



ΕΠΕΜΥ
Επιστημονική Εταιρεία
για τη Μυοσκελετική Υγεία

12^ο Πανελλήνιο Συνέδριο

*Ολοκληρωμένη διαχείριση των Φλεγμονώδων
και των Μυοσκελετικών Παθήσεων*

Ολοκληρωμένη Διαχείριση της ΨΑ στις
γυναίκες

GR-N-CZ-PsA-2000002

ΔΗΜΗΤΡΟΥΛΑΣ ΘΕΟΔΩΡΟΣ
ΕΠΙΚΟΥΡΟΣ ΚΑΘΗΓΗΤΗΣ ΑΠΘ
Δ' ΠΑΘΟΛΟΓΙΚΗ ΚΛΙΝΙΚΗ
ΙΠΠΟΚΡΑΤΕΙΟ ΝΟΣΟΚΟΜΕΙΟ ΘΕΣ/ΝΙΚΗΣ

Σύγκρουση συμφερόντων

Conflict of interest

Παρούσα παρουσίαση: UCB

Εκπαιδευτικές-ερευνητικές-συμβουλευτικές επιχορηγήσεις την
τελευταία διετία:

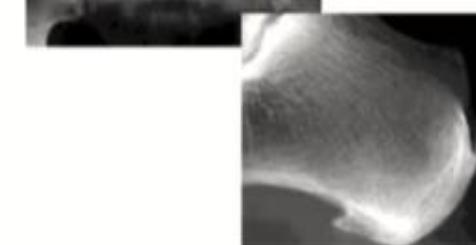
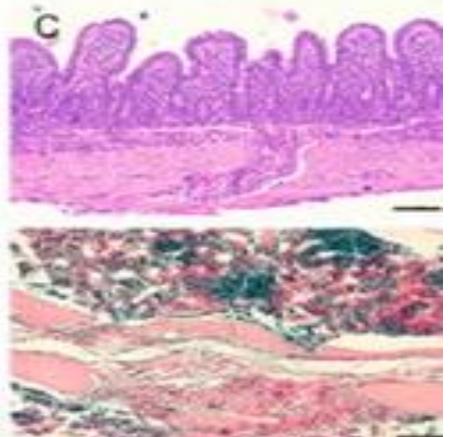
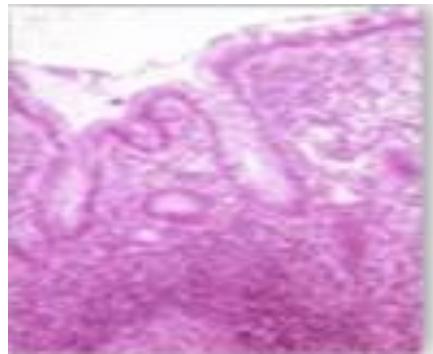
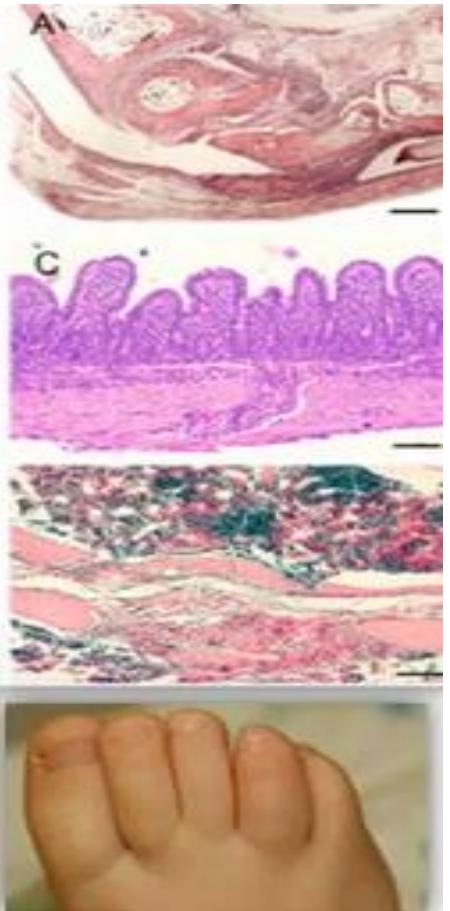
Abbvie, Amgen, Boehringer Ingelheim, Elpen, Enorasis,, JANSSEN,
Genesis Pharma, Gilead, ΚΟΠΕΡ, Lilly, Novartis, Pfizer, Mylan, MSD



ΨΩΡΙΑΣΙΚΗ ΑΡΘΡΙΤΙΔΑ

- Πόνος
- Δυσφορία
- Στρες

Ετερογένεια κλινικού φαινοτύπου στην Ψωριασική Αρθρίτιδα

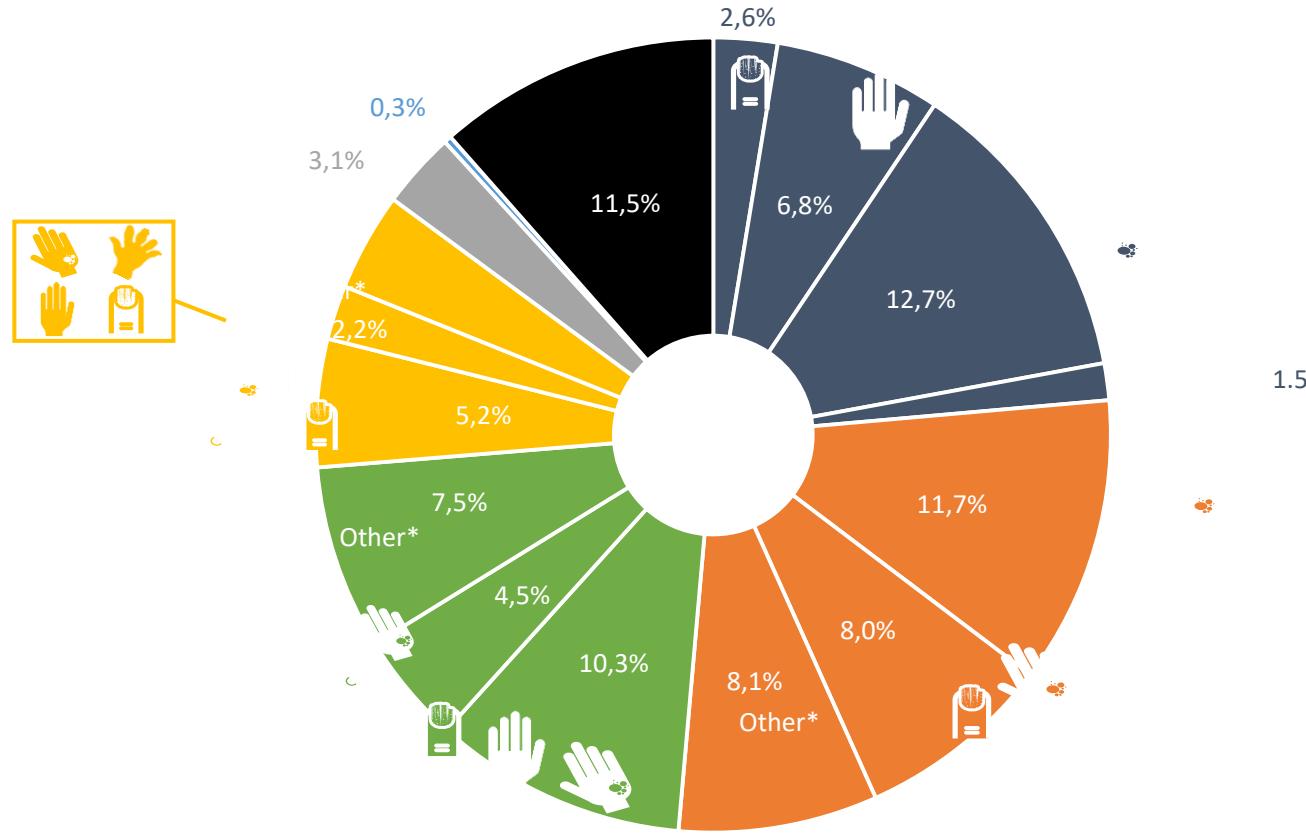
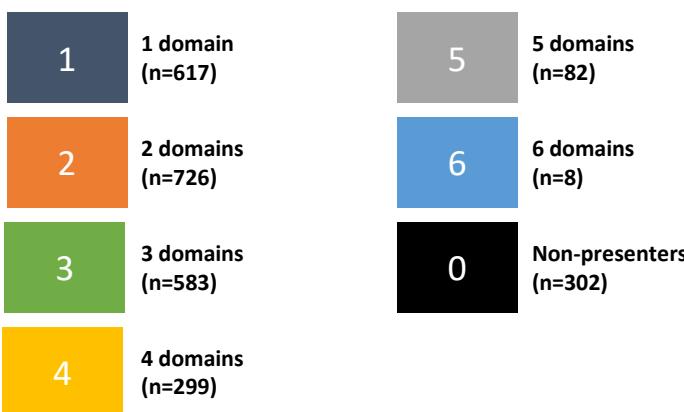
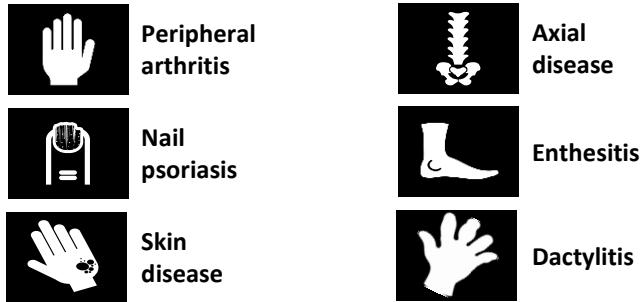


Στην Ψωριασική Αρθρίτιδα εμπλέκονται 6 πεδία της νόσου με τις αντίστοιχες κλινικές εκδηλώσεις



1. Kavanaugh A, et al. *Rheumatol Ther* 2016;3:91–102; 2. Kyriakou A, et al. *Sci World J* 2014;Article ID 508178; 3. Lee E, et al. *J Exp Med* 2004;199:125–30; 4. Lowes M, et al. *J Invest Dermatol* 2008;128:1207–11; 5. Yao Y, et al. *PLoS One* 2008;3:e2737; 6. Taylan A, et al. *Rheumatol Int* 2012;32:2511; 7. Limon-Camacho L, et al. *J Rheumatol* 2012;39:830–5.. 8. Van Kuijk A and Tak P. *Curr Rheumatol Rep* 2011;13:353–9; 9. Ritchlin C, et al. *J Rheumatol* 1998;25:1544–52; 10. Menon B, et al. *Arthritis Rheumatol* 2014;66:1272–81; 11. Celis R, et al. *Arthritis Res Ther* 2012;14:R93; 12. Spadaro A, et al. *Ann Rheum Dis* 2002;6:174–6; 13. Molteni S and Reali E. *Psoriasis: Targets and Therapy* 2012;2:55–66; 14. Siegel E, et al. *Curr Opin Rheumatol* 2015;27:111–7; 15. Lories R, et al. *Nat Med* 2012;18:1018–9; 16. Ebihara S, et al. *Autoimmunity* 2015;29:1–8; 17. Ruutu M, et al. *Arthritis Rheum* 2012;64:2211–22; 18. Sherlock J, et al. *Nat Med* 2012;18:1069–77; 19. Yamamoto M, et al. *J Invest Dermatol* 2015;135:445–53; 20. Reinhardt A, et al. *Arthritis Rheumatol* 2016;68:2476–86; 21. Coates LC, et al. *Lancet* 2015;386:2489–98.

Prevalence of Disease Domain Manifestations in Patients with PsA



Κάθε ασθενής μπορεί να παρουσιάσει ένα μοναδικό συνδυασμό των συμπτωμάτων και της βαρύτητάς τους με διαφορετικό φορτίο της νόσου γεγονός που αντανακλά τη πολυπλοκότητα της νόσου.

Adapted from Oggie A et al. Arthritis Rheumatol. 2019;71 (suppl 10). Abstract 2475.

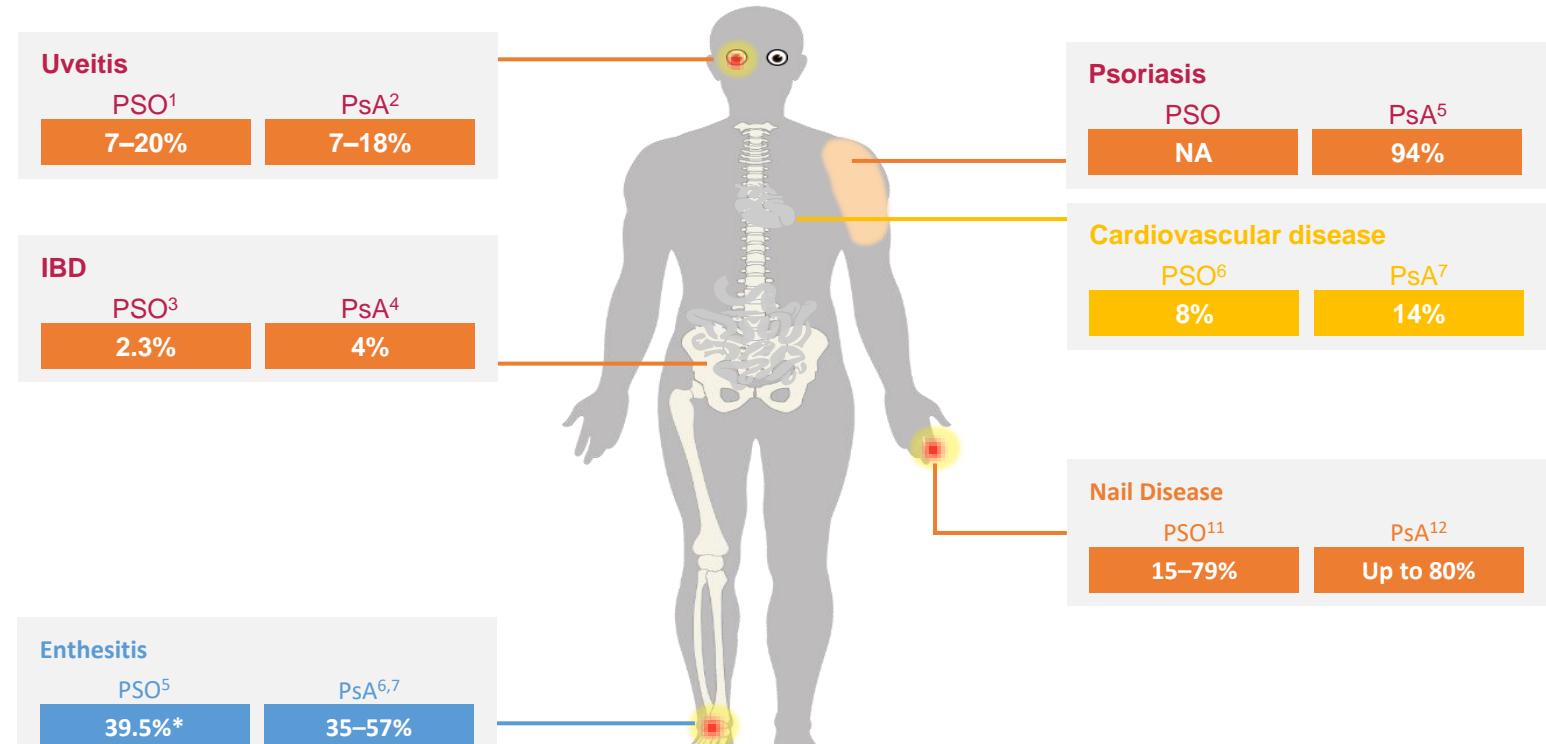
2,617 patients with PsA enrolled in the Corrona PsA/SpA Registry.
*Other (2–4 domains) presentation includes all other combinations of ≥2 domains not shown in the figure; [†]Other (1 domain) presentation includes axial disease, enthesitis and dactylitis.

Extra-musculoskeletal Manifestations and Comorbidities in Patients with Psoriatic Disease

Extra-musculoskeletal manifestations (EMMs) including psoriasis, uveitis, inflammatory bowel disease (IBD) and nail disease^{1-4,8,11-12}

Comorbidities including cardiovascular disease^{6,7}

Peripheral articular manifestations such as enthesitis⁵⁻⁷



Prevalence of EMMs and comorbidities in patients with PSO is similar to patients with PsA

1. Fraga NA et al. An Bras Dermatol. 2012;87(6):877–883.
2. Chen H and Chou C. Curr Rheumatol Rev. 2008;4:111–14.
3. Loftus E Jr et al. Poster P626. 11th Congress of ECCO, 2016. Abstract P626.
4. Williamson L et al. J Rheumatol. 2004;31:1469–1470.
5. Elnady B et al. Clin Rheumatol. 2019;38(6):1627–1635.

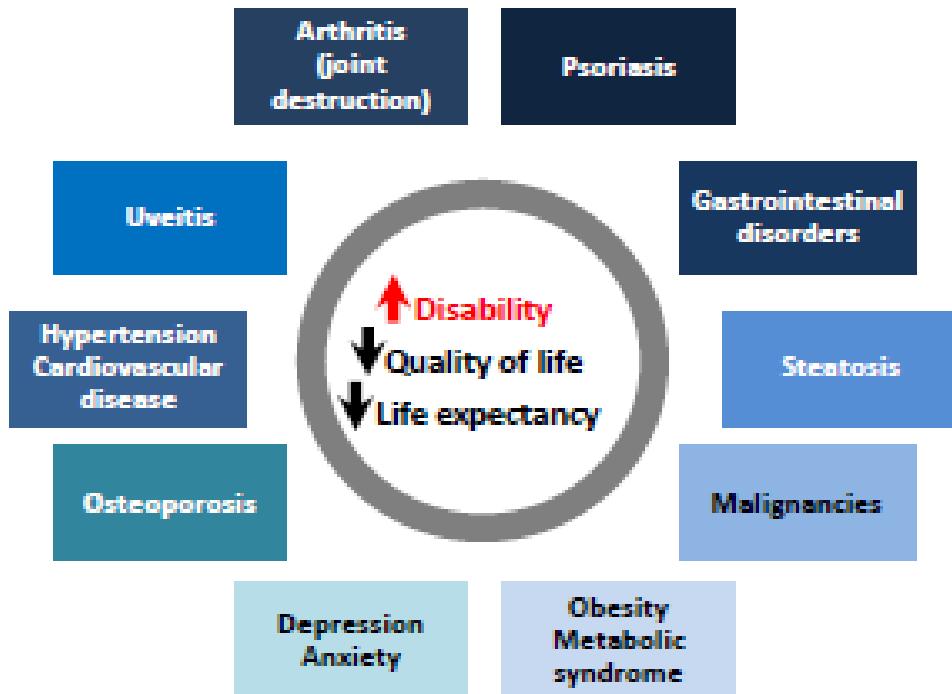
6. Kaeley GS et al. Semin Arthritis Rheum. 2018;48(1):35–43.
7. D'Agostino MA et al. Arthritis Rheum. 2003;48(2):523–533.
8. Kane D et al. Rheumatology (Oxford) 2003; 42(12): 1460–1468.
9. Xiao J et al. JEADV. 2009;23(11):1311–1315.
10. Peluso et al. Clin Rheumatol. 2015;34:745–753

11. Ventura A et al. Drug Design, Development and Therapy. 2017;11:2527–2535.
12. Sobolewski P et al. Reumatologia. 2017;55(3):131–135.

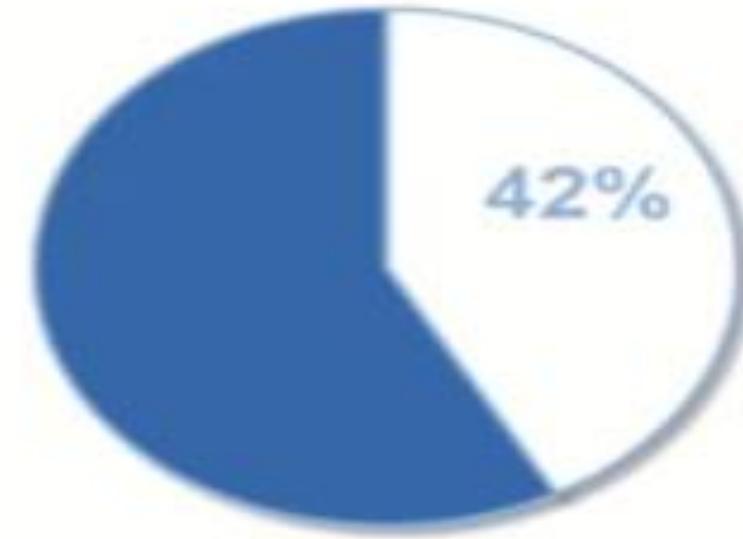
*Patients with enthesitis and/or synovitis.

