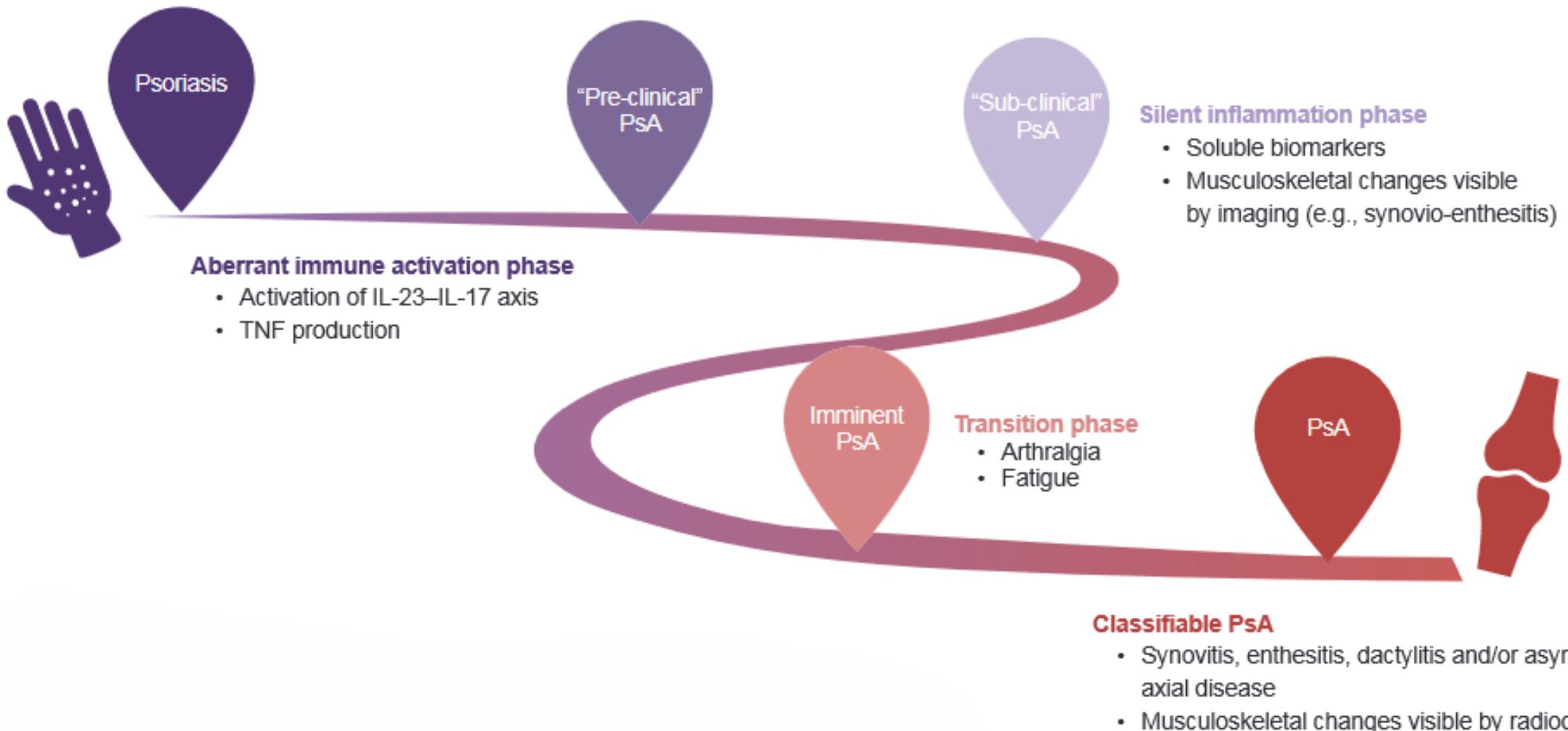


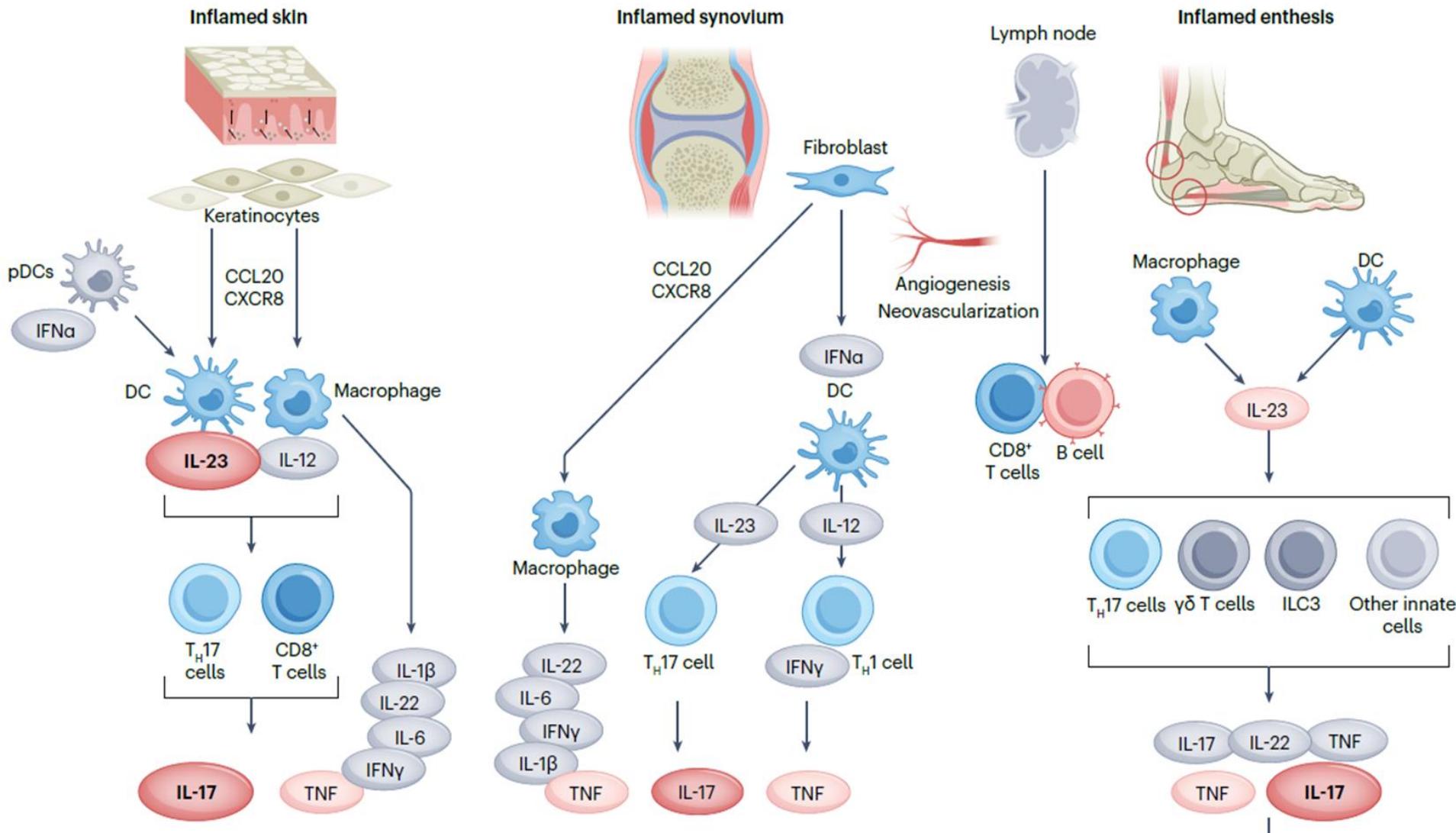
**Εξελίσσοντας τη διαχείριση της
Ψωριασικής Νόσου μέσα από την
εμπειρία των κοινών ιατρείων**

Συντονισμός-Ομιλία

- **Έλενα Σωτηρίου**, Δερματολόγος, Καθηγήτρια Δερματολογίας - Αφροδισιολογίας, Διευθύντρια Α' Δερματολογικής Κλινικής Α.Π.Θ., Θεσσαλονίκη
- **Νικόλαος Κούγκας**, Ρευματολόγος, Επιμελητής Α' ΕΣΥ, Δ' Παθολογική Κλινική ΑΠΘ, ΓΝΘ Ιπποκράτειο, Θεσσαλονίκη



Analyzing PsD from a mechanistic perspective



Patient with Psoriasis



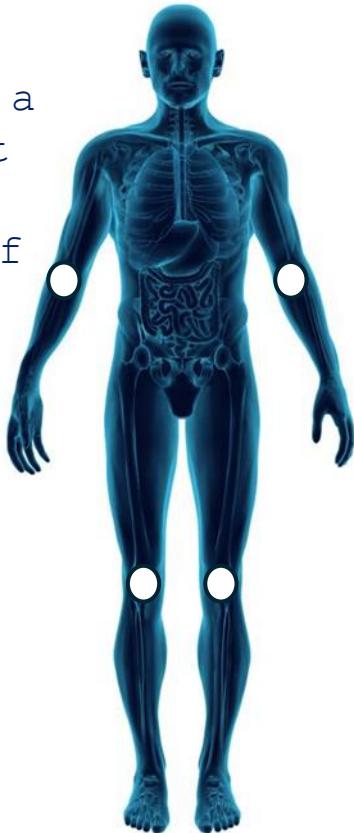
In **70%** of cases,
Pso precedes PsA
with a mean
interval of ~ **10
years**

PsA



In **13%** of cases, a
history of joint
involvement
preceded onset of
skin symptoms,
with a mean
interval of ~ **4
years**

Patient with history if joint involvement

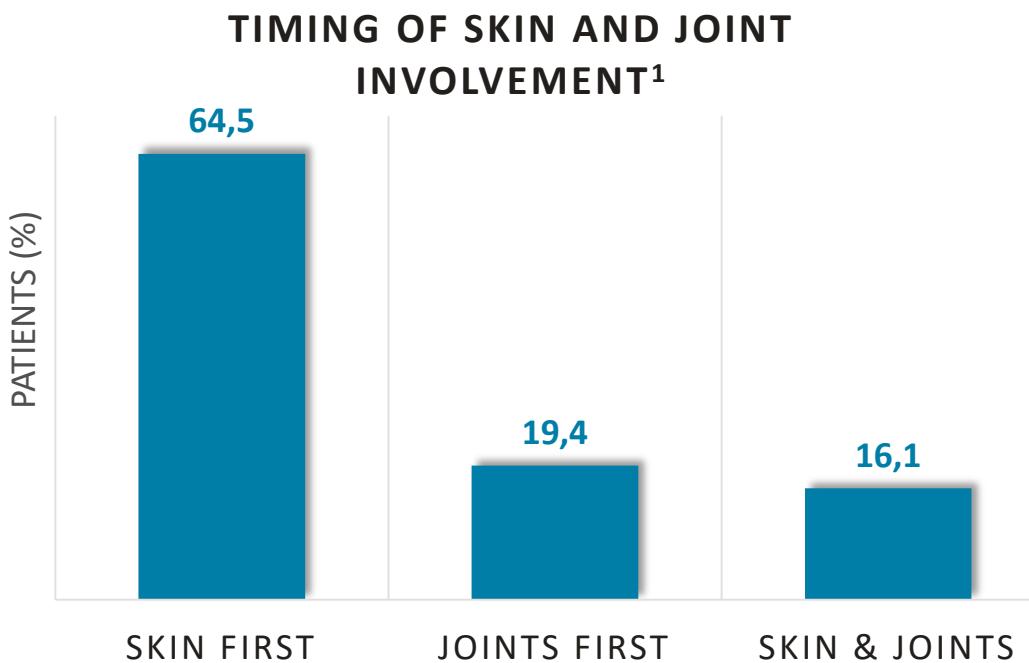


Parallel onset of skin and joint manifestations is seen in **16%** of cases

Approximately **15%** of patients with PsO who are under the care of dermatologists have an undiagnosed case of psoriatic arthritis

1. Lee, Leon Tsung-Ju et al. "Machine Learning Approaches for Predicting Psoriatic Arthritis Using Electronic Medical Records: Population-Based Study." Journal of medical Internet research vol. 25 e39972. 28 Mar. 2023, doi:10.2196/39972. 2. Stephen R. Pennington and Oliver Fitzgerald, (2021) Front. Med. 8:723944.; 2. Lourdes M. Perez-Chada, Jose U. Scher et al. Nat Rev Rheumatol. 2021; 17(4): 238-243, 3. Kumar, Ramesh et al. "Prevalence and clinical patterns of psoriatic arthritis in Indian patients with psoriasis." Indian journal of dermatology, venereology and leprology vol. 80,1 (2014): 15-23. doi:10.4103/0378-6323.125472, 4. Tan, Minjia et al. "Concurrent onset of skin and joint symptoms correlates with higher psoriatic arthritis disease activity: A single-center retrospective study." Journal of the American Academy of Dermatology vol. 89,1 (2023): 173-175. doi:10.1016/j.jaad.2023.02.045

