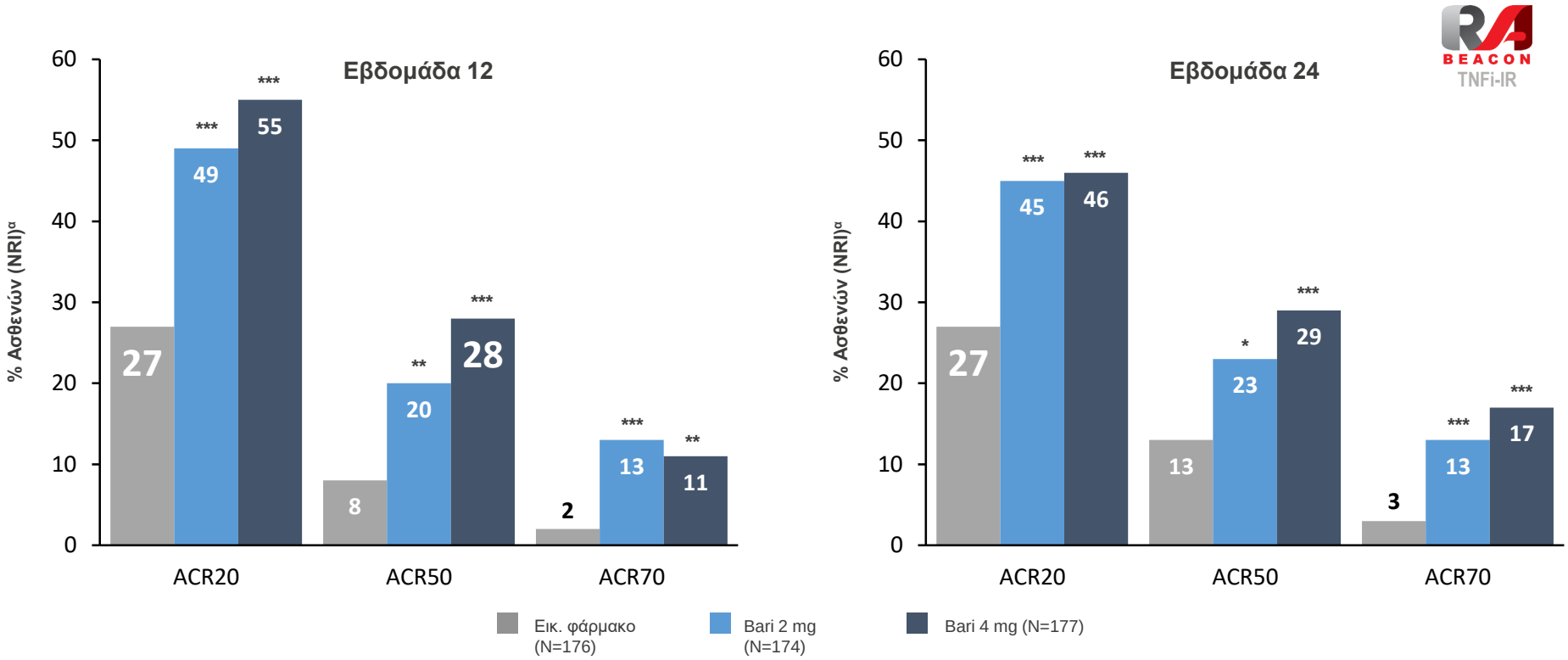


[a]Rescue treatment, Bari 4 mg QD, was available starting at Week 16.

ACR20: American College of Rheumatology 20% improvement criteria; Bari: baricitinib; bDMARD: biologic disease-modifying antirheumatic drug; cDMARDs: conventional disease-modifying antirheumatic drugs; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; hsCRP: high-sensitivity C-reactive protein; IR: inadequate responders; QD: once daily; RA: rheumatoid arthritis; TNFi: tumor necrosis factor inhibitor.

1. Genovese MC, et al. *N Engl J Med*. 2016;374(13):1243-1252.

Ανταπόκριση ACR Baricitinib vs. Placebo σε bDMARD-IR Ασθενείς

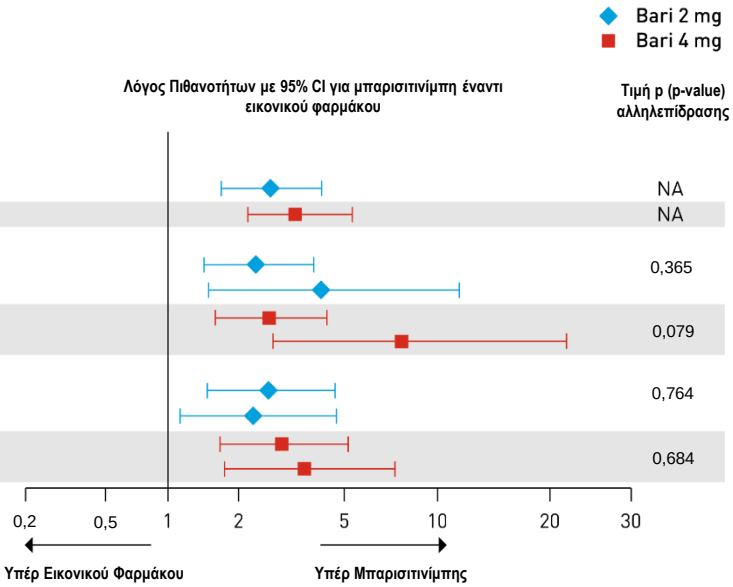


BEACON TNFi-IR

Genovese MC, et al. N Engl J Med. 2016

Η αποτελεσματικότητα του Baricitinib ήταν ανεξάρτητη από αριθμό/ τύπο προηγούμενων bDMARD

Ποσοστό ασθενών που επιτυγχάνουν ανταπόκριση ACR20 την εβδομάδα 12	n/N (%) Εικονικό Φάρμακο	Bari 2 mg	Bari 4 mg	Τιμή p (p-value) αλληλεπίδρασης
Συνολικός Πληθυσμός				
2 mg	48/176 (27)	85/174 (49)		NA
4 mg	48/176 (27)		98/177 (55)	NA
Αρ. Προηγούμενων bDMARD				
<3	42/129 (33)	66/124 (53)		0,365
≥3	6/47 (13)	19/50 (38)		
<3	42/129 (33)		74/132 (56)	0,079
≥3	6/47 (13)		24/45 (53)	
Αρ. Προηγούμενων TNFi				
1	31/104 (30)	54/102 (53)		0,764
≥2	17/69 (25)	31/72 (43)		
1	31/104 (30)		58/104 (56)	0,684
≥2	17/69 (25)		38/70 (54)	

