USZ Universitäts Spital Zürich

Psoriasis: von der Haut zum Gelenk

PD Dr. med. Raphael Micheroli MPH
Leitender Arzt
Klinik für Rheumatologie
UniversitätsSpital Zürich

26.09.2024

FAKTEN, FAKTEN, FAKTEN

Prävalenz von Psoriasis-Arthritis (PsA)

- Bis zu **30 %** der Psoriasis-Patienten haben PsA

Undiagnostizierte Psoriasis-Arthritis

- **15 %** der Psoriasis-Patienten bei Dermatologen haben nicht diagnostizierte PsA

Krankheitsverlauf

- Psoriasis geht der Arthritis im Durchschnitt um **10 Jahre** voraus
- **85%** der Fälle zuerst Psoriasis
- In **15 %** der Fälle treten Arthritis und Psoriasis gleichzeitig auf oder PsA geht der Hauterkrankung voraus

Demografische Unterschiede

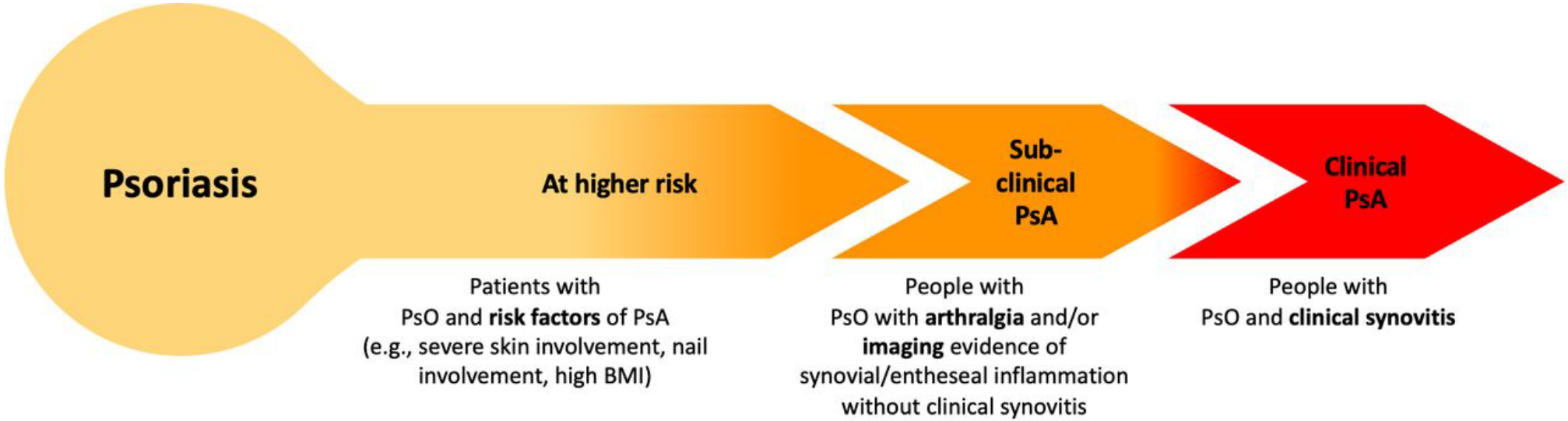
- PsA tritt selten bei Menschen asiatischer oder afrikanischer Herkunft auf
- Verhältnis **Männer zu Frauen: 1:1**

USZ Universitäts Spital Zürich

Ritchlin CT, Colbert RA, Gladman DD. Psoriatic Arthritis. N Engl J Med. 2017 Mar 9;376(10):957-970. doi: 10.1056/NEJMra1505557. Erratum in: N Engl J Med. 2017 May 25;376(21):2097. doi: 10.1056/NEJMx170005. PMID: 28273019.

Villani AP, Rouzaud M, Sevrain M, Barnetche T, Paul C, Richard MA, Beylot-Barry M, Misery L, Joly P, Le Maitre M, Aractingi S, Aubin F, Cantagrel A, Ortonne JP, Jullien D. Prevalence of undiagnosed psoriatic arthritis among psoriasis patients: Systematic review and meta-analysis. J Am Acad Dermatol. 2015 Aug;73(2):242-8. doi: 10.1016/j.jaad.2015.05.001. Epub 2015 Jun 6. PMID: 26054432.

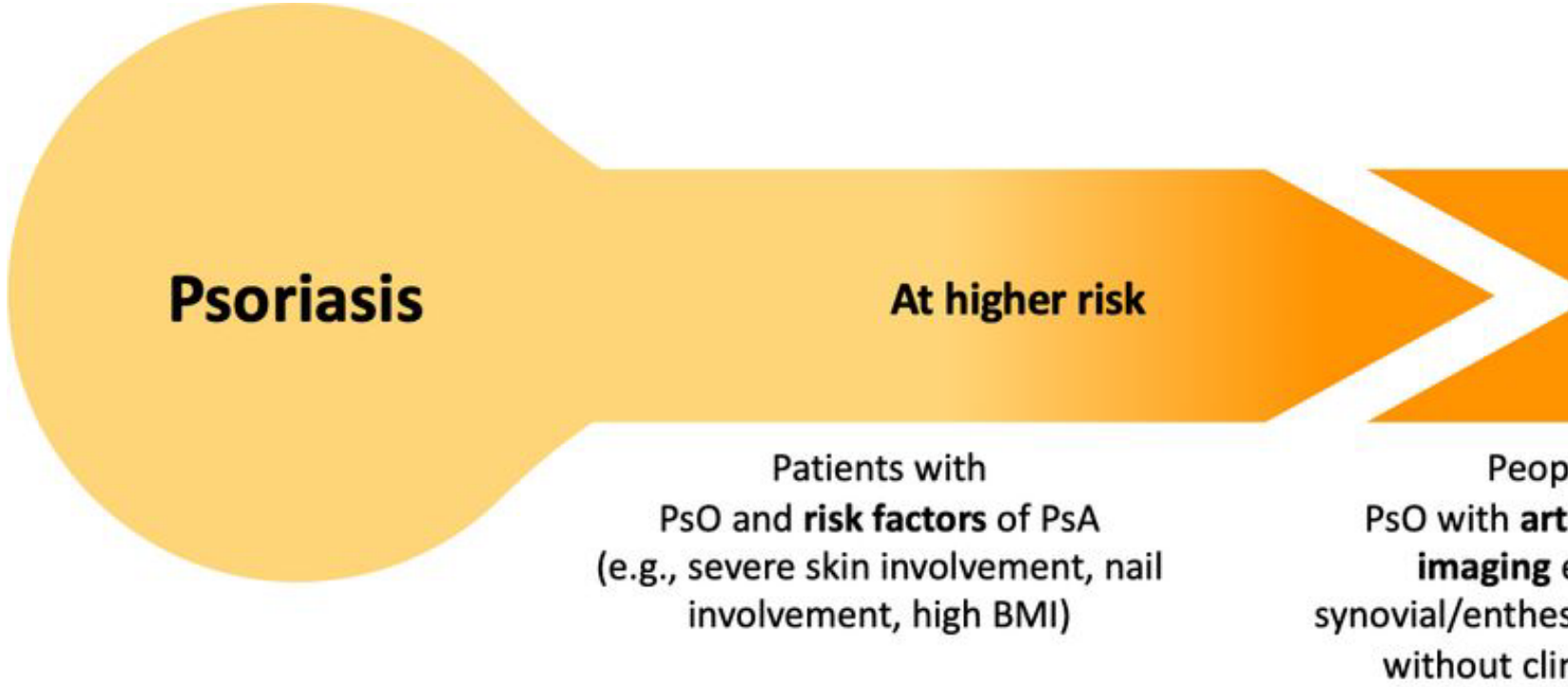
Von den Schmerzen zur Entzündung…



Nomenclature for research and prevention/interception trials in people with PsO at risk of PsA	
Phase	*Definition*
A. At higher risk	People with PsO at higher risk of PsA (i.e., severe skin involvement, nail involvement, obesity, familial history) of PsA.*
B. Sub-clinical	People with PsO with arthralgia and/or imaging evidence of synovial/entheseal inflammation without clinical synovitis
C. Clinical	People with PsO and clinical synovitis

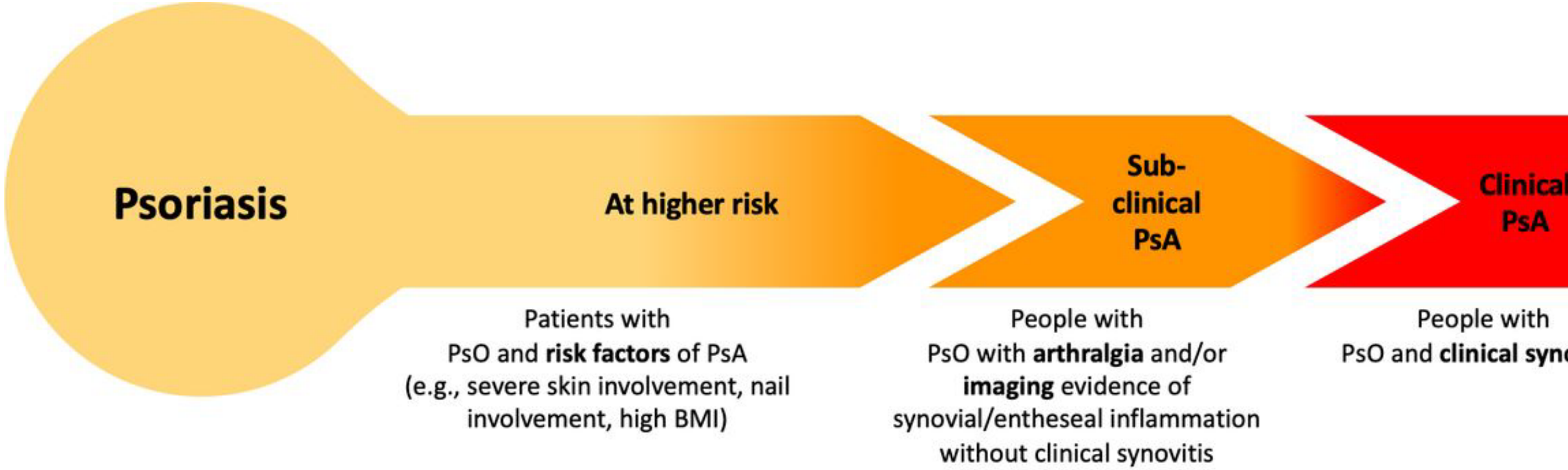
Zabotti A, De Marco G, Gossec L, Baraliakos X, Aletaha D, Iagnocco A, Gisondi P, Balint PV, Bertheussen H, Boehncke WH, Damjanov NS, de Wit M, Errichetti E, Marzo-Ortega H, Protopopov M, Puig L, Queiro R, Ruscitti P, Savage L, Schett G, Siebert S, Stamm TA, Studenic P, Tinazzi I, Van den Bosch FE, van der Helm-van Mil A, Watad A, Smolen JS, McGonagle DG. EULAR points to consider for the definition of clinical and imaging features suspicious for progression from psoriasis to psoriatic arthritis. Ann Rheum Dis. 2023 Sep;82(9):1162-1170. doi: 10.1136/ard-2023-224148. Epub 2023 Jun 9. PMID: 37295926.

Von den Schmerzen zur Entzündung…



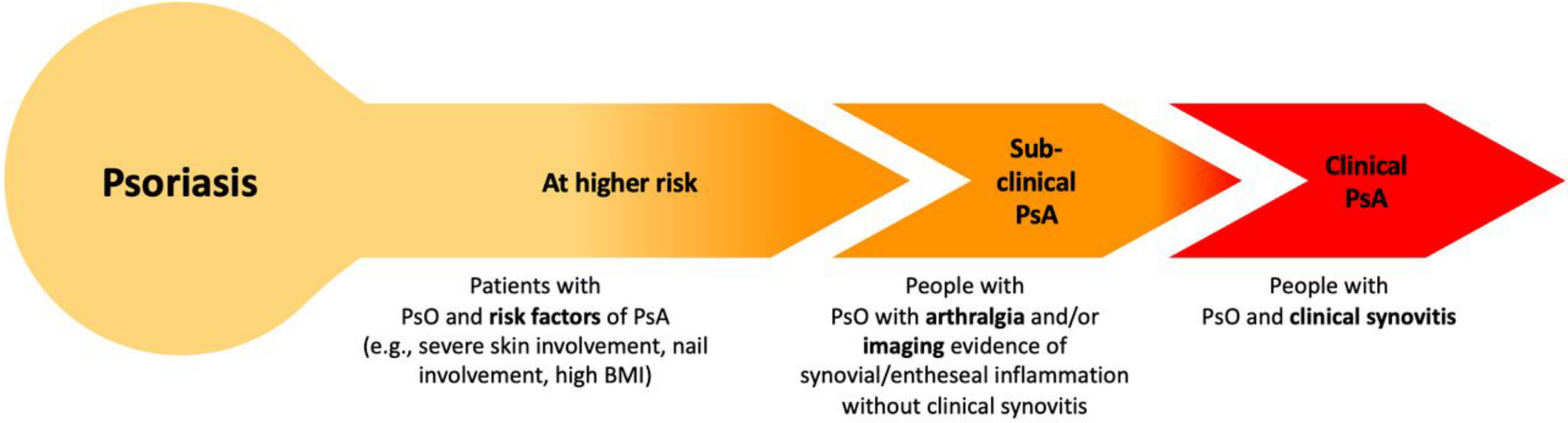
Zabotti A, De Marco G, Gossec L, Baraliakos X, Aletaha D, Iagnocco A, Gisondi P, Balint PV, Bertheussen H, Boehncke WH, Damjanov NS, de Wit M, Errichetti E, Marzo-Ortega H, Protopopov M, Puig L, Queiro R, Ruscitti P, Savage L, Schett G, Siebert S, Stamm TA, Studenic P, Tinazzi I, Van den Bosch FE, van der Helm-van Mil A, Watad A, Smolen JS, McGonagle DG. EULAR points to consider for the definition of clinical and imaging features suspicious for progression from psoriasis to psoriatic arthritis. Ann Rheum Dis. 2023 Sep;82(9):1162-1170. doi: 10.1136/ard-2023-224148. Epub 2023 Jun 9. PMID: 37295926.