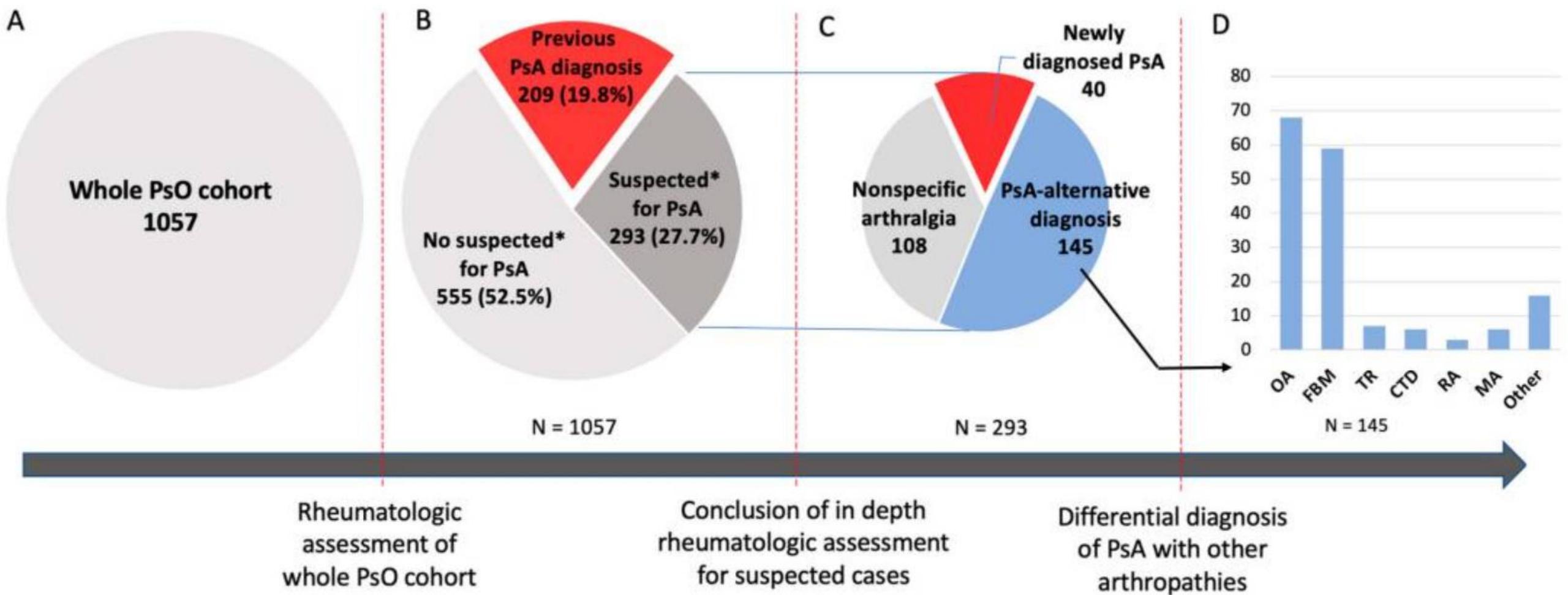
Psoriasis symptoms typically precede joint symptoms



SKIN LESIONS PRECEDE ARTHRITIS BY:



Differentiating PsA



Κλινική Περίπτωση 1



Νίκος, 54 ετών



BMI 28, ΑΥ, δυσλιπιδαιμία
Έκθεση εξανθημάτων από 6μηνου



1η εξέταση στα δερματολογικά Ε.Ι: διάγνωση ψωρίασης
κατά πλάκας στους 2 αγκώνες και στη ΔΕ κνήμη



PEST score: 0

PSORIASIS EPIDEMIOLOGY SCREENING TOOL (PEST)

HOSPITAL NO. _____

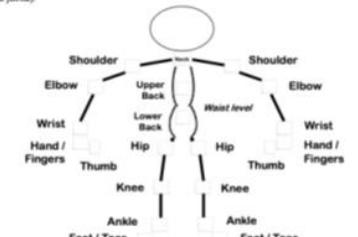
PATIENT NAME _____

DATE OF VISIT _____

The British Association for Dermatology (BAD) logo, featuring the letters 'BAD' in a stylized font inside a circular emblem with the text 'BRITISH ASSOCIATION FOR DERMATOLOGY' around it.

PEST is a validated screening tool for psoriatic arthritis (PsA) and it is recommended that patients with psoriasis who do not have a diagnosis of PsA complete an annual PEST questionnaire (NICE psoriasis guidelines 2012). A score of 3 or more indicates referral to rheumatology should be considered.

In the drawing below, please tick the joints that have caused you discomfort (i.e. stiff, swollen or painful joints).



Reproduced with kind permission of Professor Philip Hollis (University of Leeds)

Please answer the questions below and score 1 point for each question answered 'Yes'

1. Have you ever had a swollen joint (or joints)?
2. Has a doctor ever told you that you have arthritis?
3. Do your finger nails or toenails have holes or pits?
4. Have you had pain in your heel?
5. Have you had a finger or toe that was completely swollen and painful for no apparent reason?

Yes

No

Total / 5

A total score of 3 or more out of 5 is positive and indicates a referral to rheumatology should be considered

Κλινική Περίπτωση 1



Από το ιστορικό αναφερομένη χρόνια ραχιαλγία-επαγγελματική καταπόνηση και πρόσφατες συνεδρίες φυσιοθεραπειών χωρίς ιδιαίτερη βελτίωση



- Παραπομπή για εξέταση στο κοινό Ιατρείο
- Χωρίς περιφερική αρθρίτιδα ή δακτυλίτιδα
- Ραχιαλγία με φλεγμονώδη χαρακτηριστικά



Αυξημένες απαιτήσεις και υποχρεώσεις στην καθημερινότητα του Νίκου

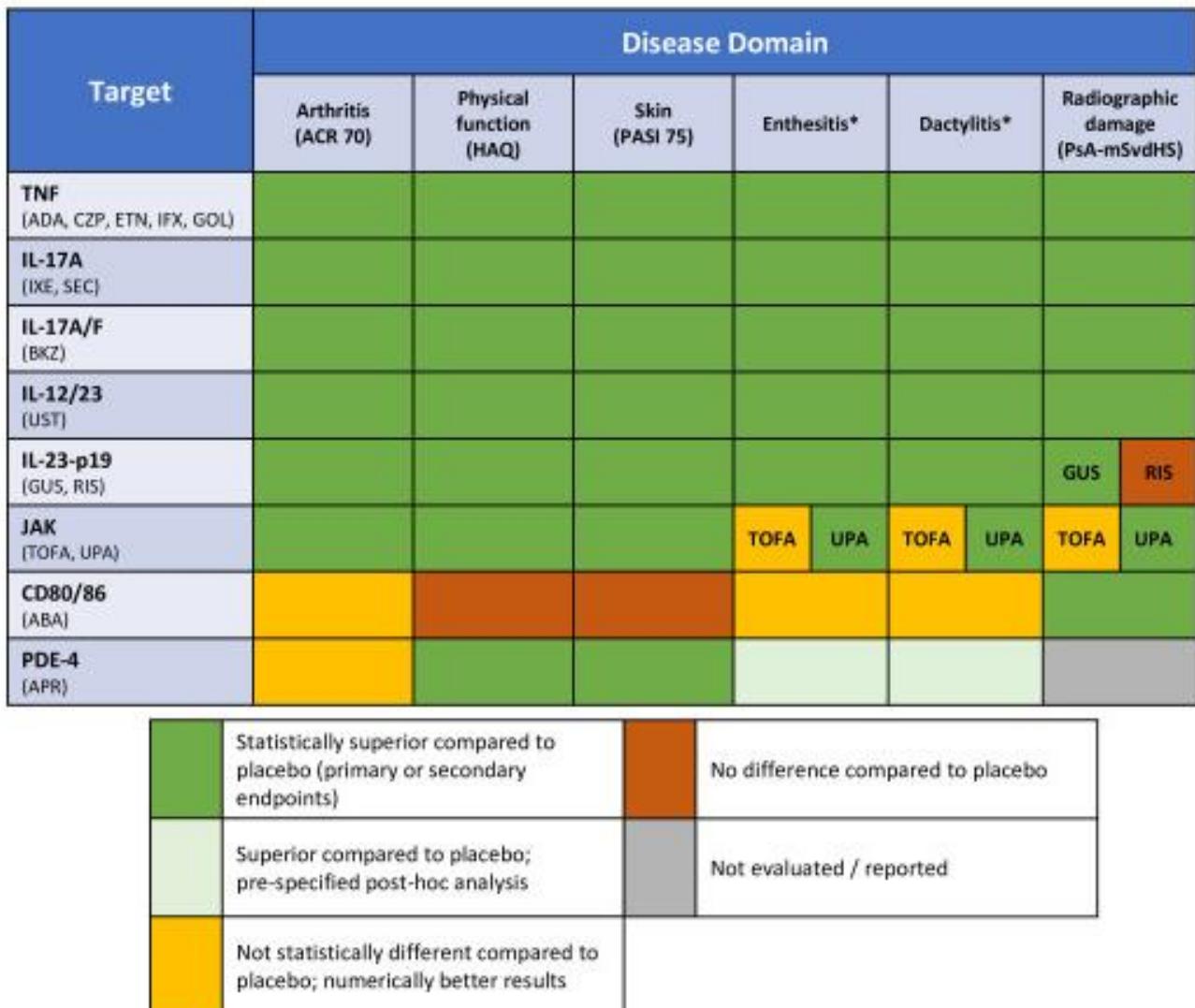
Image size: 320 x 320
View size: 1461 x 1327



- CRP 73 mg/dl
- ΤΚΕ 60 mm Hg
- Λοιπός εργαστηριακός έλεγχος κ.φ.
- Ακτινογραφία τερολαγονίων ετερόπλευρο στάδιο II (NY criteria)

Speaker's approach

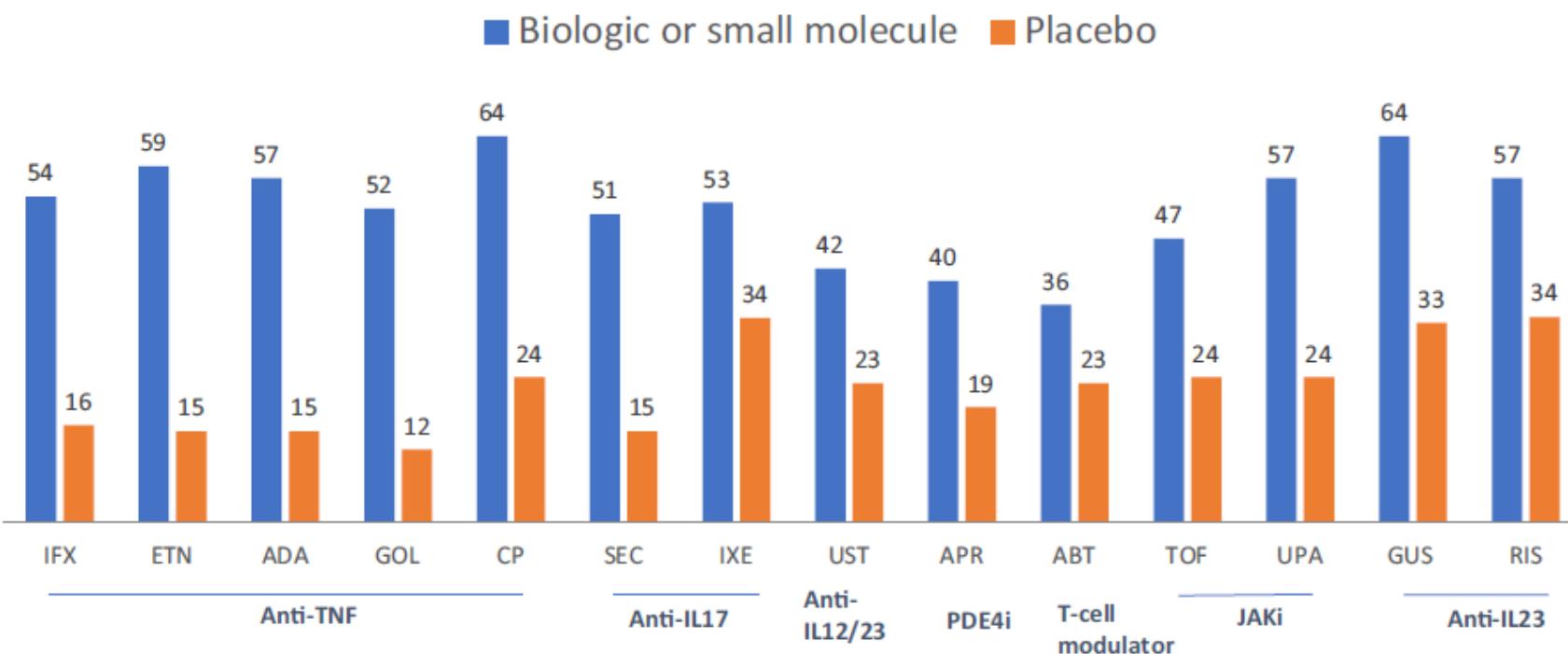
What options we have?



There are many therapeutic options for PsA to treat our patients

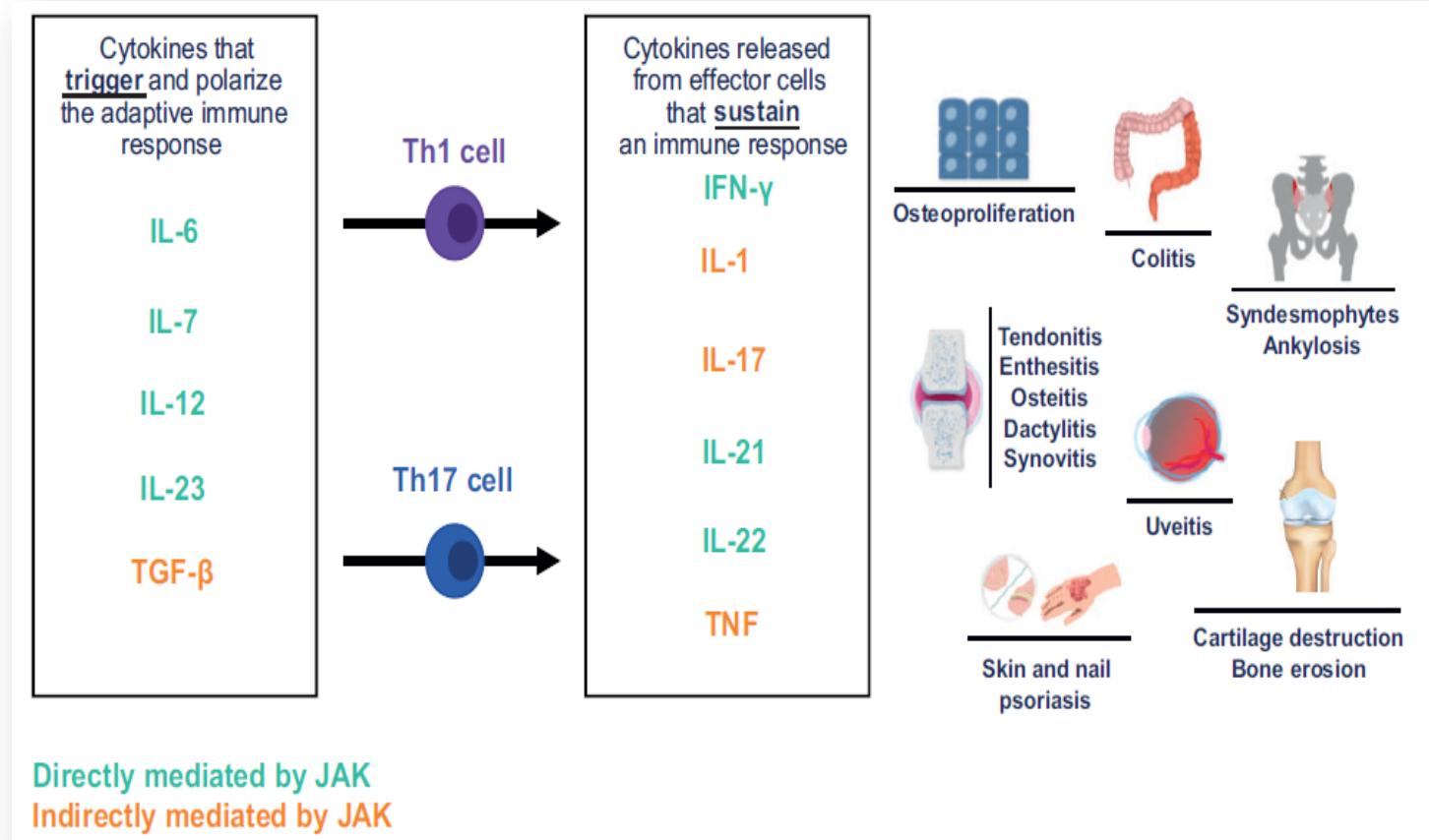
Biologic and Small-molecule Therapies for PsA: Efficacy Data from Registration Trials