ΣΥΝΝΟΣΗΡΟΤΗΤΕΣ ΚΑΙ ΨΑ

Συννοσηρότητες σε ασθενείς με ΨΑ



Ασθενείς με >3 συννοσηρότητες

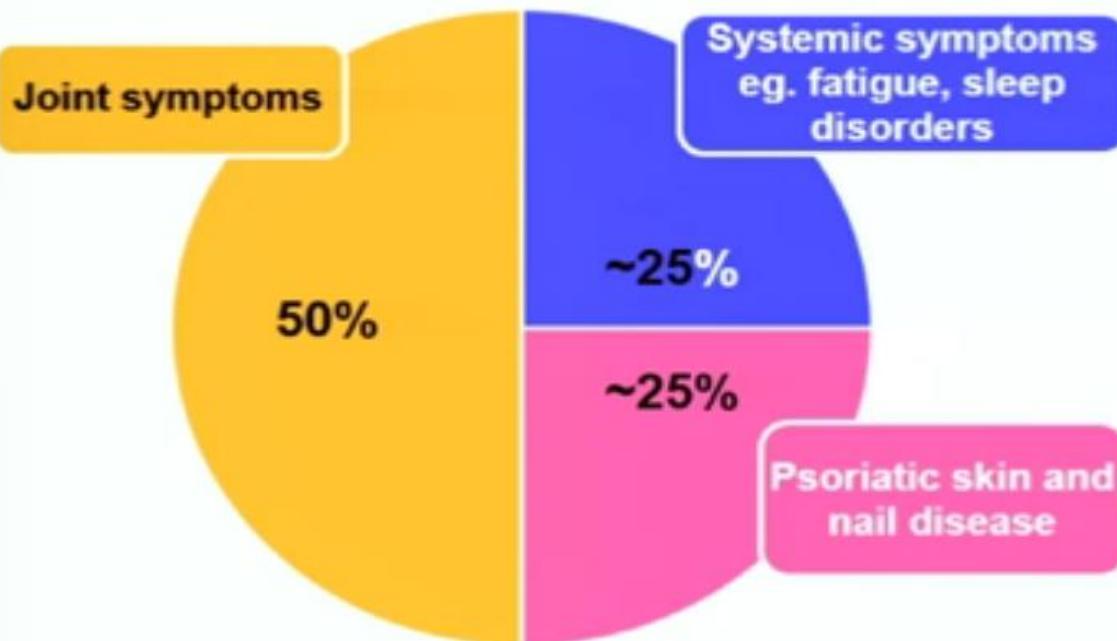


Polachek A, et al Arthr Care Res 2016
Caotes L, Arthritis Rheumatol 2016
Husted JA et al, J Rheumatol 2013

The Global Burden of PsA

Patient surveys on the global burden of disease

PsA population with predominant musculoskeletal involvement:¹



Contribution to overall burden of PsA

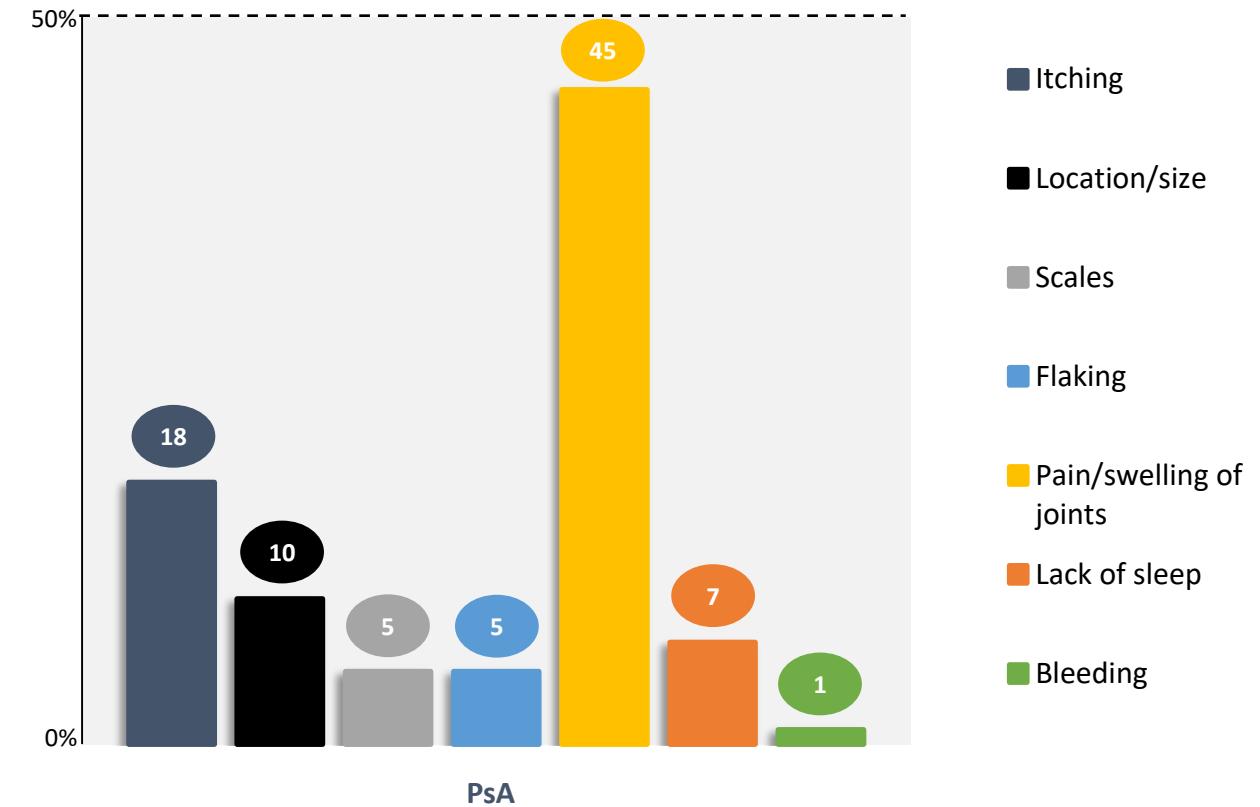
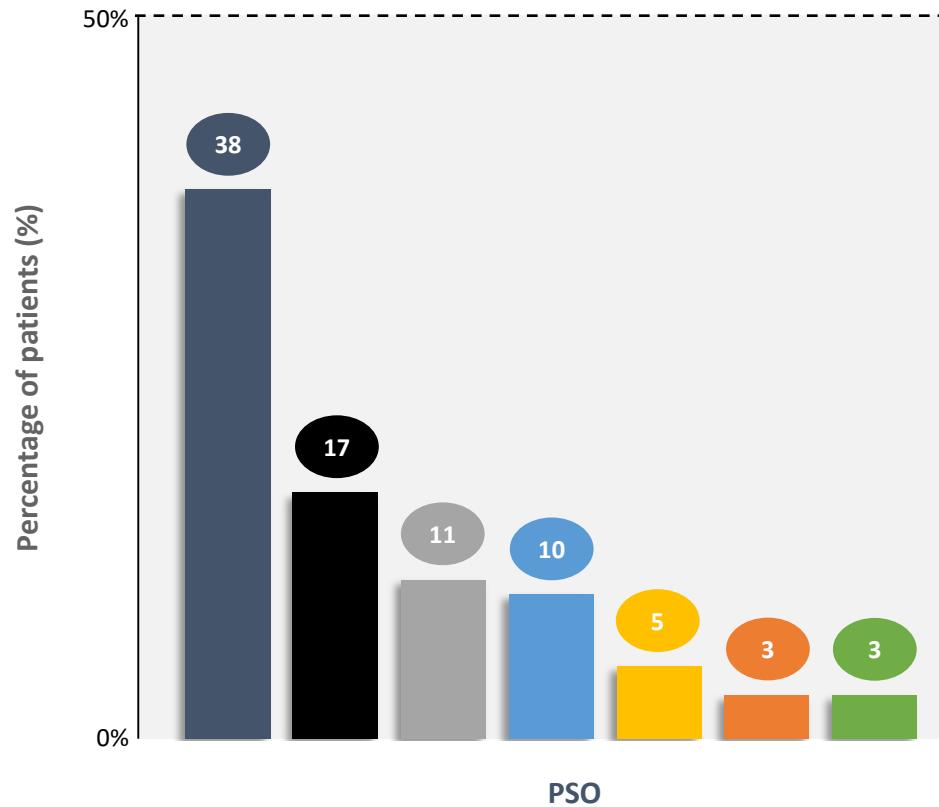
Patient-derived and patient-reported outcome measure for PsA

Domains with the highest relative importance to patients:

- Pain
- Fatigue
- Skin problems

Dandorfer et al, Semin Rheum 2012;42:32-41
Gossec et al, Ann Rheum Dis 2014;73:1012-19

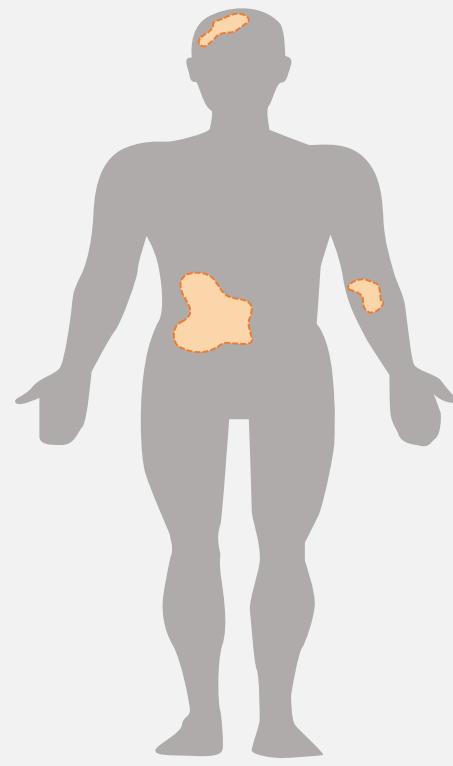
Key Factors Contributing to Disease Severity in Psoriatic Disease



Itching and location of skin involvement in psoriasis, and pain/swelling of joints upon joint involvement, are the patient-reported factors mostly contributing to disease severity

Progression of Psoriatic Disease

Psoriasis

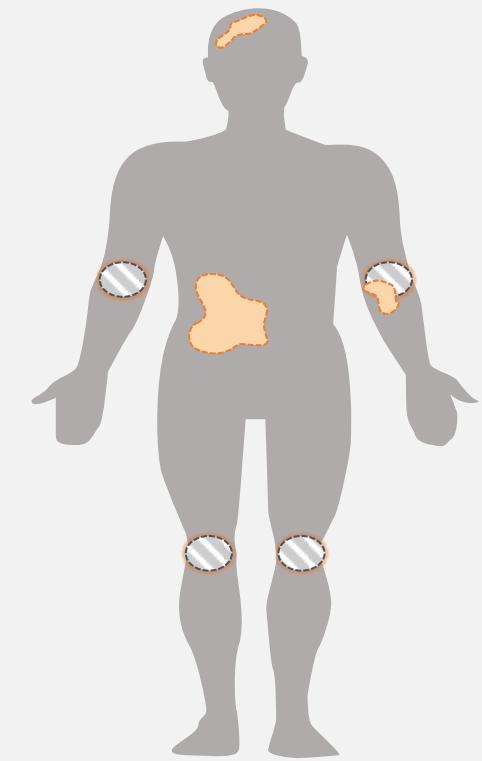


In 70% of cases, psoriasis precedes PsA,
with a mean interval of ~10 years^{3,4}

In 13% of cases, history of joint involvement precedes onset
of skin symptoms,
with a mean interval of ~4 years⁴

Parallel onset of skin and joint manifestations is seen in 15–21%
of cases^{3–5}

Psoriatic Arthritis

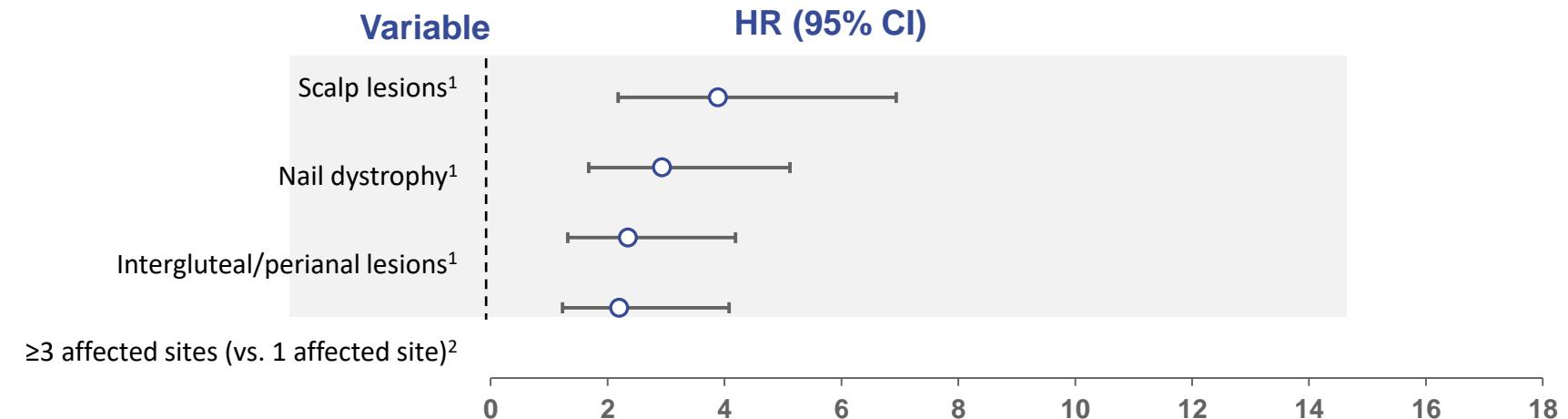


Of all PSO patients, as many as ~40% will
develop PsA^{1,2}

1. Mease PJ and Armstrong AW. Drugs. 2014;74(4):423–441.
2. Gladman DD et al. Ann Rheum Dis. 2005;64 Suppl 2:ii14–17.
3. Leung Y et al. J Postgrad Med. 2007;53:63–71.
4. Kumar R et al. Indian J Dermatol Venereol Leprol. 2014;80(1):15–23.
5. Cohen M et al. J Rheumatol. 1999;26:1752–1756.

PSO Features Associated with a Higher Risk of PsA

| Unmet Needs |



Other features found to be a risk factor for PsA included more extensive skin psoriasis³, psoriatic nail pitting⁴ and uveitis⁴

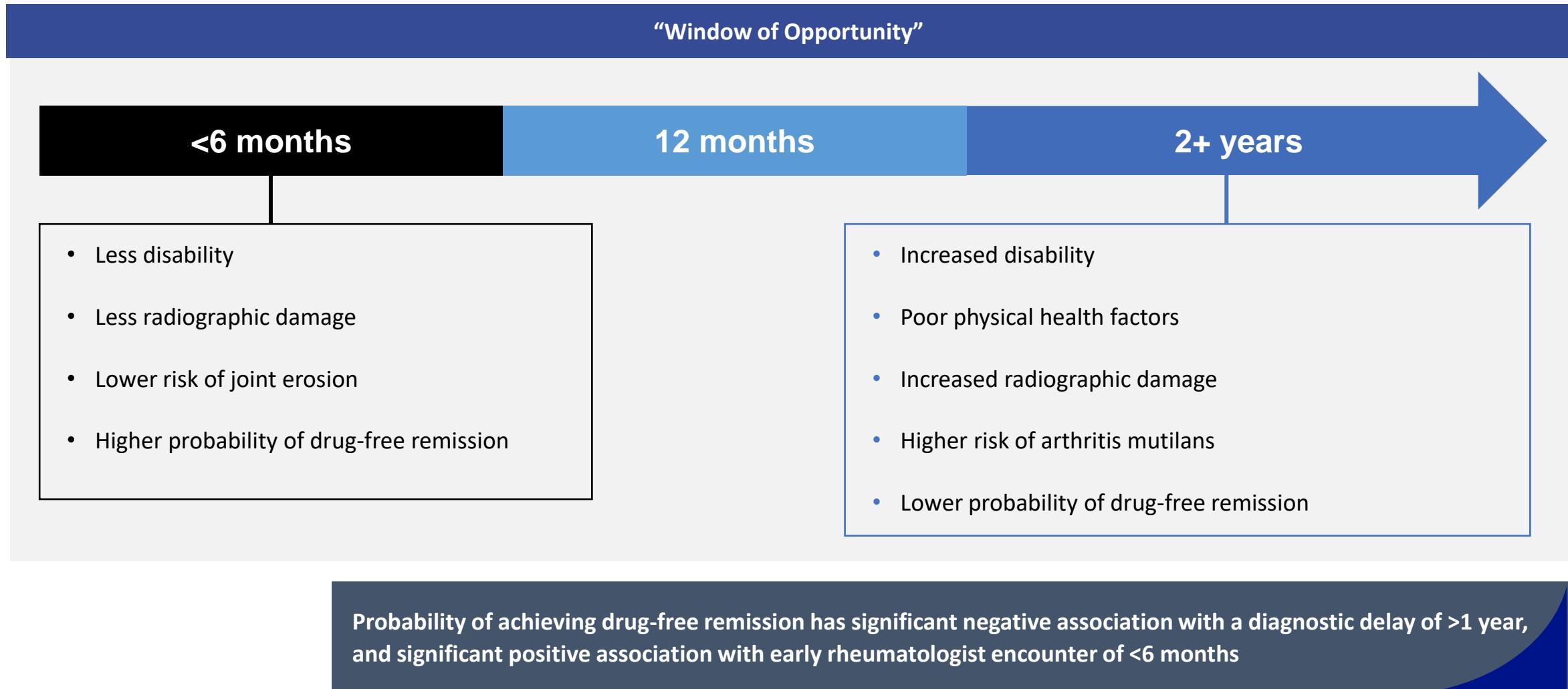
1. Wilson FC et al. Arthritis Rheum. 2009;61(2):233–239.

2. McLeod B. Evid Based Med. 2009;14(6):185.

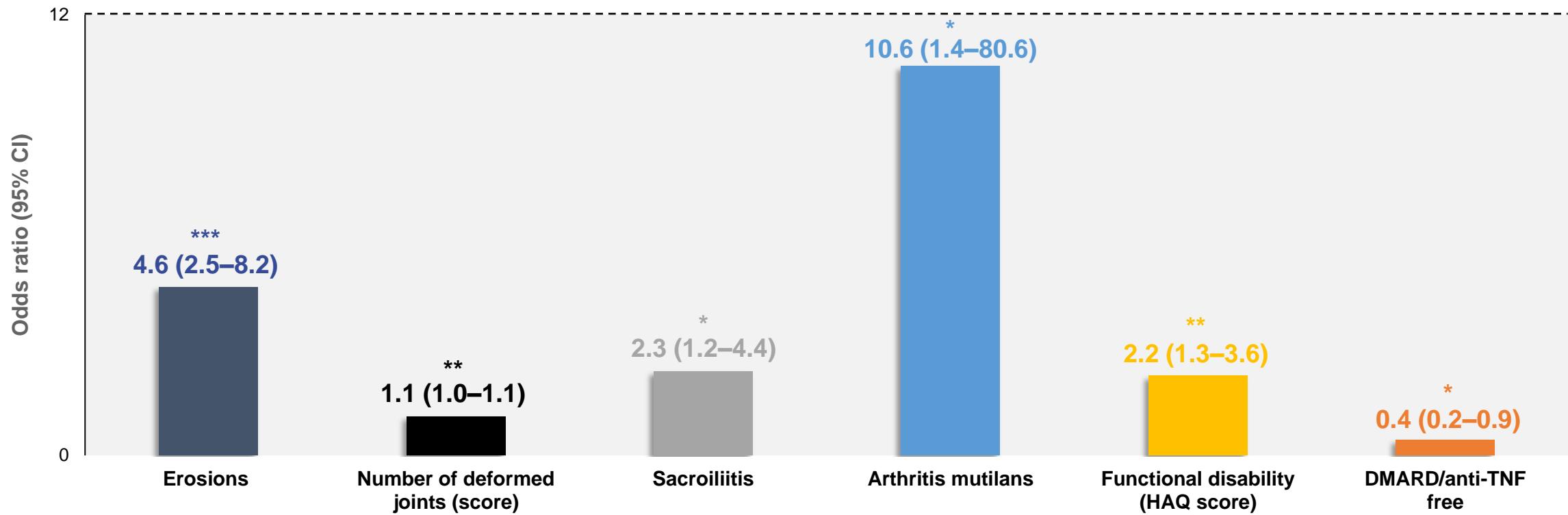
3. Oggie A. Rheumatol. 2013;52:568–575.