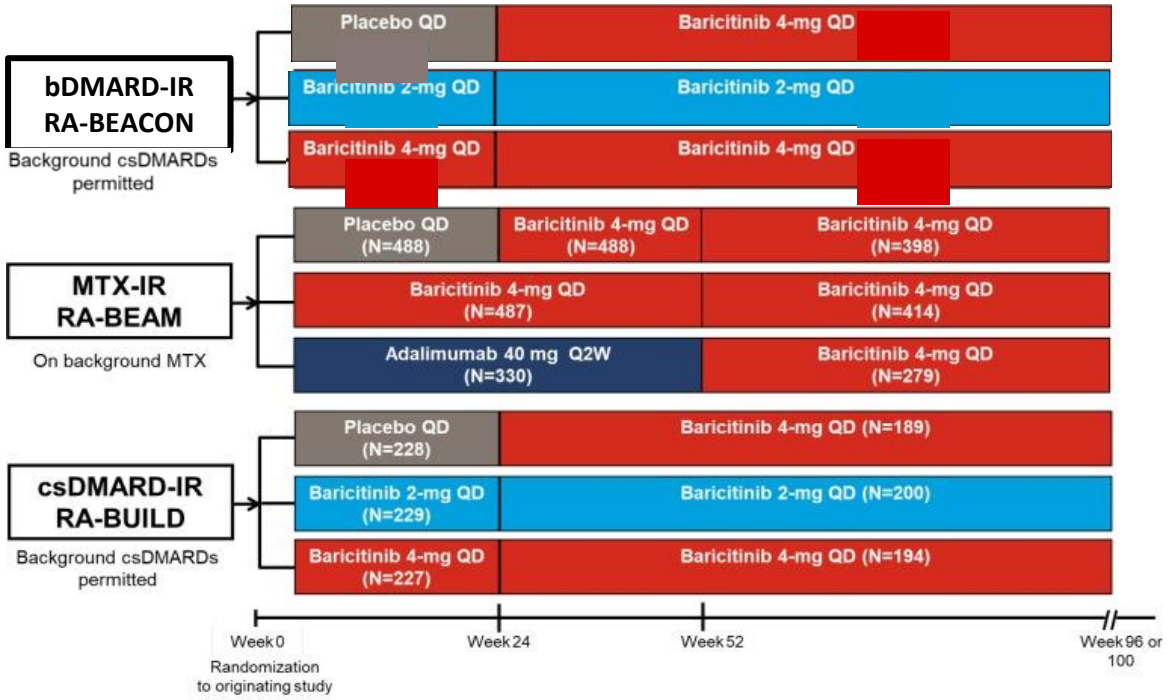


Το baricitinib επέδειξε σταθερή θεραπευτική επίδραση, μετρούμενη ως το ποσοστό των ασθενών που πέτυχαν ανταπόκριση ACR20 ή CDAI ≤ 10, ανεξάρτητα από τον αριθμό των προηγούμενων βιολογικών θεραπειών με ή χωρίς TNFi

RA BEACON TNFi-IR POST-HOC ANALYSIS

Genovese M, et al. Rheumatology. 2018

Baricitinib – Δεδομένα μακροχρόνιας αποτελεσματικότητας



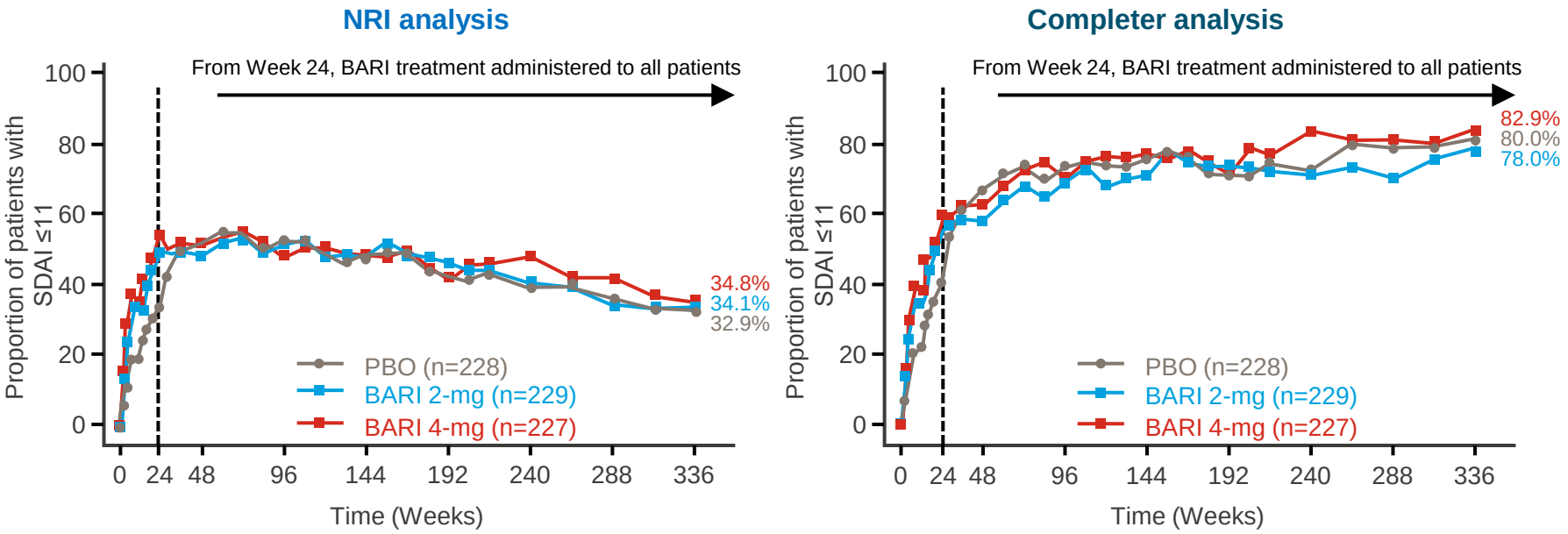
RA-BEYOND

Efficacy of baricitinib in patients with moderate-to-severe rheumatoid arthritis up to 6.5 years of treatment: results of a long-term study