Patients achieving ACR20% Response in Phase 3 PsA Trials



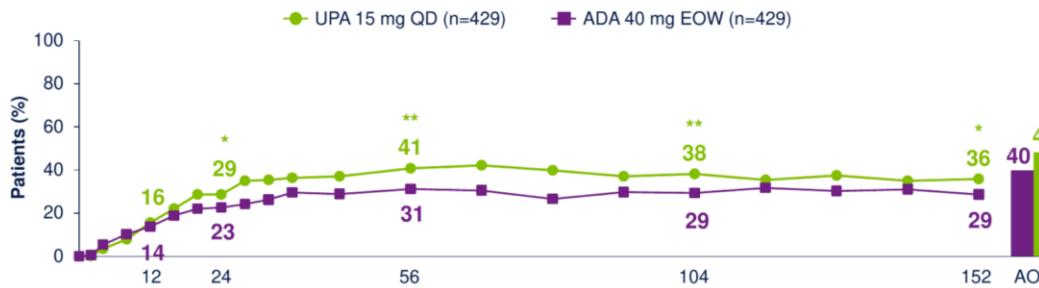
Targeting multiple pathways could lead to better results?

Η αποτελεσματικότητα των JAKi στηρίζεται στην ικανότητα τους να παρεμβαίνουν στη σηματοδότηση κυτταροκινών που εμπλέκονται με διαφορετικό τρόπο στην παθογένεια της νόσου



Maintenance of responses through week 152

ACR70



MDA



*N=321 and 315 for UPA 15 mg QD and ADA 40 mg EOW, respectively; **N=56 and 144 for PBO to UPA 15 mg QD and UPA 15 mg QD, respectively. MDA (defined as defined as meeting ≥57% of the following criteria: SJCG≤1, TJC6≤1, PASI≤1 or BSA-Ps≤3%, pain ≤1.5 [0–10 NRS], HAQ-DI ≤0.5, and LEI ≤1) was analyzed using Cochran-Mantel-Haenszel tests with NRI and are shown as response rates. ADA-as observed; bDAMARD-BSA-Ps-body surface area with psoriasis; cs-conventional synthetic; DMARD-disease-modifying antirheumatic drug; ESR-elevated sedimentation rate; IACR-improvement in American College of Rheumatology response criteria; ADA-adalimumab; AO-as observed; b-biologic; cs-conventional synthetic; DMARD-disease-modifying antirheumatic drug; EOW-every other week; IR-inadequate response; nB-nB; NRIR-non responder imputation; PBO-placebo; QD-once daily; UPA-upadacitinib.

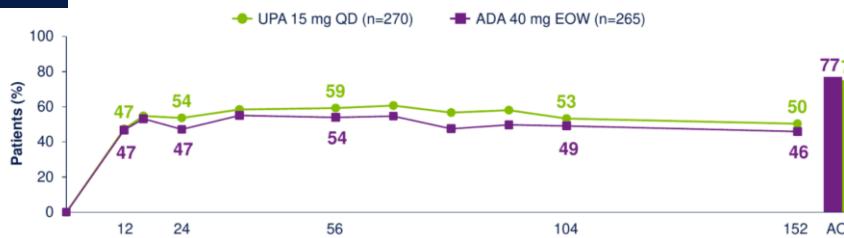
1. McInnes IB et al. *N Engl J Med* 2021;384(4):1227-1239. 2. Mease PJ et al. *Ann Rheum Dis*. 2021;80:312-320. 3. McInnes IB et al. *EULAR* 2023. POS1541. 4. Mease PJ et al. *Clin Exp Rheumatol*. 2023;41(1):2286-2297.



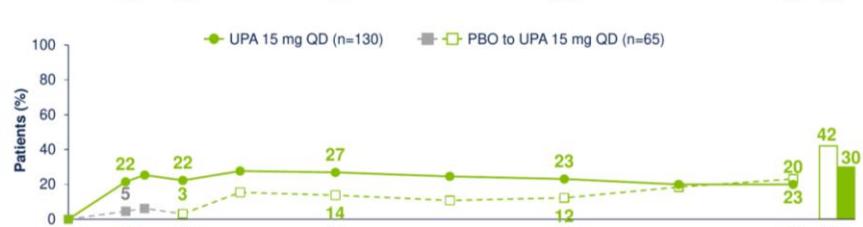
Maintenance of responses through week 152



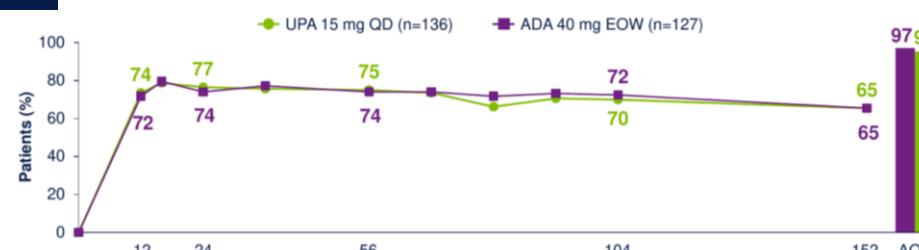
Enthesitis



PASI 100



Dactylitis



^a

^b

^c

^d

^e

^f

^g

^h

ⁱ

^j

^k

^l

^m

ⁿ

^o

^p

^q

^r

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Κλινική Περίπτωση 1



Έναρξη αγωγής με **Upadacitinib 15 mg**



- 3 μήνες αργότερα σε **πλήρη κλινική** (PASI:0 ASDAS: 1.2) **και εργαστηριακή ύφεση**
- Χωρίς ανεπιθύμητα συμβάματα

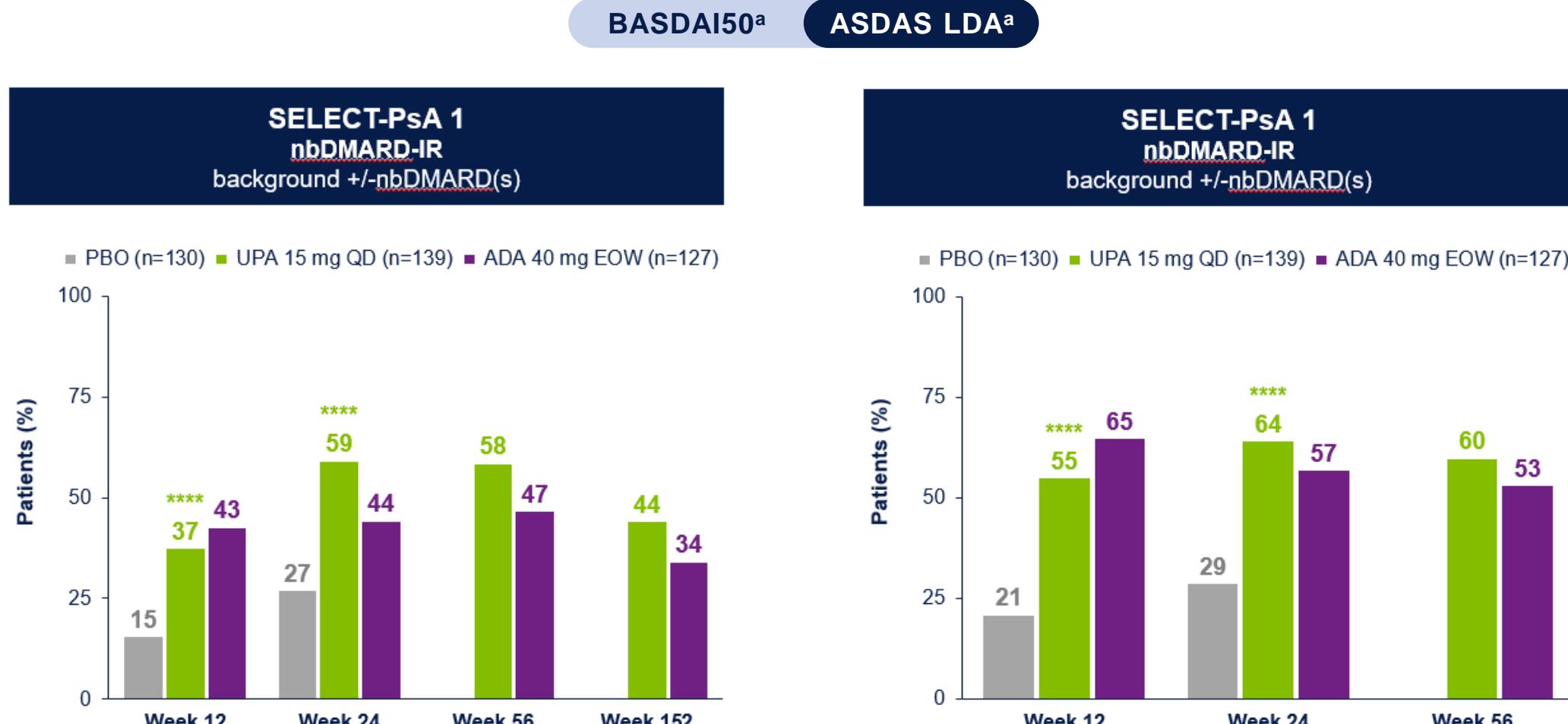


Διατήρηση της ύφεσης μέχρι και την τελευταία επίσκεψη περίπου 1 έτος από την έναρξη της θεραπείας



Ο Νίκος ανταπεξέρχεται πλέον στις απαιτήσεις και υποχρεώσεις της καθημερινότητας του

Patients with active PsA and axial involvement demonstrated significant improvements in their axial symptoms with upadacitinib¹⁻⁵



^aFor patients with axial involvement at BL, as determined by the investigator. Data were analyzed using Cochran-Mantel-Haenszel tests with NRI and are shown as response rates.

****P<0.0001 for UPA 15 mg QD vs PBO; nominal P values are shown and were not multiplicity controlled. ADA=adalimumab; ASDAS=ankylosing spondylitis disease activity score; b=biologic; BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; BASDAI50=≥50% improvement in the BASDAI; BL=baseline; DMARD=disease-modifying antirheumatic drug; EOW=every other week; IR=inadequate response; LDA=low disease activity; nb=non-biologic; PBO=placebo; PsA=psoriatic arthritis; QD=once daily; UPA=upadacitinib.

¹ McInnes IB et al. N Engl J Med. 2021;384(12):1227-1239. ² Mease PJ et al. Ann Rheum Dis. 2021;80(2):313-320. ³ Boumpas DT et al. Arthritis Res Ther. 2022;25:56. ⁴ McInnes IB et al. Ann Rheum Dis. 2022;81(10):1831-1839. ⁵ McInnes IB et al. Ann Rheum Dis. 2022;81(10):1840-1848.

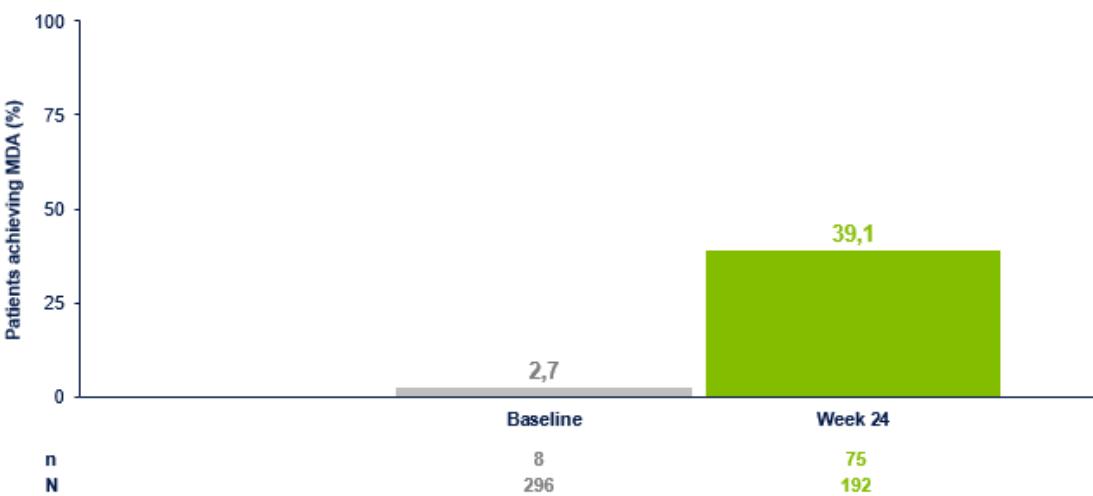
Real-world use of upadacitinib and impact on MDA and nail psoriasis in patients with PsA^{1,2}