4. Eder L et al. Arthritis Rheum. 2016;68(4):915–923.

Time to Diagnosis

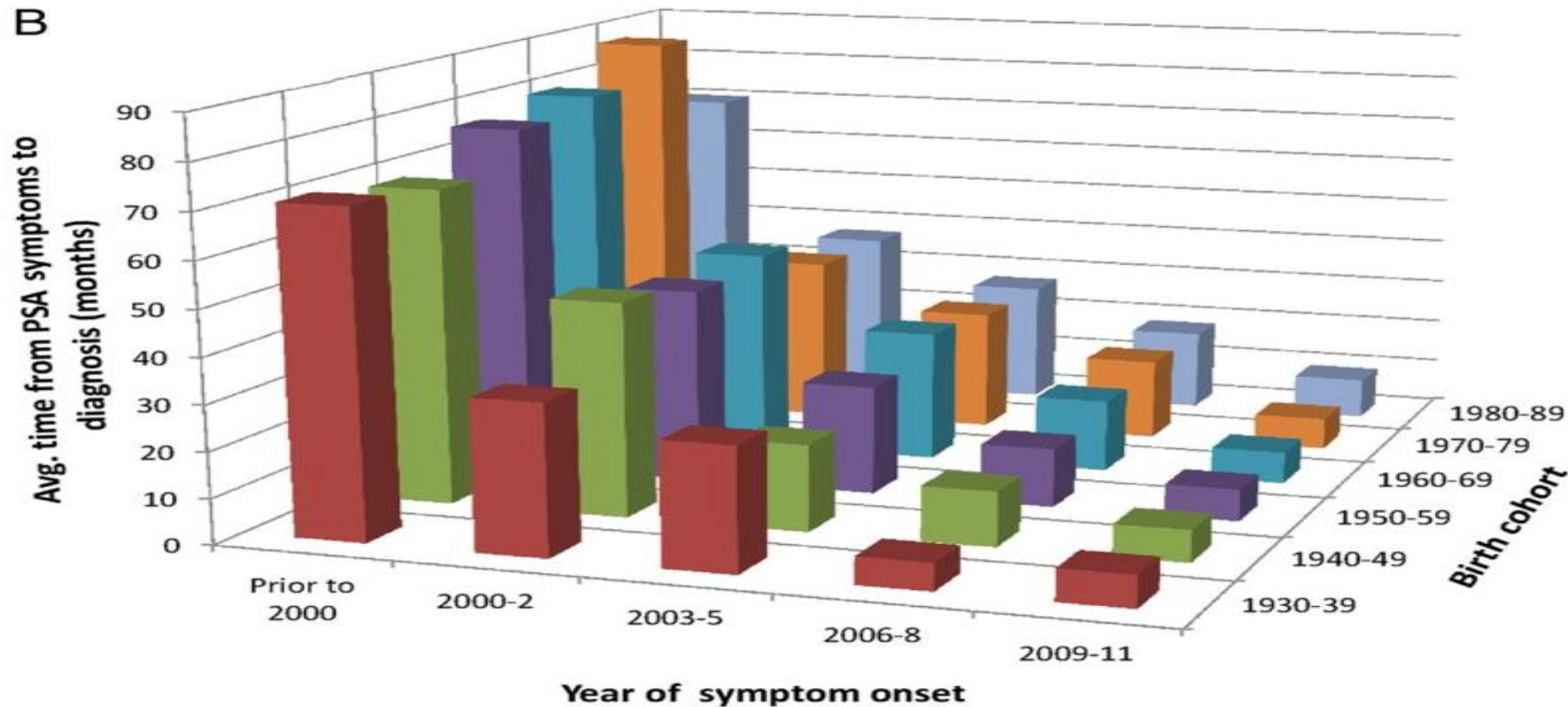


Association of Clinical Features with >6 Month Delay in Diagnosis



Delayed diagnosis of PsA is associated with poorer long-term outcomes

Η καθυστέρηση στη διάγνωση της ΨΑ φαίνεται να βελτιώνεται



Original Article

Accepted manuscript online: 4 April 2017

Clinical Characteristics, Disease Activity, and Patient-Reported Outcomes in Psoriatic Arthritis Patients With Dactylitis or Enthesitis: Results From the CORONA Psoriatic Arthritis/Spondyloarthritis Registry

Philip J. Mease MD , Chitra Karki MPH, Jacqueline B. Palmer PHARM.D, Carol J. Etzel PH.D,
 Arthur Kavanaugh MD, Christopher T. Ritchlin MD, Wendi Malley MS,
 Vivian Herrera DDS, MPH, Melody Tran PHARM.D, Jeffrey D. Greenberg MD, MPH

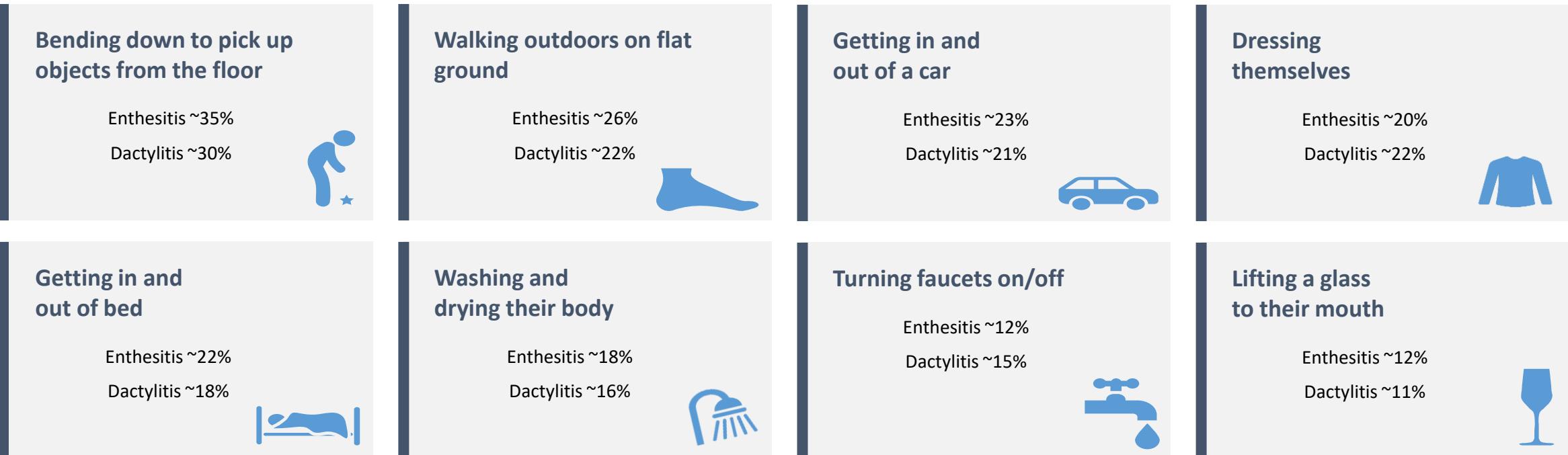


CORONA Registry 1,567 PsA patients - 420 with enthesitis, 228 with dactylitis

	Ενθεσίτιδα	Δακτυλίτιδα
Αυξημένα πιθανότητα μη επίτευξης LDA/MDA	2.53 (1.55–4.15)	1.88 (1.23–2.86)
Πόνος – VAS	7.40 (3.78–11.02)	7.31 (3.88–10.75)
Κόπωση - VAS	3.30 (-1.22–7.82)	2.47 (-1.86–6.79)
Επίπτωση στη εργασία (απώλεια ωρών εργασίας – μειωμένης απόδοσης)	1.57 (1.05–2.35)	1.21 (0.66–2.22)
Συνολικά μειωμένη δραστηριότητα	2.00 (1.37–2.93)**	1.77 (1.16–2.69)

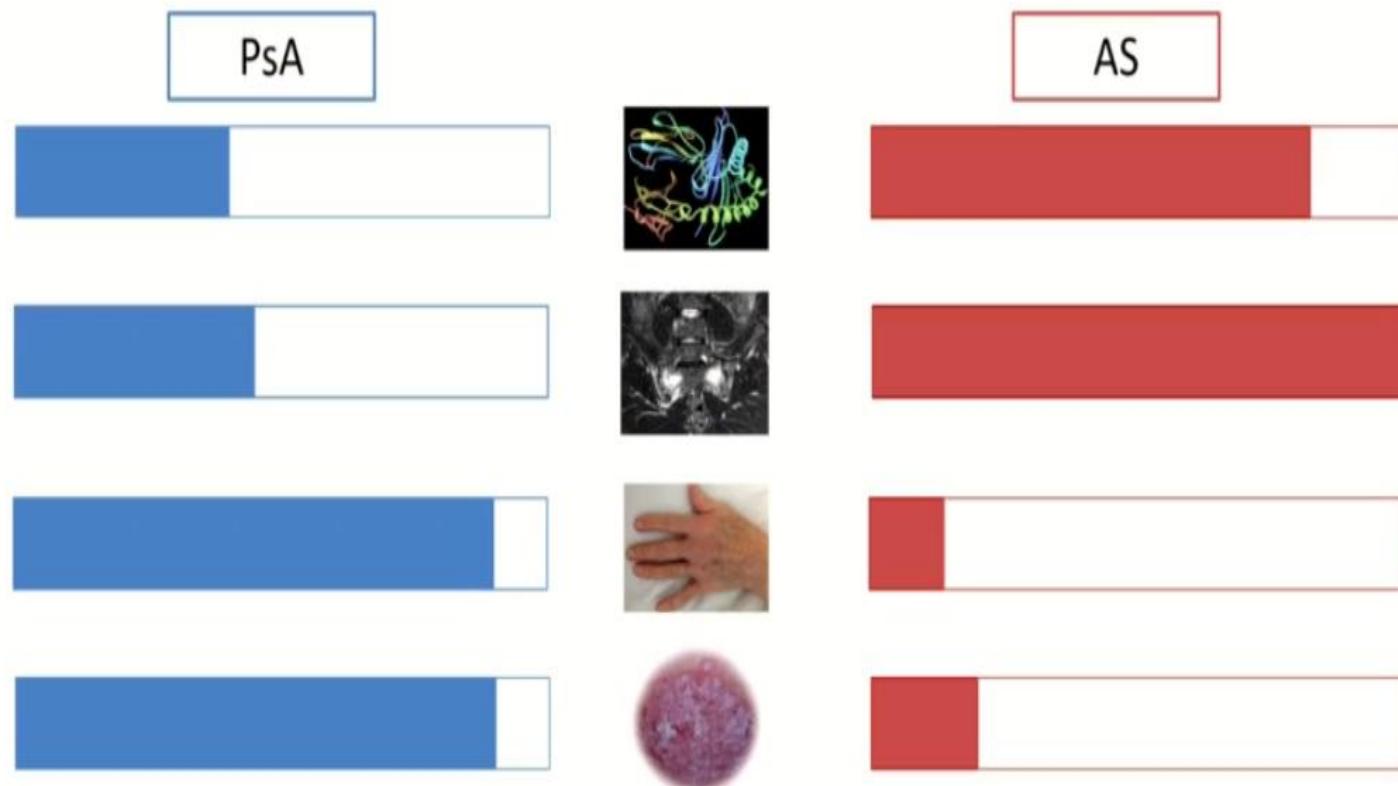
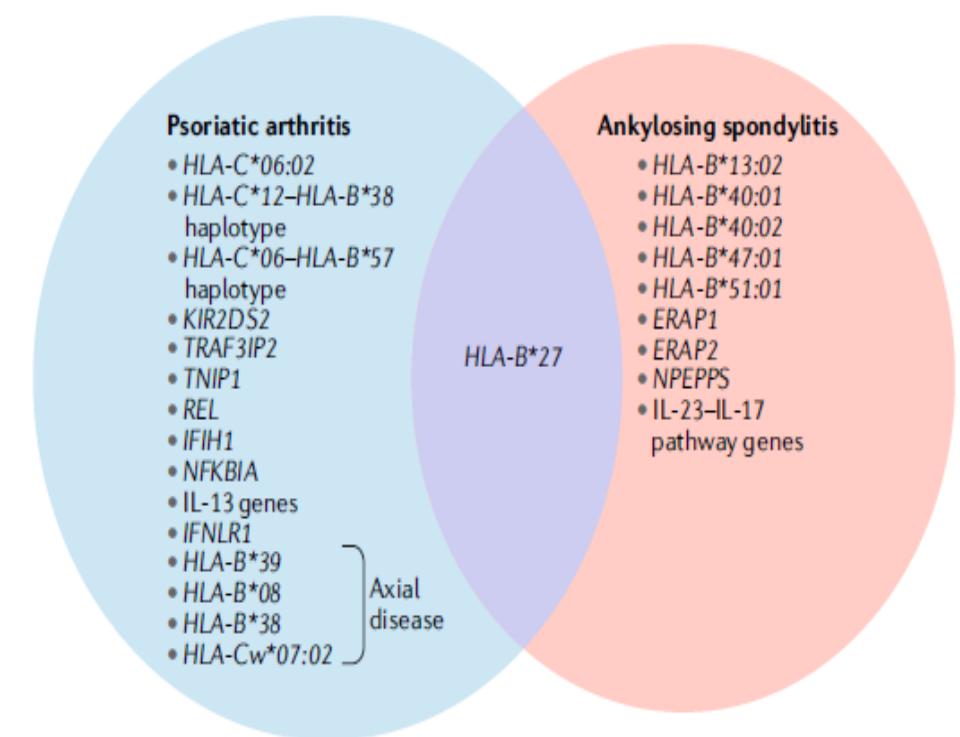
Impact of Enthesitis and Dactylitis on Physical Function

PsA patients with enthesitis and dactylitis reported more disability compared to all PsA patients in:*



Axial disease in psoriatic arthritis and ankylosing spondylitis: a critical comparison

Feld et al, 2018 Jun;14(6):363-371



EXTENDED REPORT

Axial Disease in Psoriatic Arthritis study: defining the clinical and radiographic phenotype of psoriatic spondyloarthritis

Deepak R Jadon,^{1,2} Raj Sengupta,¹ Alison Nightingale,³ Mark Lindsay,³ Eleanor Korendowych,¹ Graham Robinson,¹ Amelia Jobling,⁴ Gavin Shaddick,⁴ Jing Bi,⁵ Robert Winchester,⁵ Jon T Giles,⁵ Neil J McHugh^{1,3}

Ann Rheum Dis. 2017 Apr; 76(4): 701–707.

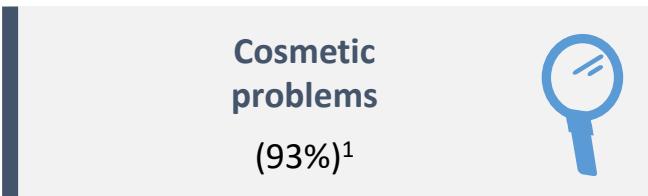
201 PsA, 201 AS



- Μεγαλύτερη διάρκεια νόσου
- Ανδρικό φύλο
- ↑ ΤΚΕ
- Πολυαρθριτικός τύπος
- HLA-B27

Burden of Nail Disease on Patients

- Among PsA patients, nail disease can cause:



PsA patients with severe nail disease are reported to have

- Higher functional impairment²
- Greater anxiety scores²
- Greater depression scores²

Severity of nail psoriasis is associated with

- Enthesitis²
- Polyarticular disease²
- Progressive arthritis in PsA²

1. Williamson L et al. *Rheum.* 2004;43:790–794.

2. Lee S et al. *P&T.* 2010;35(12):680–689.

Psoriatic Arthritis (PsA) Features^{1–7}

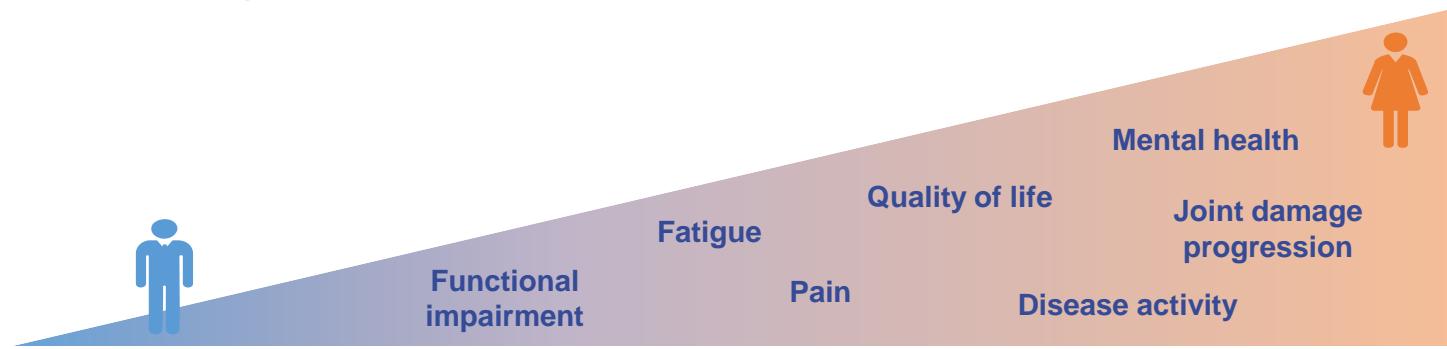
- Extra-musculoskeletal manifestations** Psoriasis, uveitis, and IBD
- Sacroiliitis and spondylitis** Inflammation of sacroiliac joints
- Peripheral articular manifestations** Peripheral arthritis, enthesitis and dactylitis
- Comorbidities** Cardiovascular disease

Progression^{8,9}



~40% of patients may progress from PSO to PsA

Diagnosis is Delayed¹⁰ and Outcomes are Worse in Women^{11,12}



Burden of Disease



Pain/swelling¹⁶



Itching¹⁷



Difficulty with every day activities¹⁸

Window of Opportunity for Diagnosis¹³

Early diagnosis

- ↓ Disability
- ↓ Radiographic damage
- ↑ Probability of drug-free remission
- ↓ Sacroiliitis
- ↓ Functional disability

Late diagnosis

- ↑ Disability
- ↑ Radiographic damage
- ↓ Probability of drug-free remission
- ↑ Sacroiliitis
- ↑ Functional disability



~15–30% of patients with PSO have undiagnosed PsA^{14,15}

Depression, anxiety and mental health^{11,19}



Quality of life reduced^{18,19}



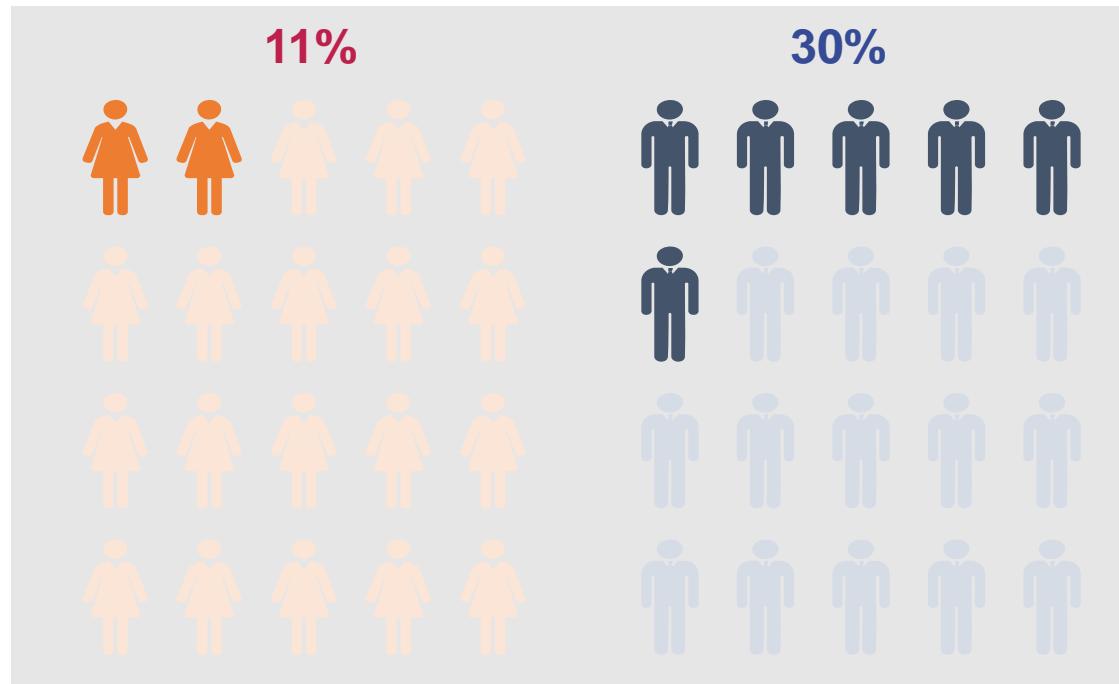
1. Garg N et al. Best Pract Res Clin Rheumatol. 2014;28(5):663–672.
2. Collantes E et al. Rheumatology. 2007;46(8):1309–1315.
3. Fraga NA et al. An Bras Dermatol. 2012;87(6):877–883.
4. Chen H and Chou C. Curr Rheumatol Rev. 2008;4:111–114.
5. Williamson L et al. J Rheumatol. 2004;31:1469–1470.
6. Kane D et al. Rheumatology (Oxford) 2003; 42(12): 1460–1468.

7. Peluso et al. Clin Rheumatol. 2015;34:745–753.
 8. Mease PJ and Armstrong AW. Drugs. 2014;74(4):423–441.
 9. Gladman DD et al. Ann Rheum Dis. 2005;64 Suppl 2:i14–17.
 10. Jovani V et al. PLoS One. 2018;13(10):e0205751.
 11. Nas K et al. Ann Rheum Dis 2019; 78(Suppl 2):920–921. Abstract FRI0456.
 12. Eder L et al. Ann Rheum Dis. 2013;72(4):578–582.
13. Haroon M et al. Ann Rheum Dis. 2015;74(6):1045–1050.

14. Villani et al. J Am Acad Dermatol. 2015;73:242–248.
15. Haroon M et al. Ann Rheum Dis. 2013;72(5):736–740.
16. Lebwohl MG et al. J Am Acad Dermatol. 2014;70(5):871–881.
17. Kavanagh A et al. Rheumatol Ther. 2016;3:91–102.
18. Picchianti-Diamanti A et al. Qual Life Res. 2010;19:821–826.
19. Salaffi F et al. Health Qual Life Outcomes. 2009;7:25.