Caporali R et al. Rheumatology, 2024, 63, 2799–2809

LDA was Maintained with Baricitinib 2- and 4-mg up to 6.5 Years[1] SDAI

Findings from RA-BUILD and RA-BEYOND (LTE study)



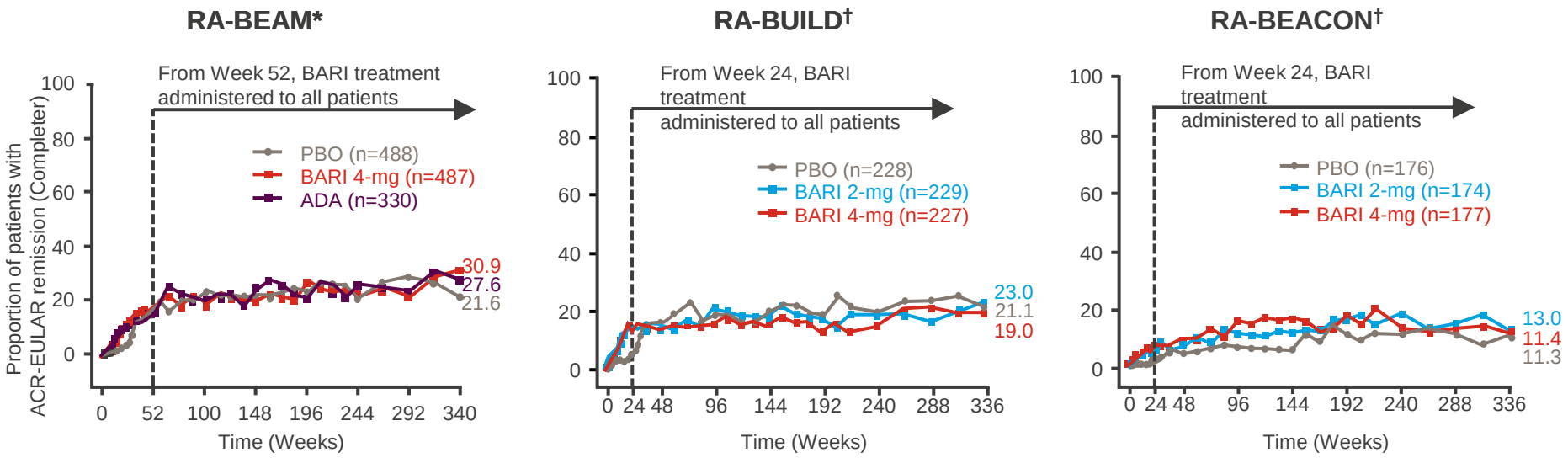
Rescue treatment was offered at Week 16. Upon entering RA-BEYOND at Week 24, patients who received PBO in RA-BUILD were switched to BARI 4-mg.

BARI=Baricitinib; csDMARD=Conventional Synthetic Disease-Modifying Antirheumatic Drug; IR=Inadequate Response; LDA=low disease activity; LTE=Long-Term Extension; NRI=Non-Responder Imputation; PBO=Placebo; RA=Rheumatoid Arthritis; SDAI=Simplified Disease Activity Index.

1. Caporali R, et al. *Rheumatology (Oxford)* 2023.

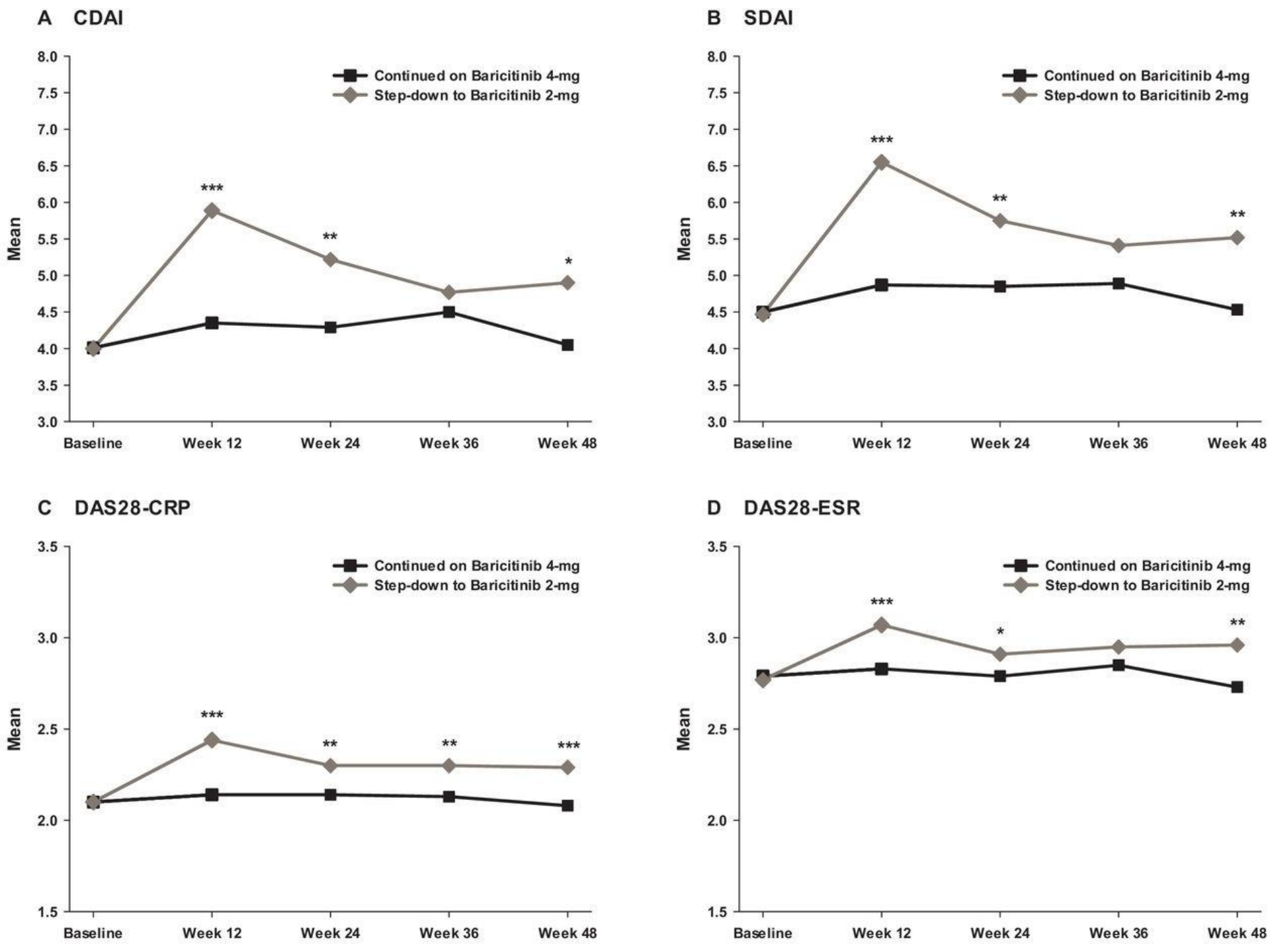
Boolean Remission rates in RA-BEYOND up to 6.5 years[1]