MDA

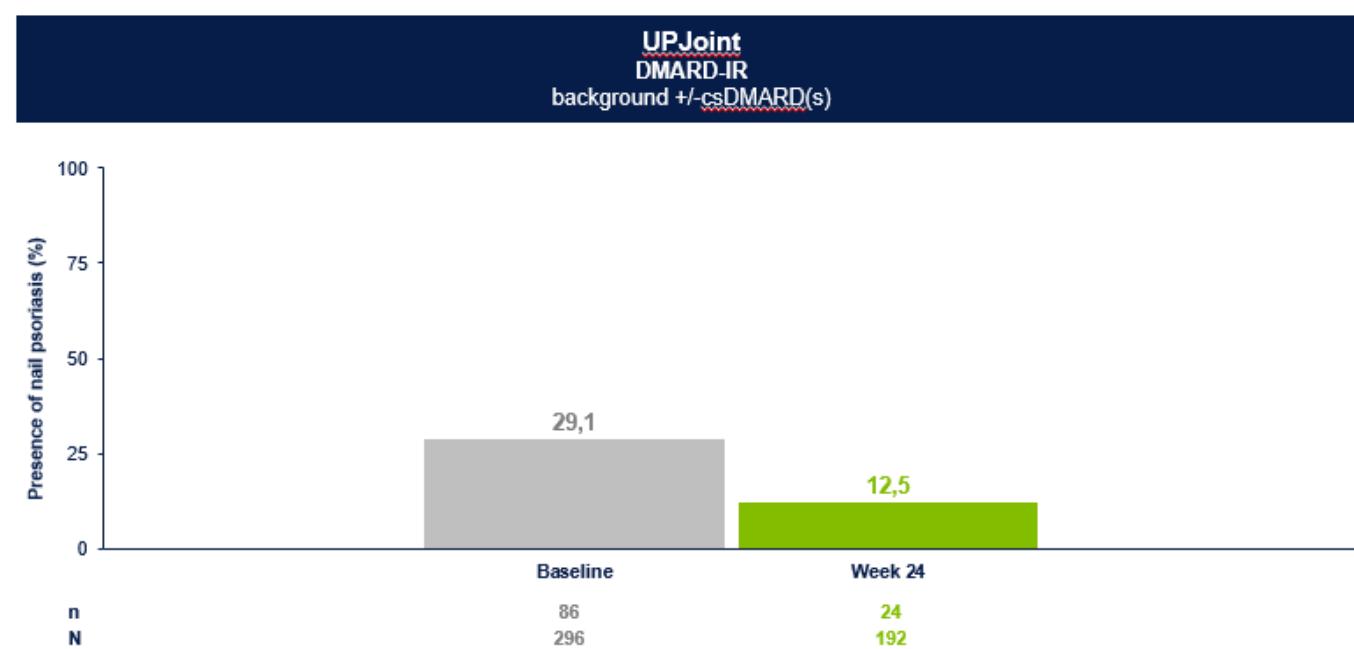
Nail psoriasis

UPJoint
DMARD-IR
background +/-csDMARD(s)



MDA Nail psoriasis

UPJoint
DMARD-IR
background +/-csDMARD(s)



Data reported as observed. cs=conventional synthetic; DMARD=disease-modifying antirheumatic drug; IR=inadequate response; MDA=minimal disease activity; PsA=psoriatic arthritis.

Data reported as observed. MDA defined as meeting ≥5/7 of the following criteria: SJC68 ≤1, TJC68 ≤1, PASI ≤1 or BSA-Ps ≤3%, pain ≤1.5 (0-10 NRS), PtGA ≤2 (0-10 NRS), HAQ-DI ≤0.5, and LEI ≤1. BSA-Ps=body surface area with psoriasis; cs=conventional synthetic; DMARD=disease-modifying antirheumatic drug; HAQ-DI=health assessment questionnaire-disability index; IR=inadequate response; LEI=Leeds Enthesitis Index; MDA=minimal disease activity; NRS=numeric rating scale.

1. Werner SG et al. *Rheumatol Ther*. 2023;10:1503-1518.

2. Werner SG et al. *Rheumatol Ther*. 2023;10:1503-1518.

The safety profile of upadacitinib has been established across 7 approved indications¹⁻³



CONSISTING OF
16
CLINICAL TRIALS across RA, PsA,
AS, nr-axSpA, AD, UC, and CD



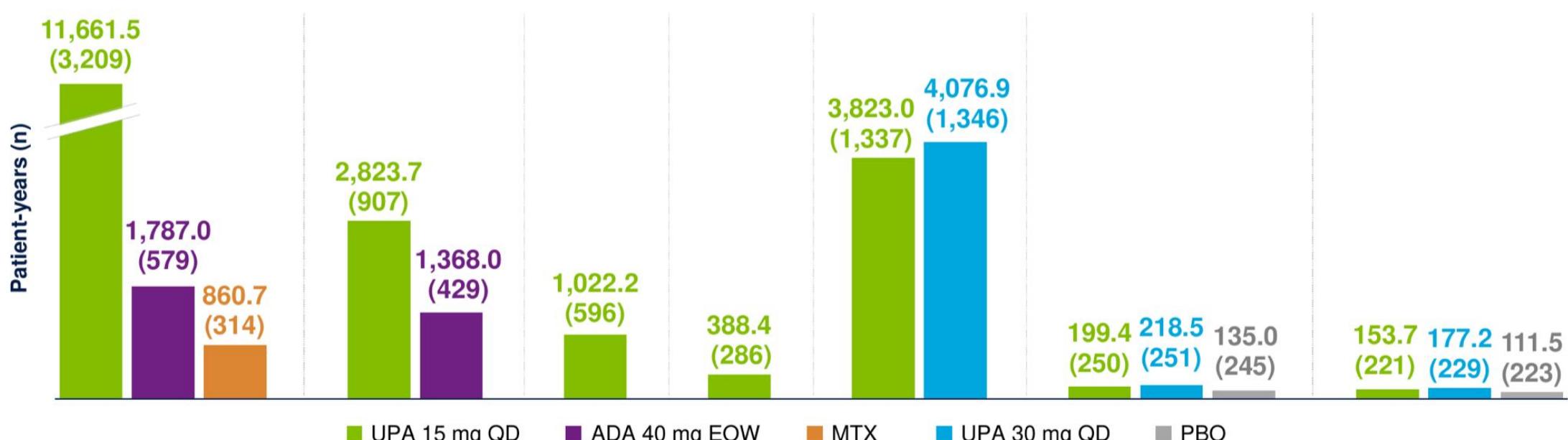
IN
8,632
PATIENTS who received
UPA **15 mg or 30 mg**



REPRESENTING
>24,000
PATIENT-YEARS of combined
exposure to UPA **15 mg and 30 mg**



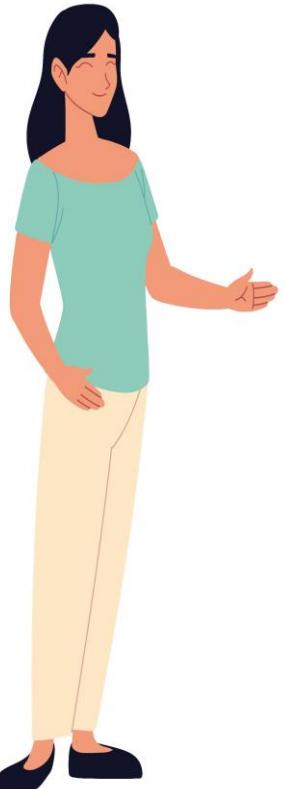
4 Rheumatology indications including
4,998 patients representing 15,895.8 patient-years



^aSafety data (cutoff date: 15 August 2023) from 11 Phase 3 UPA trials were compiled for RA (6), PsA (2), AS (2; one phase 2/3), and nr-axSpA (1) for this analysis; ^bLong-term safety for up to 5 years of UPA 15 mg and 30 mg use in adolescents and adults with moderate-to-severe AD, based on the results of integrated data from three ongoing global pivotal Phase 3 studies; ^cAssessed among patients who responded to an induction dose of UPA 45 mg QD during Week 8 (UC) or Week 12 (CD) and then received ≥1 dose of PBO, UPA 15 mg or UPA 30 mg QD in U-ACHIEVE, and U-ENDURE during the 52-week PBO-controlled randomized maintenance period. Data were integrated comprising patients from both studies. AD=atopic dermatitis; ADA=adalimumab; AS=ankylosing spondylitis; CD=Crohn's disease; CV=cardiovascular; MTX=methotrexate; nr-axSpA=non-radiographic axial spondyloarthritis; PBO=placebo; PsA=psoriatic arthritis; QD=once daily; RA=rheumatoid arthritis; UC=ulcerative colitis; UPA=upadacitinib.

1. Burmester G et al. EULAR 2024. POS0894. 2. Bunick C et al. RAD 2023. Poster 533. 3. Panaccione R et al. ACG 2023. P3631.

Κλινική Περίπτωση 2

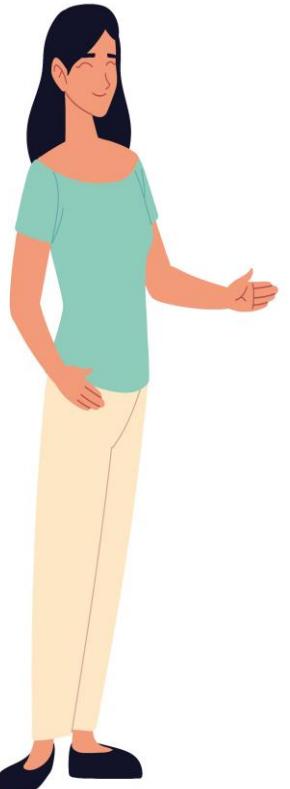


- Μαρία 49 ετών, Καπνιστρια 20 p/y, BMI 26,5 Hashimoto, δυσλιπιδαιμία, πιθανό θετικό οικογενειακό ιστορικό για φλεγμονώδη αρθρίτιδα
- Πρόσφατη διάγνωση οροαρνητικής RA (πολυαρθρίτιδα, αρνητικά αυτοαντισώματα, αυξημένη CRP)
- Έναρξη MTX 15 mg/week και κορτικοστεροειδή σε χαμηλές δόσεις
- Υποτροπή των συμπτωμάτων με τη διακοπή των στεροειδών



Αυξημένες απαιτήσεις και υποχρεώσεις στην καθημερινότητα της Μαρίας

Κλινική Περίπτωση 2



- Νέα στεροειδή και αύξηση MTX 20 mg/week
- - Αύξηση ηπατικών ενζύμων χ3, αύξηση και ΣΒ από τη χρήση των κορτικοστεροειδών
 - Απόφαση για έναρξη βιολογικής θεραπείας
- Λήψη αντιμυκητισιακής αγωγής για βλάβες νυχιών χεριών χωρίς βελτίωση
- Παραπομπή στο κοινό ιατρείο ψωριασικής νόσου



Αυξημένες απαιτήσεις και υποχρεώσεις στην καθημερινότητα της Μαρίας

Κλινική Περίπτωση 2



Διάγνωση ψωριασικής ουσχίας



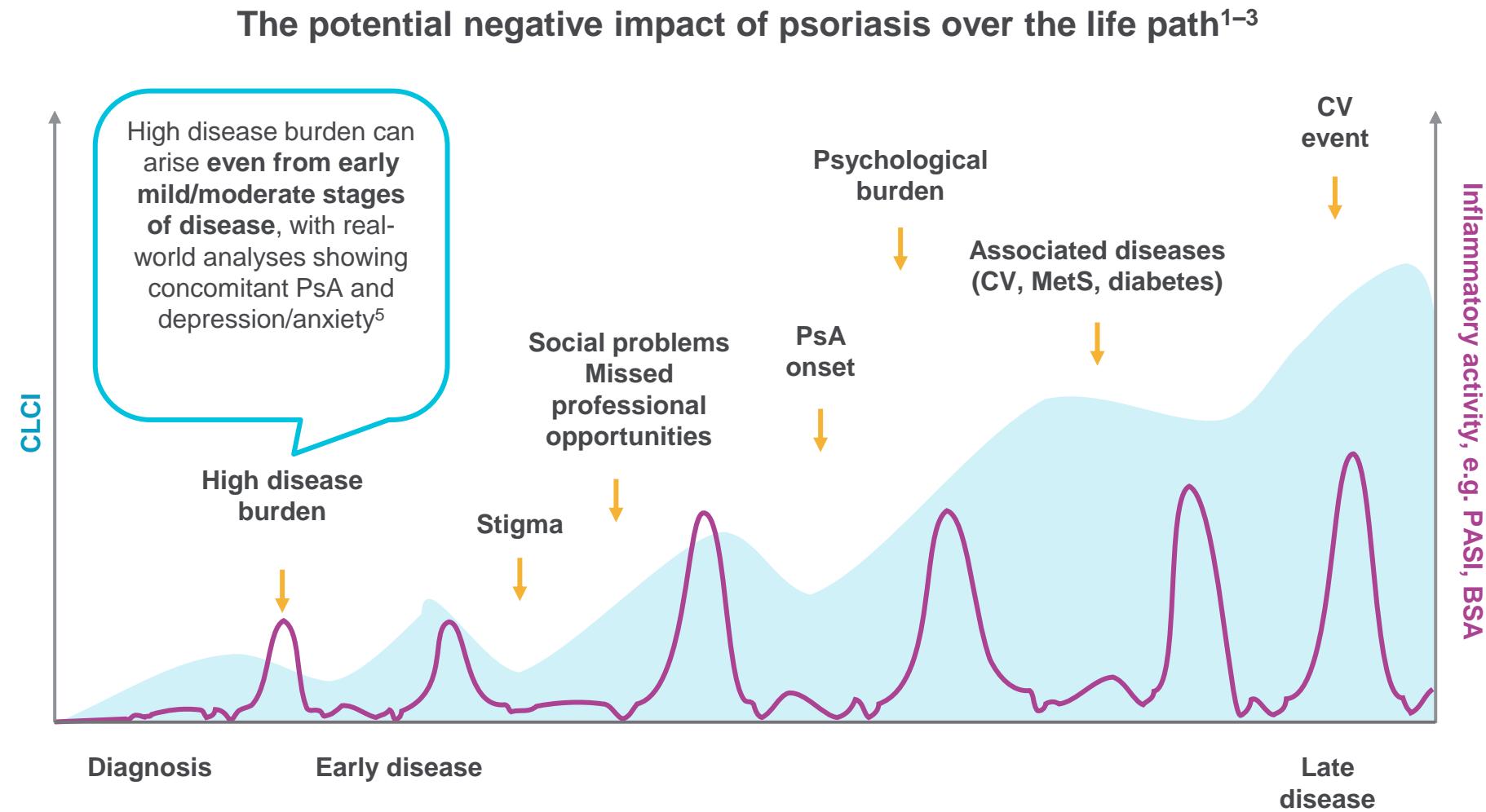
Έναρξη αγωγής με **Risankizumab**



Αυξημένες απαιτήσεις και υποχρεώσεις στην καθημερινότητα της Μαρίας

CLCI describes the potential cumulative negative impact of a patient's disease over their lifetime

- CLCI is a useful model in understanding the impact of chronic inflammatory diseases
- It describes the **compounding impact on a patient's life path**,¹⁻⁴ including on their physical health, mental health, comorbidities, daily activities, and social interaction



BSA, body surface area; CLCI, Cumulative Life Course Impairment; CV, cardiovascular; MetS, metabolic syndrome; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis.