Female Patients have a Higher Probability of Misdiagnosis

First Correct Diagnosis of SpA



Common Misdiagnoses Before SpA Diagnosis

Misdiagnosis	Women	Men
Herniated disc, n (%)	5 (10.9)	11 (19.0)
Scoliosis, n (%)	2 (4.4)	5 (8.6)
Sciatica, n (%)	9 (19.6)	4 (6.9)
Osteoarthritis, n (%)	6 (13.0)	3 (5.2)
Fibromyalgia, n (%)	3 (6.5)	1 (1.7)

Only 11% of women received a first correct diagnosis of spondyloarthritis vs 30% of men

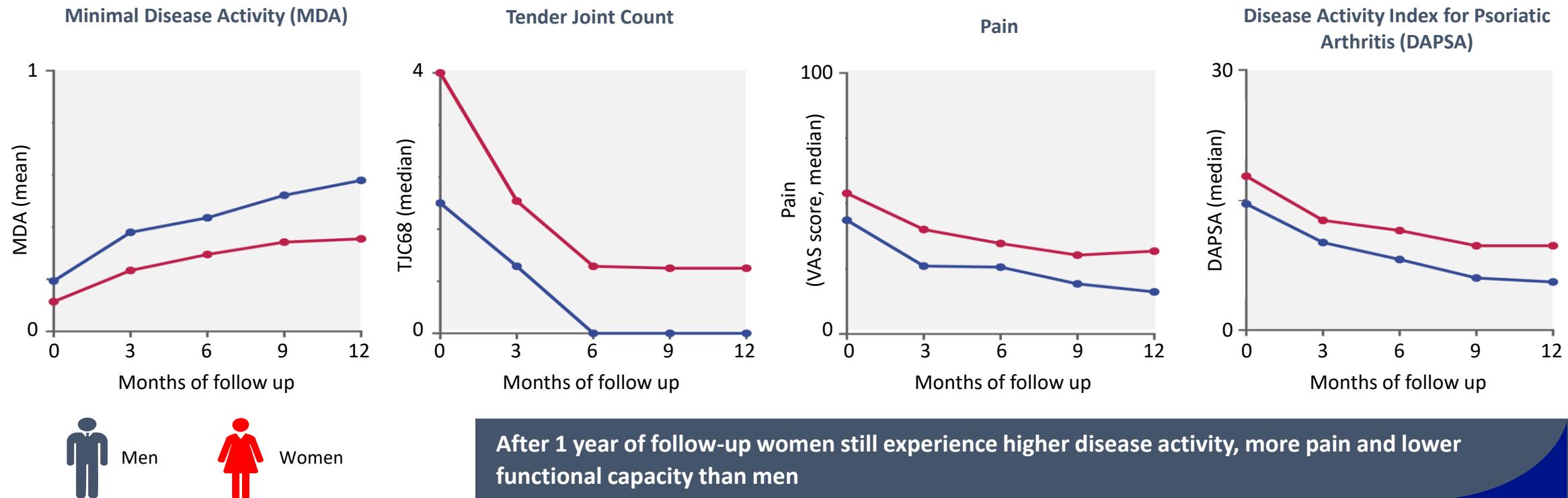
Before Definitive Diagnosis of SpA, Male Patients are Referred to Specialists More Often than Female Patients

Health Services	Attending Prior Diagnosis in Rheumatology Clinic			Referring to Rheumatology Clinic		
	Women (N=54)	Men (N=96)	P value	Women (n=54)	Men (n=96)	P value
Primary care	44 (81.5)	86 (89.6)	0.16	14 (25.9)	30 (31.3)	0.49
Orthopaedic surgery	34 (63.0)	49 (51.0)	0.16	11 (20.4)	23 (24.0)	0.62
Rehabilitation services	9 (16.7)	16 (16.7)	1	0	2 (2.0)	NA
Emergency department	21 (38.9)	15 (15.6)	0.001	9 (16.7)	6 (6.3)	0.04
Workers' compensation insurance	2 (3.7)	14 (14.6)	0.05	0	4 (4.2)	NA
Neurology	2 (3.7)	4 (4.2)	1.0	1 (1.9)	2 (2.1)	1.0
Physiotherapy	2 (3.7)	3 (3.1)	1.0	0	0	NA
Pain unit	2 (3.7)	2 (2.1)	0.62	0	0	NA
Urology	1 (1.9)	2 (2.1)	1.0	1 (1.9)	1 (1.0)	1.0
Gastroenterology	0	3 (3.1)	NA	0	2 (2.1)	NA
Ophthalmology	6 (11.1)	1 (1.0)	0.009	5 (9.3)	1 (1.0)	0.02
Rheumatology	3 (5.6)	1 (1.0)	0.13	0	0	NA
Neurosurgery	1 (1.9)	1 (1.0)	1.0	0	0	NA
General internal medicine	0	1 (1.0)	NA	0	1 (1.0)	NA
Psychology	0	1 (1.0)	NA	0	0	NA
Cardiology	0	1 (1.0)	NA	0	2 (2.1)	NA
Vascular surgery	1 (1.9)	0	NA	0	0	NA
Gynaecology	1 (1.9)	0	NA	0	0	NA
Intensive care unit	1 (1.9)	0	NA	0	0	NA
Non health services	0	0	NA	11 (20.4)	14 (14.6)	0.36
Don't know	0	0	NA	2 (3.7)	8 (8.3)	0.33

Gender Specific Differences in Early PsA

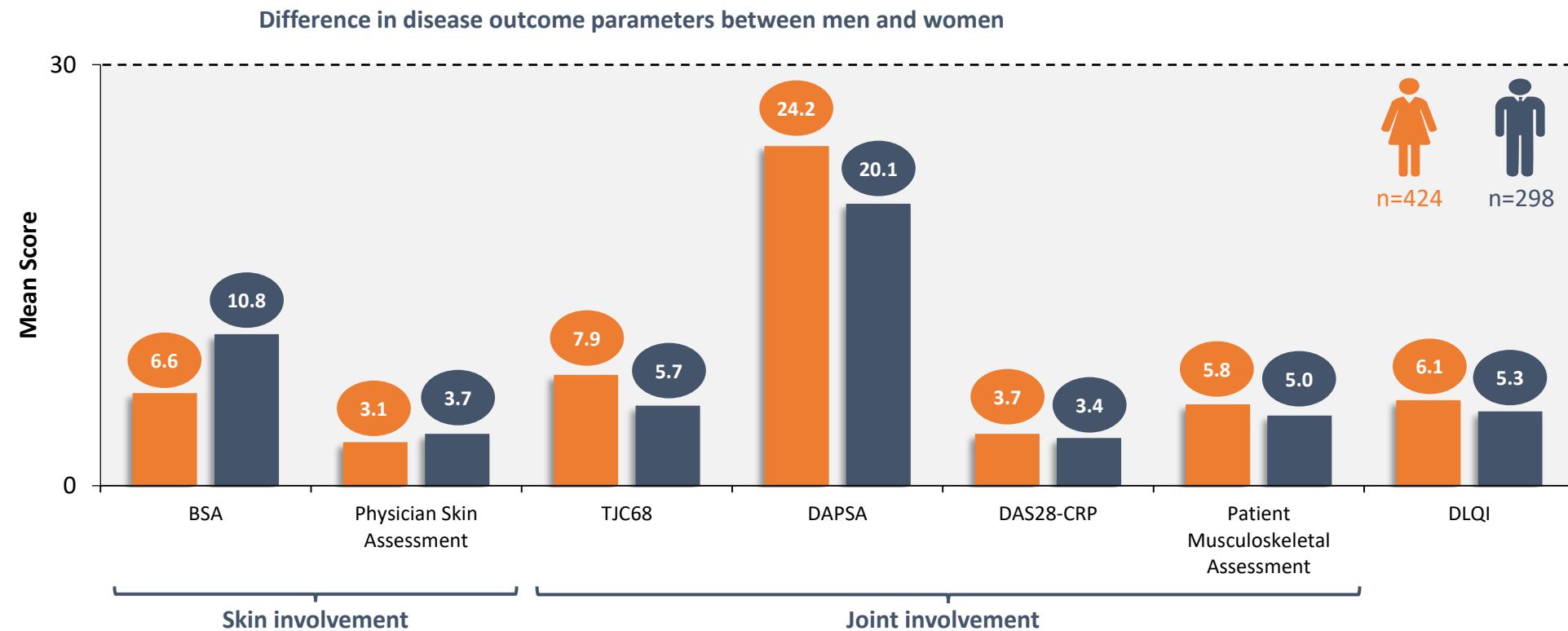
Patients with newly diagnosed PsA were included in the Dutch south-west Early Psoriatic Arthritis prospective cohort study (273 men and 294 women)

Women reported significantly longer duration of symptoms before diagnosis and significantly fewer of them were in paid employment at baseline



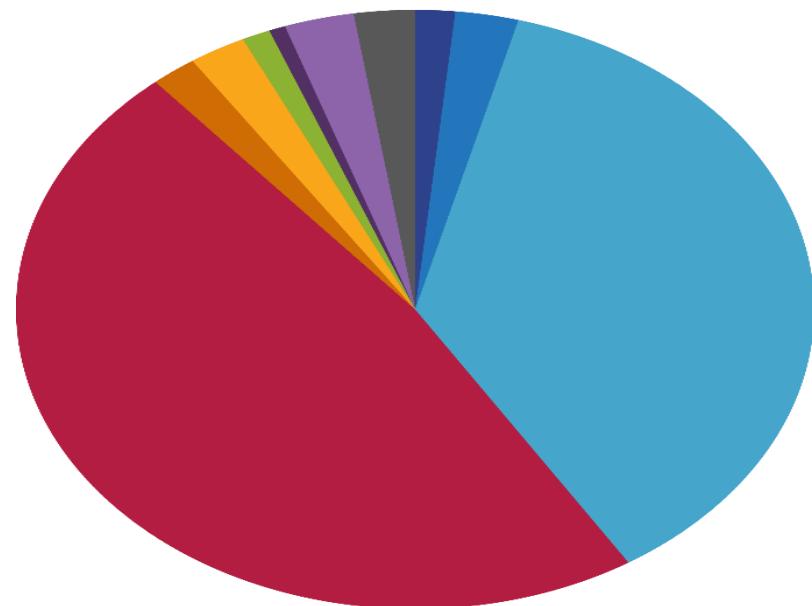
Men Have More Severe Skin Involvement, While Women Have Higher Burden of Joint Involvement*

RABBIT-SpA is a prospective longitudinal cohort study including PsA patients enrolled at start of a new csDMARD, bDMARD or tsDMARD (N=722)

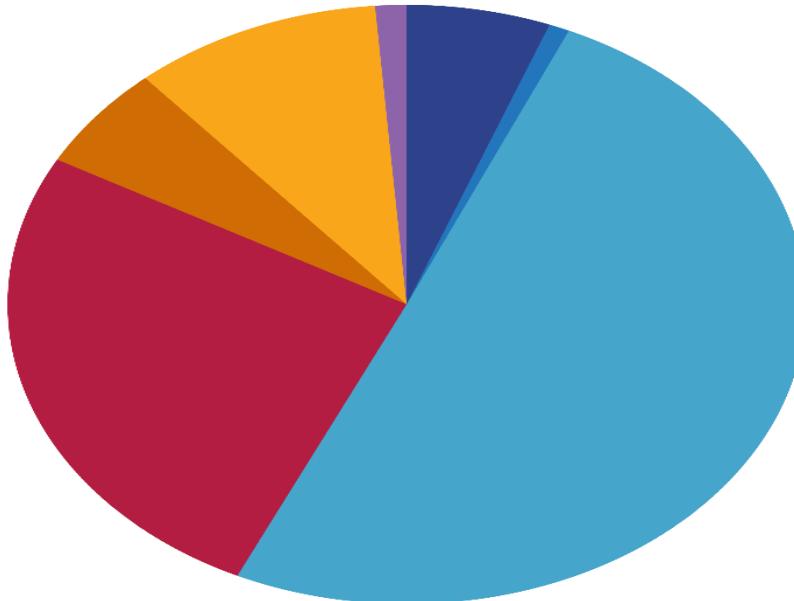


Polyarticular Joint Pattern Most Commonly Seen in Women at Presentation of PsA

Women (n=114)

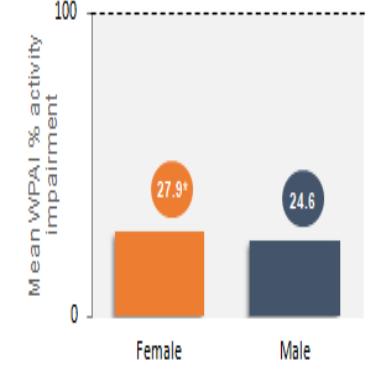
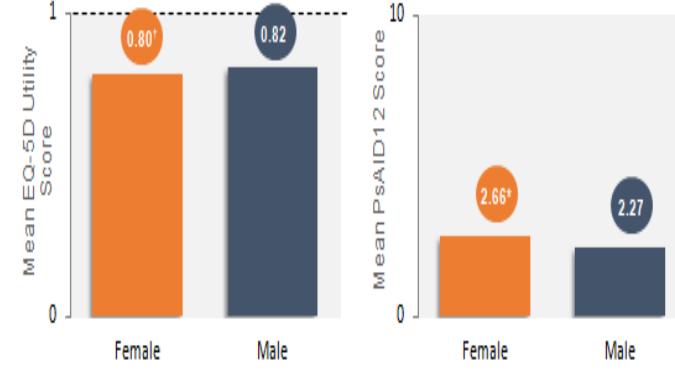
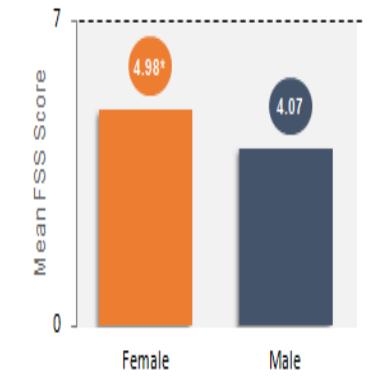
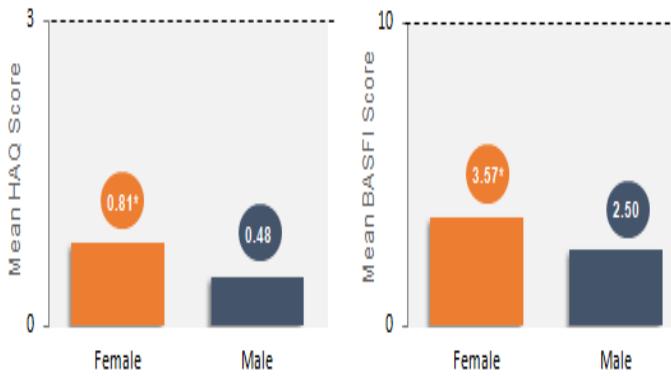


Men (n=83)



- Remission
- DIP only
- Mono/oligo only
- Poly only
- Axial only
- Axial+Peripheral
- Sapho
- Oligo+DIP
- Poly+DIP
- Abnormal ESR/CRP only

Women Experience More Limitations in Daily Function Worse Quality of Life and Greater Work Impairment



Women with PsA have significantly worse scores in PROs than males, independent of age and other disease-related variables¹

Women with PsA have significantly worse scores in QoL than males and a greater work impairment

1. Eder L et al. Int J Clin Rheumatol. 2012;7(6):641–649.

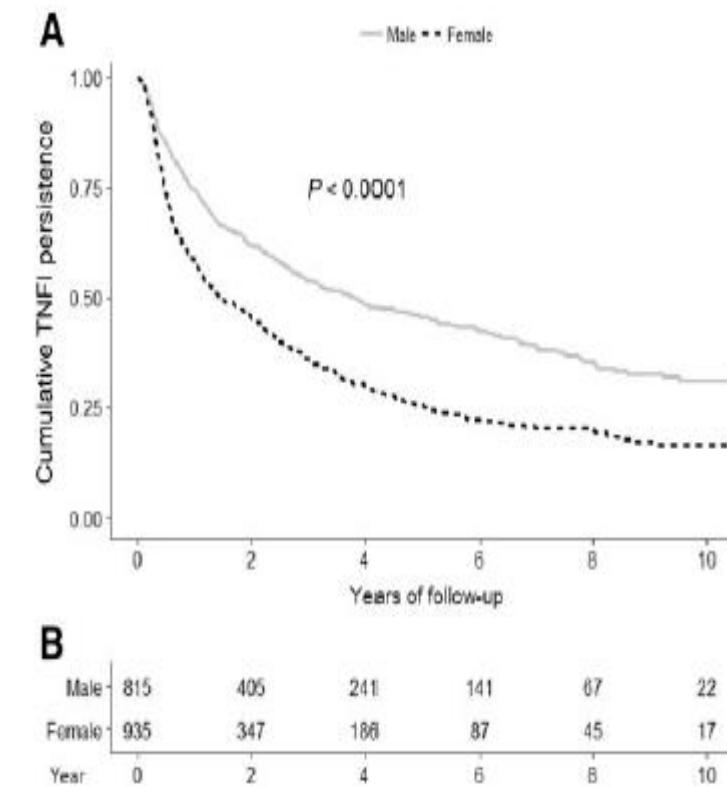
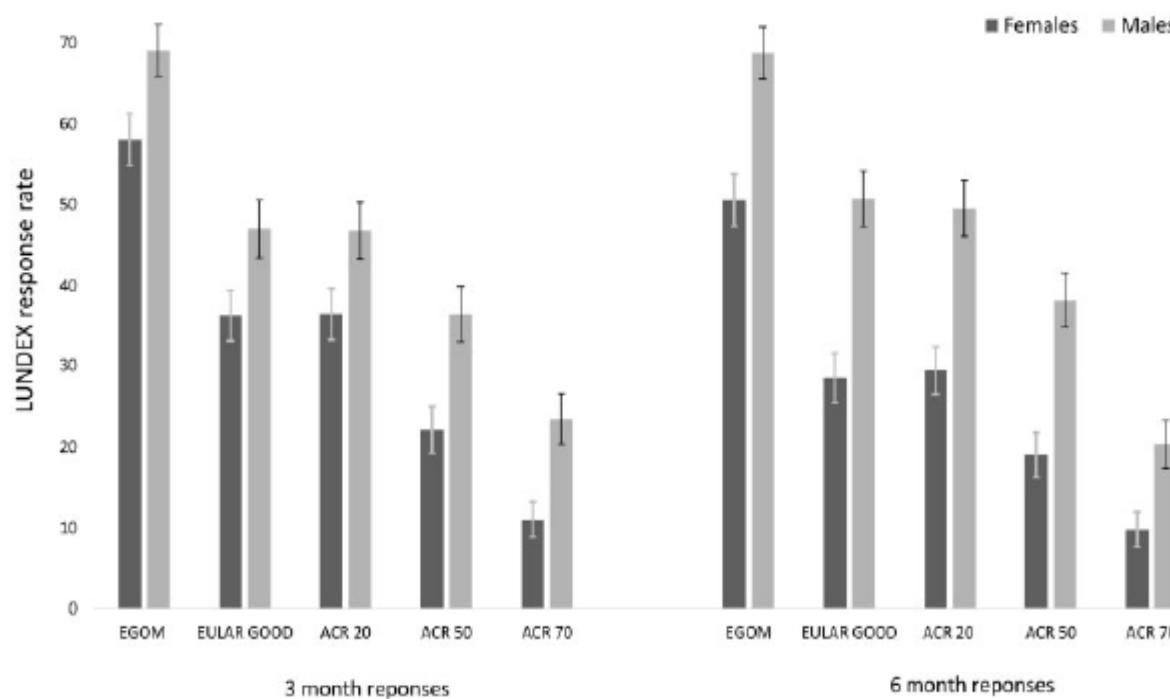
2. Eder L et al. Ann Rheum Dis. 2013;72(4):578–582.

Gender differences in biologic treatment outcomes—a study of 1750 patients with psoriatic arthritis using Danish Health Care Registers

Pil Højgaard^{1,2}, Christine Ballegaard^{1,2}, René Cordtz^{1,2}, Kristian Zobbe^{1,2}, Marianne Clausen¹, Bente Glintborg^{1,3}, Lars Erik Kristensen² and Lene Dreyer^{1,2,4}

2018 Sep 1;57(9):1651-1660.

1750 PsA patients (935 women) biologic naïve – first anti-TNF



Impact of Gender on Treatment Effectiveness in PsA

Response rates after 6 months of biologic therapy in patients with axial PsA and peripheral PsA

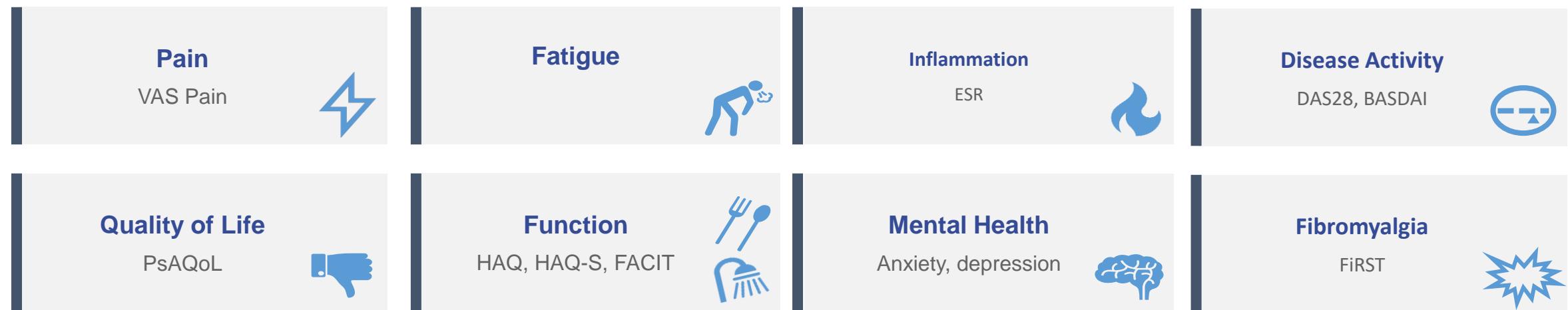
Axial PsA (n=55)				Peripheral PsA (n=54)			
	Males (n=35)	Females (n=20)	P value		Males (n=20)	Females (n=34)	P value
LDA							
ASDAS <2.1	25 (74%)	7 (37%)	0.02	DAPSA ≤14	14 (74%)	12 (39%)	0.02
BASDAI <4	24 (72%)	5 (26%)	0.02	DAS28 ≤3.2	13 (68%)	6 (31%)	0.09
Clinical improvement							
Change in ASDAS ≥1.1	20 (59%)	7 (37%)	0.15	DAPSA50	10 (53%)	11 (36%)	0.25
BASDAI50	16 (48%)	3 (16%)	0.04	Change in DAS28 ≥1.2	11 (57%)	8 (42%)	0.15

Male gender is associated with a higher rate of response to biologic treatment in axial PsA and peripheral PsA

Effect of Gender on Disease Activity, Functional Index and Quality of Life in Patients with Axial PsA