Von den Schmerzen zur Entzündung…



Zabotti A, De Marco G, Gossec L, Baraliakos X, Aletaha D, Iagnocco A, Gisondi P, Balint PV, Bertheussen H, Boehncke WH, Damjanov NS, de Wit M, Errichetti E, Marzo-Ortega H, Protopopov M, Puig L, Queiro R, Ruscitti P, Savage L, Schett G, Siebert S, Stamm TA, Studenic P, Tinazzi I, Van den Bosch FE, van der Helm-van Mil A, Watad A, Smolen JS, McGonagle DG. EULAR points to consider for the definition of clinical and imaging features suspicious for progression from psoriasis to psoriatic arthritis. Ann Rheum Dis. 2023 Sep;82(9):1162-1170. doi: 10.1136/ard-2023-224148. Epub 2023 Jun 9. PMID: 37295926.

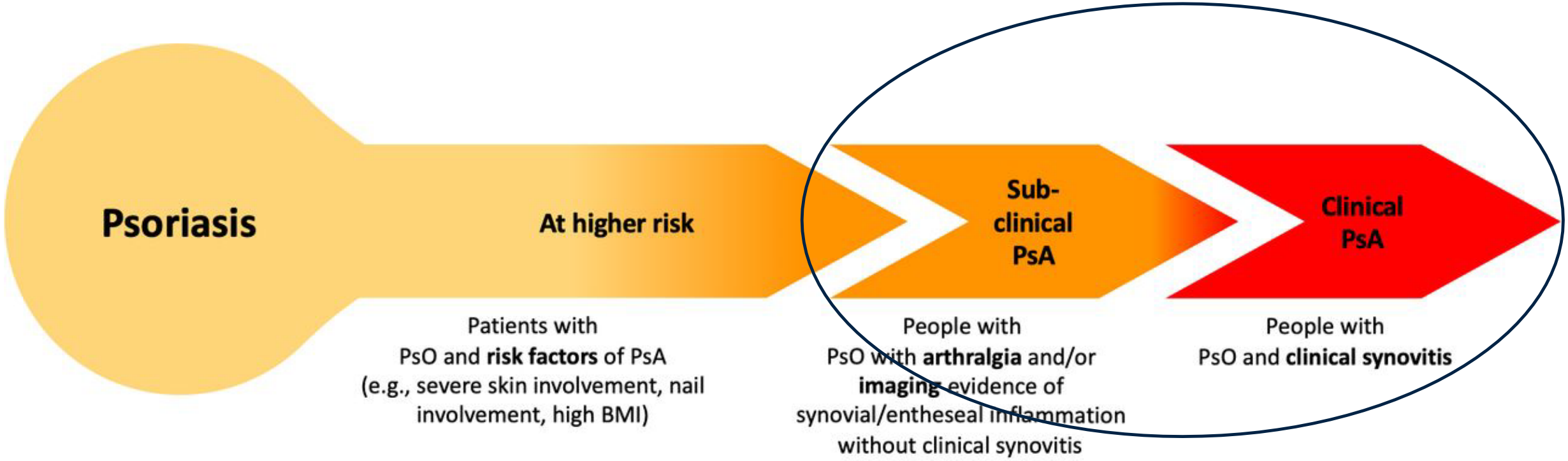
Von den Schmerzen zur Entzündung…



USZ Universitäts Spital Zürich

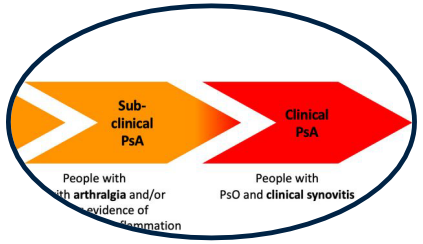
Zabotti A, De Marco G, Gossec L, Baraliakos X, Aletaha D, Iagnocco A, Gisondi P, Balint PV, Bertheussen H, Boehncke WH, Damjanov NS, de Wit M, Errichetti E, Marzo-Ortega H, Protopopov M, Puig L, Queiro R, Ruscitti P, Savage L, Schett G, Siebert S, Stamm TA, Studenic P, Tinazzi I, Van den Bosch FE, van der Helm-van Mil A, Watad A, Smolen JS, McGonagle DG. EULAR points to consider for the definition of clinical and imaging features suspicious for progression from psoriasis to psoriatic arthritis. Ann Rheum Dis. 2023 Sep;82(9):1162-1170. doi: 10.1136/ard-2023-224148. Epub 2023 Jun 9. PMID: 37295926.

Von den Schmerzen zur Entzündung…

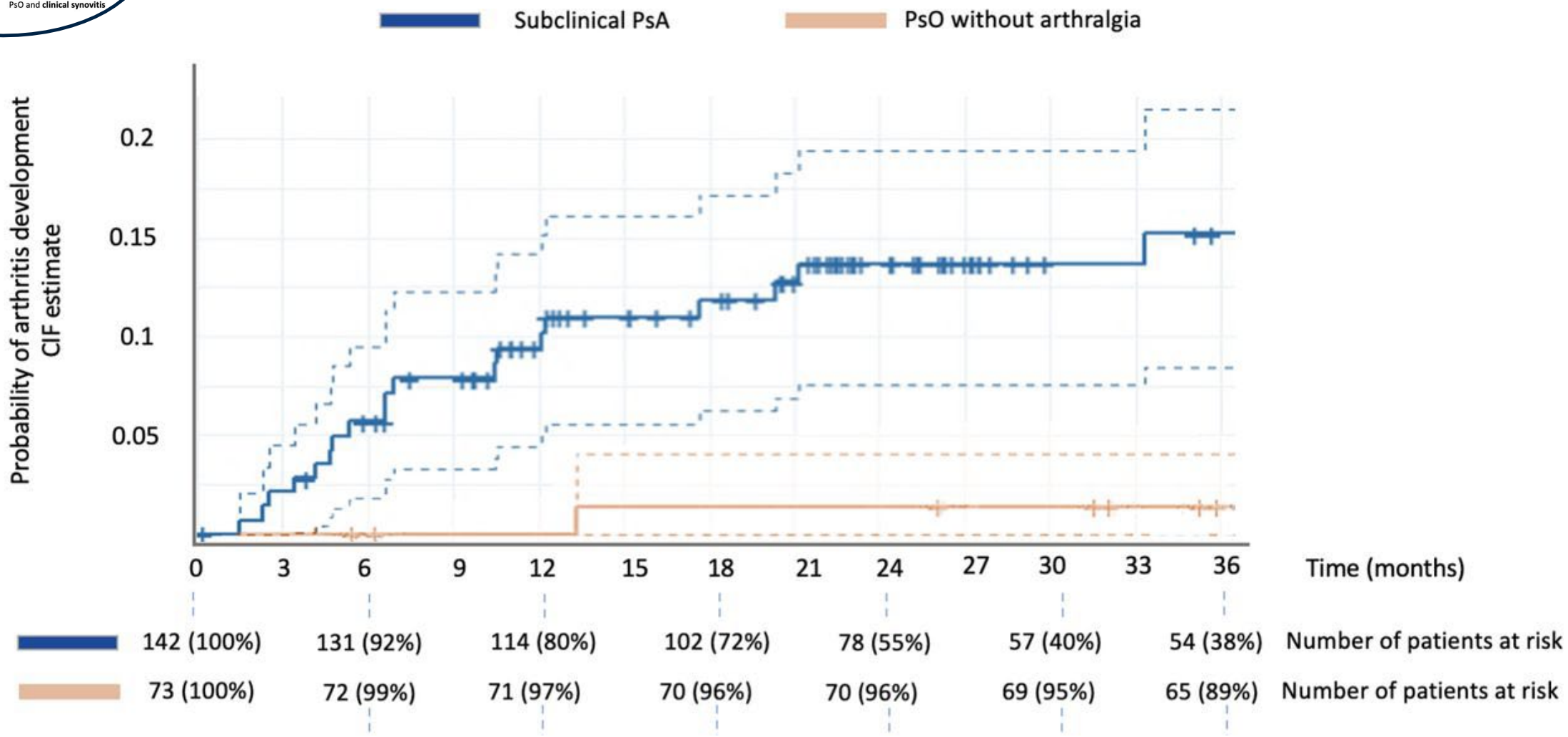


USZ Universitäts Spital Zürich

Zabotti A, De Marco G, Gossec L, Baraliakos X, Aletaha D, Iagnocco A, Gisondi P, Balint PV, Bertheussen H, Boehncke WH, Damjanov NS, de Wit M, Errichetti E, Marzo-Ortega H, Protopopov M, Puig L, Queiro R, Ruscitti P, Savage L, Schett G, Siebert S, Stamm TA, Studenic P, Tinazzi I, Van den Bosch FE, van der Helm-van Mil A, Watad A, Smolen JS, McGonagle DG. EULAR points to consider for the definition of clinical and imaging features suspicious for progression from psoriasis to psoriatic arthritis. Ann Rheum Dis. 2023 Sep;82(9):1162-1170. doi: 10.1136/ard-2023-224148. Epub 2023 Jun 9. PMID: 37295926.