Adapted from: Pariente B, et al. *Inflamm Bowel Dis.* 2011;17:1415–22. For illustrative purposes only, not intended to represent a definitive linear disease progression for every patient.

• 1. Kimball AB, et al. *J Eur Acad Dermatol Venereol.* 2010;24(9):989–1004; 2. Ros S, et al. *Actas Dermosifiliogr.* 2014;105:128–34; 3. Linder MD, et al. *Acta Derm Venereol.* 2016;96:102–8;

4. Marzano AV, et al. *Br J Dermatol.* 2021;184:133–40;

The burden of undiagnosed PsA



- A diagnostic delay of even 6 months has been shown to lead to significantly more radiographic damage and worse long-term physical function^{1,2}



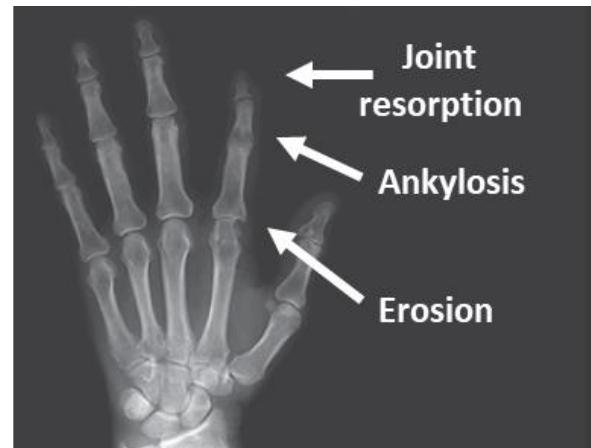
- Significantly less common drug-free remission and more common arthritis mutilans were noted among patients presenting >1 year after symptom onset¹



- Clinical and radiological damage was higher among patients presenting later than 2 years of symptom onset^{1,2}

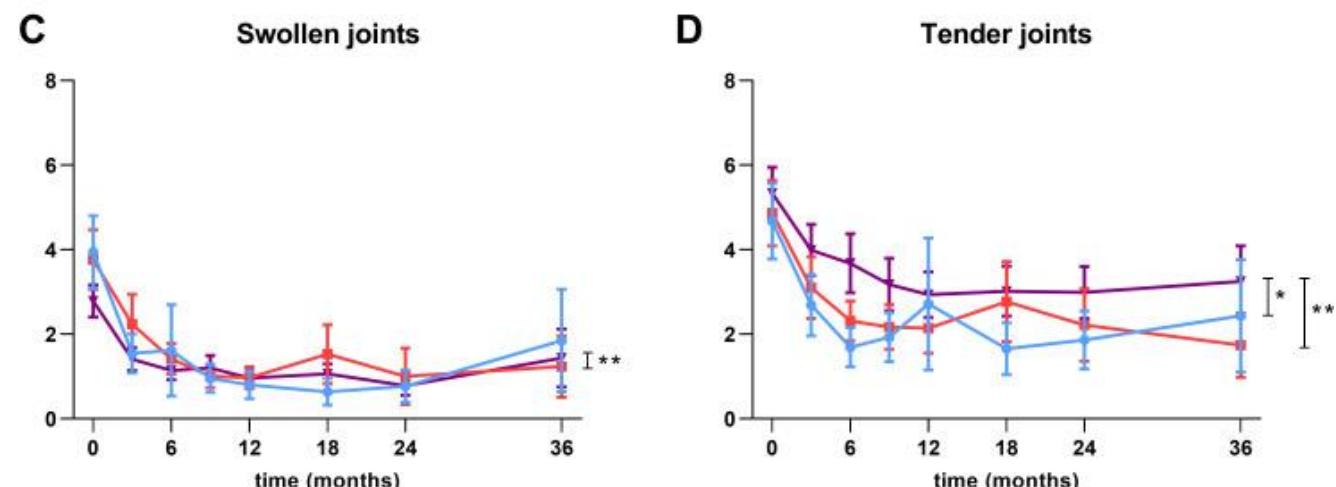
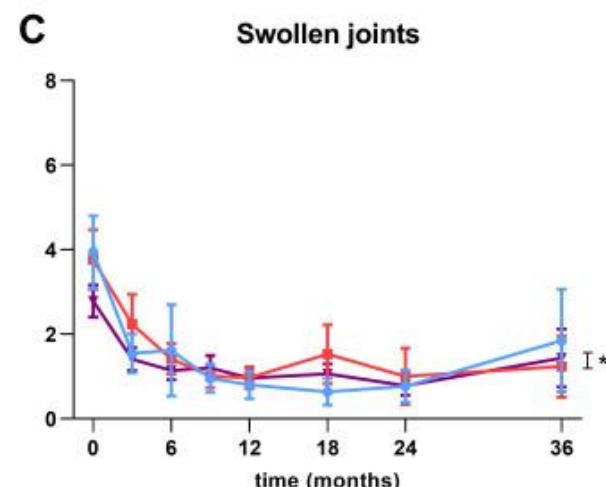
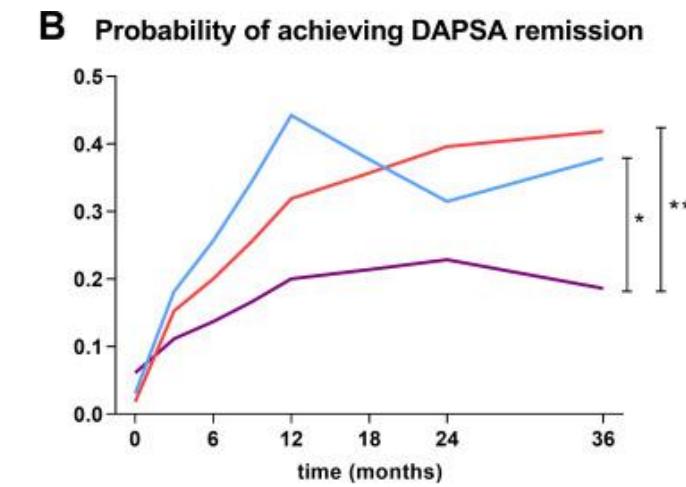
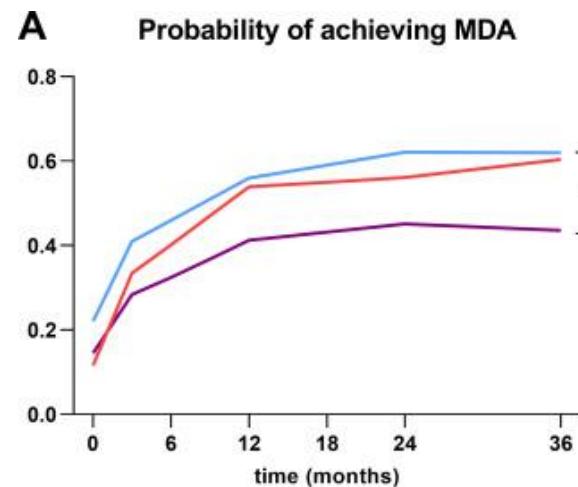
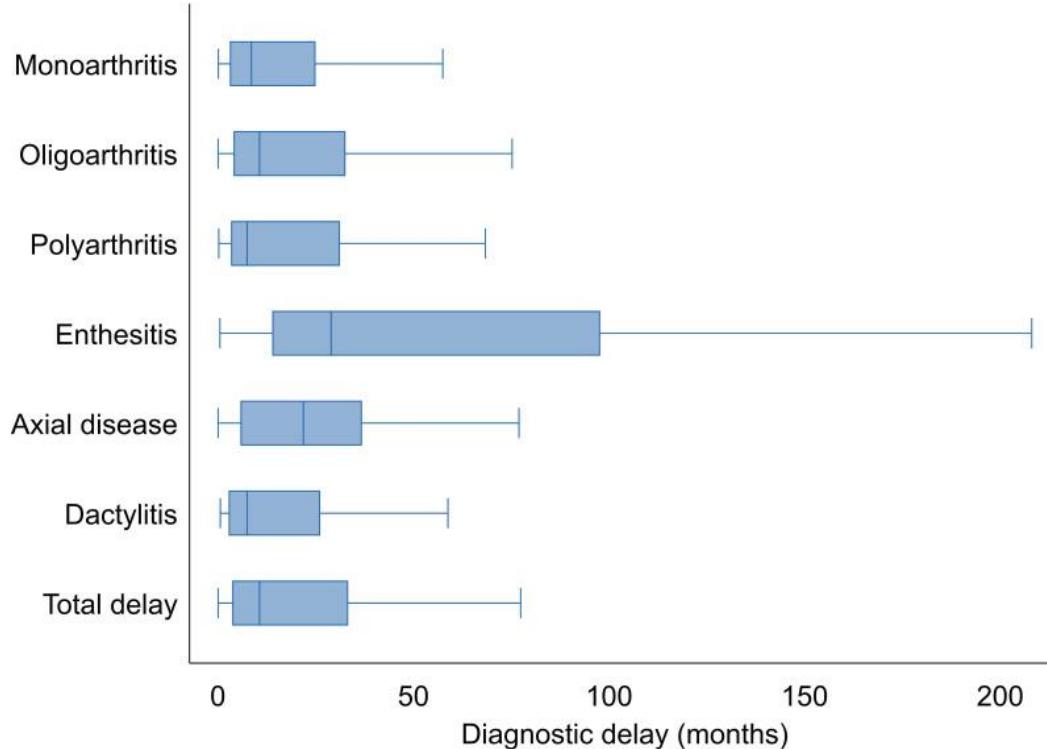
○ Almost half of patients exhibit structural damage and functional impairment within 2 years of developing symptoms

Early intervention in the PsA disease process can inhibit or delay structural joint damage, and patients are more likely to experience improvements in pain, fatigue, depression and QoL³



Arthritis mutilans, with pencil-in-cup deformities (arrow)⁴

Window of opportunity in psoriatic arthritis: the earlier the better



IL-23 therapy is associated with lower risk of developing inflammatory arthritis, including PsA

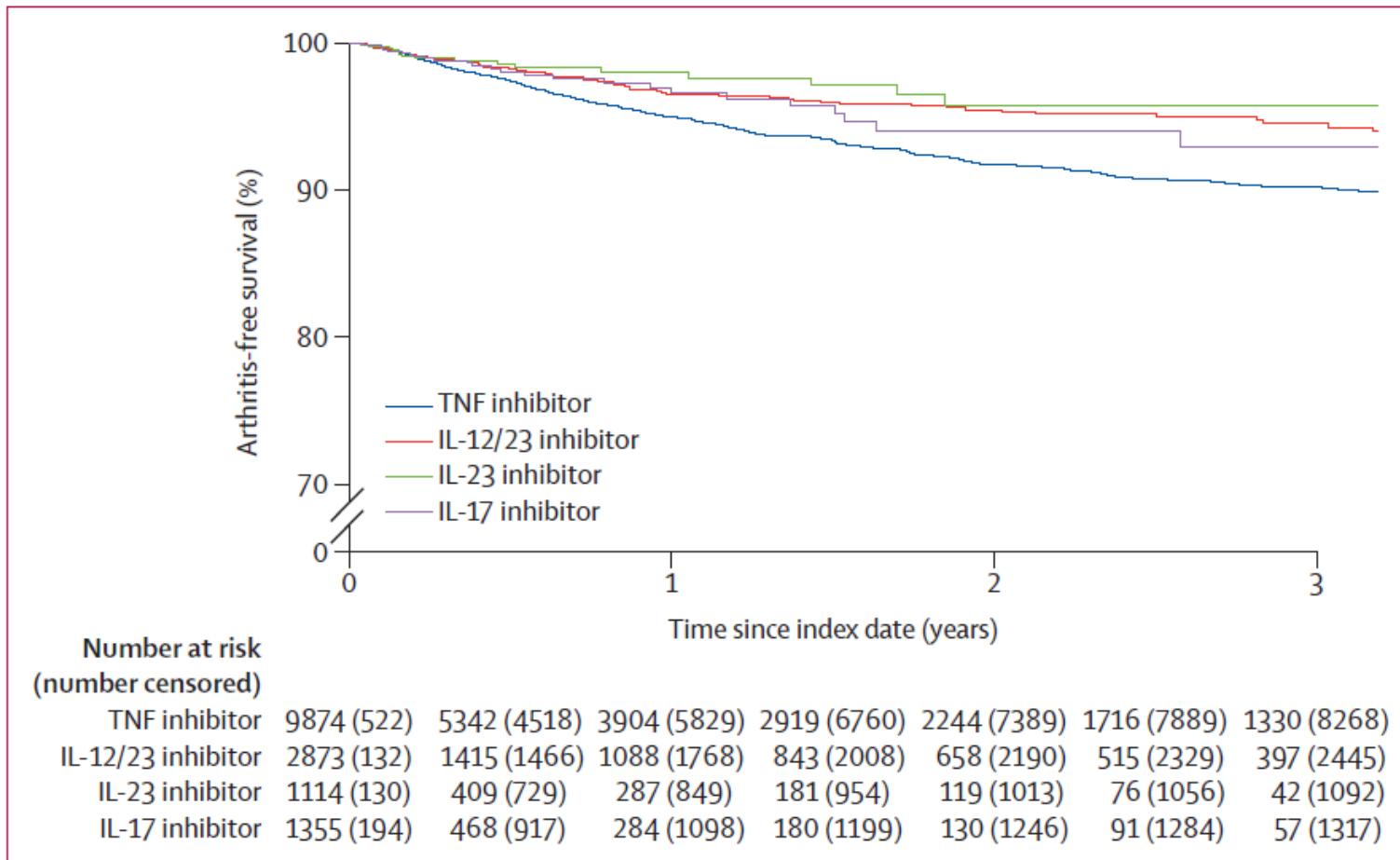


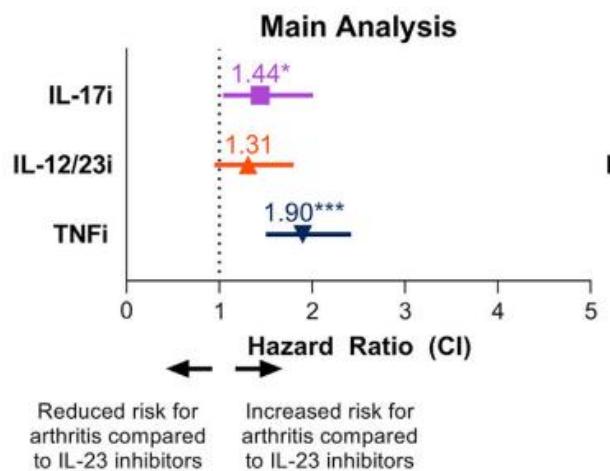
Figure 2: Time to inflammatory arthritis among patients initiating biological therapies for psoriasis (n=15 501)

TNF=tumour necrosis factor. IL=interleukin.