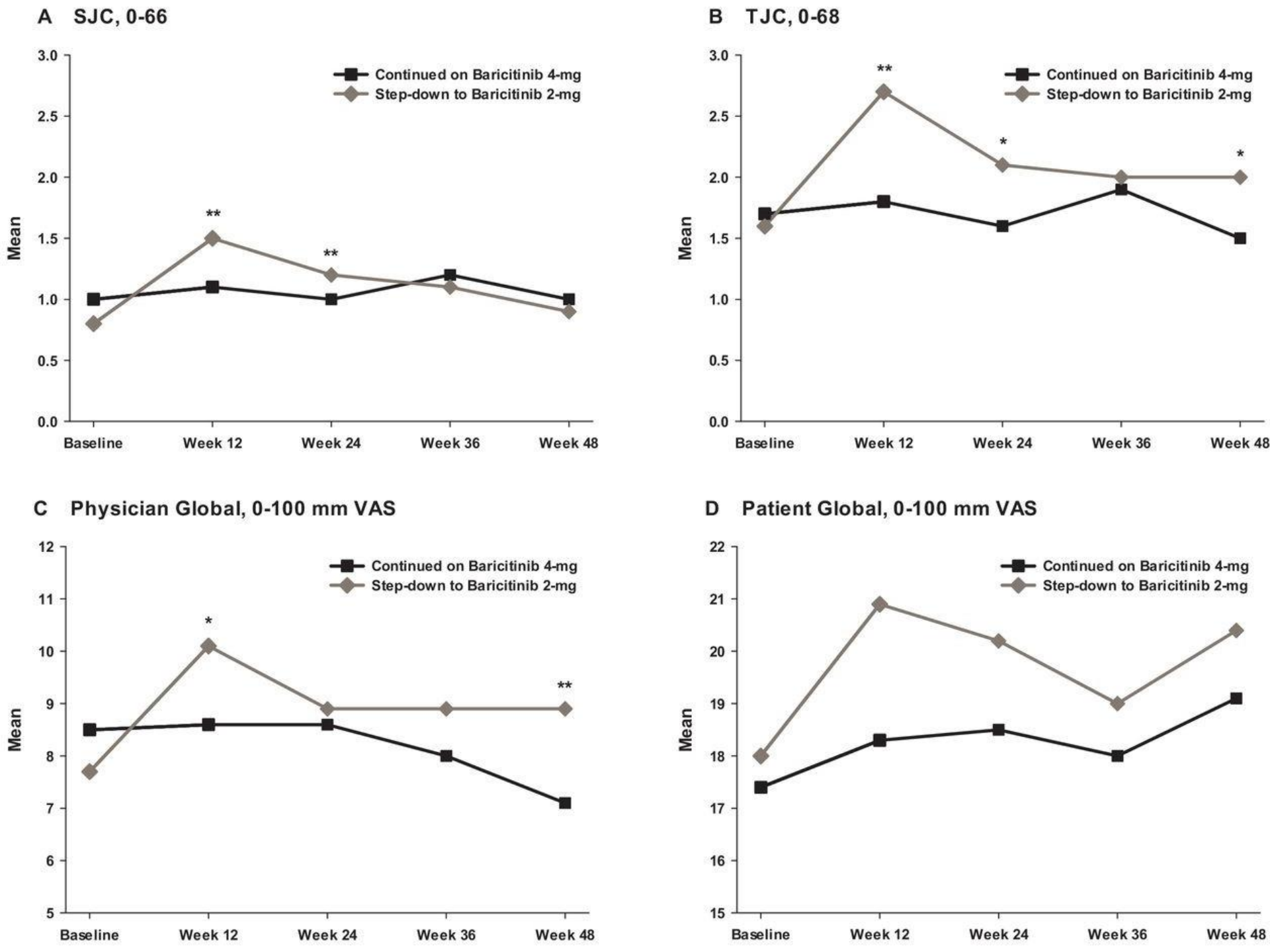
COMPLETER



Rescue treatment was offered at Week 16. *At Week 24, all patients who received PBO (+MTX) in RA-BEAM were switched to BARI 4-mg (+MTX). Upon entering RA-BEYOND at Week 52, patients who received ADA (+MTX) in RA-BEAM were switched to BARI 4-mg (+MTX). †Upon entering RA-BEYOND at Week 24, patients who received PBO in RA-BUILD and RA-BEACON were switched to BARI 4-mg.
ACR-EULAR=American College of Rheumatology-European League Against Rheumatism; ADA=Adalimumab; BARI=Baricitinib; CDAI=Clinical Disease Activity Index; MTX=Methotrexate; NRI=Non-Responder Imputation; PBO=Placebo; RA=Rheumatoid Arthritis; SDAI=Simplified Disease Activity Index.