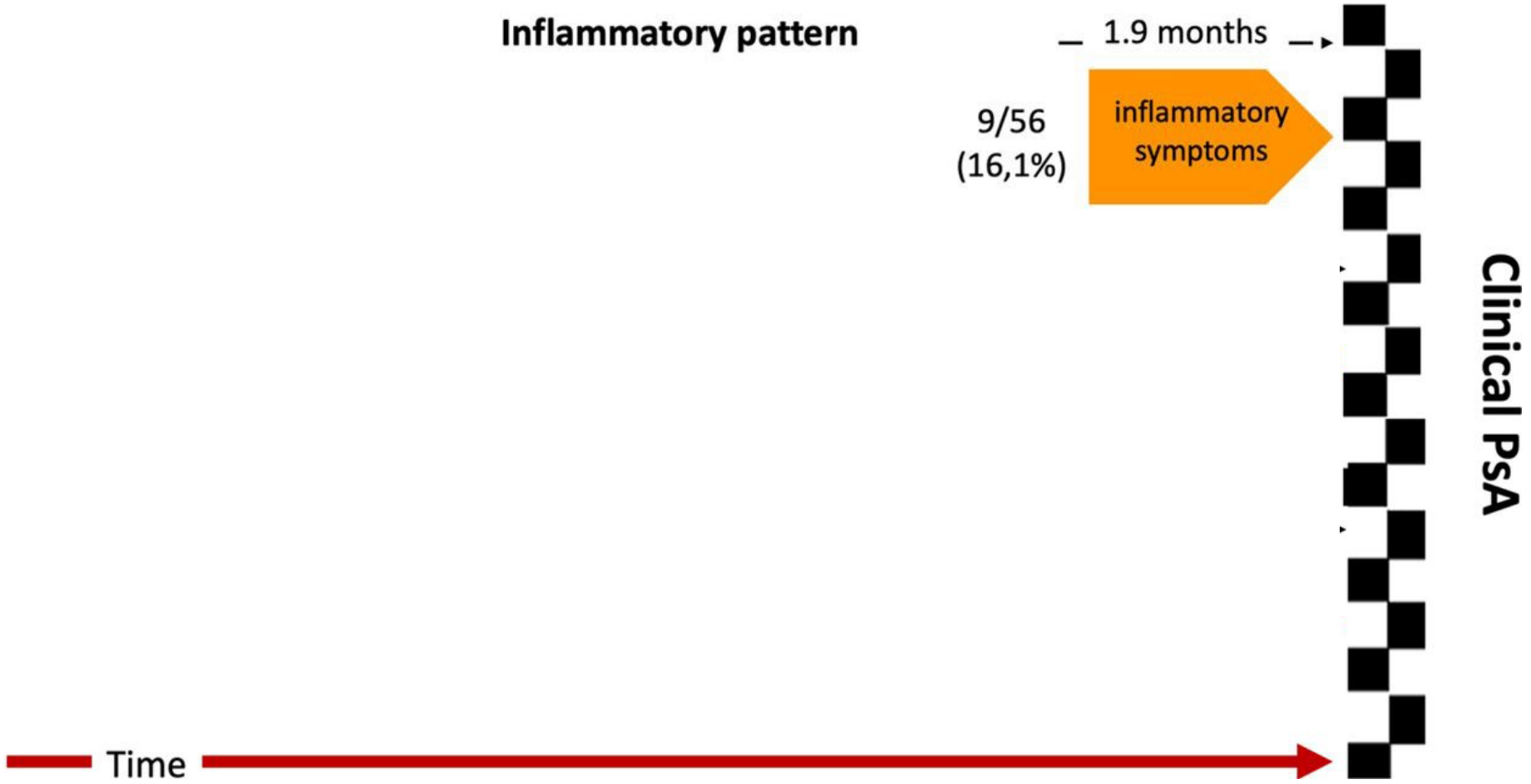
Von den Schmerzen zur Entzündung…



USZ Universitäts Spital Zürich

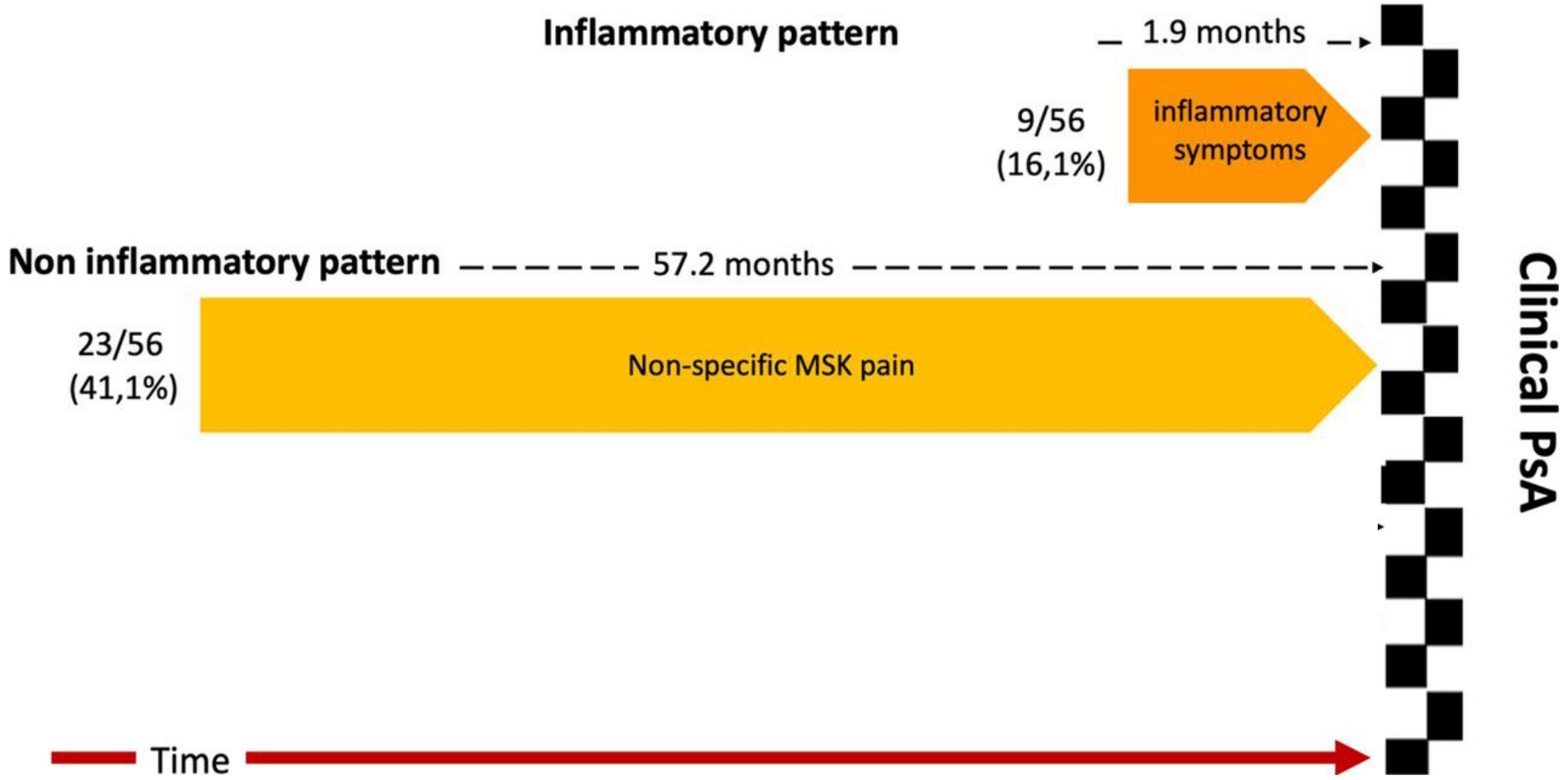
Zabotti A, Fagni F, Gossec L, *et al* Risk of developing psoriatic arthritis in psoriasis cohorts with arthralgia: exploring the subclinical psoriatic arthritis stage *RMD Open* 2024;**10:**e004314. doi: 10.1136/rmdopen-2024-004314

1. Inflammatory—when at least two of the following features were present: (a) duration of morning stiffness >30 min; (b) most severe symptoms present in the morning; (c) improvement of symptoms during the day.
2. Non-inflammatory—defined as arthralgia without inflammatory features.



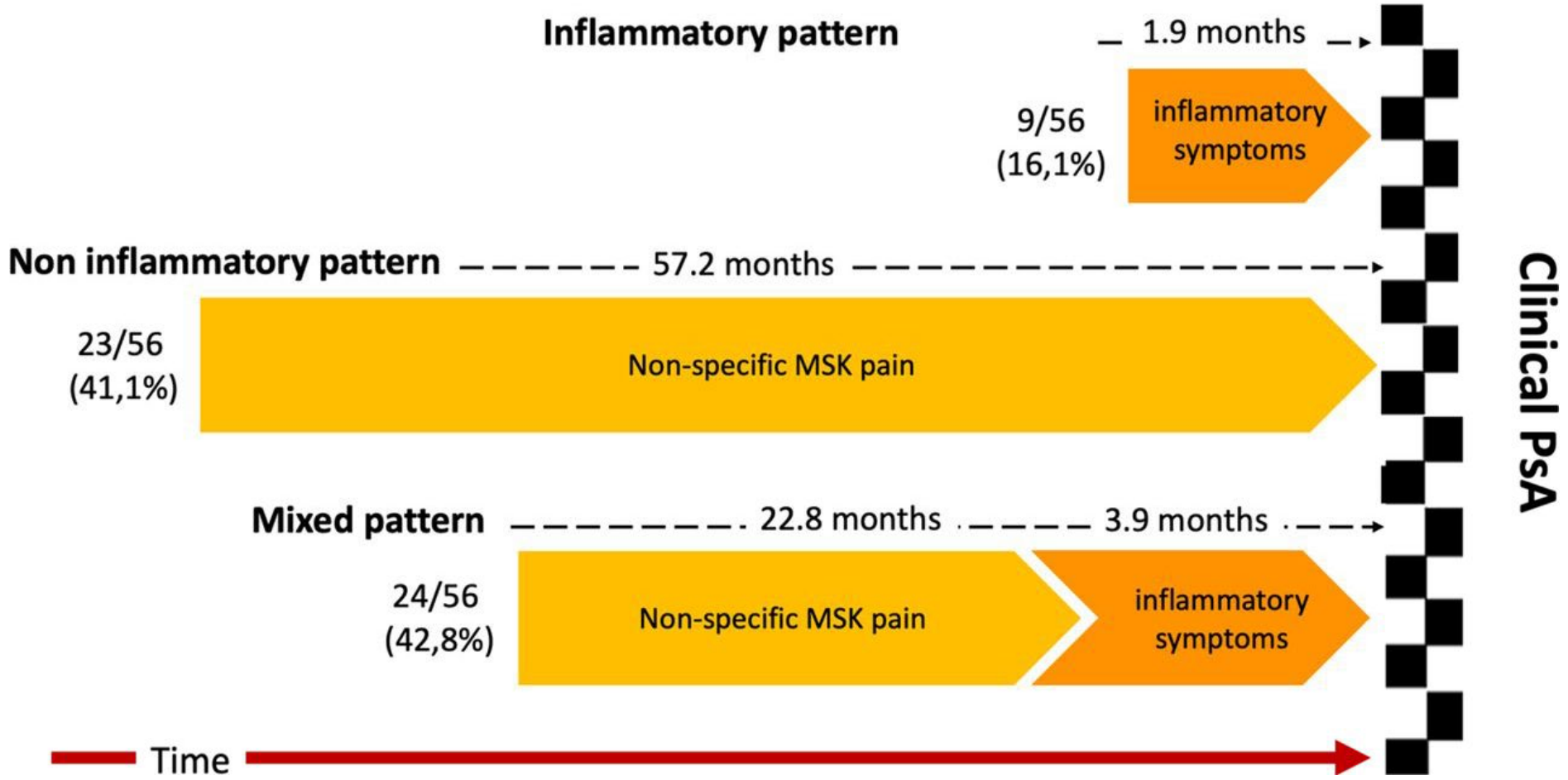
Zabotti A, Fagni F, Gossec L, *et al* Risk of developing psoriatic arthritis in psoriasis cohorts with arthralgia: exploring the subclinical psoriatic arthritis stage *RMD Open* 2024;**10:**e004314. doi: 10.1136/rmdopen-2024-004314

1. Inflammatory—when at least two of the following features were present: (a) duration of morning stiffness >30 min; (b) most severe symptoms present in the morning; (c) improvement of symptoms during the day.
2. Non-inflammatory—defined as arthralgia without inflammatory features.

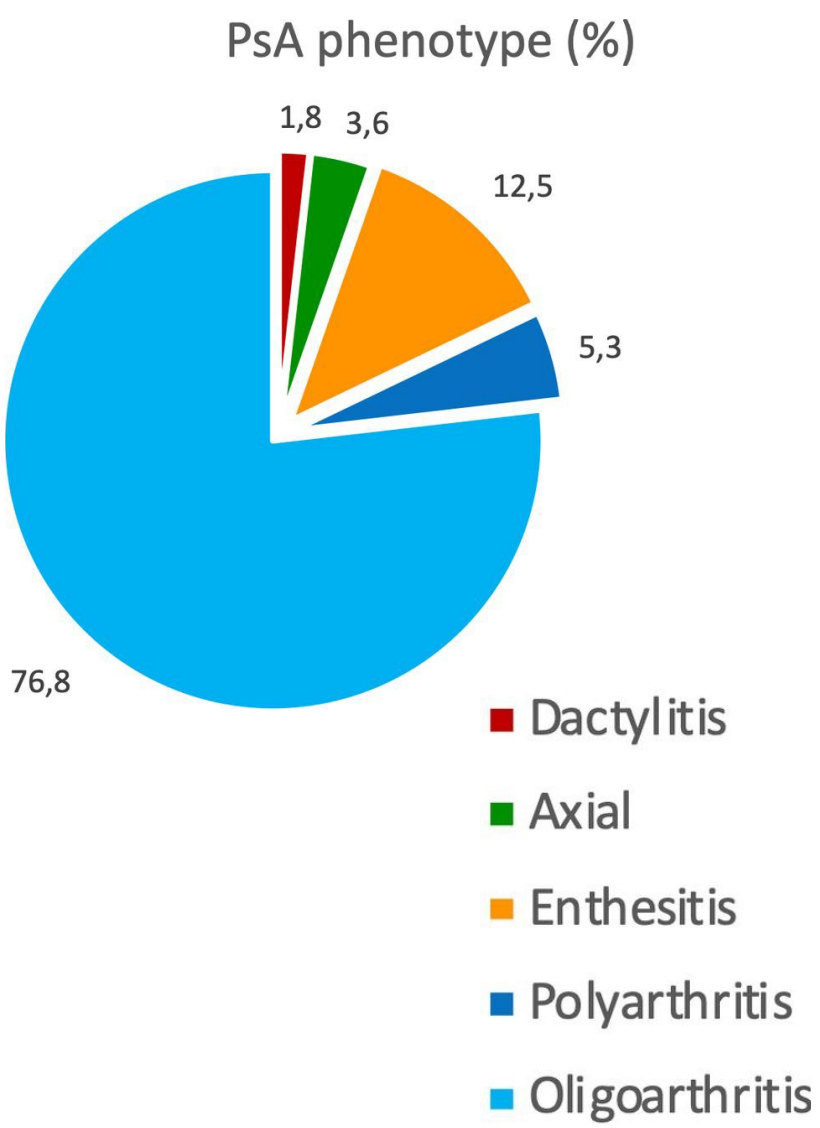


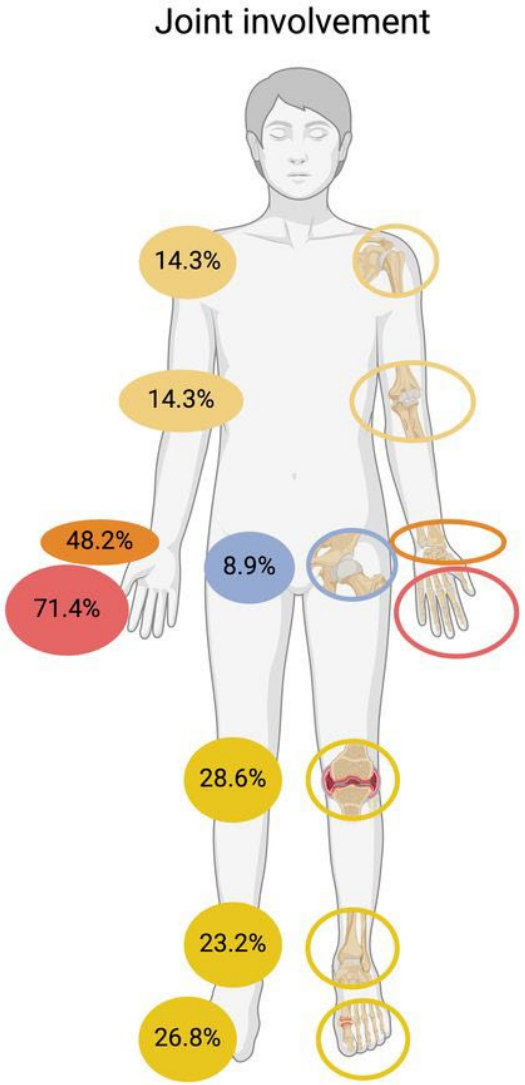
Zabotti A, Fagni F, Gossec L, *et al* Risk of developing psoriatic arthritis in psoriasis cohorts with arthralgia: exploring the subclinical psoriatic arthritis stage *RMD Open* 2024;**10:**e004314. doi: 10.1136/rmdopen-2024-004314

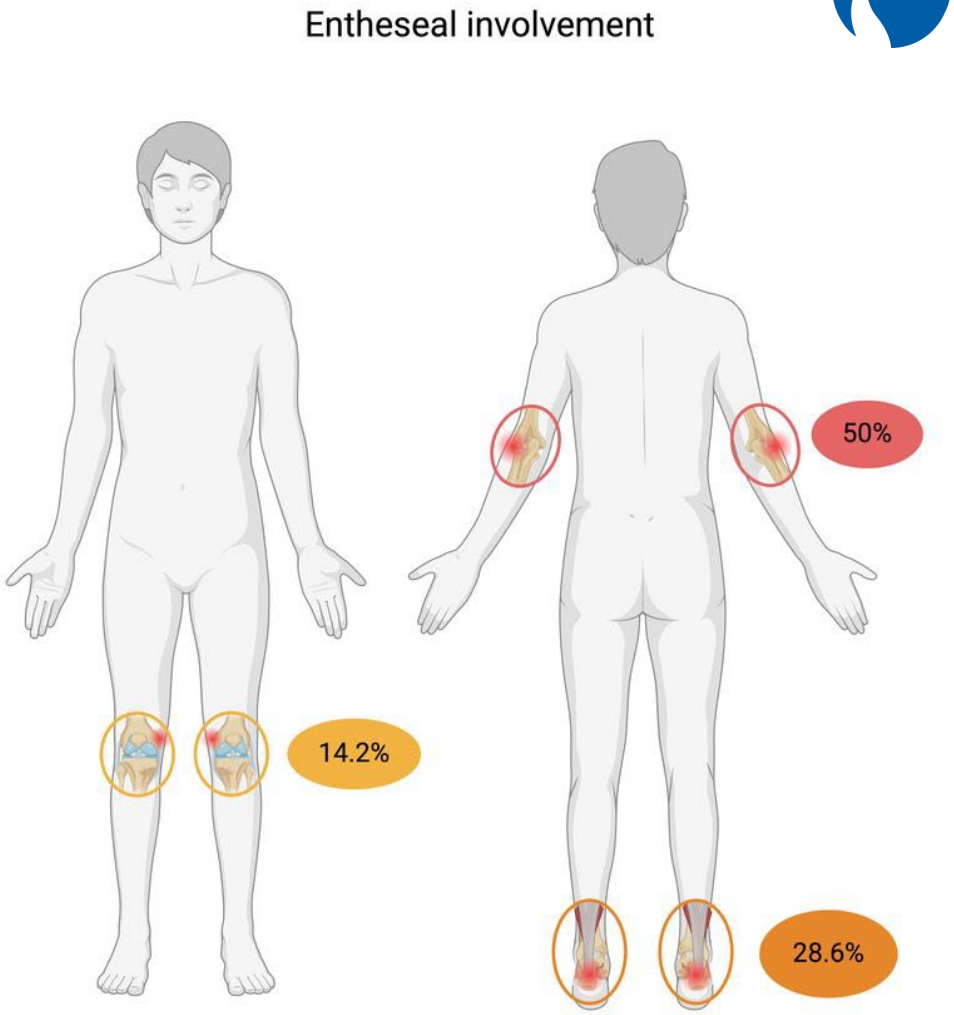
1. Inflammatory—when at least two of the following features were present: (a) duration of morning stiffness >30 min; (b) most severe symptoms present in the morning; (c) improvement of symptoms during the day.
2. Non-inflammatory—defined as arthralgia without inflammatory features.