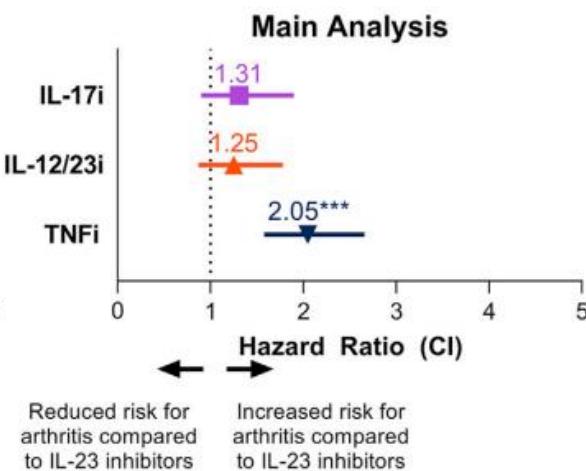
In a retrospective non-randomized study in 15.501 patients with psoriasis, **risk of developing inflammatory arthritis (including PsA) is reduced among patients who have started anti-IL12/23 or anti-IL23 therapy³**

Patients receiving IL-17, IL-12/23, or TNF inhibitors have higher incidence rates than patients receiving IL-23

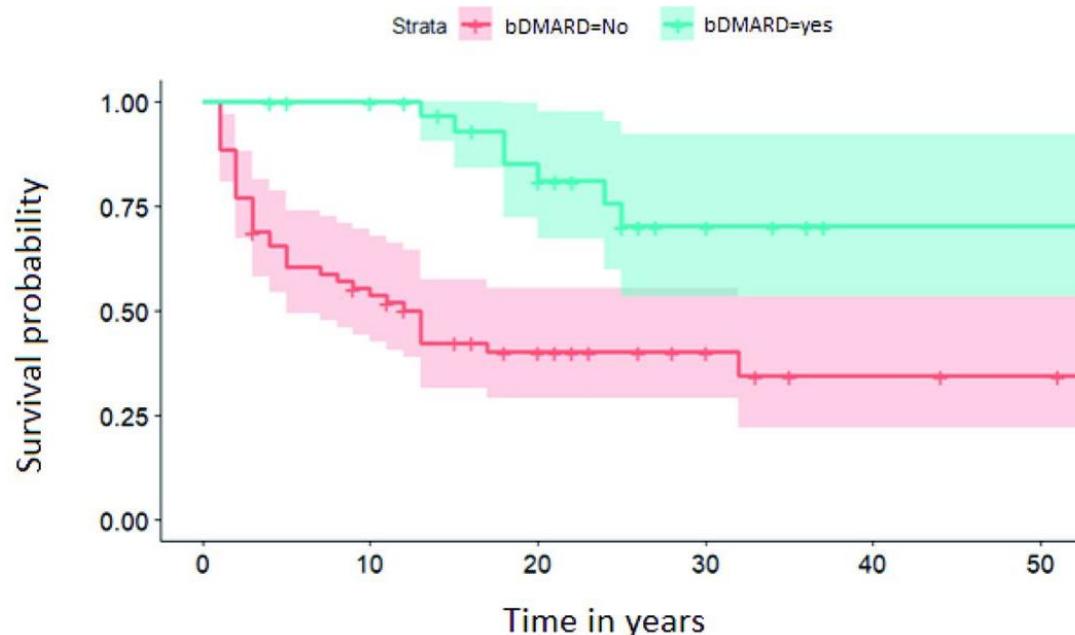
Inflammatory Arthritis



Psoriatic Arthritis



Survival curves for PsA development for different treatment groups (bDMARD yes/no)

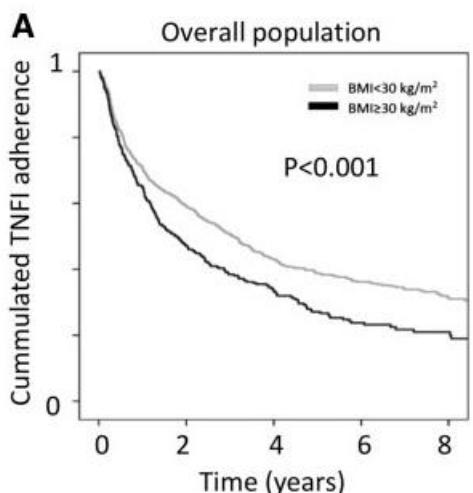


Risk of developing inflammatory arthritis in patients with psoriasis initiating treatment with biologics: A population-based analysis, Strober, Bruce et al. Journal of the American Academy of Dermatology, Volume 91, Issue 6, 1143 - 1149

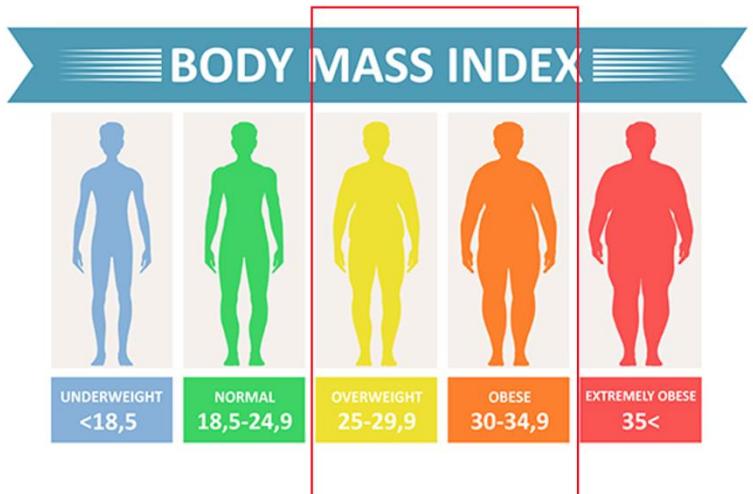
Azevedo SF, et al, POS0988 Annals of the Rheumatic Diseases 2024;83:717.

Effect of comorbidities on treatment outcomes/decisions: the obesity paradox

- ◆ ↑ risk of PsA Development in patients with Psoriasis Or in healthy individuals
- ◆ ↑ risk of not reaching outcomes
- ◆ ↑ risk of not maintaining favorable outcomes



Outcome at ≤12 months unless otherwise specified	sample size, n	n (%) events	OR (95% CI)	ORadj (95% CI)	ORadj (95% CI)
MDA					
Normal weight	306	66 (21.6)	1 (ref.)	1 (ref.)	
Overweight	285	40 (14.0)	0.59 (0.38-0.91)	0.63 (0.39-1.03)	
Obese	183	19 (10.4)	0.43 (0.25-0.74)	0.45 (0.24-0.82)	
DAPSA-remission					
Normal weight	306	51 (16.7)	1 (ref.)	1 (ref.)	
Overweight	285	20 (7.0)	0.38 (0.22-0.66)	0.44 (0.24-0.79)	
Obese	183	12 (6.6)	0.36 (0.19-0.70)	0.42 (0.21-0.85)	

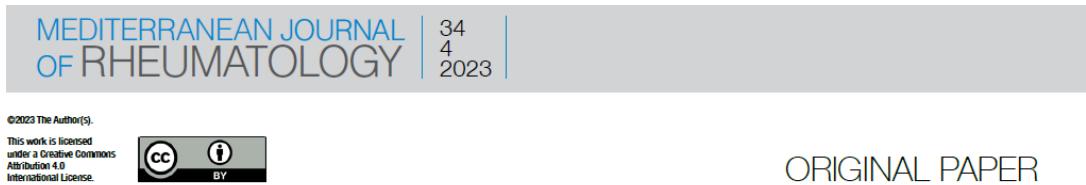


Drug category	RA	PsA	AxSpA
Abatacept			
JAK inhibitors			
IL-17 inhibitors			
IL-23 inhibitors			
IL-6R inhibitors			
Rituximab			
TNF inhibitors			

PsA

Data from Greece

923 patients (55% females)
median (IQR) age of 57 (48-65) years



ORIGINAL PAPER

Disease Profile and Achievement of Therapeutic Goals in a Modern, Nationwide Cohort of 923 Patients with Psoriatic Arthritis

George E. Fragoulis^{1*}, Charalampos Papagoras^{2*}, Sousana Gazi³, Evangelia Mole³, Michael Krikellis³, Paraskevi V. Voulgaris⁴, Evripidis Kaltonoudis⁴, Nikolaos Koletsos⁴, Pelagia Katsimpi⁵, Dimitrios Boumpas⁵, Dimitrios Katsifis⁵, Nikolaos Kougkas⁶, Theodoros Dimitroulas⁶, Petros P. Sfikakis¹, Maria G. Tektonidou¹, Chrysoula Gialouri¹, Dimitrios P. Bogdanos⁷, Theodora Simopoulou⁷, Christos Koutsianas⁸, Eugenia Mavrea⁹, Gkikas Katsifis⁹, Konstantinos Kottas⁹, Maria Konsta¹⁰, Matthoula Tziafalia¹⁰, Evangelia Kataxaki¹¹, Eleni Kalavri¹², Kalliopi Klavdianou¹², Eleftheria P. Grika¹³, Charalampos Sfontouris¹³, Dimitrios Daoussis¹⁴, George Iliopoulos¹⁴, Ilias Bourazos¹⁵, Dimitrios Karokis¹⁵, Konstantinos Georganas¹⁵, Dimos Patrikios¹⁵, Dimitrios Vassilopoulos⁸