1. Caporali R, et al. *Rheumatology (Oxford)* 2023.


A CDAI
B SDAI
C DAS28-CRP
D DAS28-ESR
Continued on Baricitinib 4-mg
Step-down to Baricitinib 2-mg
Mean
Baseline
Week 12
Week 24
Week 36
Week 48
***
**
*


A SJC, 0-66
B TJC, 0-68
C Physician Global, 0-100 mm VAS
D Patient Global, 0-100 mm VAS
Continued on Baricitinib 4-mg
Step-down to Baricitinib 2-mg
Mean
Baseline
Week 12
Week 24
Week 36
Week 48
**
*

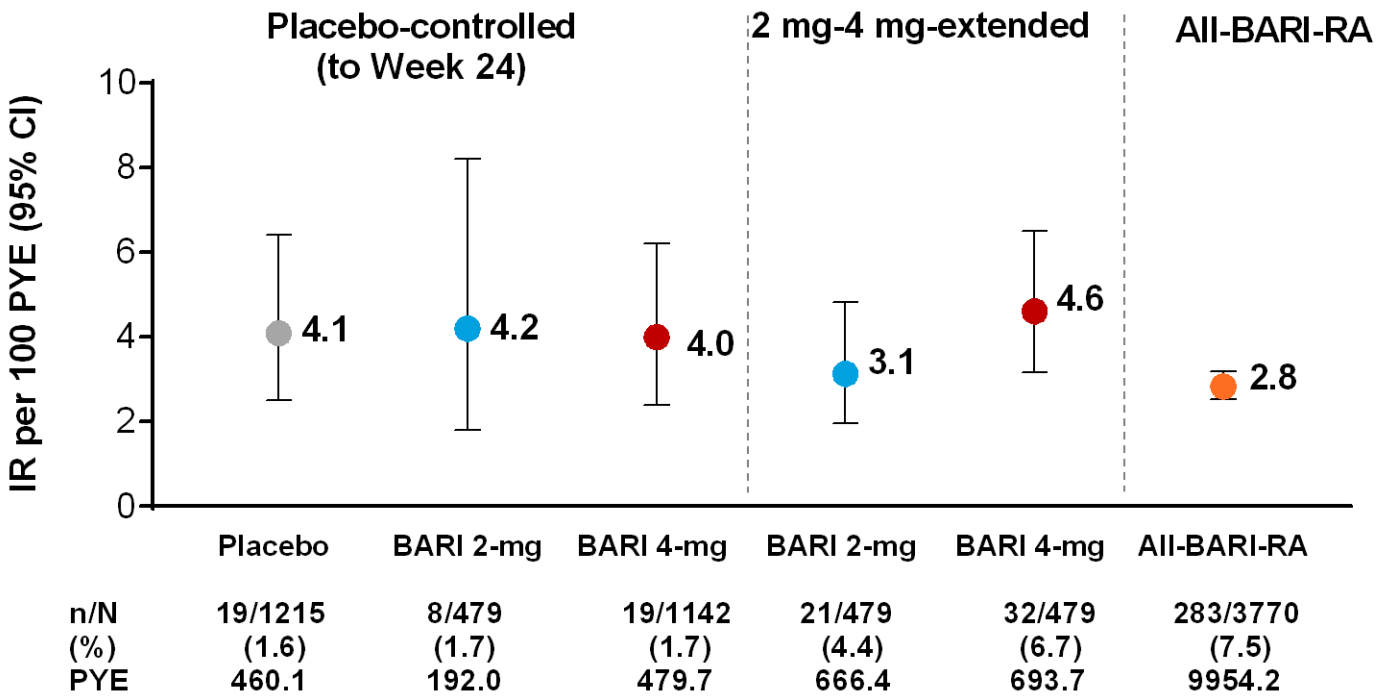
Safety Profile of Baricitinib for the Treatment of Rheumatoid Arthritis up to 7 Years: An Updated Integrated Safety Analysis

Mark C. Genovese,[1] Josef S. Smolen,[2] Tsutomu Takeuchi,[3] Gerd Burmester,[4] Dennis Brinker,[5] Terence P. Rooney,[5] Jinglin Zhong,[6] Daojun Mo,[5] Chadi Saifan,[5] Anabela Cardoso,[5] Maher Issa,[5] Wen-Shuo Wu,[5] Kevin L. Winthrop[7]

[1]Division of Immunology and Rheumatology, Stanford University, Palo Alto, USA; [2]Division of Rheumatology, Department of Medicine, Medical University of Vienna, Vienna, Austria; [3]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan; [4]Department of Rheumatology and Clinical Immunology, Charité-University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany; [5]Eli Lilly and Company, Indianapolis, USA; [6]IQVIA, Morrisville, USA; [7]Oregon Health Sciences University, Portland, USA

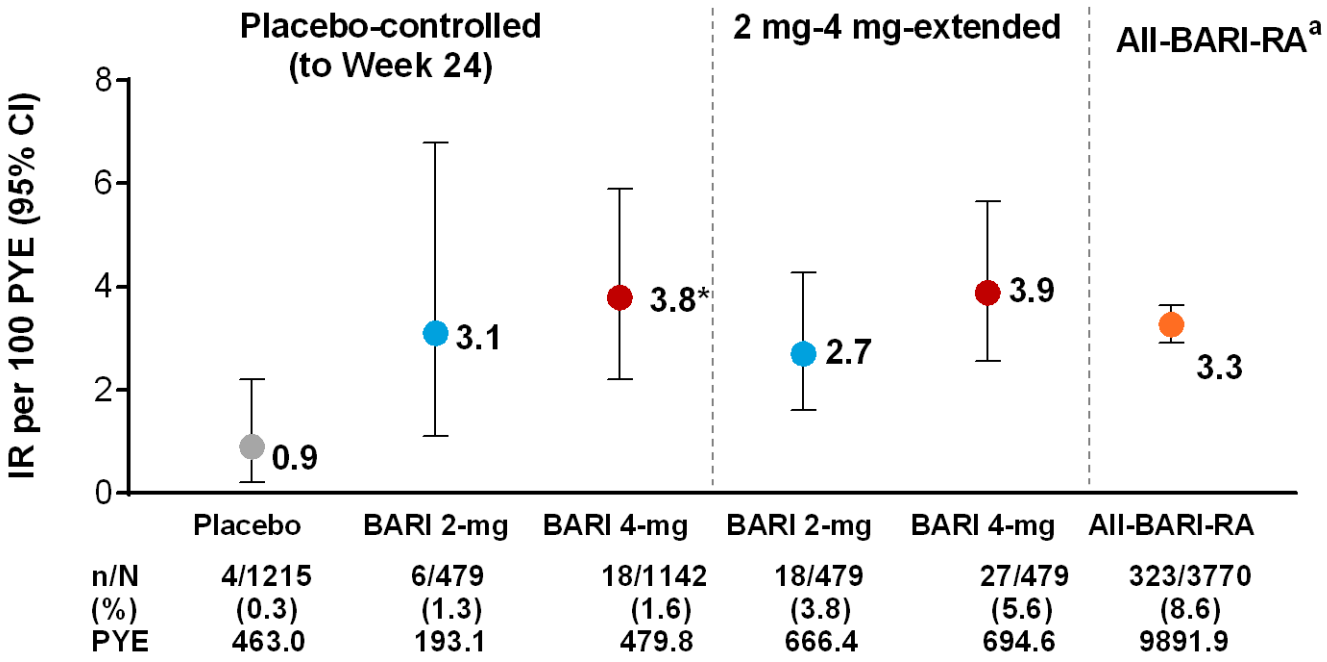
European League Against Rheumatism (EULAR); Madrid, Spain; June 12-15 2019