- TLAR-Network PsA Study:
- 251 women and 169 men with PsA and axial involvement

Outcomes were Significantly Worse in Female PsA Patients with Axial Involvement



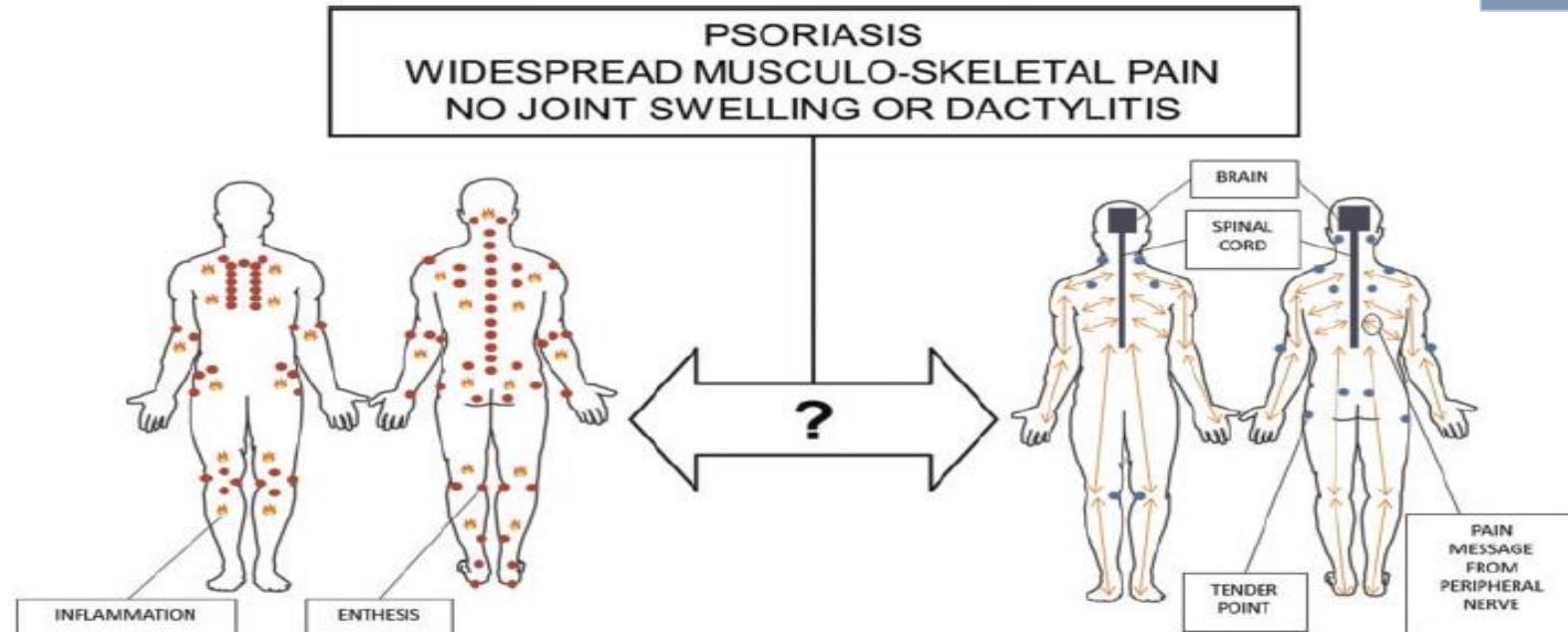
Female patients with PsA who have axial involvement have higher disease activity, physical disability, functional limitation and higher depression and anxiety risk than male patients

The problem in differentiation between psoriatic-related polyenthesitis and fibromyalgia

Antonio Marchesoni¹, Gabriele De Marco^{2,3}, Mira Merashli⁴, Frank McKenna⁵, Ilaria Tinazzi⁶, Helena Marzo-Ortega^{2,3} and Dennis G. McGonagle^{2,3}

Ραχιαλγία στην ΨΑ: Ενθεσίτιδα ή Ινομυαλγία;

5-8% PsA patients suffer from FMS



MULTI-ENTHESITIC PsA

- Stiffness after prolonged immobility
- Anterior chest wall pain
- Heel swelling
- Favourable response to:
 - NSAIDs
 - Biologics
 - DMARDs?

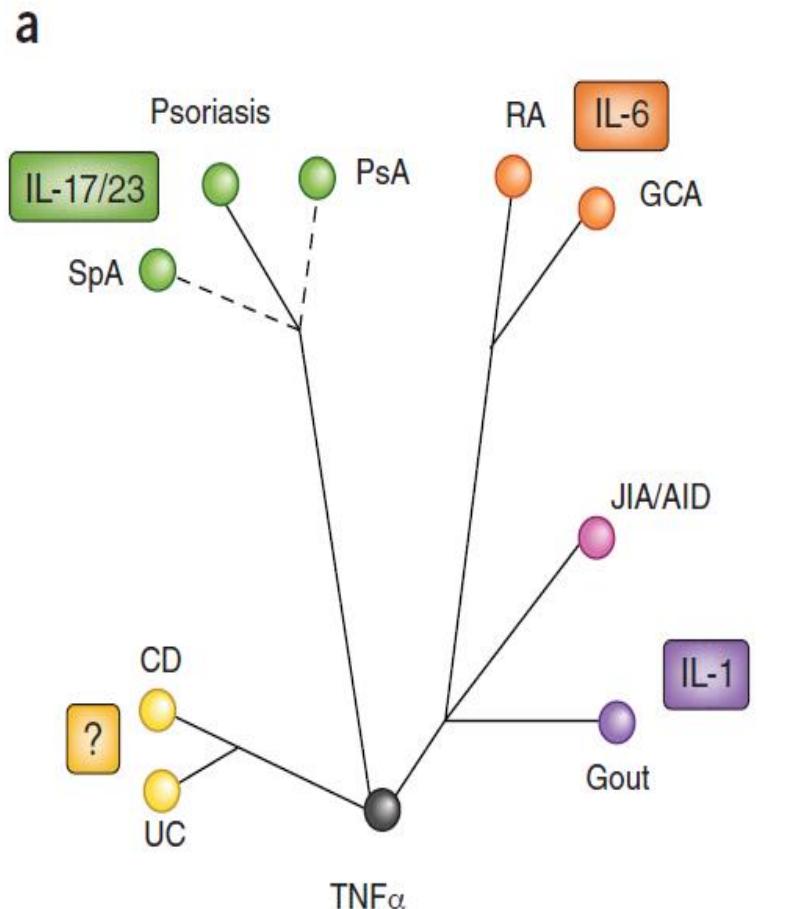
FMS

- Somatoform symptoms:
 - Sleep disturbances
 - Cognitive impairment
 - Anxiety
 - Migraine
 - Raynaud's phenomenon
 - Irritable bowel
- Indifference to emotional stimulations

Σημεία σχετιζόμενα με ενθεσοπάθεια στην ΨΑ και σύνδρομα ινομυαλγίας. Οι δυο οντότητες μπορεί να αλληλεπικαλύπτονται και οι δείκτες φλεγμονής να είναι φυσιολογικοί. Ακόμη και η απεικόνιση μπορεί να μην είναι διαγνωστική.

Toward a cytokine-based disease taxonomy

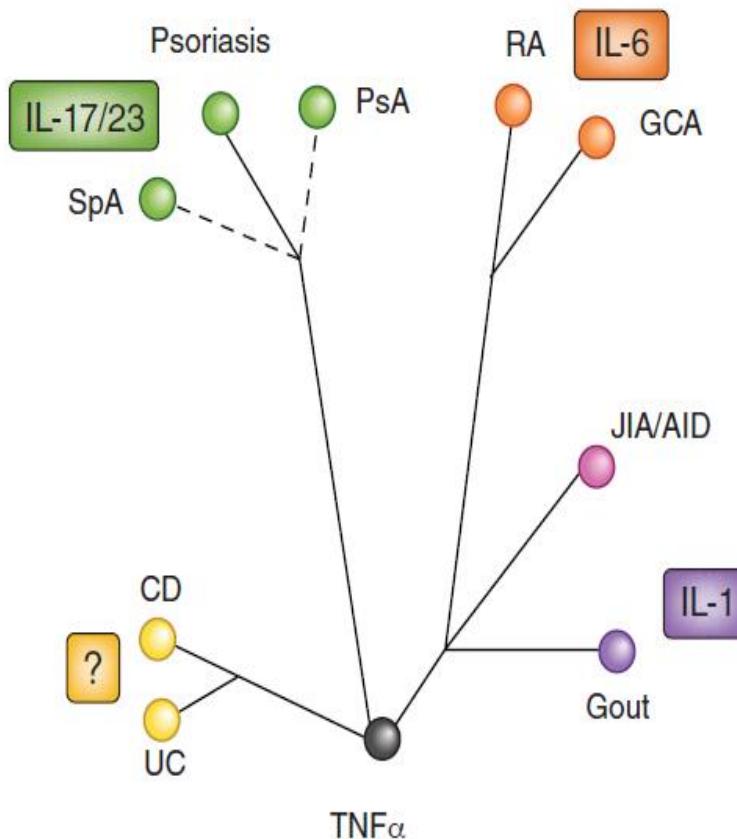
Georg Schett, Dirk Elewaut, Iain B McInnes, Jean-Michel Dayer & Markus F Neurath



Toward a cytokine-based disease taxonomy

Georg Schett, Dirk Elewaut, Iain B McInnes, Jean-Michel Dayer & Markus F Neurath

a



TNF α inhibitors

- Adalimumab
- Certolizumab
- Etanercept
- Infliximab
- Golimumab

IL-12/IL-23 inhibitors

- Ustekinumab

IL-17A inhibitors

- Ixekizumab
- Secukinumab

TNF α

IL-23

IL-17A



Activated
dendritic cells



Th17 cells
T cells



Target
cell

PDE4 inhibitors

- Apremilast

JAK inhibitors

SPECIAL ARTICLE

Group for Research and Assessment of Psoriasis and Psoriatic Arthritis 2015 Treatment Recommendations for Psoriatic Arthritis

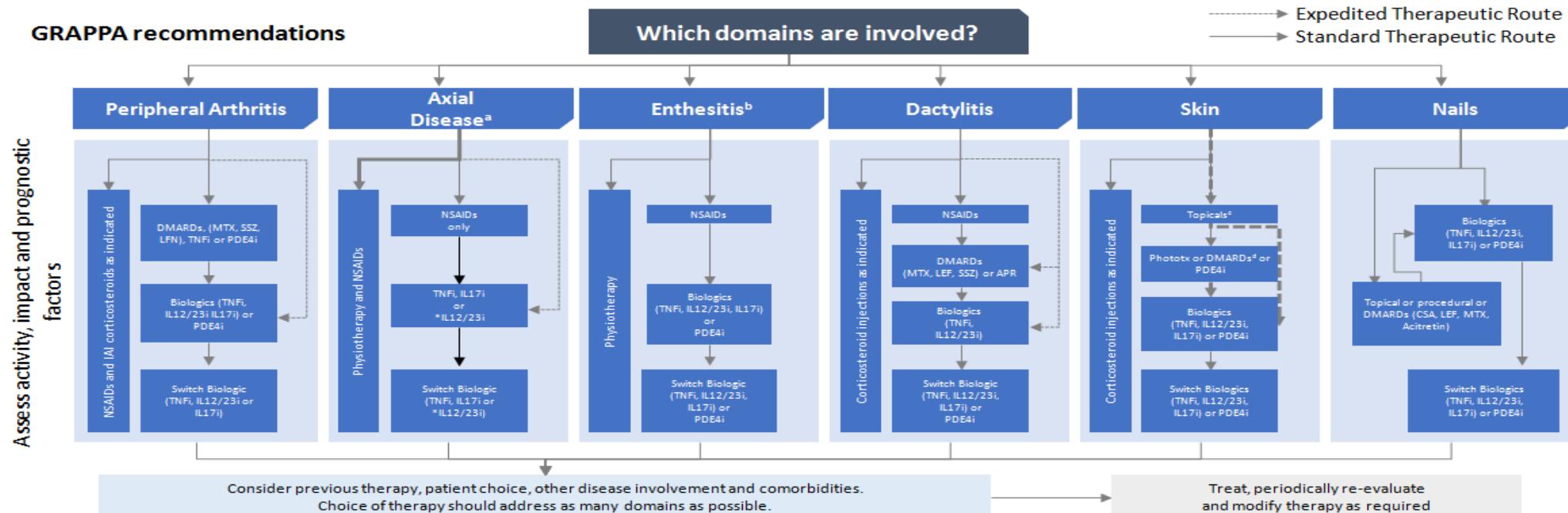
Laura C. Coates,¹ Arthur Kavanaugh,² Philip J. Mease,³ Enrique R. Soriano,⁴ Maria Laura Acosta-Felquer,⁴ April W. Armstrong,⁵ Wilson Bautista-Molano,⁶ Wolf-Henning Boehncke,⁷ Willemina Campbell,⁸ Alberto Cauli,⁹ Luis R. Espinoza,¹⁰ Oliver FitzGerald,¹¹ Dafna D. Gladman,¹² Alice Gottlieb,¹³ Philip S. Hellier,¹⁴ M. Elaine Husni,¹⁵ Thorvardur J. Love,¹⁶ Ennio Lubrano,¹⁷ Neil McHugh,¹⁸ Peter Nash,¹⁹ Alexis Ogdie,²⁰ Ana-Maria Orbai,²¹ Andrew Parkinson,²² Denis O'Sullivan,²³ Cheryl F. Rosen,²⁴ Sergio Schwartzman,²⁵ Evan L. Siegel,²⁶ Sergio Toloza,²⁷ William Tuong,²⁸ and Christopher T. Ritchlin²⁹

Recommendation



EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update

Laure Gossec ^{1,2}, Xenofon Baraliakos,³ Andreas Kerschbaumer ^{10,4}, Maarten de Wit ^{10,5}, Iain McInnes,⁶ Maxime Dougados,⁷ Jette Primdahl ^{10,8,9}, Dennis G McGonagle,^{10,11} Daniel Aletaha,¹² Andra Balanescu,¹³ Peter V Balint,¹⁴ Heidi Bertheussen,¹⁵ Wolf-Henning Boehncke,¹⁶ Gerd R Burmester,¹⁷ Juan D Canete ¹⁸, Nemanja S Damjanov,¹⁹ Tue Wenzel Kragstrup,^{20,21} Tore K Kvien,²² Robert B M Landewé,^{23,24} Rik Jozef Urbain Lories,^{25,26} Helena Marzo-Ortega,^{10,11} Denis Poddubnyy ^{27,28}, Santiago Andres Rodrigues Manica ^{29,30}, Georg Schett ^{10,31}, Douglas J Veale ^{10,32}, Filip E Van den Bosch,³³ Désirée van der Heijde ^{10,22,34}, Josef S Smolen^{35,36}

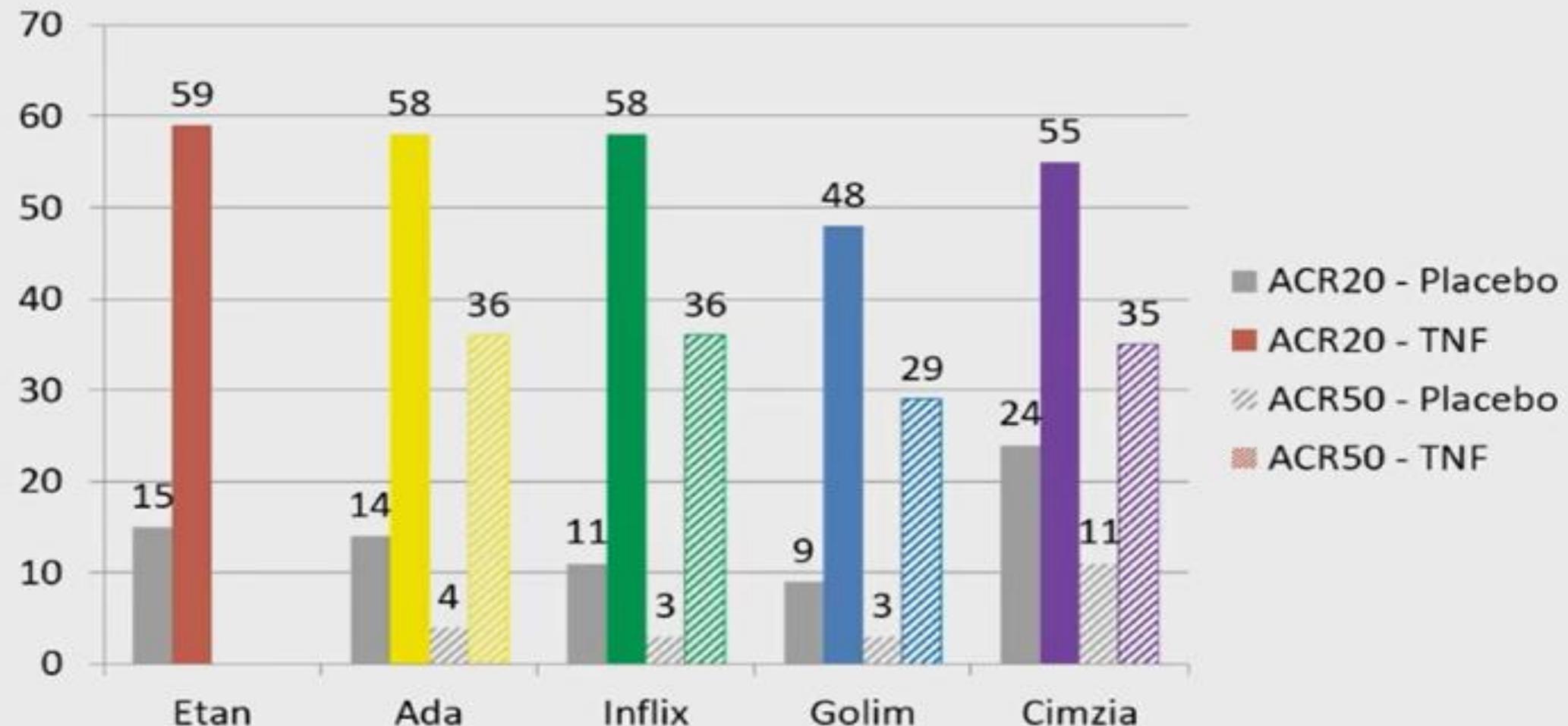


CSA, cyclosporine A; DMARD, disease-modifying anti-rheumatic drug; IAI, intra-articular injection; IL12/23i, interleukin 12/23 inhibitor; IL17i, interleukin 17 inhibitor; LFN, leflunomide; MTX, methotrexate; NSAID, non-steroidal anti-inflammatory drug; PDE4i, phosphodiesterase 4 inhibitor; phototox, phototherapy; SSZ, sulfasalazine; TNFi, tumor necrosis factor inhibitor.

*No direct evidence for therapies in axial PsA, recommendations based on axial SpA literature; ^bCorticosteroid injections: consider on an individual basis due to potential for serious side effects; no clear evidence for efficacy; ^cKeratolytics, steroids, vitamin D analogues, emollients calcineurin; ^dMTX, CSA, Acitretin, Fumaric acid esters

Coates LC, et al. *Arthritis Rheumatol.* 2016;68:1060–71.