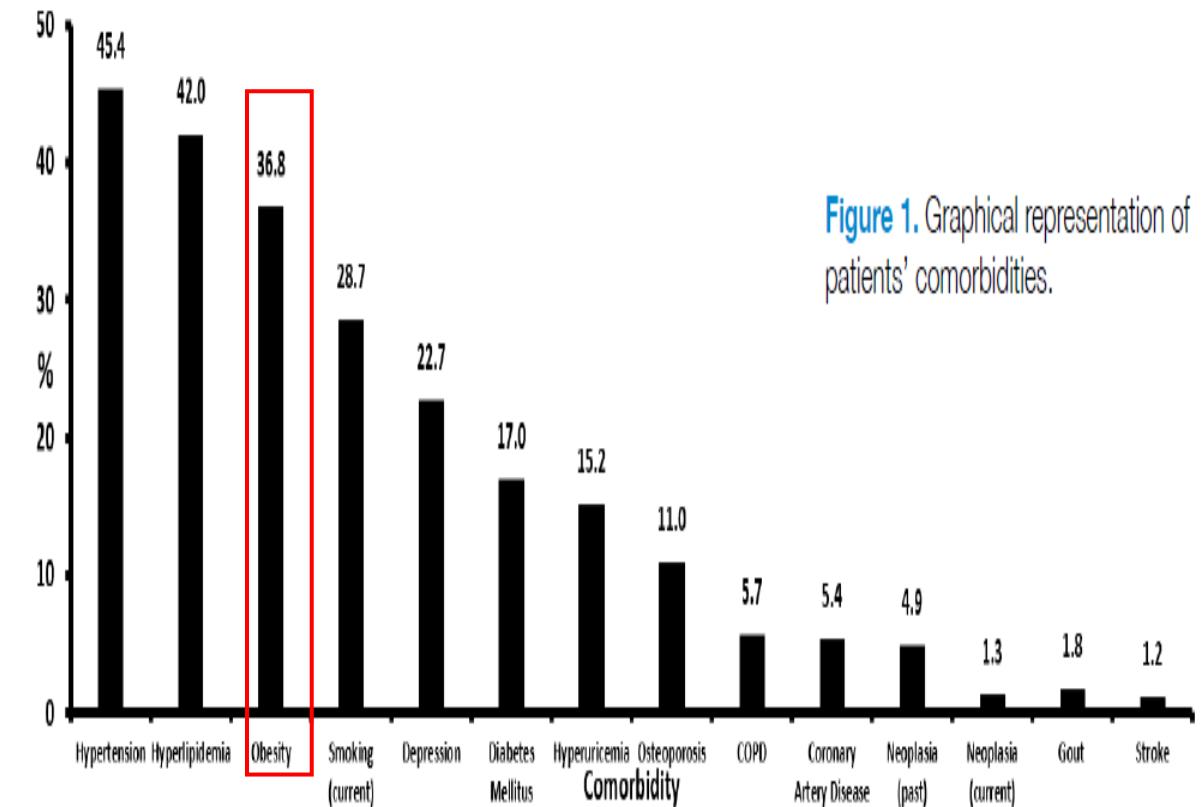
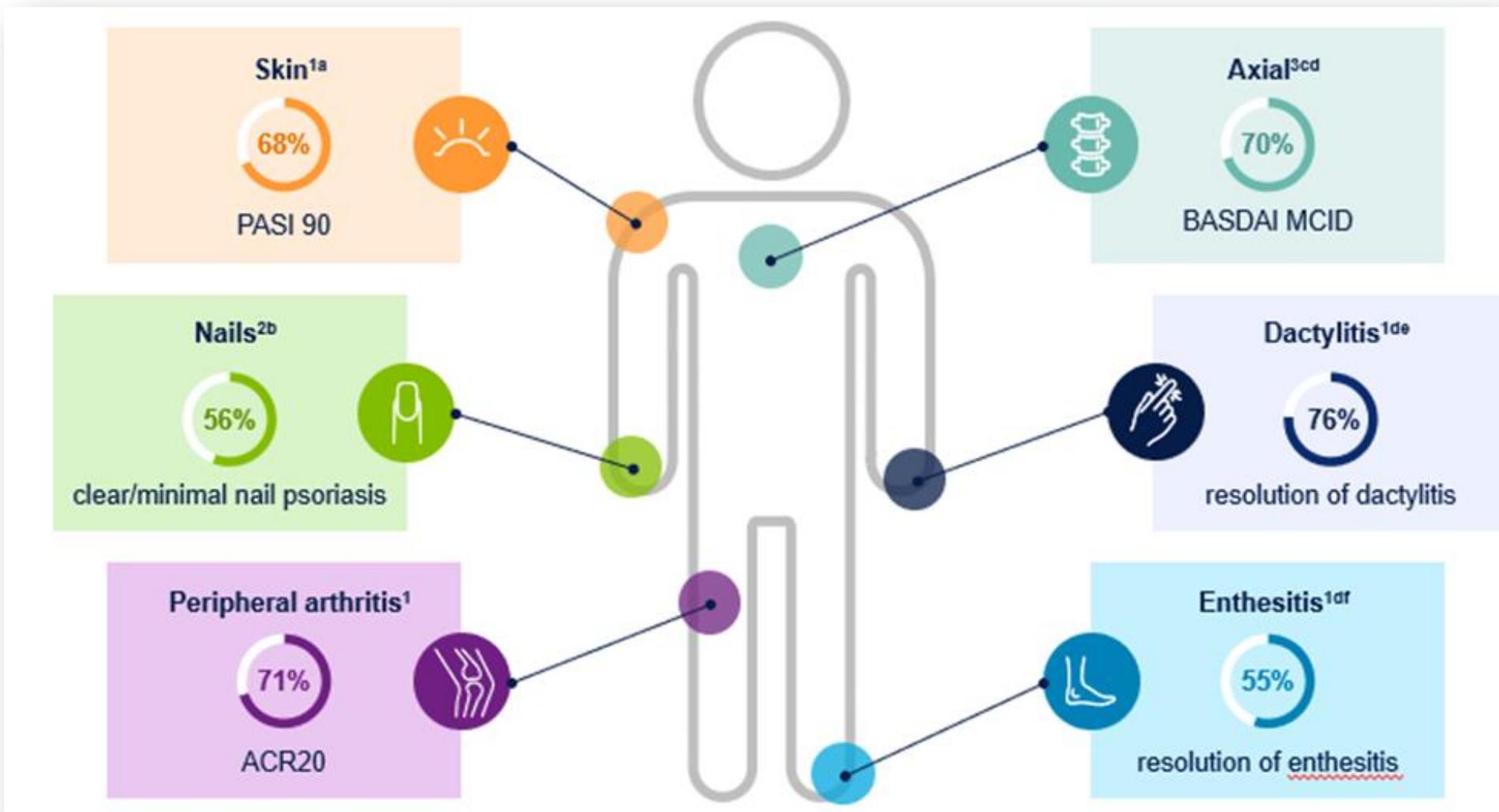
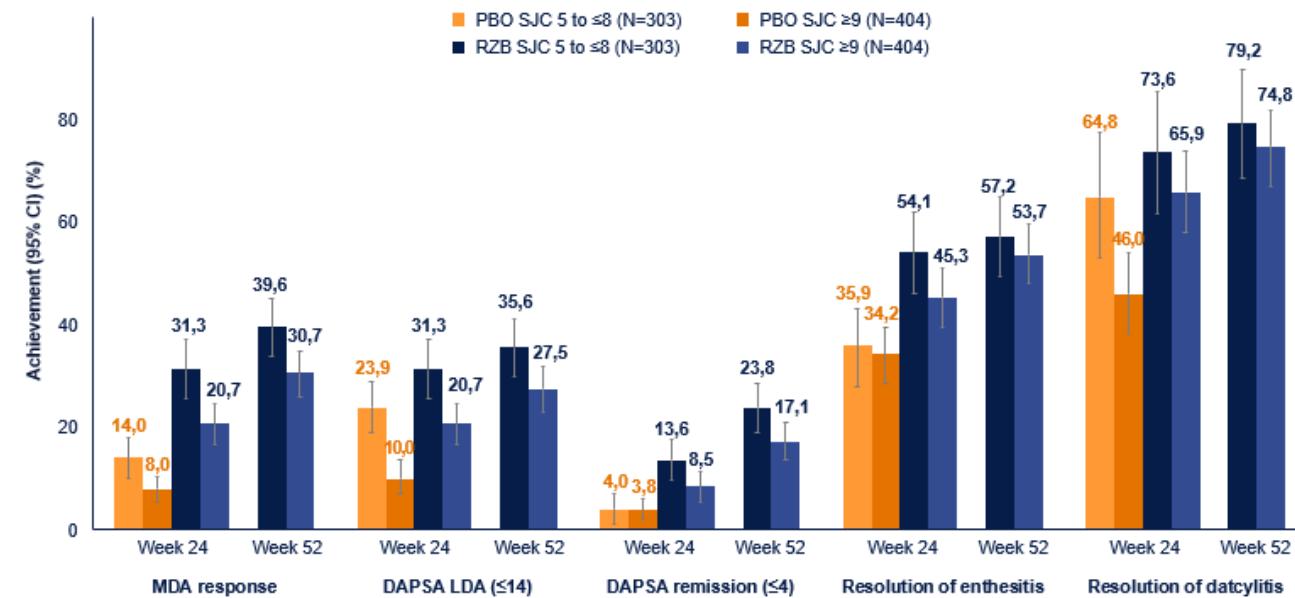
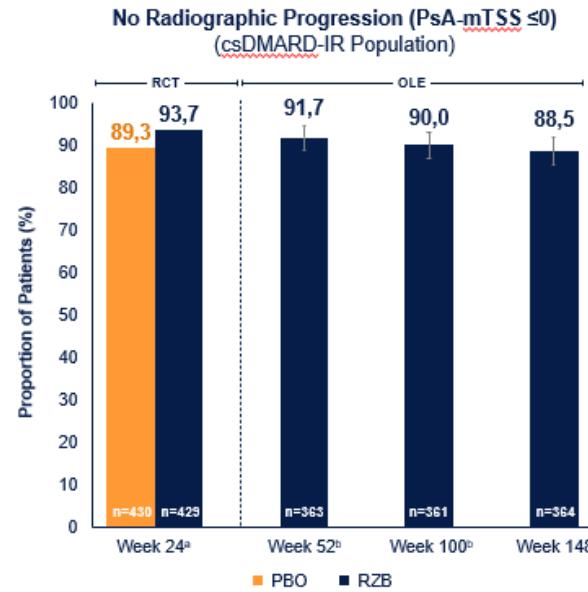
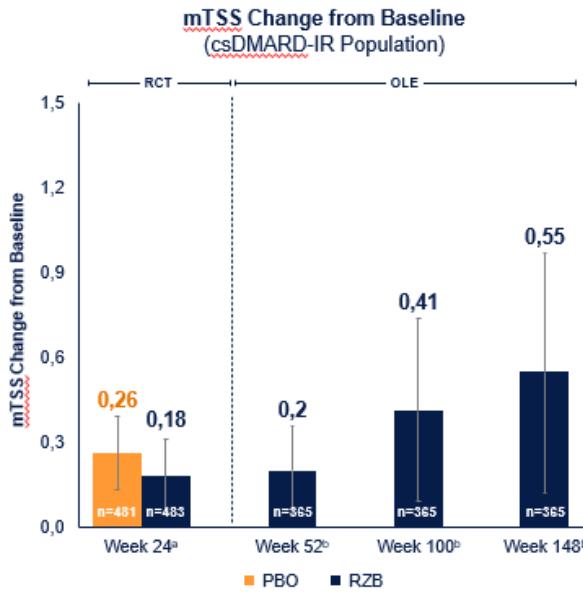


Figure 1. Graphical representation of patients' comorbidities.

Risankizumab: efficacy across all domains



High, durable responses can be achieved with IL-23 inhibition^{1,2}

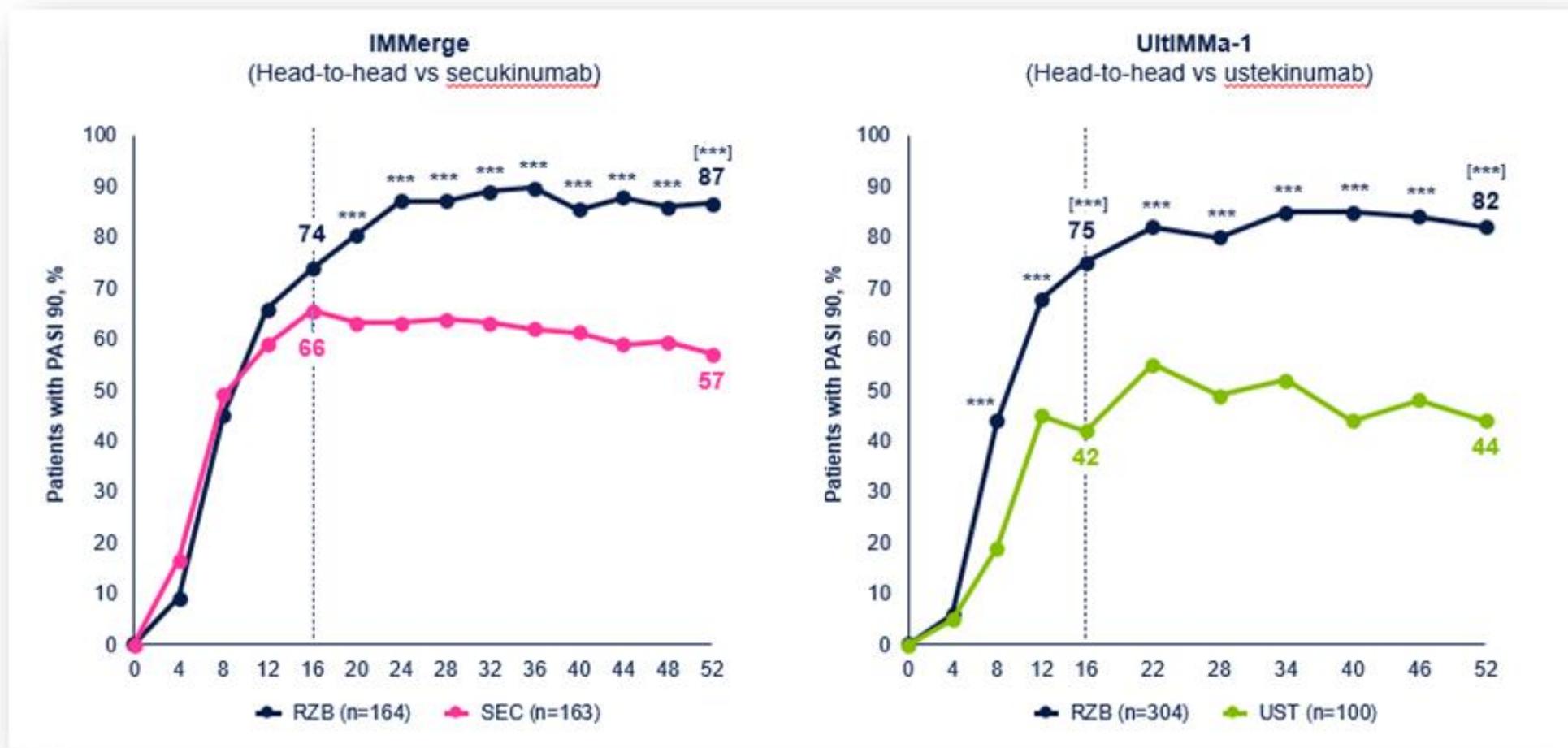


*p≤0,05 vs PBO; ^aBased on full analysis set, NRI-C. ^bBased on full analysis set, NRI (as observed with imputation, except those missing due to COVID-19) was used for missing data. Vertical dashed line represents the point at which all PBO patients were switched to RZB 150 mg. csDMARD-IR=inadequate response to conventional synthetic disease-modifying antirheumatic drugs; mTSS=modified total sharp score; OLE=open label extension; PBO=placebo; PsA=; RCT=randomized controlled trial; RZB=risankizumab.