Zabotti A, Fagni F, Gossec L, *et al* Risk of developing psoriatic arthritis in psoriasis cohorts with arthralgia: exploring the subclinical psoriatic arthritis stage *RMD Open* 2024;**10:**e004314. doi: 10.1136/rmdopen-2024-004314







USZ Universitäts Spital Zürich

Zabotti A, Fagni F, Gossec L, *et al* Risk of developing psoriatic arthritis in psoriasis cohorts with arthralgia: exploring the subclinical psoriatic arthritis stage *RMD Open* 2024;**10:**e004314. doi: 10.1136/rmdopen-2024-004314

Screening-Tools für Nicht-Rheumatologen

Questionnaire	True positive (*n*)	False positive (*n*)	True negative (*n*)	False negative (*n*)	Sensitivity (%)	Specificity (%)	AUC
EARP	**41**	**31**	**226**	**4**	**91**	**88**	**0·95**
PASE 44	36	14	243	9	80	95	0·93
PEST	24	12	245	21	53	95	0·92
ToPAS II	20	7	250	25	44	97	0·93

Mishra S et al, Br J Dermatol 2017;176:765–70

EARP (>3 Punkte assoziiert mit PsA)

Question	Yes	No
Do your joints hurt?	1	0
Have you taken anti-inflammatory more than twice a week for joint pain in the last 3 months?	1	0
Do you wake up at night because of low back pain?	1	0
Do you feel stiffness in your hands for more than 30 minutes in the morning?	1	0
Do your wrists and fingers hurt?	1	0
Do your wrists and fingers swell?	1	0
Does one finger hurt and swell for more than 3 days?	1	0
Does your Achilles tendon swell?	1	0
Do your feet or ankles hurt?	1	0
Do your elbow or hips hurt?	1	0

Tinazzi I et al, Rheumatology (Oxford) 2012; 51:2058–63.

Früherkennung – axiale PsA

Question	Response
1. Is the patient 18 years of age or older?	□ Yes □ No
2. Does the patient have a confirmed diagnosis of psoriasis (current or past)?	□ Yes □ No
3. Does the patient suffer from back pain?	□ Yes □ No
3b. Has the patient's back pain been chronic (≥ 3 months)?	□ Yes □ No
3c. Did the patient's back pain start before the age of 45 years?	□ Yes □ No
4. Has the patient been treated with a biologic or targeted synthetic DMARD in the past 12 weeks (e.g. Tofacitinib)?	□ Yes □ No

Studienergebnisse

- 151 Patienten mit chronischen Rückenschmerzen (≥3 Monate) an Rheumatologen überwiesen
- 14 Diagnosen mit axPsA, 5 mit PsA ohne axiale Beteiligung

Wichtigkeit der Bildgebung

- MRT entscheidend für axPsA-Diagnose (auch nur axial – ohne ISG-Beteiligung)
- Entzündliche Rückenschmerzen führen häufig zu Überdiagnosen ohne MRT

Früherkennung - axPsA

Question	Response
1. Is the patient 18 years of age or older?	□ Yes □ No
2. Does the patient have a confirmed diagnosis of psoriasis (current or past)?	□ Yes □ No
3. Does the patient suffer from back pain?	□ Yes □ No
3b. Has the patient's back pain been chronic (≥ 3 months)?	□ Yes □ No
3c. Did the patient's back pain start before the age of 45 years?	□ Yes □ No
4. Has the patient been treated with a biologic or targeted synthetic DMARD in the past 12 weeks (e.g. Tofacitinib)?	□ Yes □ No

Sensitivität: 100%
Spezifität: 48.50%
Positiver prädiktiver Wert (PPV): 14%
Negativer prädiktiver Wert (NPV): 100%

ANNAHME: Nur Patienten mit Rückenbeschwerden haben entzündliche MRI Veränderungen bei PsA

Früherkennung - axPsA

Table 6. Relation between inflammatory back pain and other clinical, radiological, and MRI findings

		Inflammatory back pain		
		Absent (n=36)	Present (n=14)	p value
Clinical sacroiliitis	Absent	31 (86.1%)	11 (78.6%)	0.68
	Present	5 (13.9%)	3 (21.4%)	
Schober test	Normal	30 (83.3%)	7 (50%)	0.029*
	Abnormal	6 (16.7%)	7 (50%)	
Lateral flexion test	Normal	31 (86.1%)	7 (50%)	0.023*
	Abnormal	5 (13.9%)	7 (50%)	
MRI of the LSS	Normal	23 (63.9%)	6 (42.9%)	0.16
	Abnormal	13 (36.1%)	9 (64.3%)	
MRI-diagnosed sacroiliitis	Normal	34 (94.4%)	11 (78.6%)	0.12
	Abnormal	2 (5.5%)	3 (21.4%)	
X-ray-diagnosed sacroiliitis	Normal	34 (94.4%)	13 (92.8%)	0.6
	Abnormal	2 (5.5%)	1 (7.1%)	
X-ray of the LSS	Normal	33 (91.6%)	10 (71.4%)	0.08
	Abnormal	4 (11.1%)	4 (28.5%)	

MRI: magnetic resonance imaging; LSS: lumbosacral spine

Q	Response
1.	□ Yes □ No
2	sis (current or past)? □ Yes □ No
3	□ Yes □ No
3	s)? □ Yes □ No
3	years? □ Yes □ No
	ed synthetic DMARD in □ Yes □ No

- Negativer prädik… e axiale Psoriasis-Arthritis

ABER:
MRI auch bei asymptomatischen positiv

Hamdy M, Omar G, Elshereef RR, Ellaban AS, Amin M. Early detection of spondyloarthropathy in patients with psoriasis by using the ultrasonography and magnetic resonance image. Eur J Rheumatol. 2015 Mar;2(1):10-15. doi: 10.5152/eurjrheumatol.2015.0075. Epub 2015 Mar 1. PMID: 27708913; PMCID: PMC5047236.

Table 6. Relation between inflammatory back pain and other clinical, radiological, and MRI findings

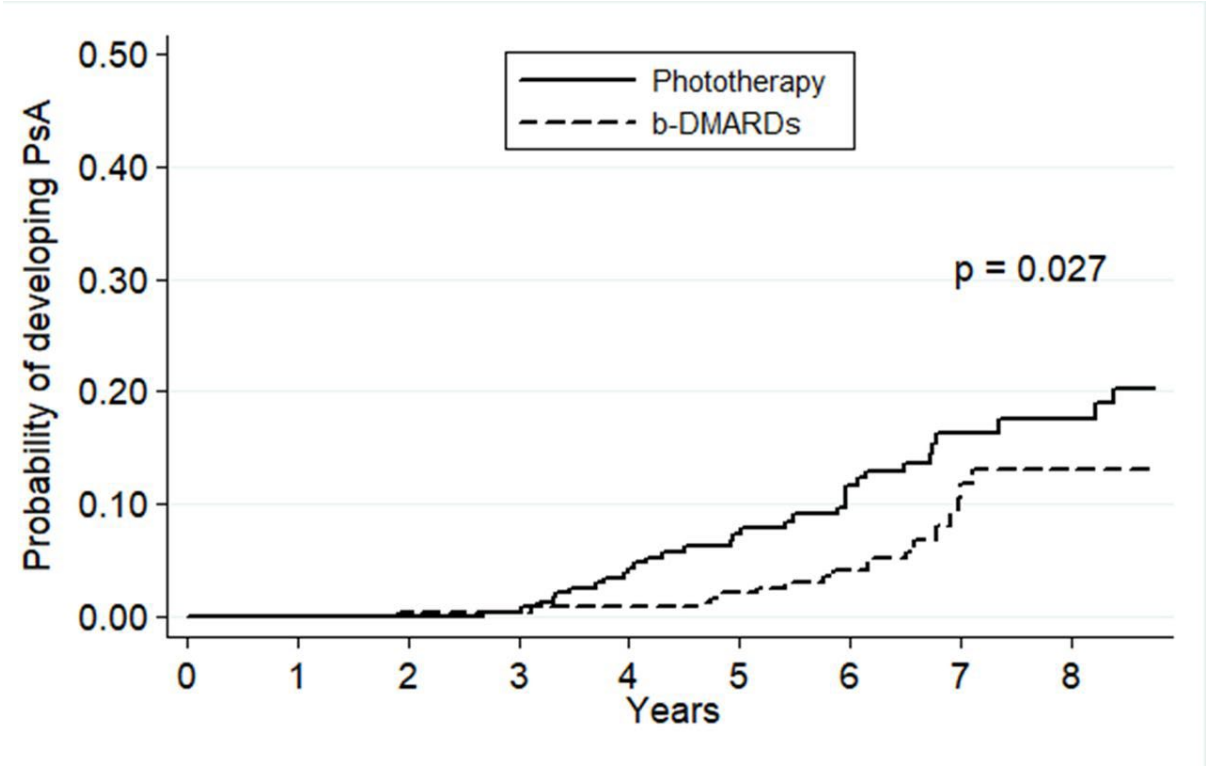
		Inflammatory back pain		
		Absent (n=36)	Present (n=14)	p value
Clinical sacroiliitis	Absent	31 (86.1%)	11 (78.6%)	0.68
	Present	5 (13.9%)	3 (21.4%)	
Schober test	Normal	30 (83.3%)	7 (50%)	0.029*
	Abnormal	6 (16.7%)	7 (50%)	
Lateral flexion test	Normal	31 (86.1%)	7 (50%)	0.023*
	Abnormal	5 (13.9%)	7 (50%)	
MRI of the LSS	Normal	23 (63.9%)	6 (42.9%)	0.16
	Abnormal	13 (36.1%)	9 (64.3%)	
MRI-diagnosed sacroiliitis	Normal	34 (94.4%)	11 (78.6%)	0.12
	Abnormal	2 (5.5%)	3 (21.4%)	
X-ray-diagnosed sacroiliitis	Normal	34 (94.4%)	13 (92.8%)	0.6
	Abnormal	2 (5.5%)	1 (7.1%)	
X-ray of the LSS	Normal	33 (91.6%)	10 (71.4%)	0.08
	Abnormal	4 (11.1%)	4 (28.5%)	

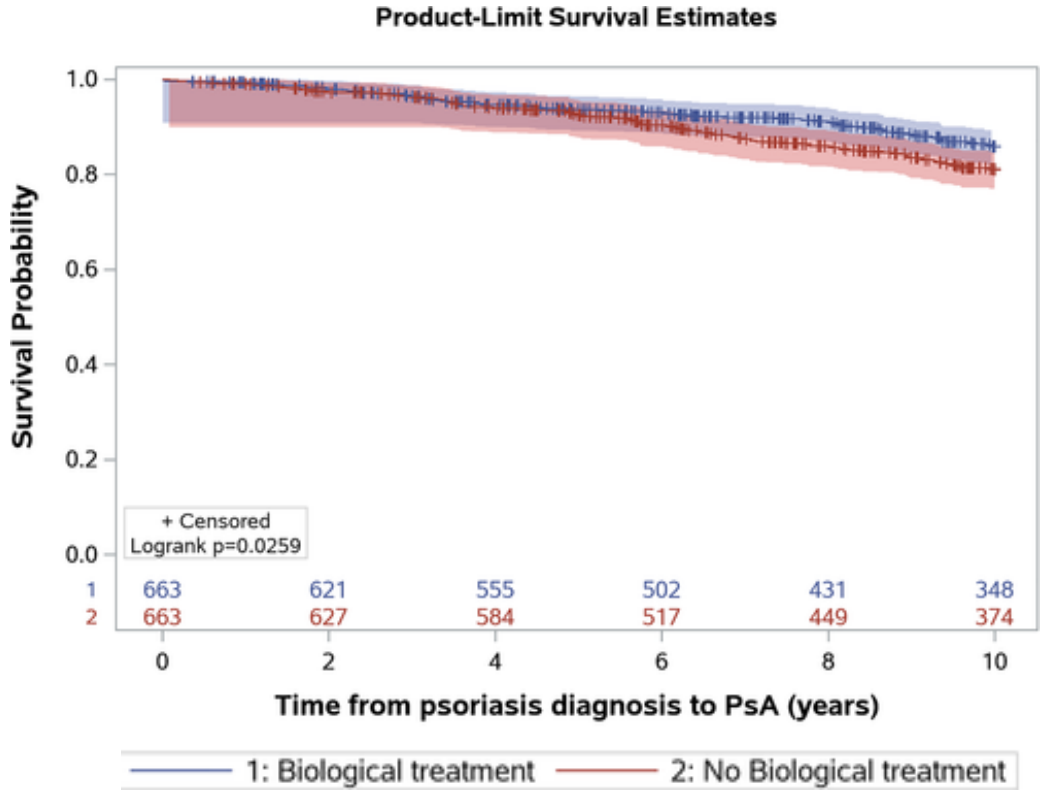
MRI: magnetic resonance imaging; LSS: lumbosacral spine

ABER:
MRI auch bei asymptomatischen positiv

Hamdy M, Omar G, Elshereef RR, Ellaban AS, Amin M. Early detection of spondyloarthropathy in patients with psoriasis by using the ultrasonography and magnetic resonance image. Eur J Rheumatol. 2015 Mar;2(1):10-15. doi: 10.5152/eurjrheumatol.2015.0075. Epub 2015 Mar 1. PMID: 27708913; PMCID: PMC5047236.