Serious Infections by Analysis Set



BARI=baricitinib; CI=confidence interval; IR=incidence rate; n/N=number of patients with events/total number of patients; PYE=patient years of exposure; RA=rheumatoid arthritis

Herpes Zoster by Analysis Set



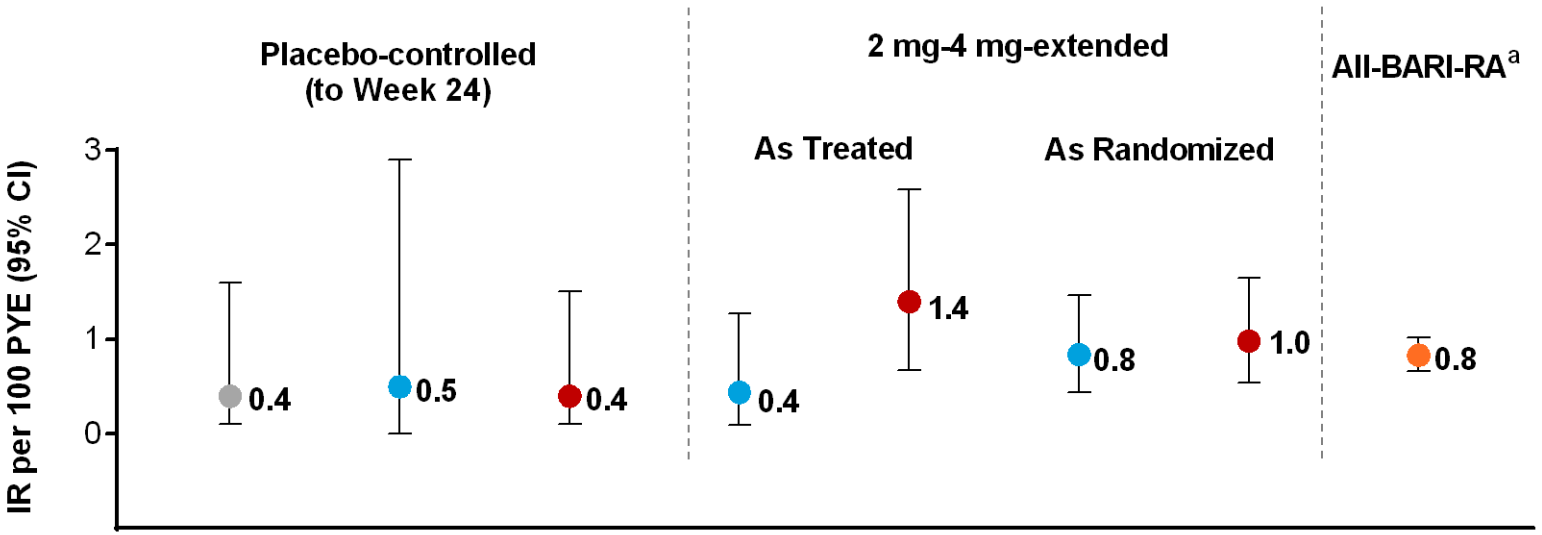
- Herpes zoster IR was significantly higher for baricitinib 4-mg versus placebo

p<0.05 for BARI 4-mg vs. placebo

[a] Maximum severity: mild, 41.5%; moderate, 53.3%; severe, 5.2%. Multidermatomal (7.7). IRs were the highest in Asia (26.1)

BARI=baricitinib; CI=confidence interval; IR=incidence rate; n/N=number of patients with events/total number of patients; PYE=patient years of exposure; RA=rheumatoid arthritis

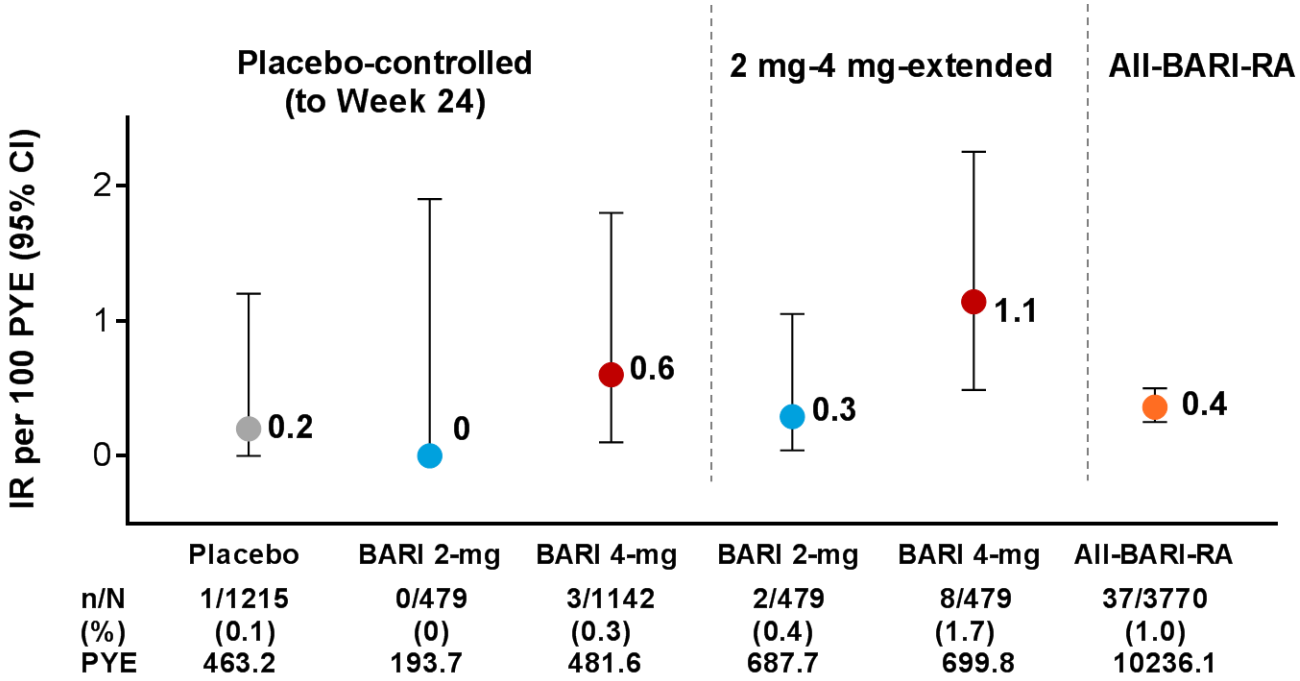
Malignancy (Excluding NMSC) by Analysis Set