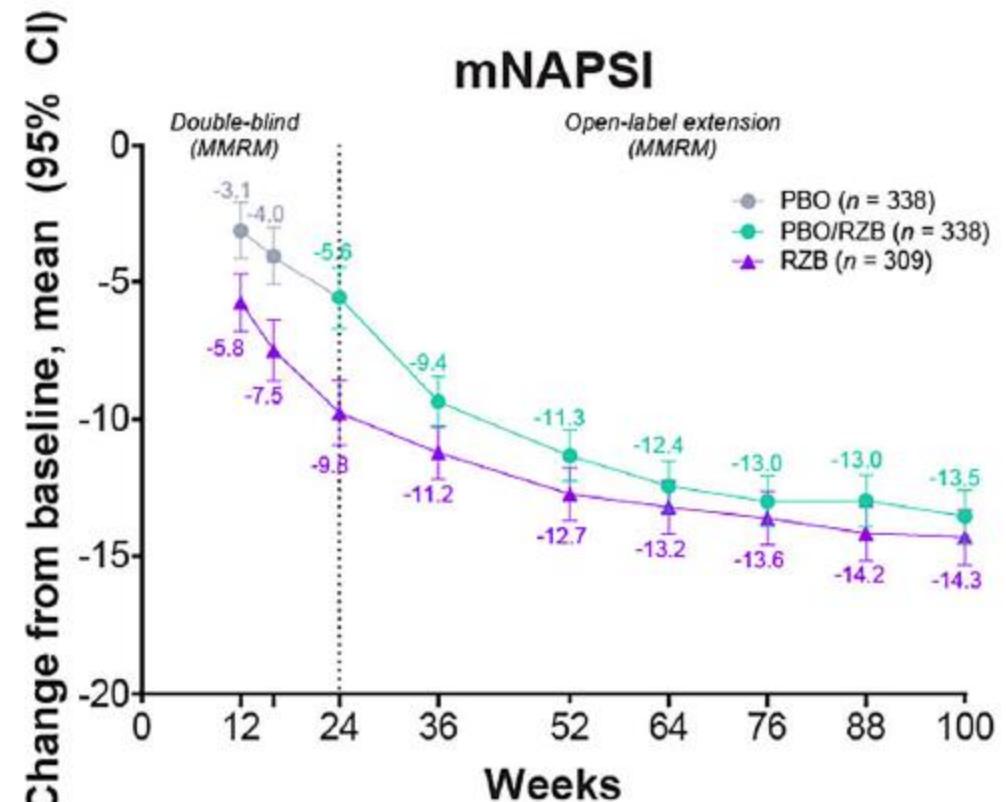
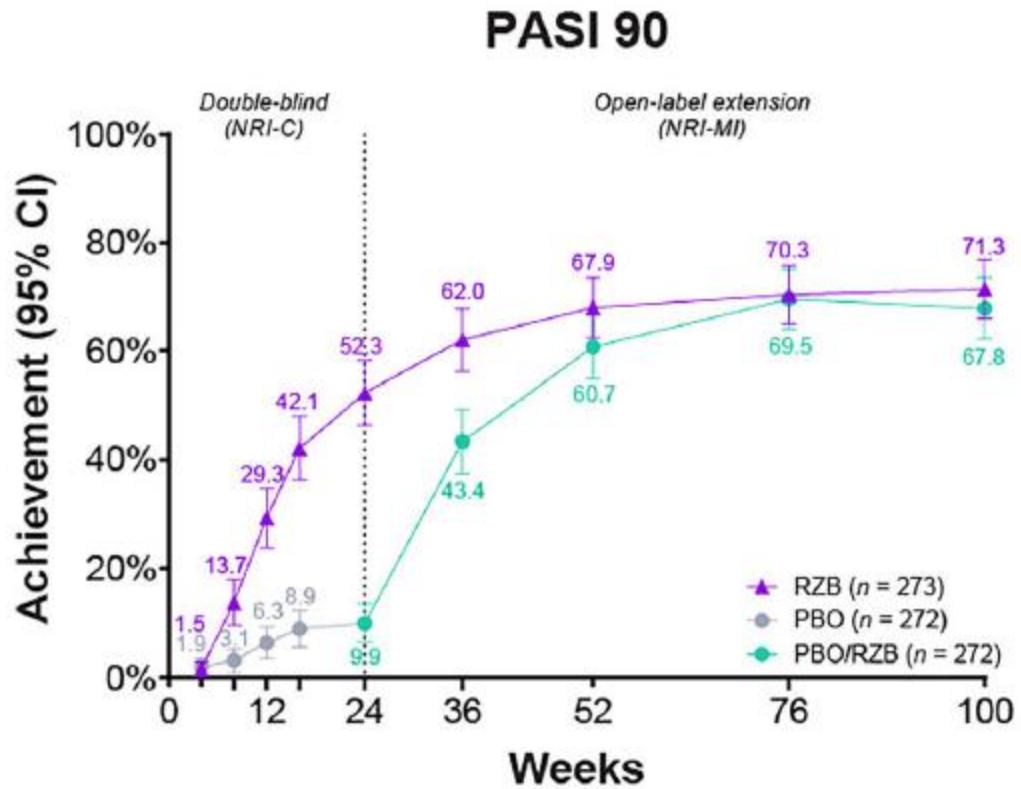
1. Kristensen LE et al. Ann Rheum Dis. 2021;80:1315-1316. 2. Kristensen LE et al. P2383; presented at EADV 2023. Resolution of enthesitis for patients with LEI ≥1 at baseline: SJC 5 to ≤8 PBO N=167, RZB N=159; SJC ≥9 PBO N=281, RZB N=285. Resolution of dactylitis LEI ≥1 at baseline: SJC 5 to ≤8 PBO N=54, RZB N=53; SJC ≥9 PBO N=150, RZB N=135. Week 24 results reported by non-responder imputation with multiple imputations accounting for COVID-19. Week 52 results reported by as observed with imputation. CI=confidence interval; DAPSA=Disease Activity Index for Psoriatic Arthritis; LDA=low disease activity; LEI=Leds Enthesitis Index; MDA=minimal disease activity; PBO=placebo; RZB=risankizumab; SJC=swollen joint count.

Oncode R et al. Poster #1494; presented at ACR 2022.

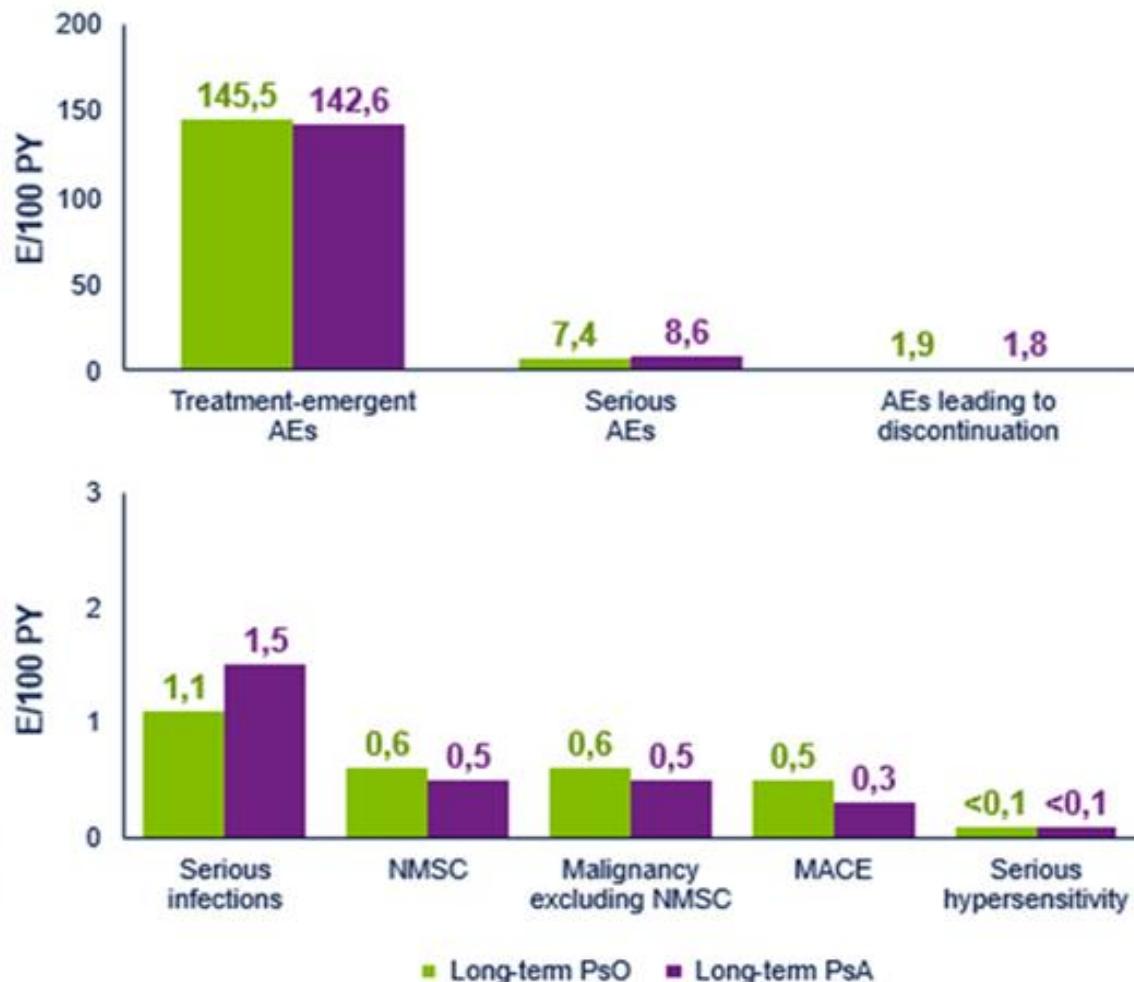
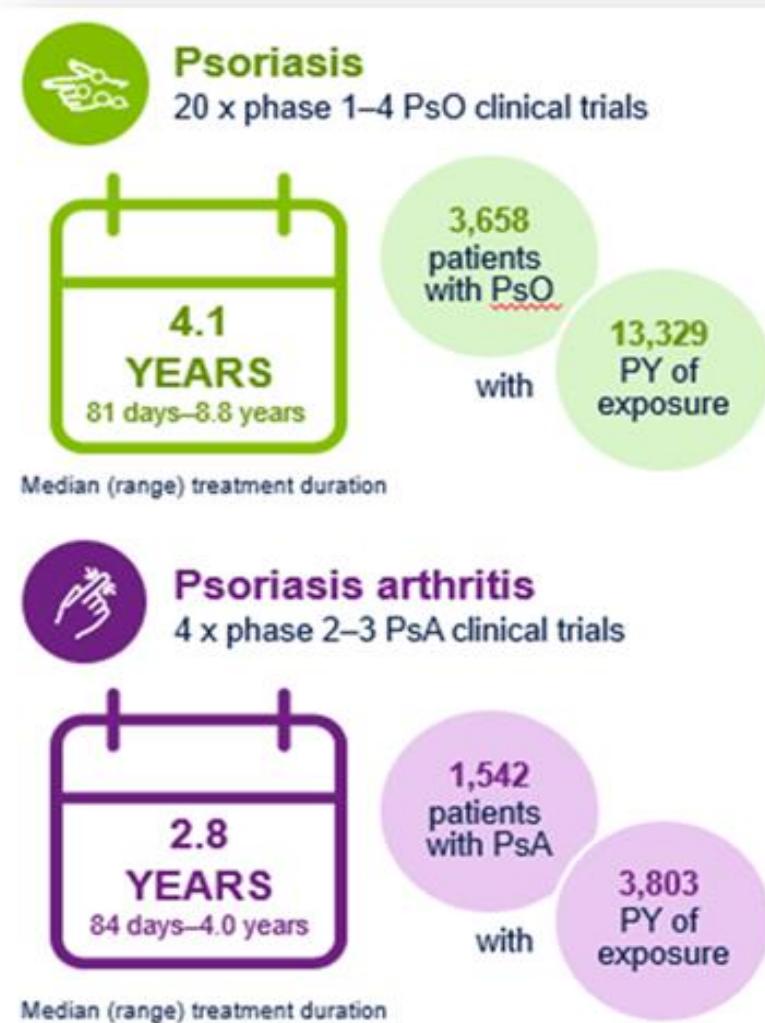
Superiority of Risankizumab vs Secukinumab and Ustekinumab



High, durable responses can be achieved with IL-23 inhibition



Risankizumab: safety



Κλινική Περίπτωση 2



6 μήνες αργότερα **πλήρης ύφεση** της ουσχίας και της αρθρίτιδας



Φυσιολογικές τιμές ηπατικών ενζύμων και αρνητικοί δείκτες φλεγμονής



Η Μαρία συνεχίζει την καθημερινότητά της έχοντας επαναφέρει το βιοτικό της επίπεδο στο βέλτιστο

Psoriatic disease – Multidisciplinary treatment approach: Where do we stand, where do we need to go?

New directions in the management of patients with psoriatic disease

Multidisciplinary collaboration

Improve
management of
patients with PsO
& PsA

Facilitate early
diagnosis of PsA

Identify early
abnormalities not
limited to skin &
joints

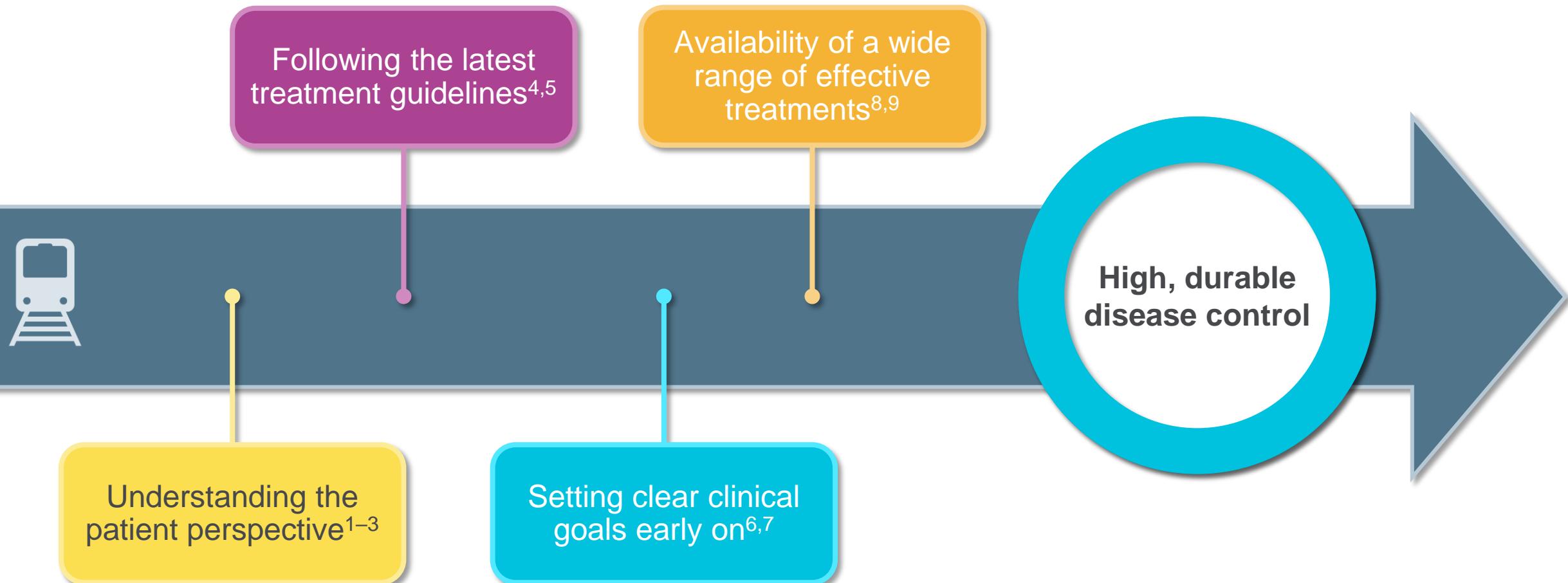
Train physicians
in the global
vision of psoriatic
disease



Models of multidisciplinary collaboration?



We have many means to help us reach our destination of high, durable disease control



1. Kouwenhoven TA, et al. *J Dermatolog Treat*. 2020;31(1):13–7; 2. Armstrong A, et al. *J Eur Acad Dermatol Venereol*. 2018;32(12):2200–7; 3. Korman NJ, et al. *J Dermatolog Treat*. 2022;33(2):733–9; 4. Nast A, et al. EuroGuiderm guideline for the systemic treatment of psoriasis vulgaris. www.guidelines.edf.one//uploads/attachments/clrf2t72k3ttodtjrokdem0cy-0-euroguiderm-pso-gl-draft-2024.pdf. September 2023. Accessed 23 April 2024; 5. Foley P, et al. *Australas J Dermatol*. 2023;64(4):476–87; 6. Strober BE, et al. *Dermatol Ther (Heidelb)*. 2019;9(1):5–18; 7. Romero IB, et al. *Annals of Medicine*. 2021;53(1):1727–36; 8. Sawyer LM, et al. *PLoS One*. 2019;14(8):e0220868; 9. Armstrong AW, et al. *Dermatol Ther (Heidelb)*. 2022;12:167–84.