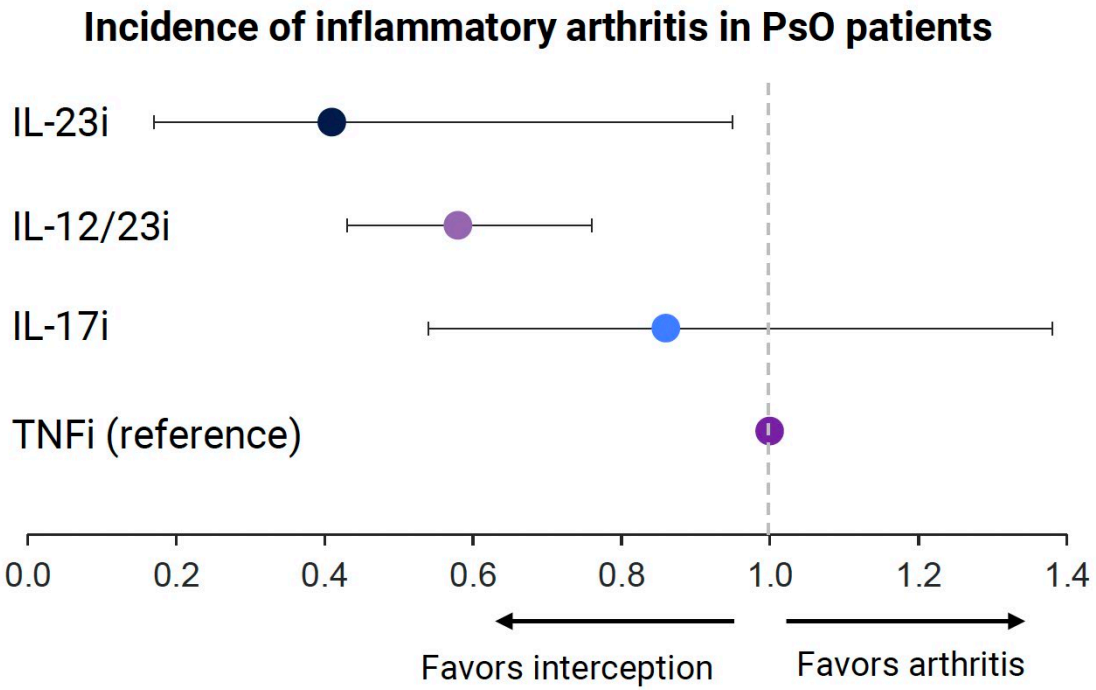
Können wir bei PsO mittels Biologika-Therapie die Entwicklung einer PsA verhindern? Observational data

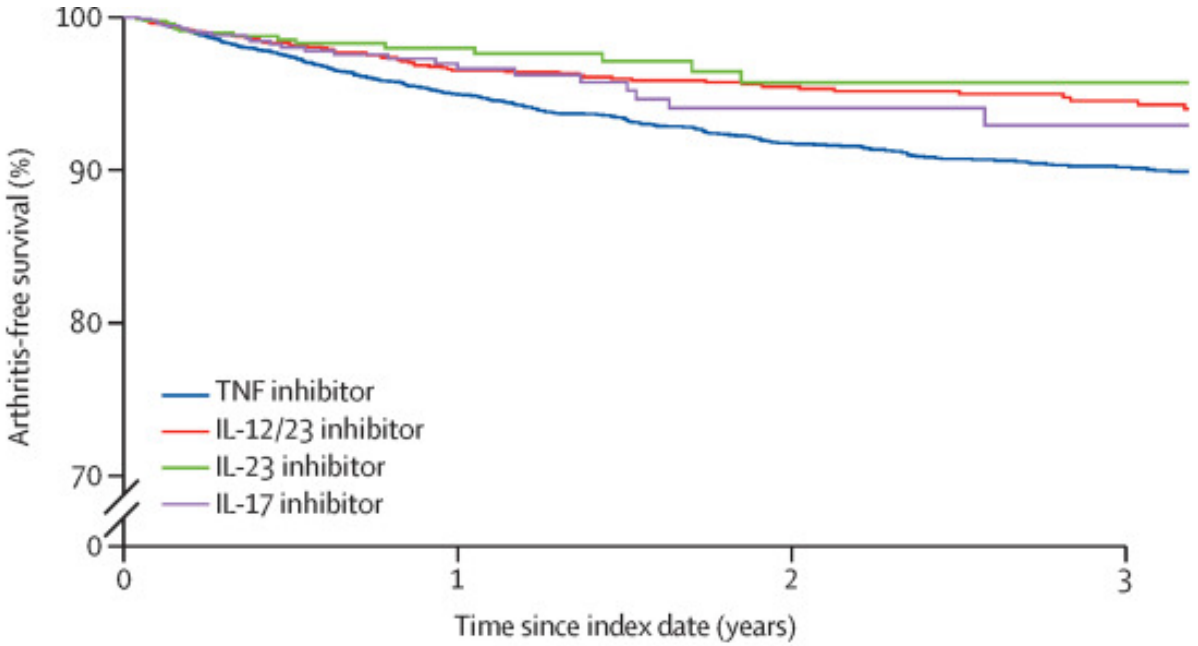




Felquer et al. ARD (2021), Gisondi et al. ARD (2021), Rosenthal et al. Rheumatology (2021)

Können wir bei PsO mittels Biologika-Therapie die Entwicklung einer PsA verhindern? Health record data

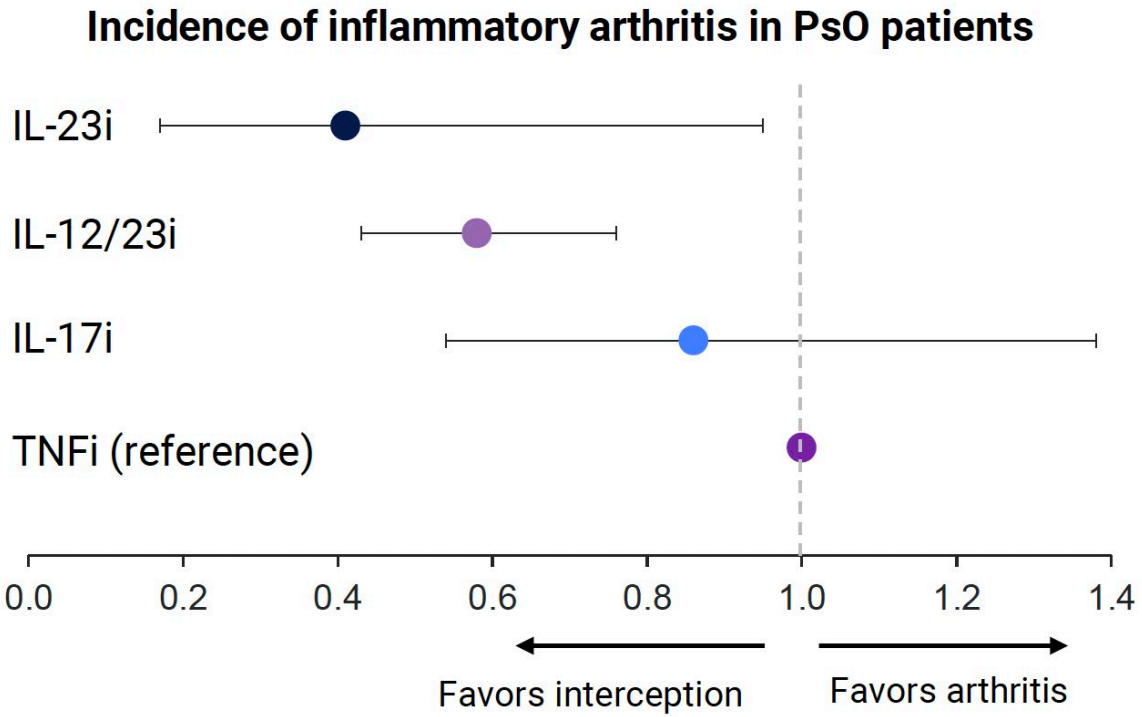


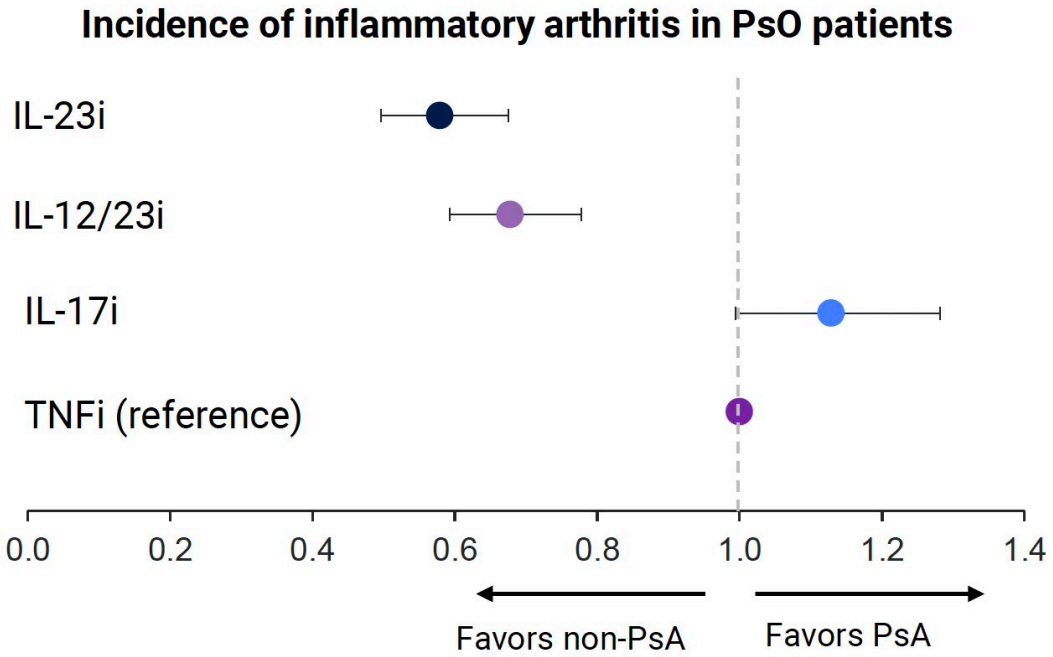


USZ Universitäts Spital Zürich

Singla et al. Lancet (2023)

Können wir bei PsO mittels Biologika-Therapie die Entwicklung einer PsA verhindern? Health record data