[a] The 3 most commonly reported malignancies were: breast (n=14); lung (n=12); and lymphoma (n=8)

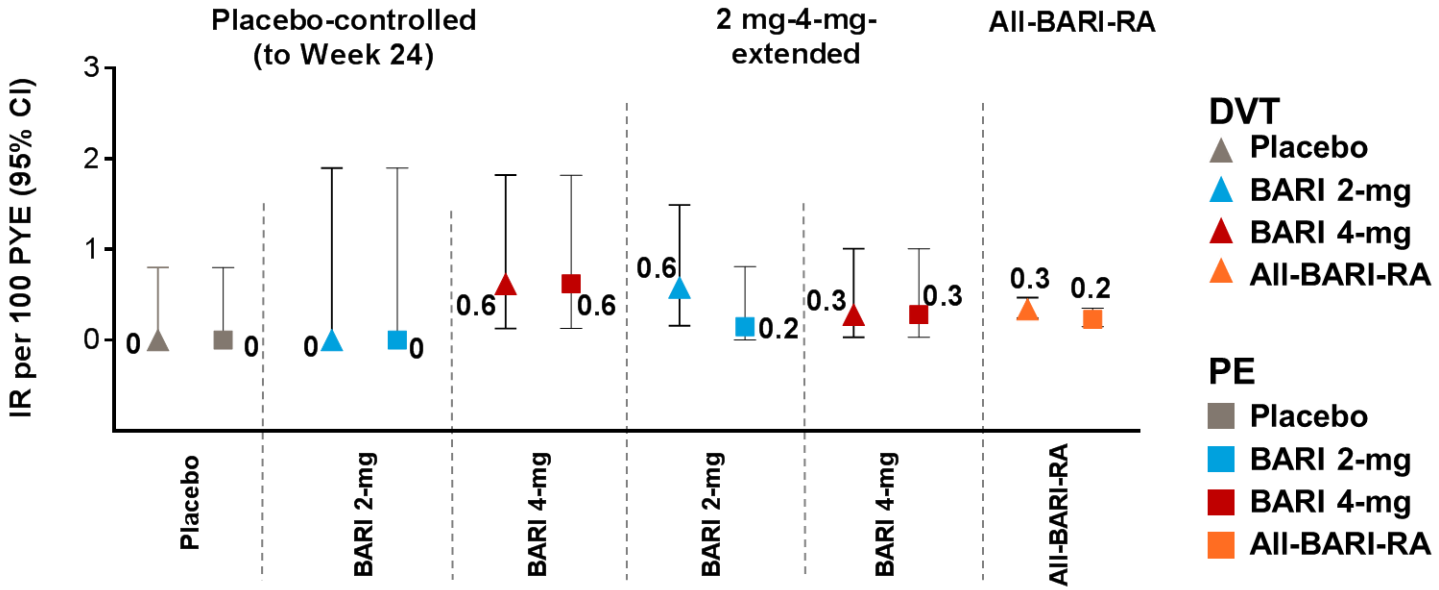
BARI=baricitinib; CI=confidence interval; IR=incidence rate; n/N=number of patients with events/total number of patients; NMSC=non-melanoma skin cancer; PYE=patient years of exposure; RA=rheumatoid arthritis

NMSC by Analysis Set



BARI=baricitinib; CI=confidence interval; IR=incidence rate; n/N=number of patients with events/total number of patients; NMSC=non-melanoma skin cancer; PYE=patient years of exposure; RA=rheumatoid arthritis

DVT and PE by Analysis Set[a]



DVT	n/N	0/1215	0/479	3/1142	4/479	2/479	35/3770
	(%)	(0)	(0)	(0.3)	(0.8)	(0.4)	(0.9)
	PYE	463.4	193.7	481.4	685.7	712.2	10252.6
PE	n/N	0/1215	0/479	3/1142	1/479	2/479	24/3770
	(%)	(0)	(0)	(0.3)	(0.2)	(0.4)	(0.6)
	PYE	463.4	193.7	481.4	686.7	713.2	10270.4

[a] A previous report suggested the risk of DVT and PE was about double in patients with RA compared to controls[4]

BARI=baricitinib; BMI=body mass index; CI=confidence interval; DVT=deep vein thrombosis; IR=incidence rate; n/N=number of patients with events/total number of patients; PYE=patient years of exposure; RA=rheumatoid arthritis; PE=pulmonary embolism

JAKi vs. TNFi

Μεγαλύτερης ηλικίας, με μεγαλύτερη διάρκεια νόσου, υψηλότερα ποσοστά προηγούμενης αποτυχίας και πιο πολλές συννοσηρότητες