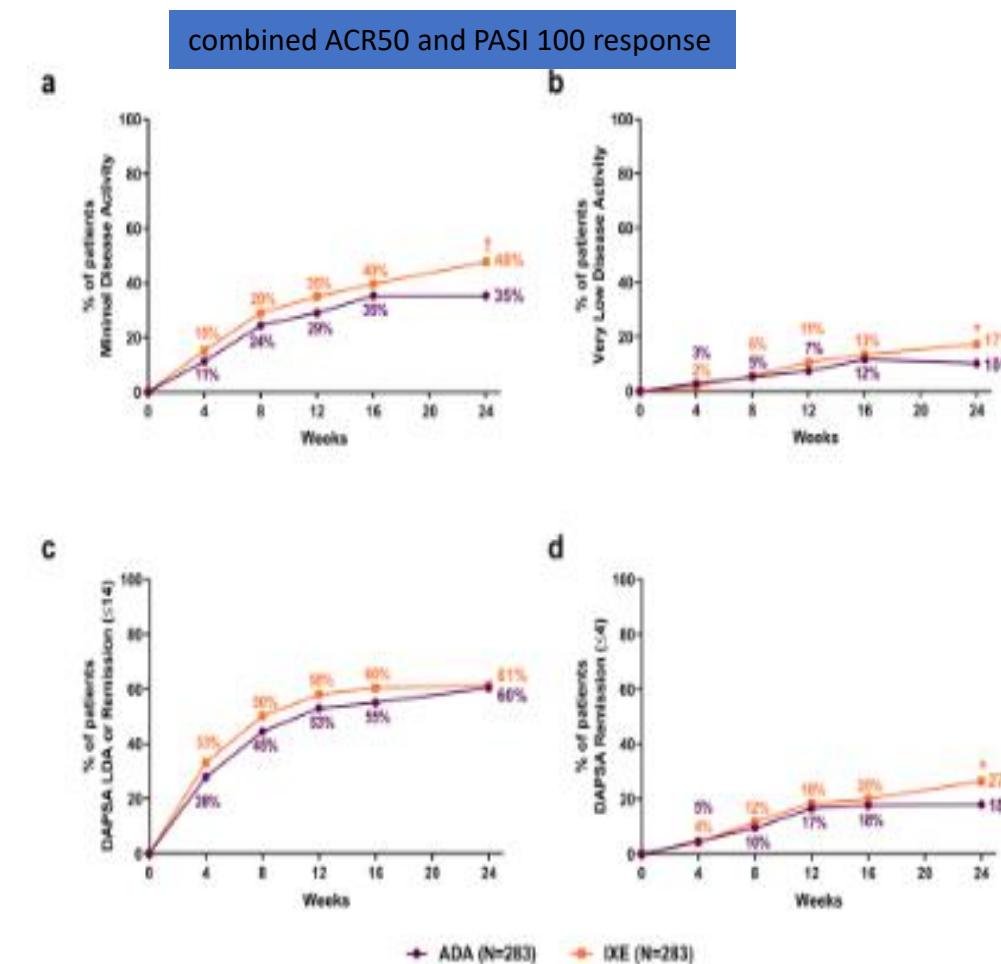
ΑΝΑΣΤΟΛΕΙΣ ΤΟΥ TNF- α



Mease et al, A&R 2004; 50(7):2264, Antoni et al, ARD 2005; 64(8):1150, Mease A&R 2005; 52(10):3279, Kavanaugh et al, A&R 2009; 60(4):976

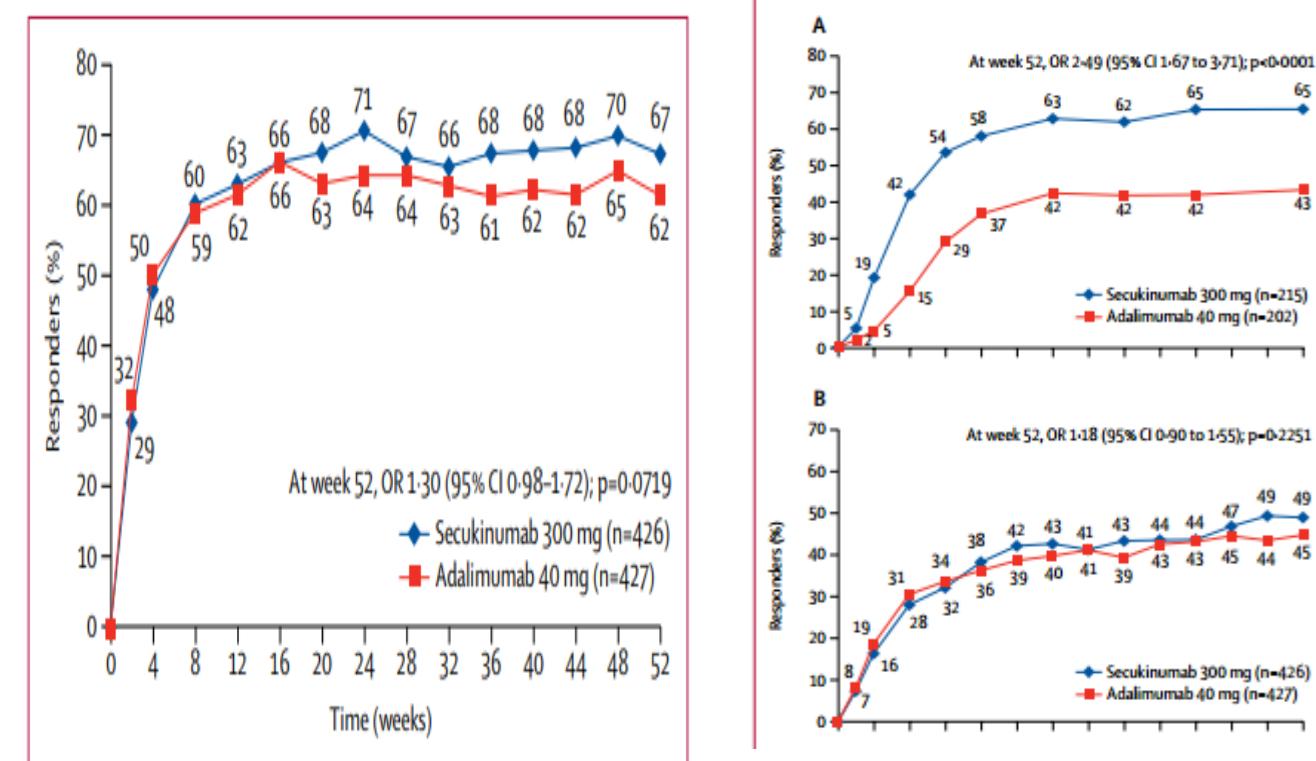
A head-to-head comparison of the efficacy and safety of ixekizumab and adalimumab in biological-naïve patients with active psoriatic arthritis: 24-week results of a randomised, open-label, blinded-assessor trial

Philip J Mease ^{1,10}, Josef S Smolen, ² Frank Behrens, ³ Peter Nash, ⁴ Soyi Liu Leage, ⁵ Lingnan Li, ⁵ Hasan Tahir, ⁶ Melinda Gooderham, ⁷ Eswar Krishnan, ⁵ Hong Liu-Seifert, ⁵ Paul Emery ¹⁰, ^{8,9} Sreekumar G Pillai, ⁵ Philip S Helliwell, ¹⁰ The SPIRIT H2H study group

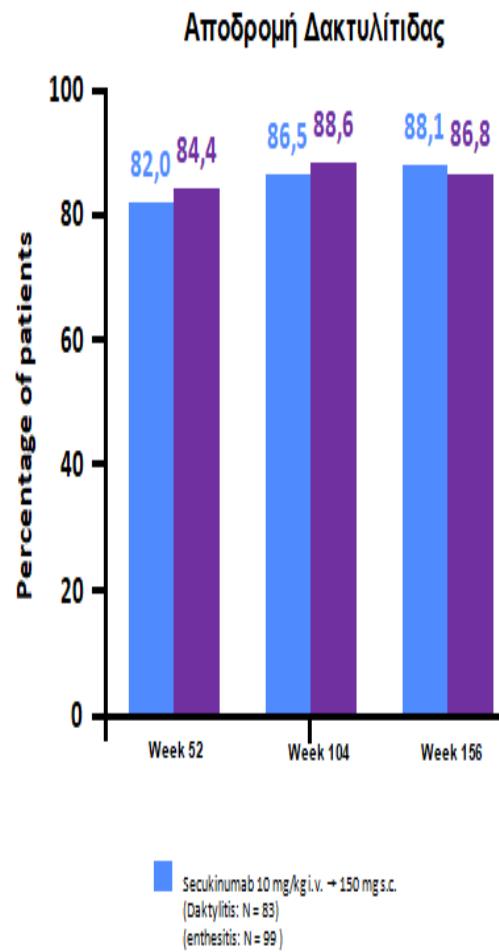


Secukinumab versus adalimumab for treatment of active psoriatic arthritis (EXCEED): a double-blind, parallel-group, randomised, active-controlled, phase 3b trial

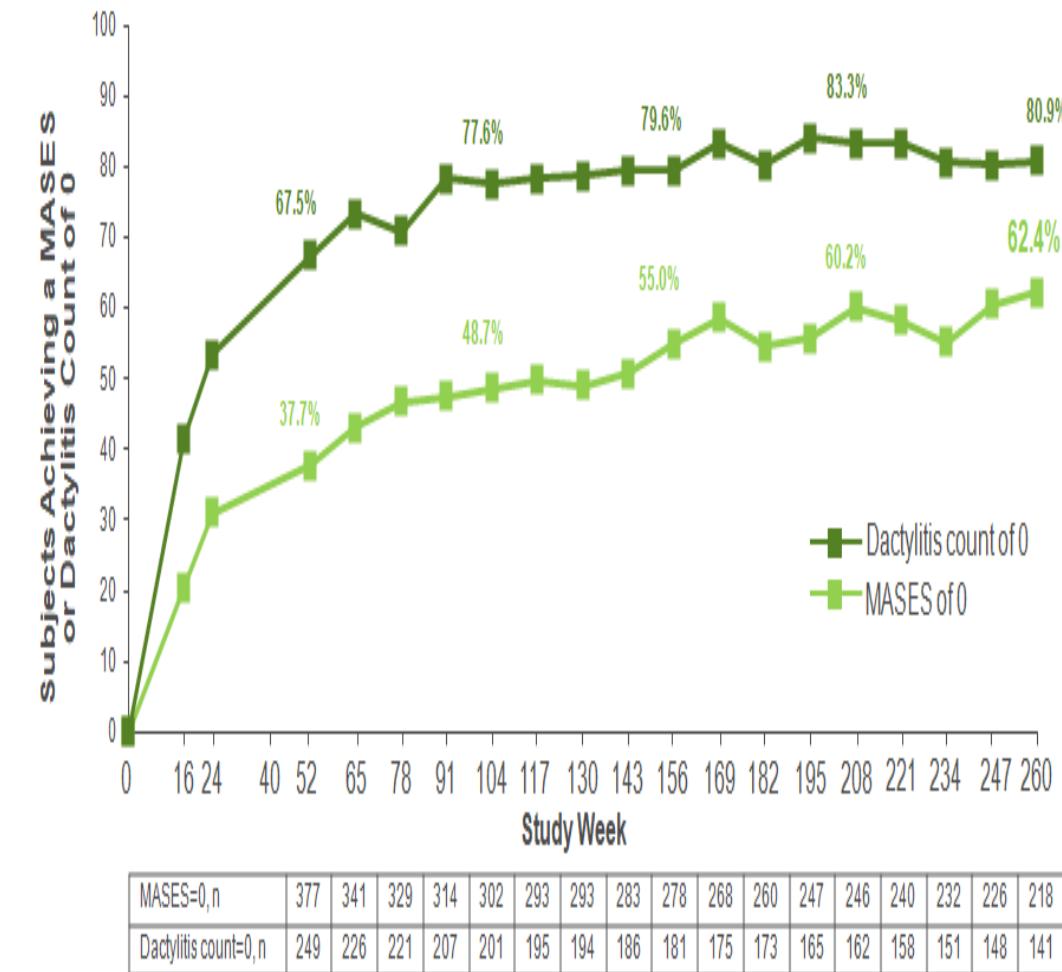
Iain B McInnes, Frank Behrens, Philip J Mease, Arthur Kavanaugh, Christopher Ritchlin, Peter Nash, Jordi Gratacós Masmitja, Philippe Gouille, Tatiana Korotaeva, Alice B Gottlieb, Ruvie Martin, Kevin Ding, Pascale Pellet, Shephard Mpofu, Luminita Pricop, on behalf of EXCEED Study Group



FUTURE -1 - SECUKINUMAB



PALACE 1-3 – APREMILAST



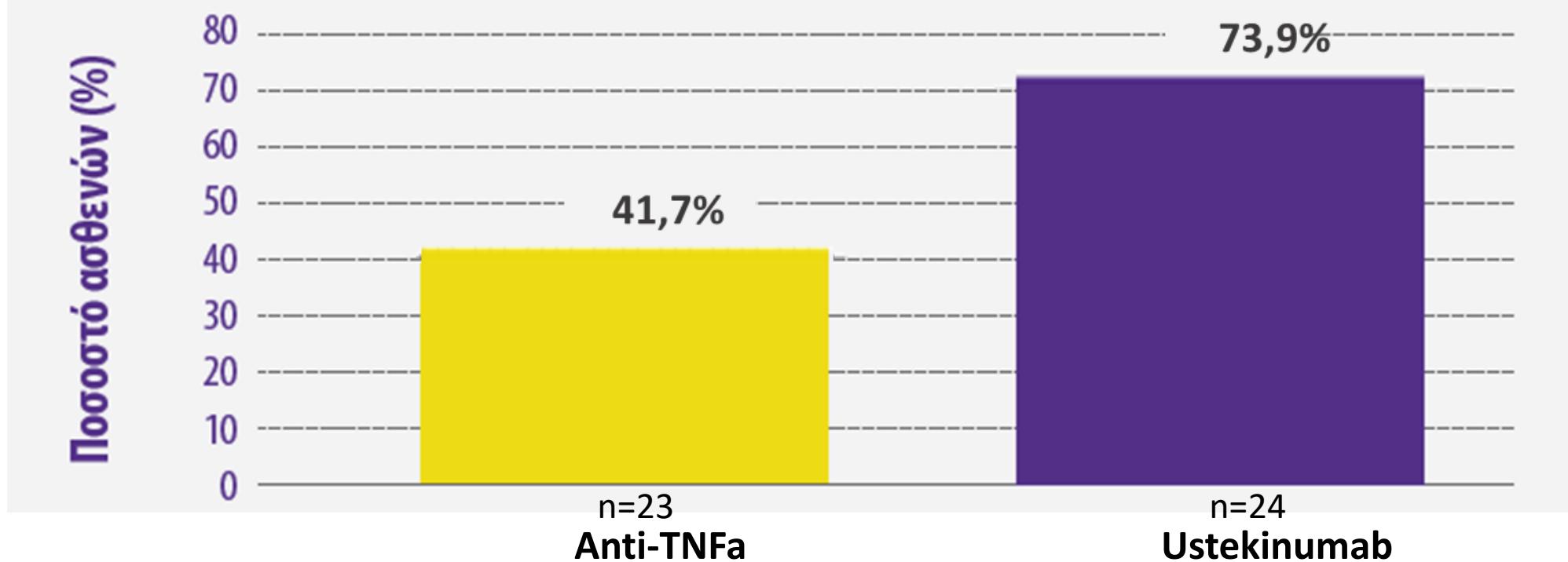


Semin Arthritis Rheum. 2019 Feb;48(4):632-637. doi: 10.1016/j.semarthrit.2018.05.011. Epub 2018 Jun 13.

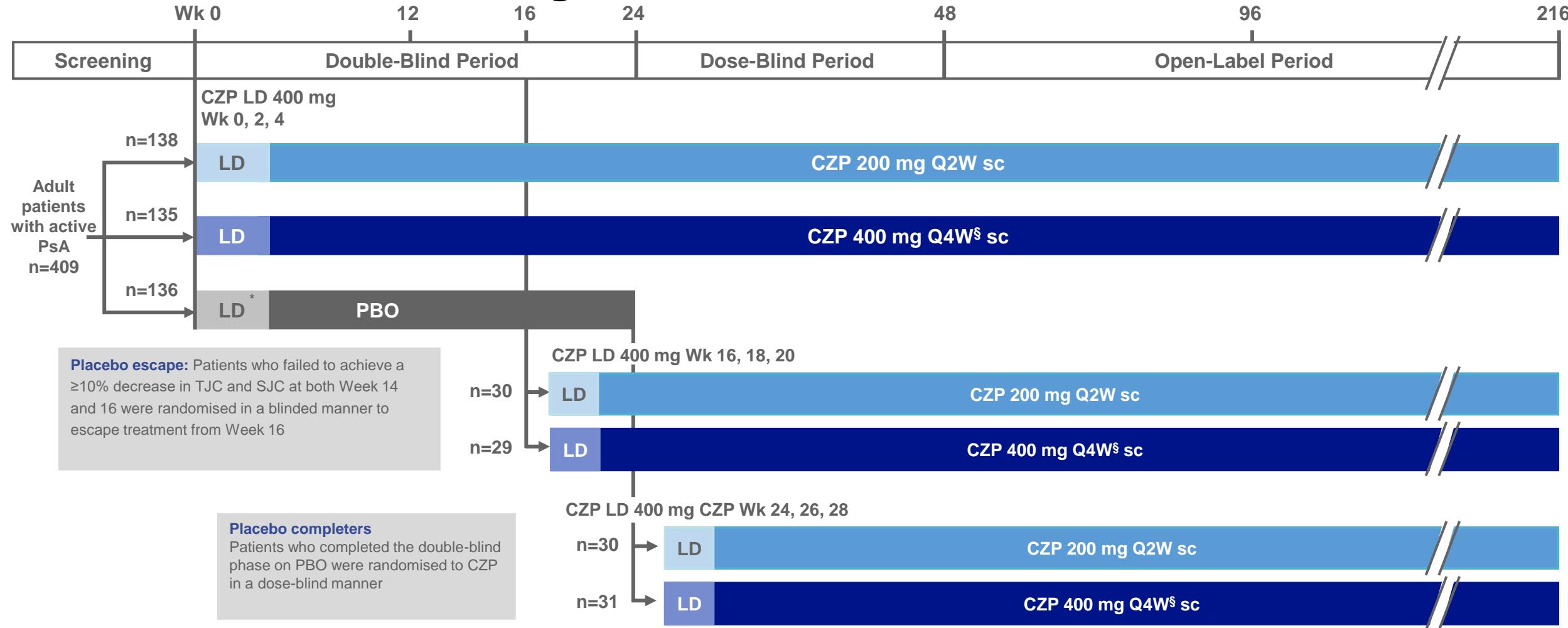
Effects of ustekinumab versus tumor necrosis factor inhibition on enthesitis: Results from the enthesial clearance in psoriatic arthritis (ECLIPSA) study.

Araujo EG¹, Englbrecht M¹, Hoepken S¹, Finzel S¹, Kampylafka E¹, Kleyer A¹, Bayat S¹, Schoenau V¹, Hueber A¹, Rech J¹, Schett G².

Ποσοστό ασθενών με κάθαρση ενθεσίτιδας (SPARCC)=0 στους 6 μήνες



RAPID-PsA Trial Design to Week 216

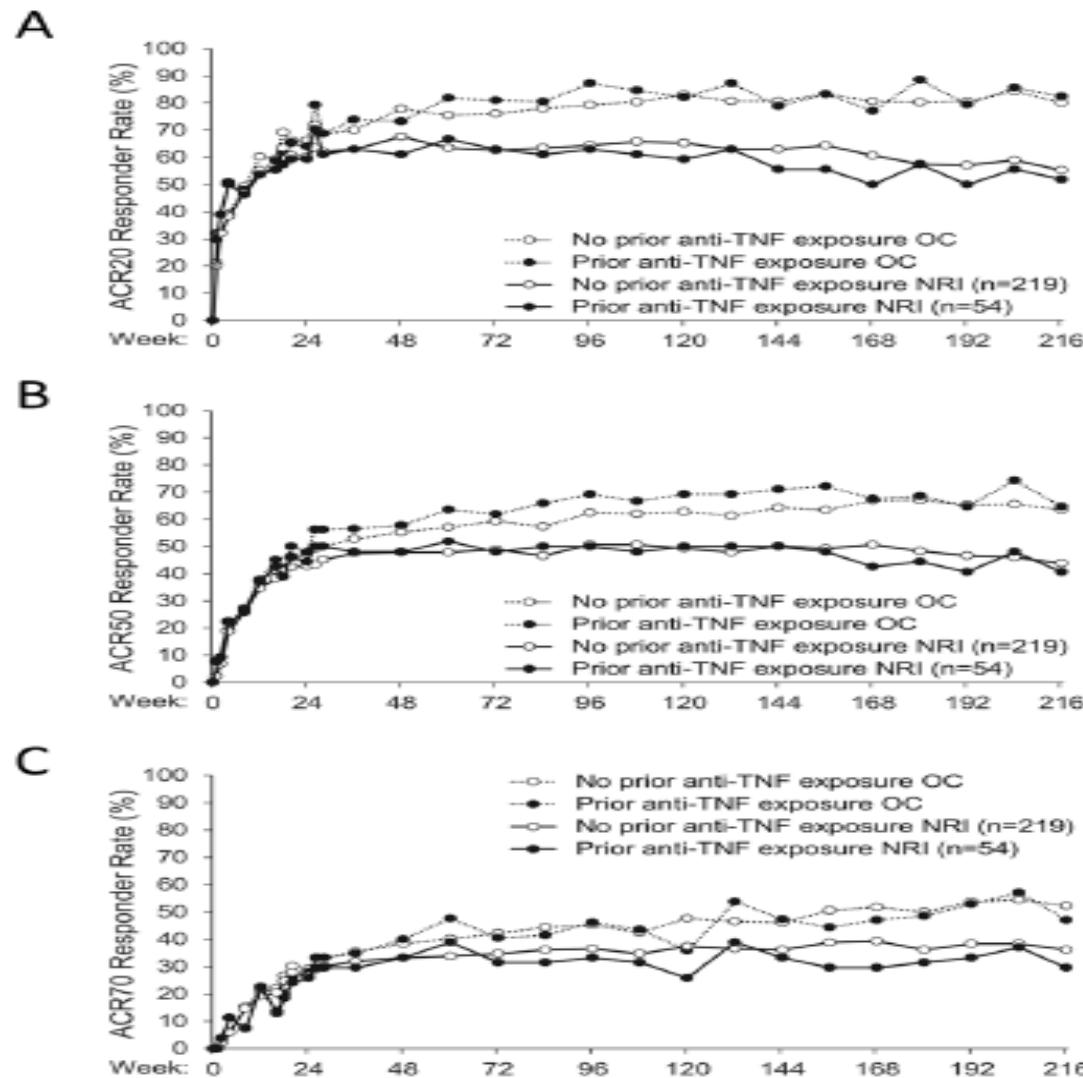
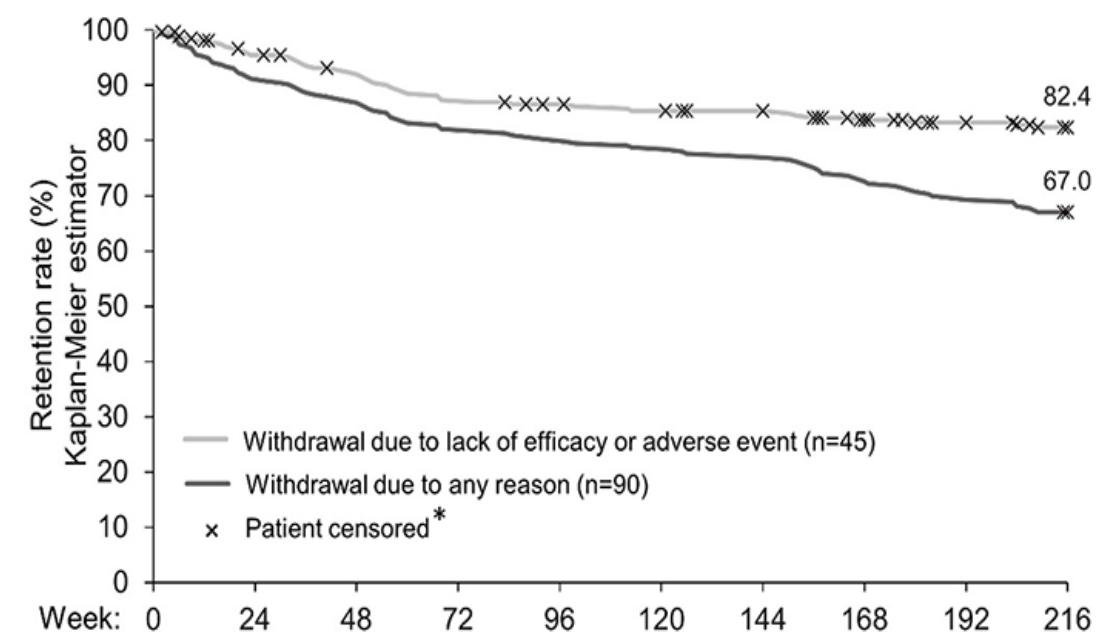


Adapted from Mease PJ et al. RMD Open. 2015;1(1):e000119.