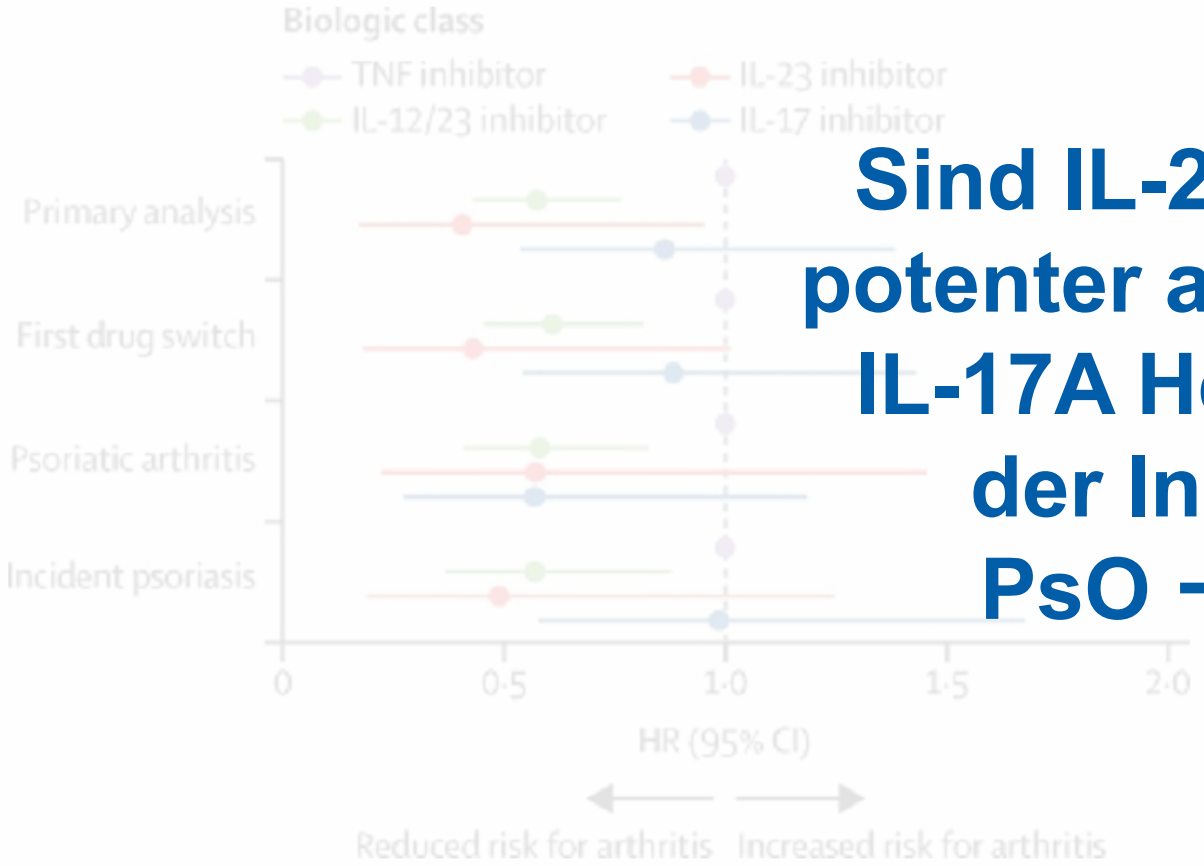




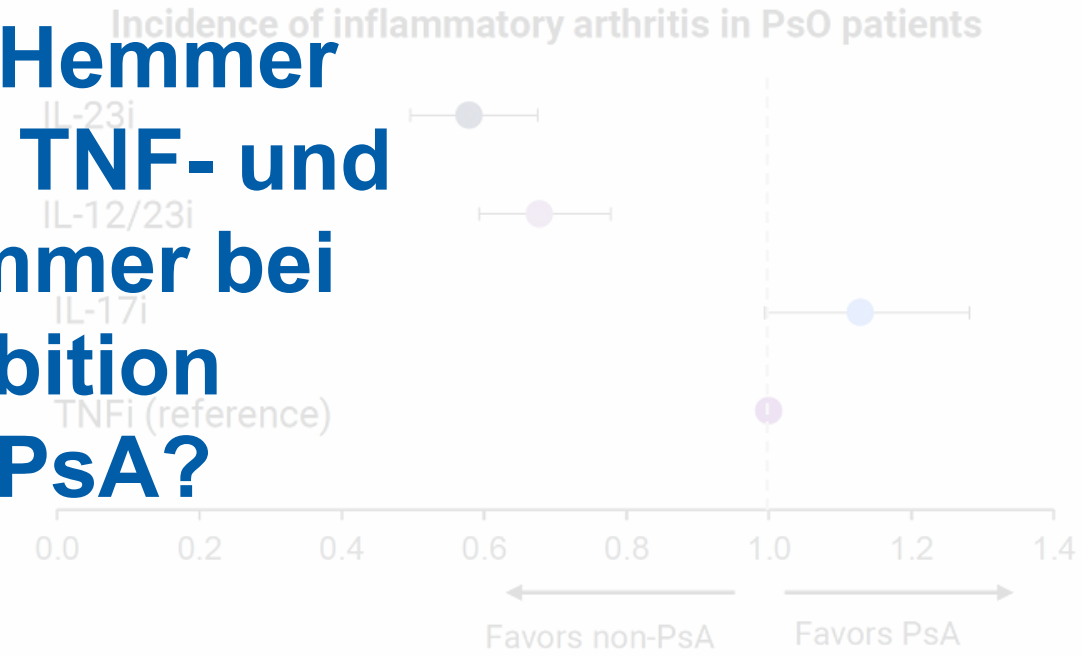
Retrospective study based on electronic history data included in Trinetx, a global network of electronic records of 199,875,420 patients

Singla et al. Lancet (2023) & Joven-Ibanez B et al. Ann Rheum Dis. 2024;83:168-169.

Können wir bei PsO mittels Biologika-Therapie die Entwicklung einer PsA verhindern?



Sind IL-23 Hemmer potenter als TNF- und IL-17A Hemmer bei der Inhibition PsO → PsA?



Retrospective study based on electronic history data included in Trinetx, a global network of electronic records of 199,875,420 patients

Singla et al. Lancet (2023) & Joven-Ibanez B et al. Ann Rheum Dis. 2024;83:168-169.

GRAPPA 2021 recommendations algorithm for the treatment of PsA

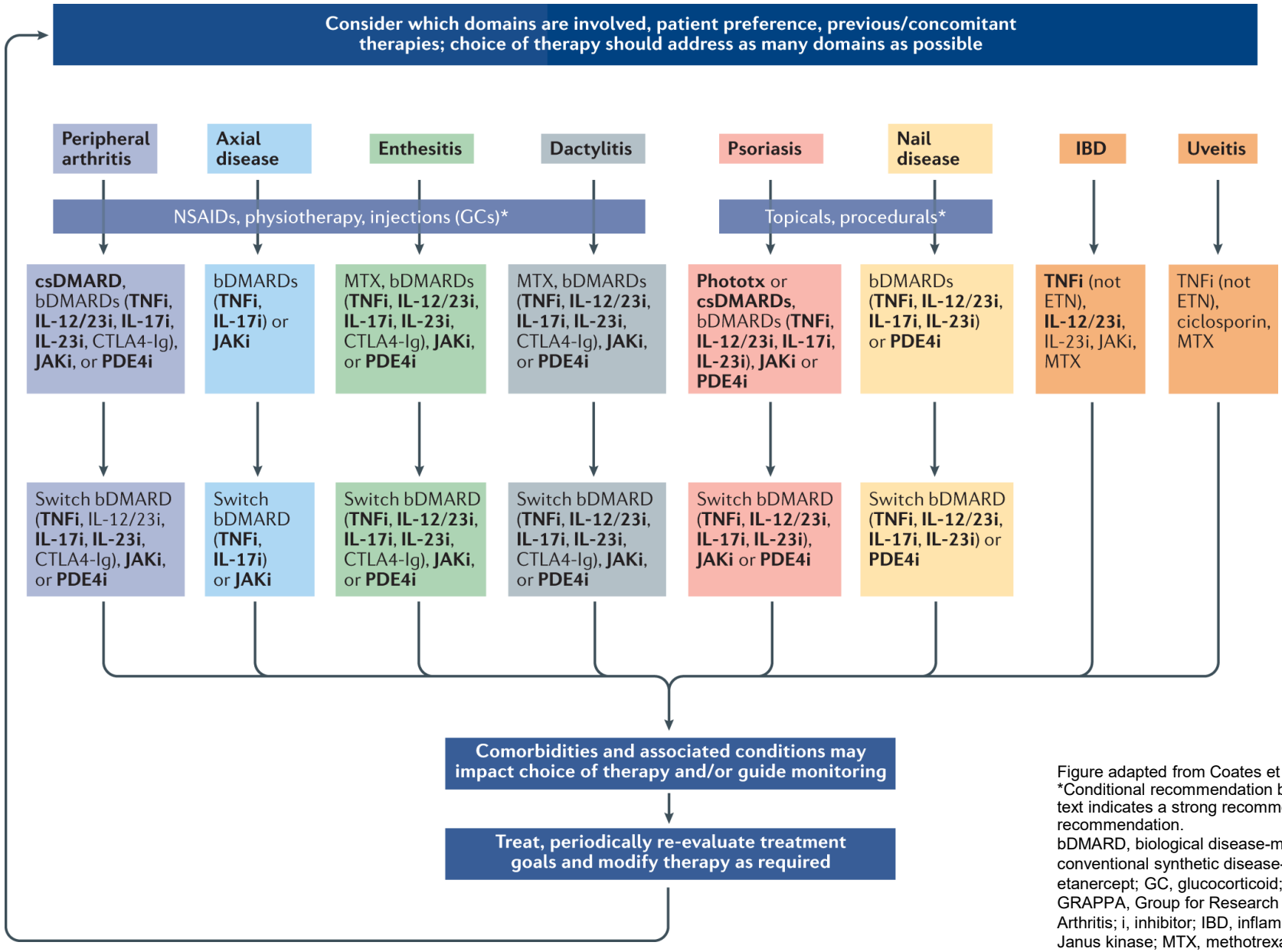
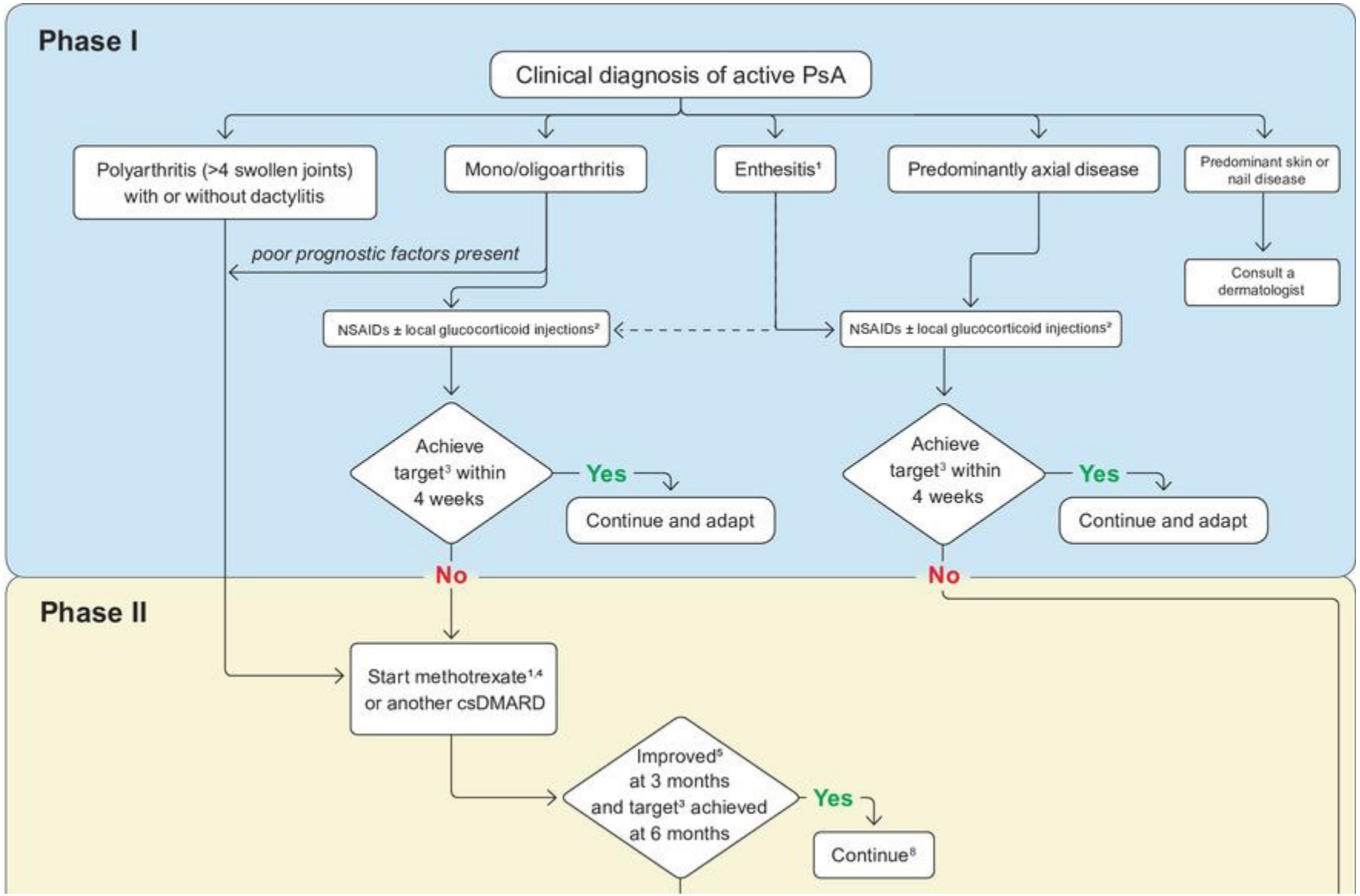


Figure adapted from Coates et al. 2022.
*Conditional recommendation based on data from abstracts only. Bold text indicates a strong recommendation, standard text a conditional recommendation.
bDMARD, biological disease-modifying antirheumatic drug; csDMARD, conventional synthetic disease-modifying antirheumatic drug; ETN, etanercept; GC, glucocorticoid;
GRAPPA, Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; i, inhibitor; IBD, inflammatory bowel disease; IL, interleukin; JAK, Janus kinase; MTX, methotrexate; NSAID, non-steroidal anti-inflammatory drug; PDE4, phosphodiesterase-4; phototx, phototherapy; TNF, tumour necrosis factor.

Coates LC, et al. Nat Rev Rheumatol. 2022;18(8):465-79.

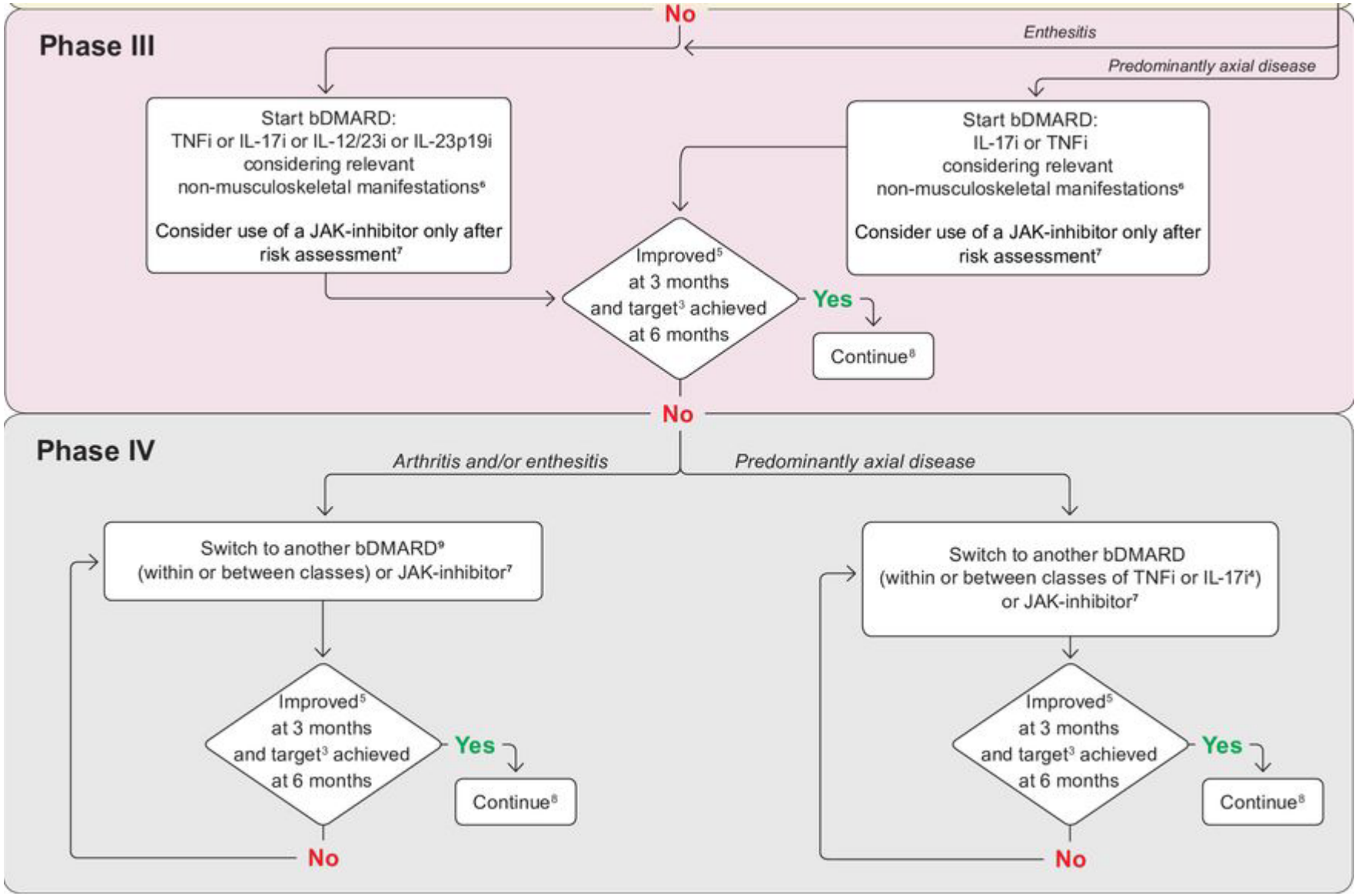
2023 EULAR recommendations algorithm for the management of PsA



USZ Universitäts Spital Zürich

Gossec L, Kerschbaumer A, Ferreira RJO, et al EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2023 update Annals of the Rheumatic Diseases 2024;83:706-719.