	Overall patients				CV risk patients			
n (%)	**JAKi**	**TNFi**	**Other bDMARDs**	**csDMARDs**	**JAKi**	**TNFi**	**Other bDMARDs**	**csDMARDs**
No. of treatment episodes	3058	3694	3150	4301	1845	2010	1866	2643
Treatment start before 2021	2457 (80.4)	3100 (83.9)	2793 (88.7)	3700 (86.0)	1475 (80.0)	1675 (83.3)	1658 (88.9)	2282 (86.3)
Time on treatment, months, mean (SD)	18.2 (14.3)	19.2 (15.3)	16.5 (13.7)	12.6 (13.6)	18.4 (14.2)	18.6 (14.8)	15.8 (13.2)	12.7 (13.7)
Age, years [mean (SD)]	60.2 (11.8)	57.7 (13.3)	60.4 (11.9)	61.3 (12.3)	64.7 (8.9)	64.0 (9.0)	65.2 (8.8)	66.0 (9.1)
Age (≥65 years)	1023 (33.5)	1122 (30.4)	1116 (35.4)	1722 (40.0)	826 (44.8)	869 (43.2)	874 (46.8)	1372 (51.9)
Male	721 (23.6)	962 (26.0)	842 (26.7)	1111 (25.8)	491 (26.6)	598 (29.8)	570 (30.6)	764 (28.9)
Disease duration, years [mean (SD)]	12.5 (9.5)	9.6 (8.7)	13.6 (9.7)	12.4 (9.8)	13.3 (9.8)	10.5 (9.5)	14.5 (10.1)	13.3 (10.0)
DAS28-ESR [mean (SD)]	4.2 (1.4)	4.3 (1.4)	4.0 (1.5)	3.6 (1.4)	4.4 (1.4)	4.5 (1.3)	4.1 (1.5)	3.7 (1.4)
Sum of CV comorbidities, [mean (SD)]	1.1 (1.1)	1.0 (1.1)	1.2 (1.2)	1.2 (1.2)	1.6 (1.1)	1.6 (1.1)	1.7 (1.2)	1.7 (1.1)
Hypertension	1456 (47.6)	1534 (41.5)	1484 (47.1)	2126 (49.4)	1357 (73.6)	1431 (71.2)	1390 (74.5)	2027 (76.7)
Coronary heart disease	251 (8.2)	257 (7.0)	310 (9.8)	423 (9.8)	246 (13.3)	254 (12.6)	299 (16.0)	415 (15.7)
History of stroke	72 (2.4)	81 (2.2)	91 (2.9)	124 (2.9)	63 (3.4)	73 (3.6)	85 (4.6)	113 (4.3)
Hyperlipoproteinemia	392 (12.8)	336 (9.1)	461 (14.6)	535 (12.4)	371 (20.1)	318 (15.8)	443 (23.7)	519 (19.6)
History of malignancy	137 (4.5)	138 (3.7)	190 (6.0)	282 (6.6)	99 (5.4)	109 (5.4)	140 (7.5)	210 (8.0)

Meissner Y, et al. RMD Open 2023;9:e003489.

Συχνότητα εμφάνισης MACEs: JAKi vs. TNFi[1]

		Overall patients				CV risk patients			
		JAKi	TNFi	Other bDMARDs	csDMARDs	JAKi	TNFi	Other bDMARDs	csDMARDs
Main analysis	No. of treatment episodes	3058	3694	3150	4301	1845	2010	1866	2643
	Patient years of follow-up	5013.17	7264.00	4615.92	4326.58	3142.75	3985.58	2746.83	2712.17
	No. of events	34	45	35	41	29	41	32	40
	IR (95% CI)	**0.68** (0.47–0.95)	**0.62** (0.45–0.83)	0.76 (0.53–1.06)	0.95 (0.68–1.29)	**0.92** (0.62–1.33)	**1.03** (0.74–1.40)	1.17 (0.80–1.65)	1.48 (1.05–2.01)
Male	No. of treatment episodes	721	962	842	1111	491	598	570	764
	Patient years of follow-up	1226.08	1959.67	1223.17	1103.00	862.33	1234.08	815.00	733.42
	No. of events	15	20	13	17	12	18	11	17
	IR (95% CI)	**1.22** (0.69–2.02)	**1.02** (0.62–1.58)	1.06 (0.57–1.82)	1.54 (0.90–2.47)	**1.39** (0.72–2.43)	**1.46** (0.86–2.31)	1.35 (0.67–2.42)	2.32 (1.35–3.71)
Female	No. of treatment episodes	2337	2732	2308	3190	1354	1412	1296	1879
	Patient years of follow-up	3787.08	5304.33	3392.75	3223.58	2280.42	2751.50	1931.83	1978.75
	No. of events	19	25	22	24	17	23	21	23
	IR (95% CI)	**0.50** (0.30–0.78)	**0.47** (0.31–0.70)	0.65 (0.41–0.98)	0.75 (0.48–1.11)	**0.75** (0.43–1.19)	**0.84** (0.53–1.25)	1.09 (0.67–1.66)	1.16 (0.74–1.74)

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Τι μάθαμε

- Το Baricirinib είναι ο πρώτος (1ος) JAKi που έδειξε ανωτερότητα στην σύγκριση με το ADA καθιερωμένη θεραπεία στη ΡΑ.

- Πρώιμα Baricirinib σε T2T στρατηγική: καλύτερα αποτελέσματα για ασθενείς με ρευματοειδή αρθρίτιδα vs TNFi (μελέτη PERFECT-RA) διάρκειας ενός έτους)

(3 επιπλέον ασθενείς κάθε 10 ασθενείς, είναι πιθανό να επιτύχουν ύφεση όταν λαμβάνουν θεραπεία με 75% Baricitinib vs 46% ADA , την εβδομάδα 12)

- Έχει ταχεία έναρξη δράσης, με μείωση της φλεγμονής και του πόνου με καλύτερο έλεγχο της νόσου.

Τι μάθαμε

- Ασθενείς χωρίς παράγοντες κινδύνου μπορούν να λάβουν JAKis αλλά και ασθενείς που δεν ανταποκρίνονται σε άλλους μηχανισμούς

- Ευελιξία στη δοσολογία 4&2 mg (↓↑), επιτρέπει την εξατομίκευση & δυνατότητα και για μονοθεραπεία, ανάλογα με τις ανάγκες του ασθενούς).

- Τα δεδομένα των κλινικών μελετών επαληθεύονται πλέον και από την εμπειρία της καθημερινής κλινικής πρακτικής και πλέον συχνότερα χρησιμοποιείται και ως 1η προωθημένη θεραπεία αμέσως μετά την αποτυχία της MTX εφόσον δεν υπάρχουν παράγοντες κινδύνου

Pharmasrve-Lilly Επιστημονική Εκδήλωση Ρευματολογίας, ΕΠΕΝΜΥ 2026
Σάββατο 9 Μαΐου 2026, Ξενοδοχείο Hermes, Σύρος

Η άποψη σας είναι πολύτιμη…

…σας ευχαριστούμε!