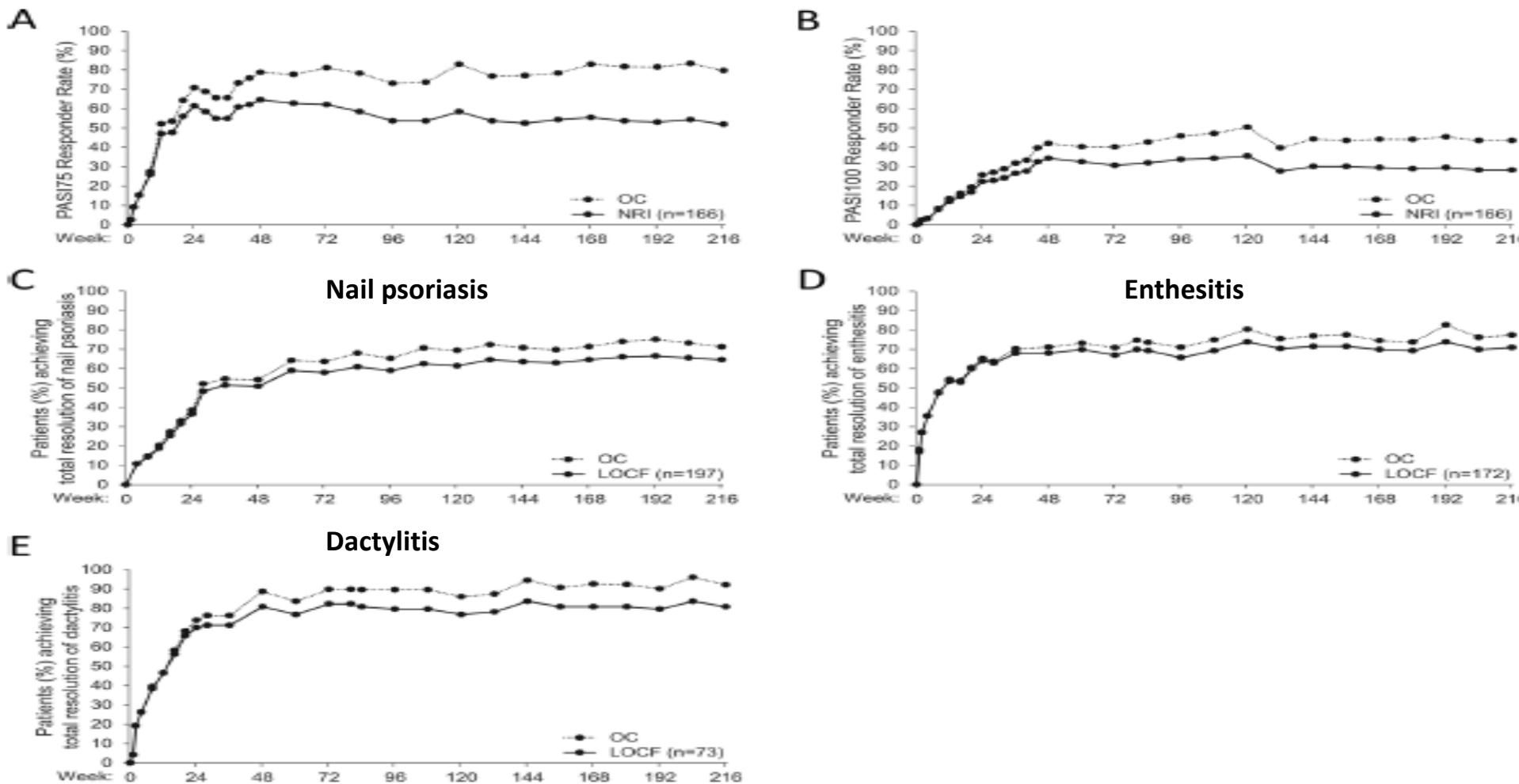
[§]For maintenance in PsA, CZP 400 mg Q4W before clinical response is confirmed is not an approved dose in the European Union.

*Loading dose of PBO.

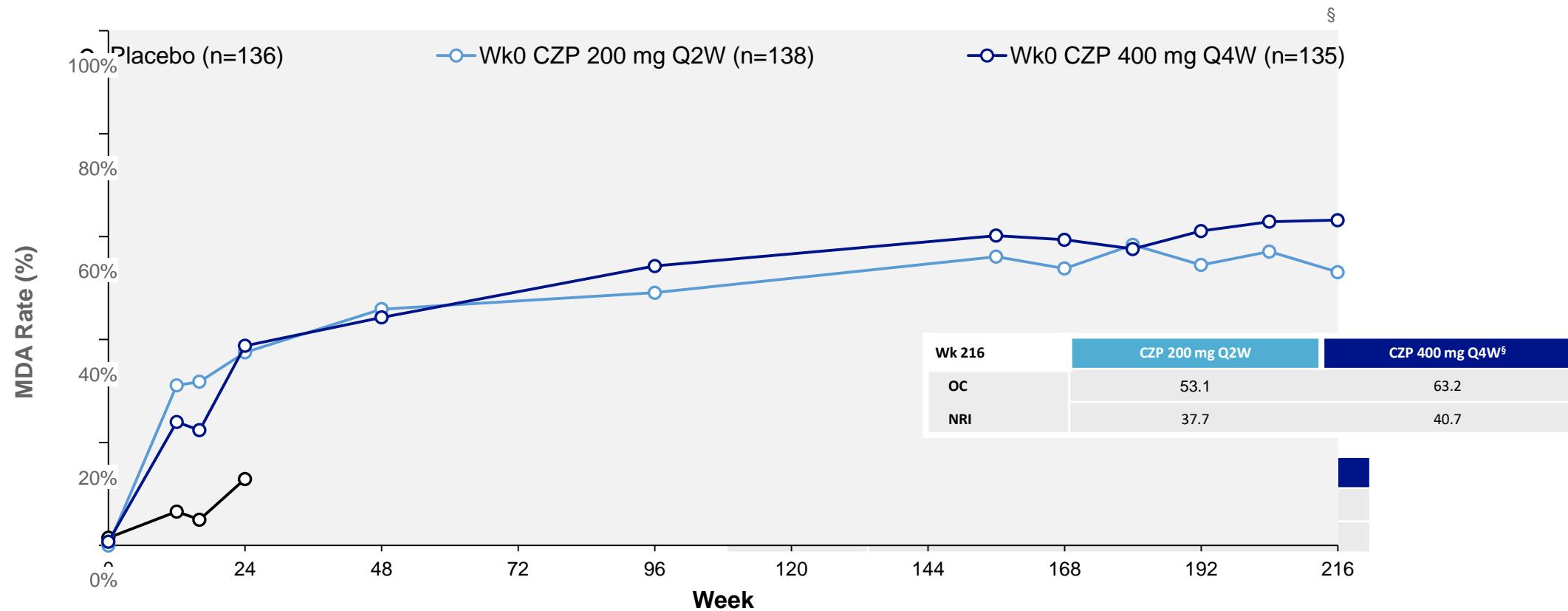
4-year results from the RAPID-PsA phase 3 randomised placebo-controlled trial of certolizumab pegol in psoriatic arthritis



4-year results from the RAPID-PsA phase 3 randomised placebo-controlled trial of certolizumab pegol in psoriatic arthritis



MDA Rate Over 216 Weeks (Observed Case)



Sustained improvement in disease activity from Week 24 to Week 216

Wk 24, 48 and 216 values from van der Heijde D et al. RMD Open. 2018; 4:e000582.

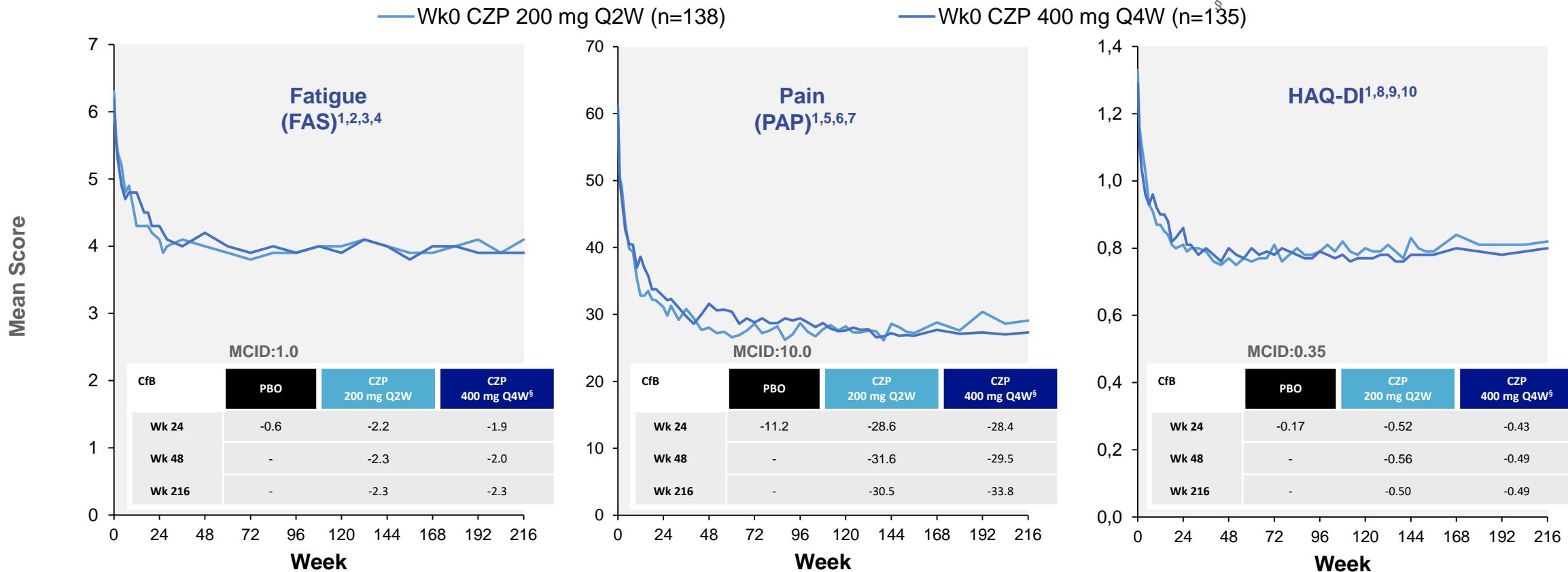
Exact data values from UCB Data on File (PsA001 Wk216 Final Tables 2016, Table 4.58.1, 4.58.2) – Data are available on request.

Placebo data from UCB Data on File (PsA001 Wk24 Post-hoc Tables, Table 4.75.2) – Data are available on request.

[§]For maintenance in PsA, CZP 400 mg Q4W before clinical response is confirmed is not an approved dose in the European Union.

Randomised set (observed case). Placebo arm taken from Week 24 dataset, for comparison.

Fatigue, Pain and HAQ-DI Over 216 Weeks (LOCF)



Pain improved by more than 50% by Week 216

1. Wk 0, 24, 48 and 216 data from van der Heijde D et al. RMD Open. 2018; 4:e000582.
2. UCB Data on File (PsA001 Wk216 Final Tables. 2016. Table 4.32.1).
3. Placebo data from UCB Data on File (PsA001 Wk24 Final Tables. 2012. Table 4.34).
4. MCID value from UCB Data on File (Protocol Study PsA001 Amendment 5. 2013. p59).
5. UCB Data on File (PsA001 Wk24 Final Tables. 2016 Table 4.25.1).
6. Placebo data from UCB Data on File (PsA001 Wk24 Final Tables. 2012. Table 4.27.1).

7. MCID value from UCB Data on File (Protocol Study PsA001 Amendment 5. 2013. p58).
8. UCB Data on File (PsA001 Wk216 Final Tables. 2016. Table 4.6.1).
9. Placebo data from UCB Data on File (PsA001 Wk24 Final Tables. 2012. Table 4.22.1).
10. MCID value Mease PJ et al. J Rheumatol. 2011;38:2461–246.

[§]For maintenance in PsA, CZP 400 mg Q4W before clinical response is confirmed is not an approved dose in the European Union.

Randomised set (LOCF). Placebo arm taken from Week 24 dataset, for comparison.

RAPID-PsA

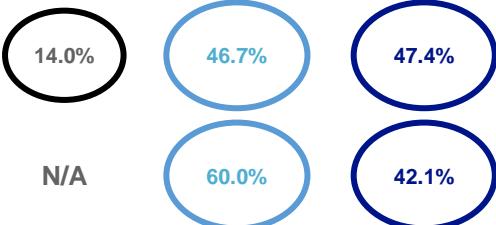
The first published randomised controlled trial of an anti-TNF in **PsA** to include patients with prior anti-TNF exposure¹



PASI75*

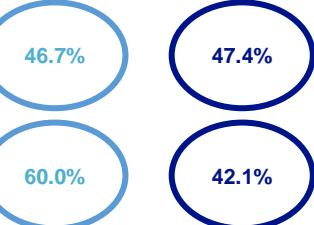
Significant and sustained responses in PASI75 to Week 216

Week 12¹



Week 216²

N/A



Enthesitis^{‡2}

Sustained resolution to Week 216

Week 216



Dactylitis^{‡2}

Sustained resolution to Week 216

Week 216



1. Mease PJ et al. Ann Rheum Dis. 2014;73(1):48–55.

2. van der Heijde D et al. RMD Open. 2018; 4:e000582.

3. Gottlieb AB et al. J Am Acad Dermatol. 2018;79(2):302–314.

4. Lebwohl M et al. J Am Acad Dermatol. 2018;79(2):266–276.

Significant responses in PASI75 were also reported in PSO studies, CIMPASI 1/2 and CIMPACT^{3,4}

ACR responses demonstrated regardless of prior anti-TNF use² or +/- concomitant DMARD use⁵



Fatigue^{2,6}

Sustained improvements in fatigue through to Week 216



Pain^{2,7}

Pain improved by more than 50% by Week 216



↓ FAS Improvement

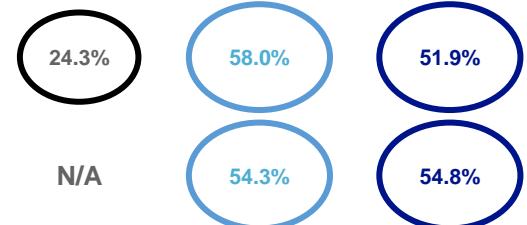
↓ PAP Improvement



ACR20**

Sustained responses in ACR20 to Week 216

Week 12¹



Week 216²

N/A



Nail Disease^{‡2}

Sustained resolution to Week 216

Week 216



Safety Profile

No new safety signals identified with increased exposure to CZP and safety outcomes were in line with those published previously²

PBO

CZP 200 mg Q2W

CZP 400 mg Q4W[§]

5. Walsh JA et al. Clin Rheumatol. 2018;37(12):3285–3296.

6. UCB Data on File (PsA001 Wk216 Final Tables. 2016. Table 4.32.1).

7. UCB Data on File (PsA001 Wk216 Final Tables. 2016 Table 4.25.1).

§For maintenance in PsA, CZP 400 mg Q4W before clinical response is confirmed is not an approved dose in the European Union.

*In patients with psoriasis involving ≥3% BSA at baseline (n=86, n=90, n=76); †In patients with enthesitis at baseline (n=88, n=84); ‡In patients with dactylitis at baseline (n=35, n=38); [‡]In patients with nail psoriasis at baseline (n=92, n=105); **ACR20 (n=136, n=138, n=135).

OP0053 SECUKINUMAB IMPROVES CLINICAL AND IMAGING OUTCOMES IN PATIENTS WITH PSORIATIC ARTHRITIS AND AXIAL MANIFESTATIONS WITH INADEQUATE RESPONSE TO NSAIDS: WEEK 52 RESULTS FROM THE MAXIMISE TRIAL FREE

X. Baraliakos¹, L. Gossec², E. Pournara³, S. Jeka⁴, R. Blanco⁵, S. D'angelo⁶, G. Schett⁷, B. Schulz³, M. Rissler³, K. Nagar⁸, C. Perella³, L. C. Coates⁹

Phase 3b, double-blind, placebo (PBO)-controlled, multicentre 52-wk trial included 498 pts (aged ≥ 18 years) with a diagnosis of PsA and classified by CASPAR criteria, **spinal pain VAS score $\geq 40/100$ and BASDAI score ≥ 4** despite use of at least two NSAIDs



Figure 1.

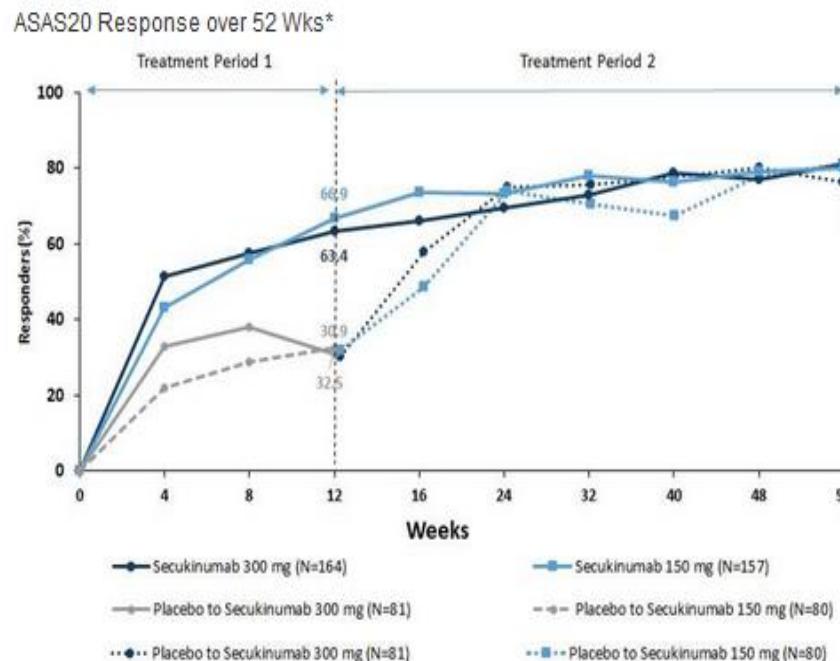
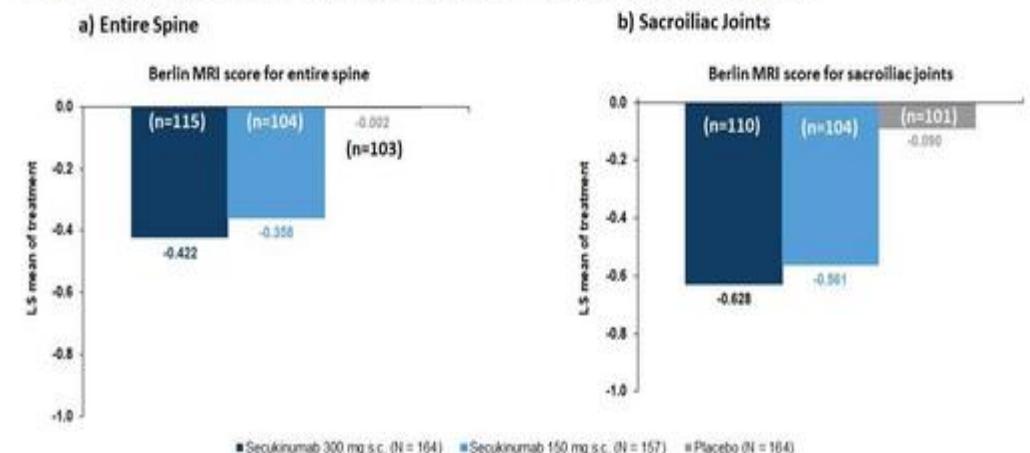


Figure 2.