2023 EULAR recommendations algorithm for the management of PsA



USZ Universitäts Spital Zürich

Gossec L, Kerschbaumer A, Ferreira RJO, et al EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2023 update Annals of the Rheumatic Diseases 2024;83:706-719.

Kombinationstherapien - Observationsstudie

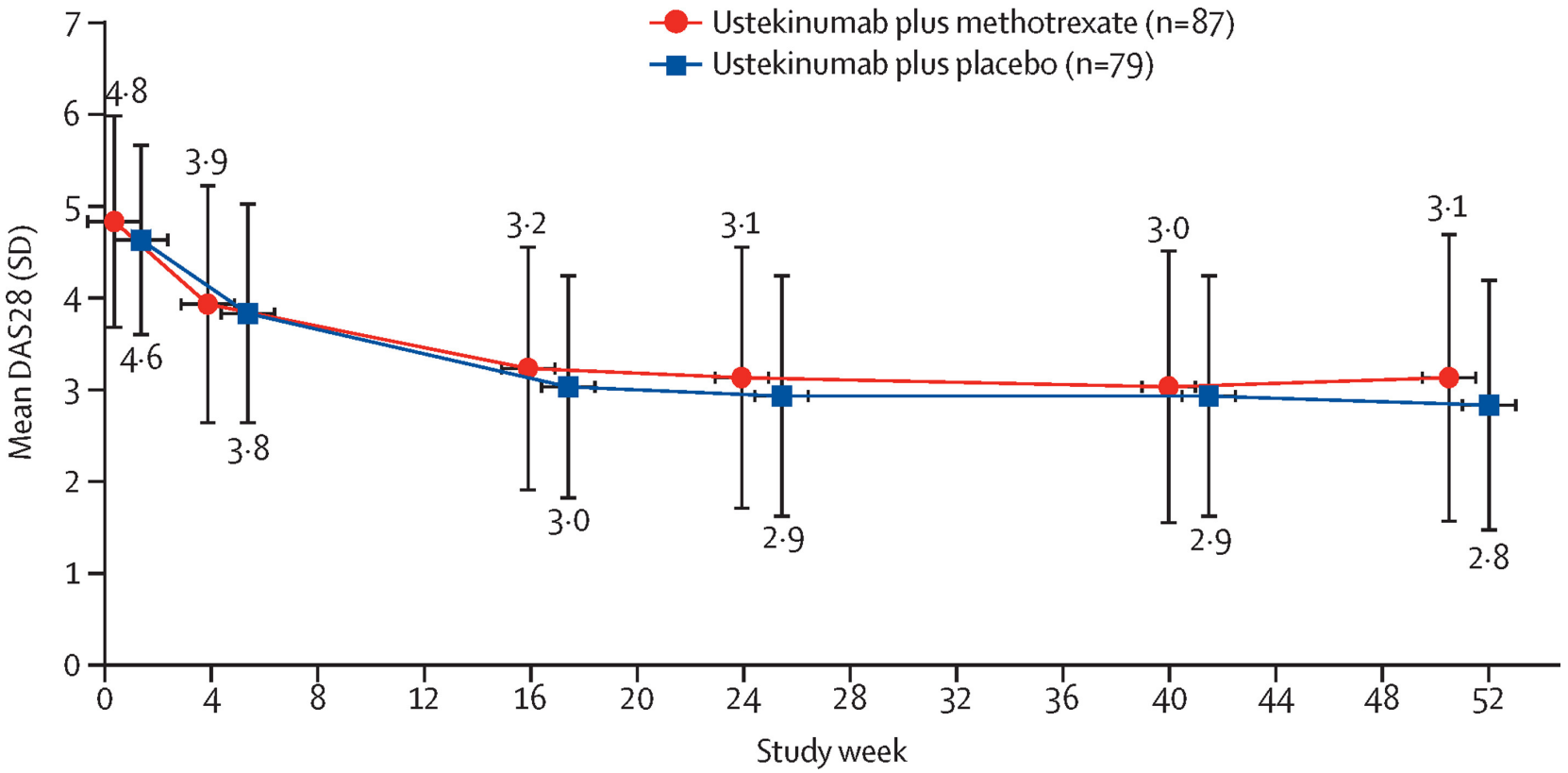
Insgesamt; Kein zusätzlicher Nutzen durch Kombinationstherapie MTX + TNFi

Table 2 Crude TNFi retention and adjusted HR for TNFi discontinuation (upper part of table), and crude proportion achieving remission and adjusted OR for clinical remission (lower part of table) for infliximab, adalimumab and etanercept, in co-medication with methotrexate compared with monotherapy

		Infliximab	Adalimumab	Etanercept
One-year TNFi retention (%) and adjusted* HR for TNFi discontinuation (ref=monotherapy)				
Czech republic	co-med/mono	NA	92%/79%	89%/89%
	HR (95% CI)	NA	**0.36 (0.17 to 0.77)**	1.06 (0.31 to 3.63)
Finland	co-med/mono	NA	87%/90%	95%/96%
	HR (95% CI)	NA	1.18 (0.41 to 3.35)	2.08 (0.31 to 13.94)
Italy	co-med/mono	80%/87%	82%/88%	85%/89%
	HR (95% CI)	1.45 (0.63 to 3.35)	1.63 (0.98 to 2.72)	1.45 (0.84 to 2.51)
Portugal	co-med/mono	NA	89%/97%	89%/84%
	HR (95% CI)	NA	**7.39 (1.46 to 37.54)**	0.60 (0.28 to 1.30)
Spain	co-med/mono	NA	82%/82%	77%/78%
	HR (95% CI)	NA	0.70 (0.26 to 1.90)	0.76 (0.30 to 1.90)
Slovenia	co-med/mono	NA	80%/67%	NA
	HR (95% CI)	NA	0.90 (0.41 to 1.96)	NA
Iceland	co-med/mono	81%/78%	NA	NA
	HR (95% CI)	0.81 (0.39 to 1.70)	NA	NA
Switzerland	co-med/mono	77%/73%	79%/72%	80%/78%
	HR (95% CI)	0.78 (0.39 to 1.58)	0.67 (0.45 to 1.00)	0.81 (0.49 to 1.35)
Sweden	co-med/mono	71%/63%	78%/66%	76%/74%
	HR (95% CI)	**0.65 (0.50 to 0.85)**	**0.58 (0.47 to 0.72)**	0.94 (0.77 to 1.14)
Norway	co-med/mono	NA	83%/68%	81%/70%
	HR (95% CI)	NA	0.59 (0.24 to 1.48)	0.59 (0.35 to 1.01)
Denmark	co-med/mono	64%/45%	71%/70%	70%/72%
	HR (95% CI)	**0.56 (0.41 to 0.78)**	0.93 (0.70 to 1.24)	1.12 (0.77 to 1.62)
Crude proportion (%) reaching remission at 12 months and adjusted* OR for clinical remission (ref=monotherapy)				
Pooled	co-med/mono	38%/32%	47%/38%	44%/42%
	OR (95% CI)	**1.55 (1.21 to 1.98)**	**1.45 (1.23 to 1.72)**	1.12 (0.95 to 1.31)

Lindström U, Di Giuseppe D, Delcoigne B, *et al*
Effectiveness and treatment retention of TNF inhibitors when used as monotherapy versus comedication with csDMARDs in 15 332 patients with psoriatic arthritis. Data from the EuroSpA collaboration
Annals of the Rheumatic Diseases 2021;**80:**1410-1418.

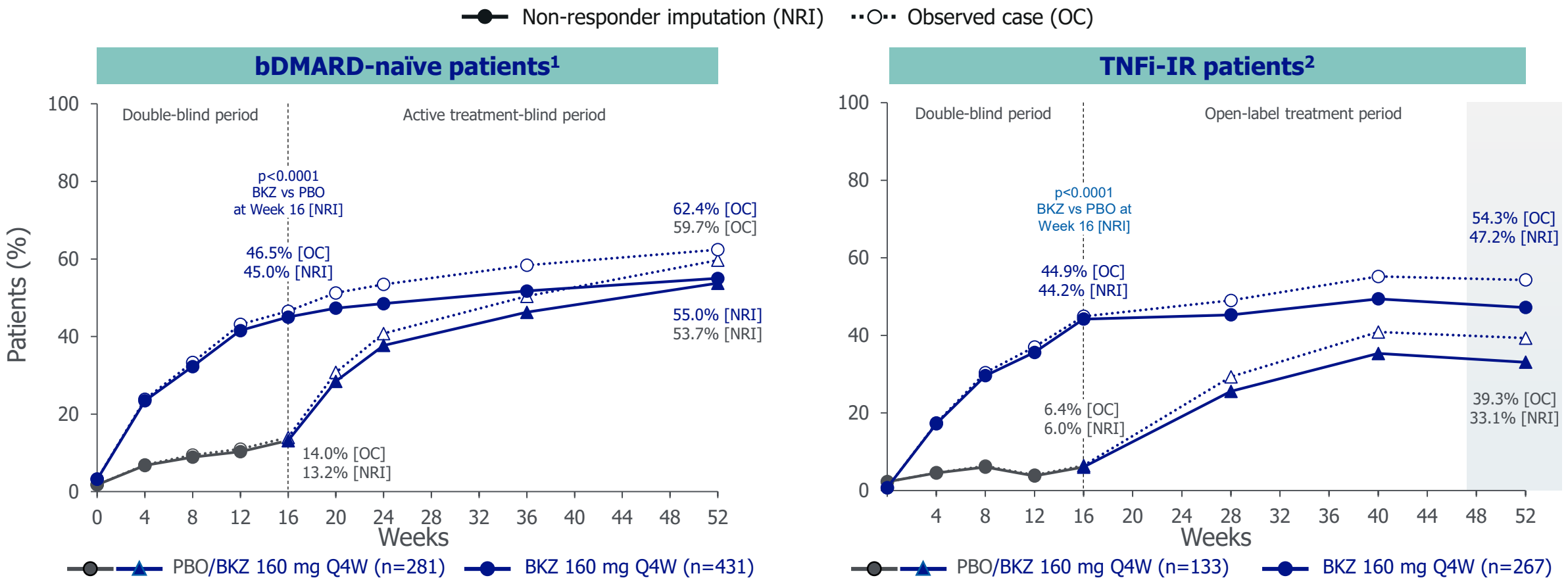
Kombinationstherapien - RCT



Phase IIIb MUST trial: Kein Benefit von MTX zu Ustekinumab

Koehm M, Rossmanith T, Foldenauer AC, Herrmann E, Brandt-Jürgens J, Burmester GR, Kellner H, Kiltz U, Kofler DM, Rech J, Mojtahed-Poor S, Jonetzko C, Burkhardt H, Behrens F; MUST Investigator Group. Methotrexate plus ustekinumab versus ustekinumab monotherapy in patients with active psoriatic arthritis (MUST): a randomised, multicentre, placebo-controlled, phase 3b, non-inferiority trial. Lancet Rheumatol. 2023 Jan;5(1):e14-e23. doi: 10.1016/S2665-9913(22)00329-0. PMID: 38251504.

MDA response - Bimekizumab in bDMARD-Naïve and TNFi-IR PsA Patients



Consistent MDA responses were also observed **irrespective of concomitant MTX** in bDMARD-naïve patients

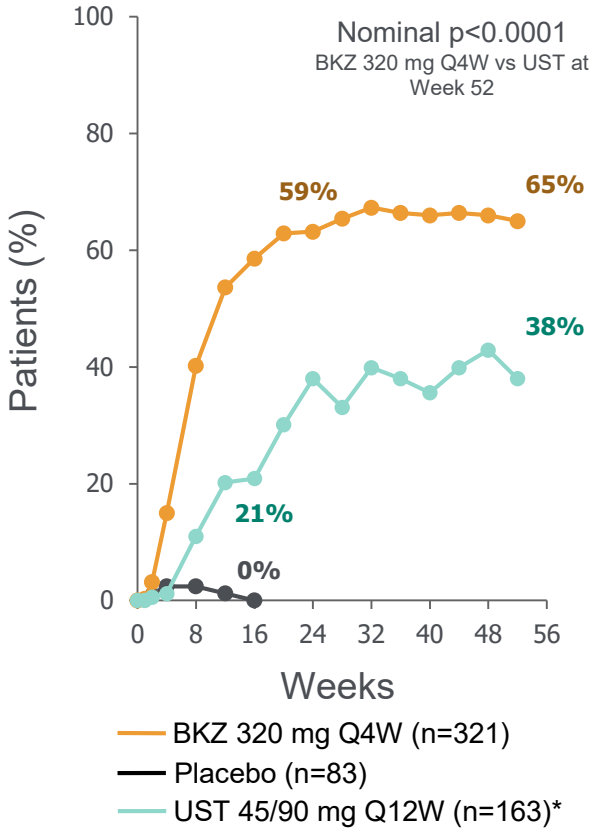
USZ Universitäts Spital Zürich

1. Adapted from Ritchlin CT, et al. Ann Rheum Dis. 2023;82(11):1404–14. 2. Adapted from Coates LC, et al. RMD Open. 2024;10(1):e003855. 3. McInnes I, et al. Ann Rheum Dis. 2023;82:1133–34. Non-responder imputation; observed case. Randomised set. Data from BE OPTIMAL (bDMARD-naïve patients) and BE COMPLETE + OLE (TNFi-IR patients). BE OPTIMAL: p value was calculated using a logistic regression model with treatment, bone erosion at baseline, and region as stratification factors; BE COMPLETE: p value was calculated using a logistic regression model with treatment, prior TNFi exposure and region as stratification factors. bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; MDA: minimal disease activity; MTX: methotrexate; NRI: non-responder imputation; OC: observed case; OLE: open-label extension; PBO: placebo; Q4W: every 4 weeks; TNFi-IR: tumour necrosis factor inhibitor-inadequate response.