Total Berlin MRI score for the Entire Spine and Sacroiliac Joints at Wk 12



LS Mean difference

Secukinumab 300 mg vs placebo: -0.4 [0.14], $p=0.0031$
Secukinumab 150 mg vs placebo: -0.4 [0.15], $p=0.0145$

*MRI, Magnetic resonance imaging

LS Mean difference

Secukinumab 300 mg vs placebo: -0.5 [0.18], $p=0.0032$
Secukinumab 150 mg vs placebo: -0.5 [0.18], $p=0.0107$

EXTENDED REPORT

Efficacy of tumour necrosis factor blockers in reducing uveitis flares in patients with spondylarthropathy: a retrospective study

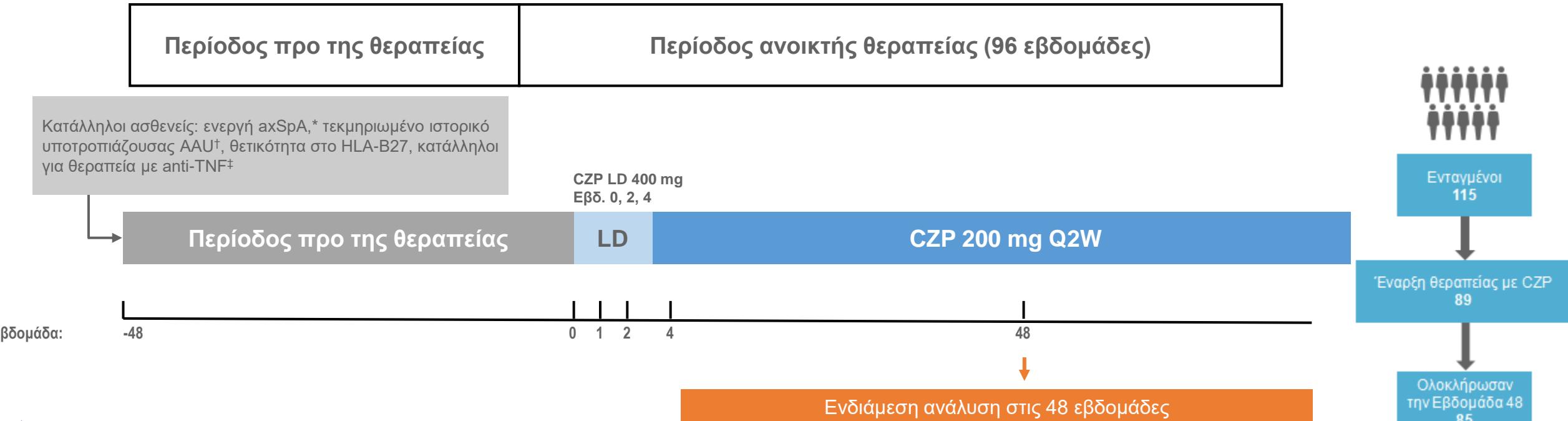
S Guignard, L Gossec, C Salliot, A Ruyssen-Witrand, M Luc, M Duclos, M Dougados



Ann Rheum Dis 2006;65:1631–1634. doi: 10.1136/ard.2006.052092

Anti-TNF (n= patients)	Period before anti-TNF treatment			Period during anti-TNF treatment			p Value*
	Duration of period (years)	Number of uveitis flares/patient Mean (SD)	Number of uveitis flares/100 patient-years Mean (SD)	Treatment period (years)	Number of uveitis flares/patient Mean (SD)	Number of uveitis flares/100 patient-years Mean (SD)	
	Mean (SD)	(SD)	(SD)	Mean (SD)	(SD)	(SD)	
All anti-TNF n=46	15.2 (10.2)	6.3 (9.7)	51.8 (65.0)	1.2 (1.1)	0.2 (1.0)	21.4 (74.9)	0.03
Soluble TNF receptor (etanercept) n=13	11.5 (10.4)	3.6 (4.1)	54.6 (78.2)	1.2 (1.1)	0.5 (0.8)	58.5 (121.9)	0.92
Anti-TNF antibodies (adalimumab and infliximab) n=33	16.7 (9.8)	7.3 (11.1)	50.6 (61.0)	1.2 (1.1)	0.1 (1.0)	6.8 (39.3)	0.001
Infliximab n=25	16.8 (10.4)	7.3 (12.1)	47.4 (58.9)	1.4 (1.3)	0.2 (1.2)	9.0 (45.2)	0.008
Adalimumab n=8	16.2 (8.7)	7.2 (7.8)	60.5 (70.4)	0.6 (0.2)	0	0	0.04

C-VIEW Σχεδιασμός της μελέτης^{1,2} open-label, phase 4 study.



- ✓ Η πρώτη μελέτη που συμπεριέλαβε ασθενείς με nr-axSpA και r-axSpA/AS, οι οποίοι ήταν θετικοί στο HLA-B27, για την εκτίμηση της επίδρασης του CZP στη μείωση των εξάρσεων AU σε ασθενείς με axSpA και ιστορικό AU

Πρωτεύον καταληκτικό σημείο:
Αριθμός διακριτών επεισοδίων έξαρσης της AAU κατά την περίοδο θεραπείας (έως την Εβδομάδα 96), σε σύγκριση με τα ιστορικά ποσοστά

To CZP δεν έχει εγκριθεί για τη θεραπεία της ραγοειδίτιδας στην Ευρωπαϊκή Ένωση

* Η axSpA ορίζεται με βάση τα κριτήρια ASAS και η ενεργή νόσος στην προκαταρκτική αξιολόγηση ορίζεται με βάση βαθμολογία BASDAI ≥ 4 και βαθμολογία άλγους της σπονδυλικής στήλης ≥ 4 σε μία NRS 0-10 (από το στοιχείο 2 του BASDAI). Οι ασθενείς με nr-axSpA πρέπει να έχουν CRP>ULN και/ή τρέχουσες ενδείξεις ιερολαγονίτιδας στην MRI σύμφωνα με τα κριτήρια ASAS. Οι ασθενείς με AS πρέπει να έχουν ενδείξεις ιερολαγονίτιδας στην ακτινογραφία του πληρούν τα κριτήρια mNY κατά την κρίση του ερευνητή.

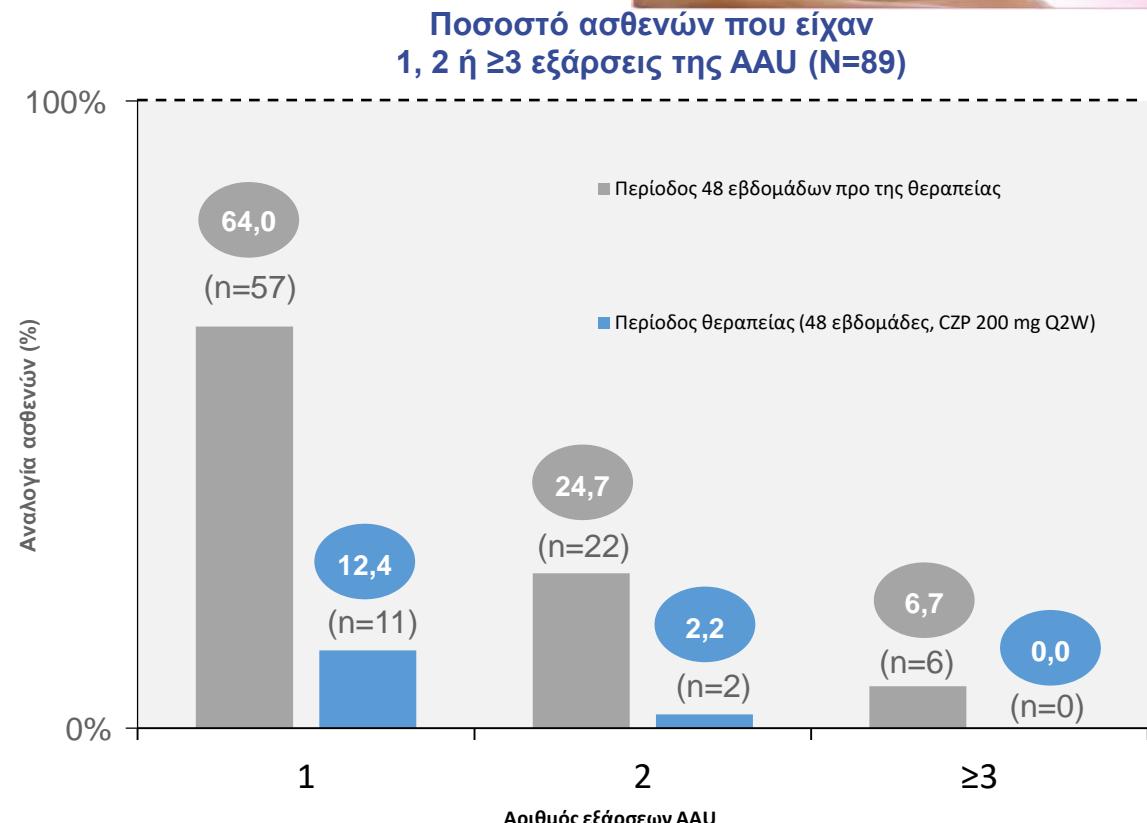
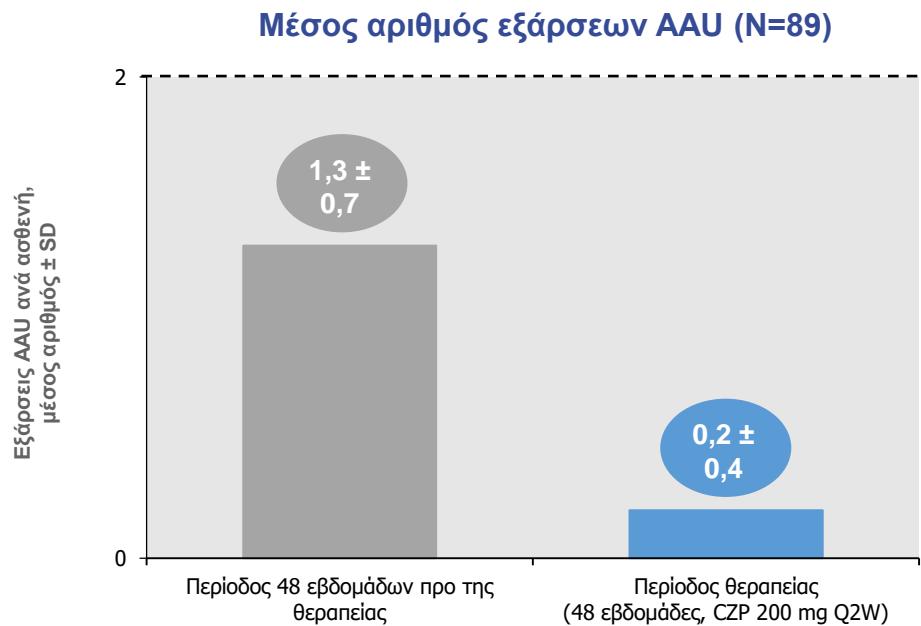
† Διαγνωσμένη από οφθαλμίατρο και ≥ 2 εξάρσεις AAU στο παρελθόν, από τις οποίες ≥ 1 τουλάχιστον 12 μήνες πριν από την έναρξη.

‡ Ενεργή axSpA, προηγούμενη αποτυχία με ≥ 2 ΜΣΑΦ, δεν έχουν λάβει βιολογικούς παράγοντες, ή προηγούμενη αποτυχία με ≤ 1 αντι-TNF.

1. ClinicalTrials.gov NCT03020992. Accessed 10.01.2020.

2. van der Horst-Bruinsma I et al. Arthritis Rheumatol. 2019; 71(suppl 10). Abstract 935.

Ενδιάμεση ανάλυση στις 48 εβδομάδες (δεδομένα παρατηρήσεων) (1/2)



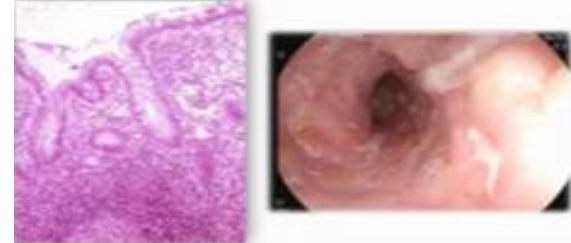
Επίπτωση προσαρμοσμένη κατά Poisson:*

Προ της θεραπείας: 1,5 Στη διάρκεια της θεραπείας: 0,2

87% μείωση της επίπτωσης AAU

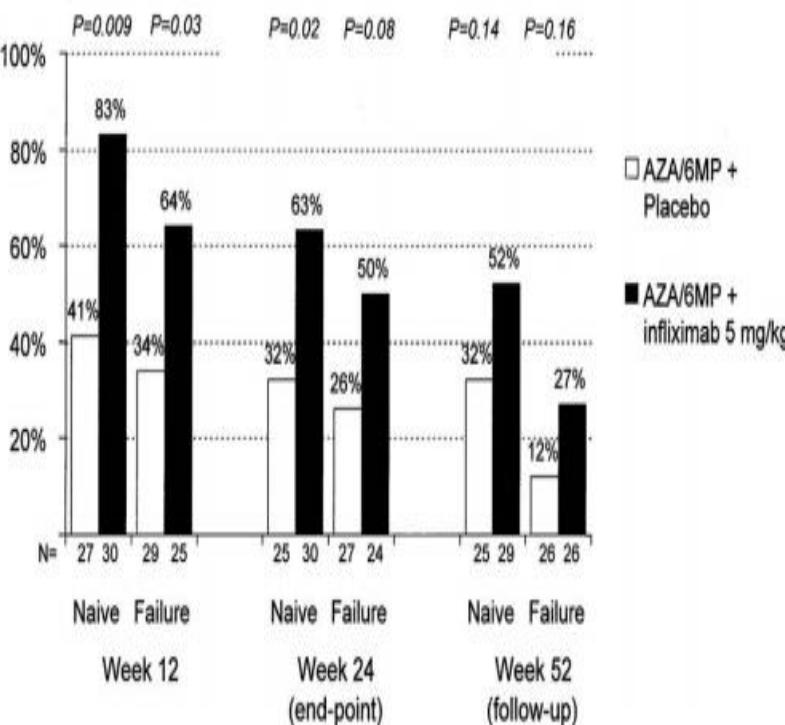
Σημαντική μείωση στο ποσοστό εξάρσεων AAU στις πρώτες 48 εβδομάδες της θεραπείας με CZP

ЕНТЕРИКΗ ΦΛΕΓΜΟΝΗ

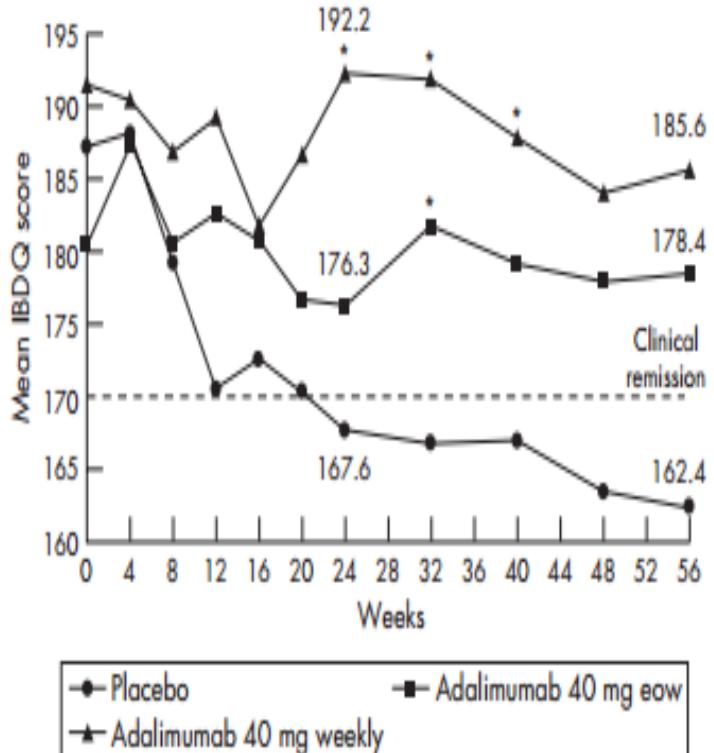


Infliximab

Remission and off steroids



Adalimumab



Certolizumab pegol

Clinical response rate (%)

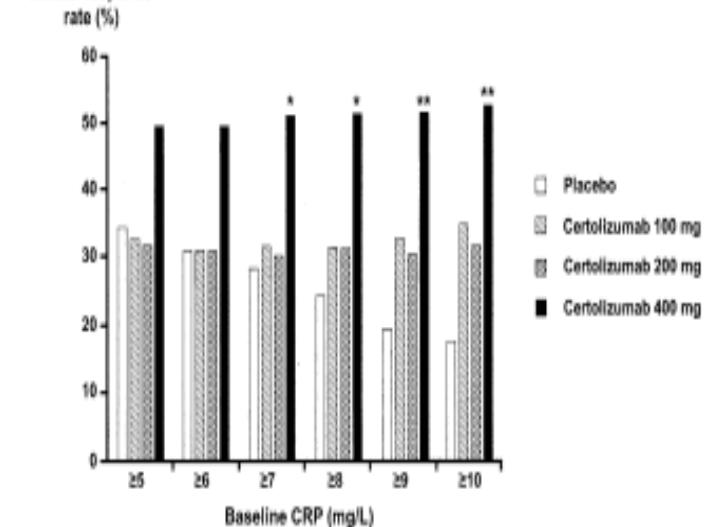
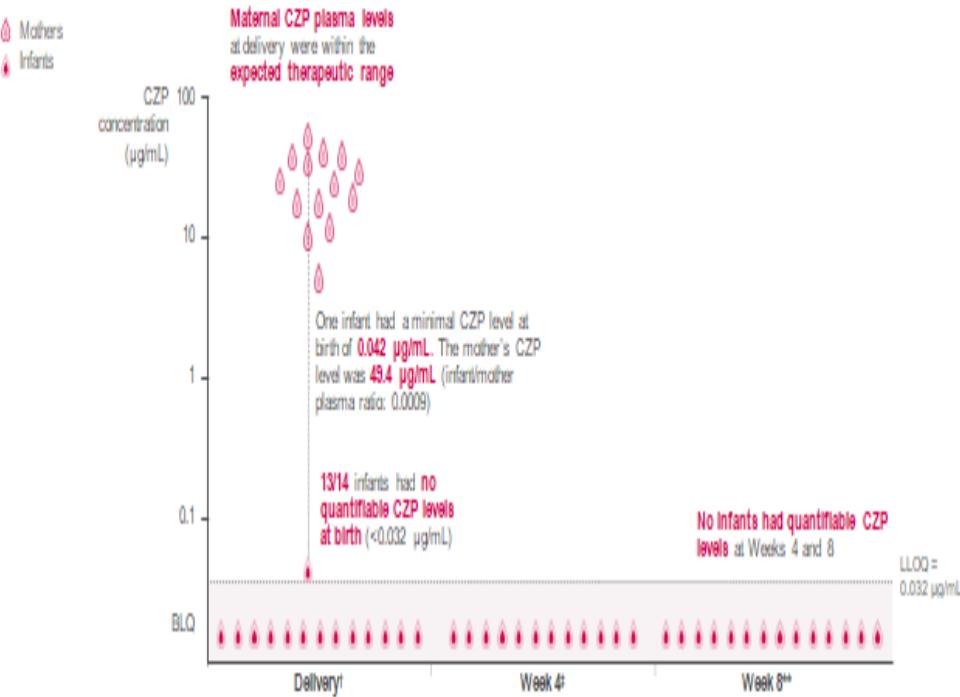


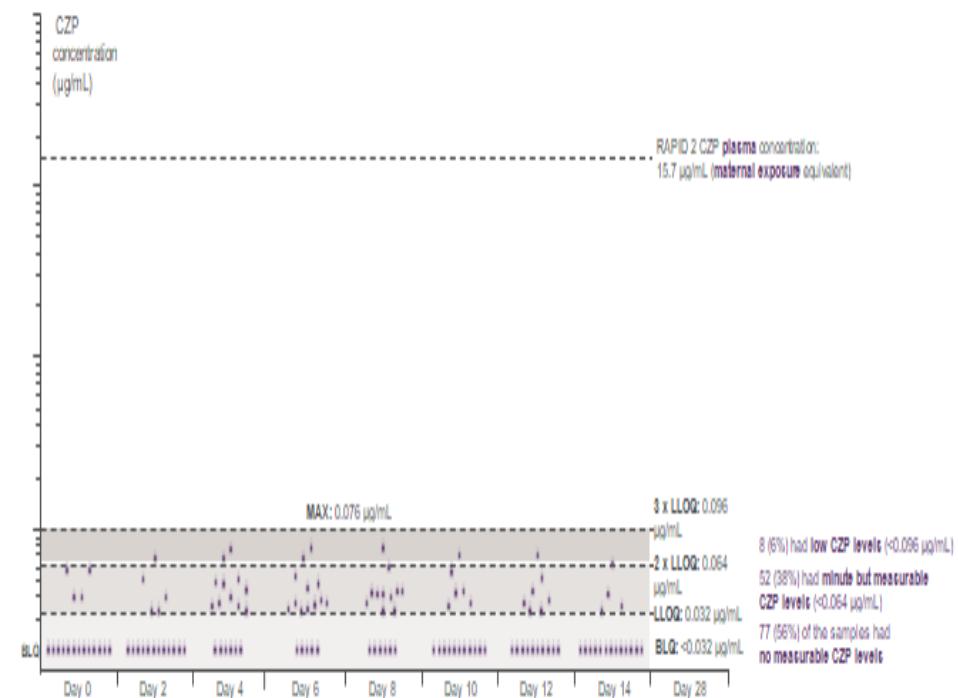
Figure 6. Clinical response rates (decrease in CDAI score ≥ 100 points or remission [CDAI score, ≤ 150 points]) to certolizumab 100, 200, and 400 mg and placebo at week 12 according to mean baseline CRP concentrations. **P* $\leq .05$, ***P* $\leq .01$ compared with placebo.

CRIB Study

CRADLE: Breast Milk Transfer Study



CZIP showed no to minimal (<0.1% of the adult therapeutic level) placental transfer from mother to infant.¹ CZIP should only be used during pregnancy if clinically needed.²



CZIP can be used during breastfeeding due to minimal transfer to breast milk

ΣΥΜΠΕΡΑΣΜΑΤΑ

Η ΨΑ αποτελεί μία ετερογενή νόσο με κλινικές εκδηλώσεις από διάφορα συστήματα και πλήθος συννοσυροτήτων που καθιστούν δύσκολη την αντιμετώπιση και επιλογή της κατάλληλης θεραπευτικής αγωγής

Το γυναικείο φύλο σχετίζεται με καθυστερημένη παραπομπή και διάγνωση της νόσου γεγονός που συνοδεύεται από σημαντικότερες επιπτώσεις σε ότι αφορά το συνολικό φορτίο και τις συνέπειες της ΨΑ σε δραστηριότητες της καθημερινής ζωής

Η καλύτερη γνώση και κατανόηση των μηχανισμών της νόσου έχει οδηγήσει σε νέες θεραπευτικές προσεγγίσεις και στρατηγικές θεραπείας που αποσκοπούν στην ολοκληρωμένη αντιμετώπιση της ΨΑ

Το certolizumab-pegol αποτελεί τον μοναδικό αναστολέα του TNF-α με μακροχρόνια δεδομένα που αφορούν όλα τα πεδία της ΨΑ καθώς και στις εξωαρθρικές εκδηλώσεις και αποτελεί αξιόπιστη επιλογή για την αντιμετώπιση του συνόλου των ετερογενών εκδηλώσεων της νόσου.