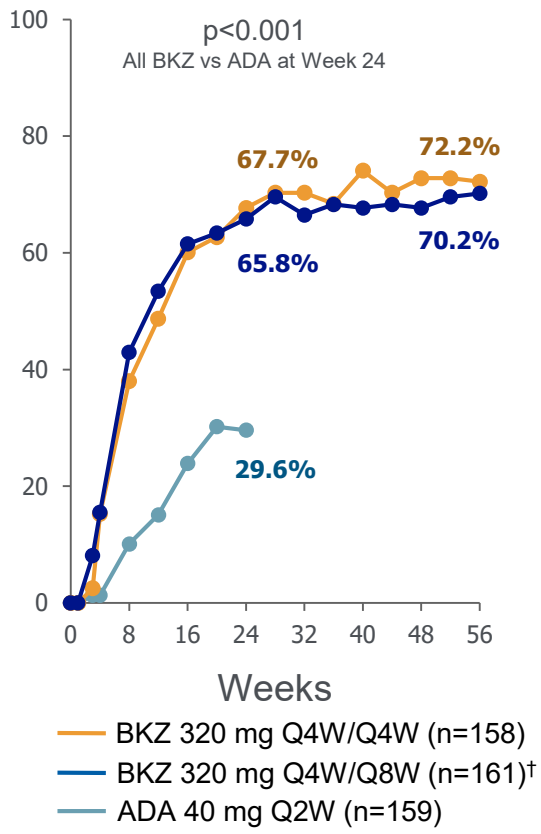
Bimekizumab vs Ustekinumab, Adalimumab and Secukinumab in PsO - RCT

PASI100 during Year 1 with BKZ vs active comparators

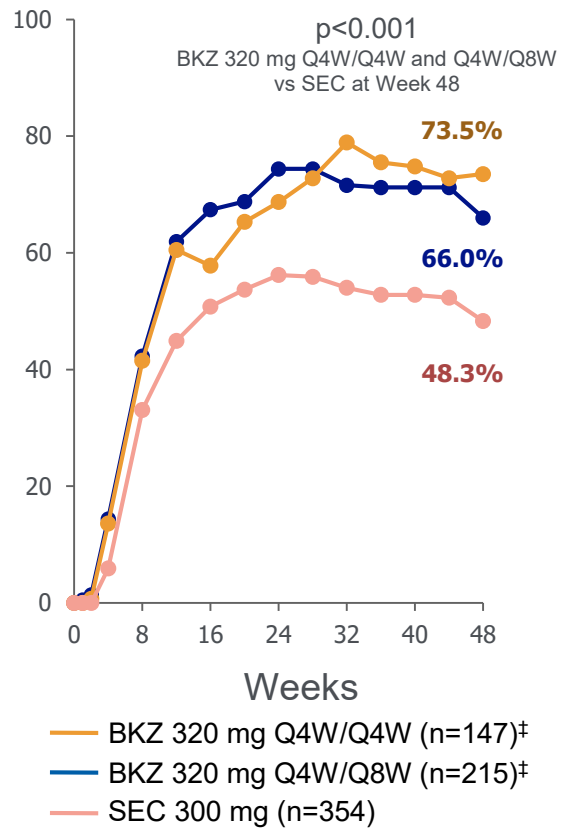
BE VIVID (BKZ vs UST)[1]



BE SURE (BKZ vs ADA)[2]



BE RADIANT (BKZ vs SEC)[3]



USZ Universitäts Spital Zürich

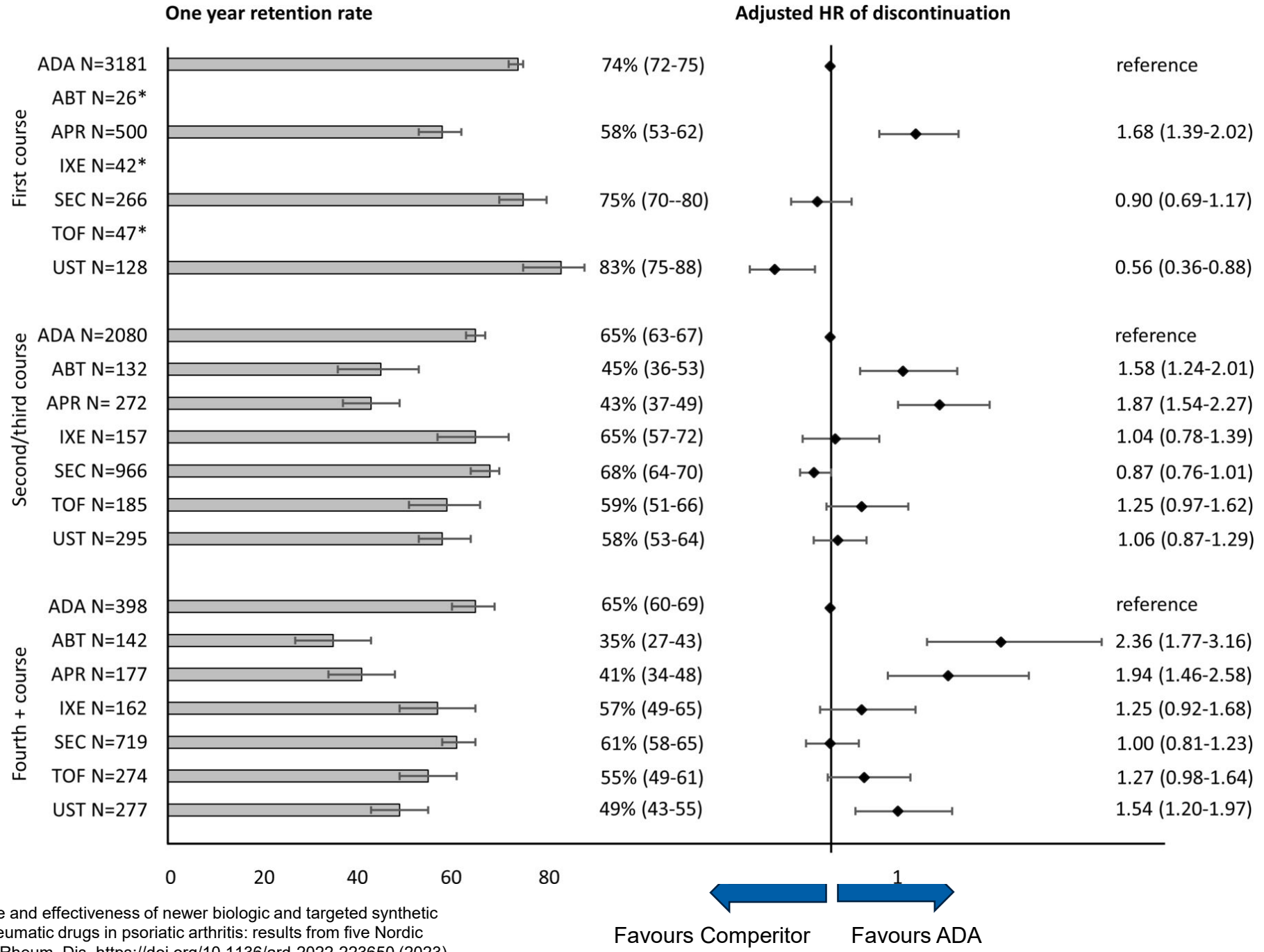
Non-responder imputation. In BE VIVID, PASI100 at Week 16 was a ranked secondary endpoint. In BE SURE, PASI100 at Week 24 was a ranked secondary endpoint. In BE RADIANT, PASI100 at Week 48, was a ranked secondary endpoint. In BE SURE, patients in the BKZ Q4W/Q8W arm switched at Week 16 from Q4W to BKZ Q8W. *45 mg for patients ≤100 kg or 90 mg for patients >100 kg, starting with a loading dose of 45/90 mg at weeks 0 and 4, and then 45/90 mg Q12W thereafter; †Patients received bimekizumab at a dose of 320 mg Q4W to Week 16, then Q8W thereafter. ‡Patients received BKZ at a dose of 320 mg Q4W or SEC at a dose of 300 mg weekly to Week 4, followed by Q4W to Week 48. At Week 16, patients receiving BKZ underwent randomisation in a 1:2 ratio, to receive maintenance dosing Q4W or Q8W to Week 48.

1. Adapted from Reich K et al. Lancet. 2021;397(10273):487–498.
2. Adapted from Warren RB et al. N Engl J Med. 2021;385(2):130–141.
3. Adapted from Reich K et al. N Engl J Med. 2021;385(2):142–152.
4. Coates LC et al. Nat Rev Rheumatol. 2022;18(8):465–479.

Retention in PsA in observational registries

Retention rate and treatment discontinuation at 1-year follow-up.

Results of multivariable Cox regression analyses presented by b/tsDMARD treatment course.



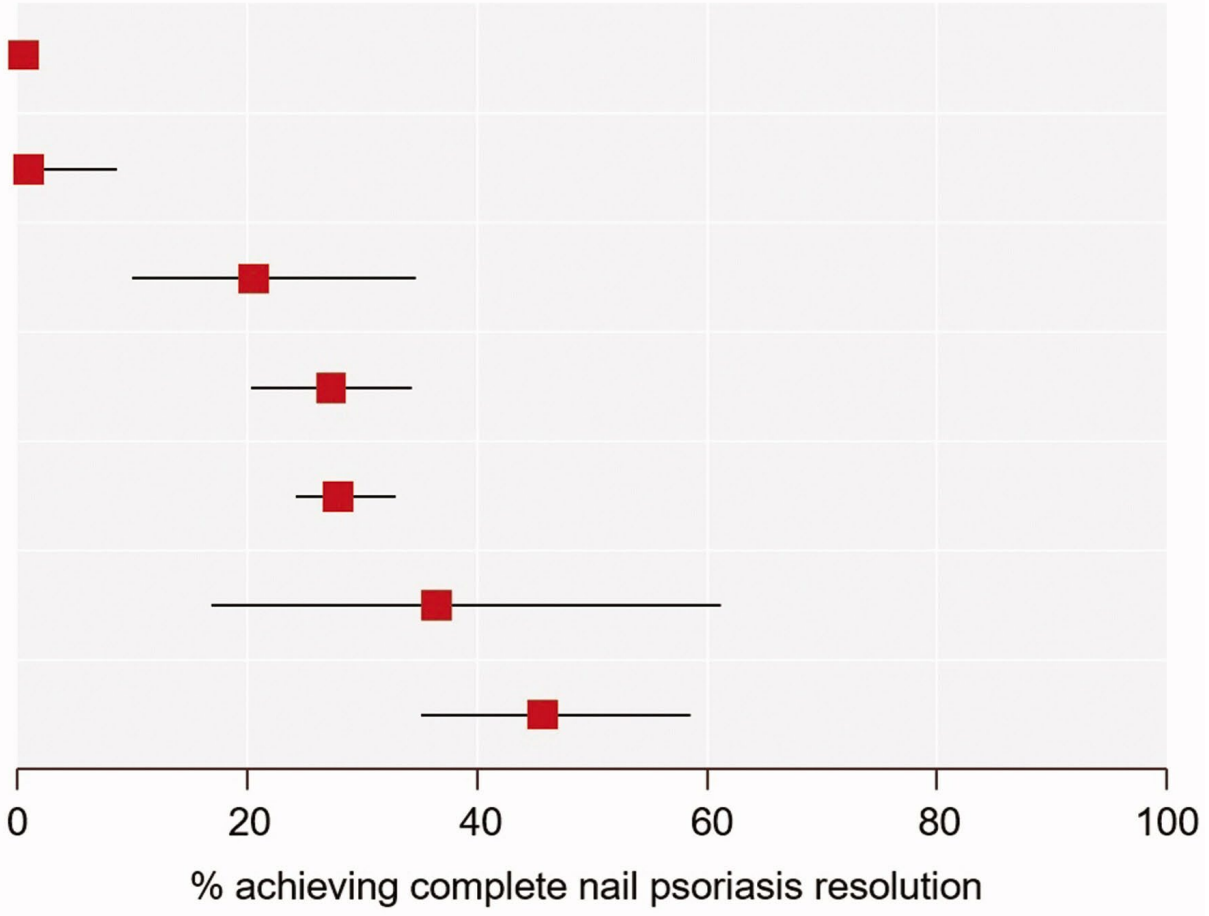
USZ Universitäts Spital Zürich

Glintborg, B. et al. Uptake and effectiveness of newer biologic and targeted synthetic disease-modifying antirheumatic drugs in psoriatic arthritis: results from five Nordic biologics registries. Ann. Rheum. Dis. https://doi.org/10.1136/ard-2022-223650 (2023).

Nagelpsoriasis – Network Meta Analysis

Forest plot of treatment differences (and 95% credibility intervals) for complete resolution of nail psoriasis at weeks 24–26.

Placebo	0.12 (0.00-1.13)
Infliximab	0.80 (0.00-8.90)
Ustekinumab	20.81 (10.19-35.18)
Guselkumab	27.70 (21.07-35.13)
Adalimumab	28.30 (24.37-32.36)
Brodalumab	36.98 (16.99-60.96)
Ixekizumab	46.45 (35.06-58.04)

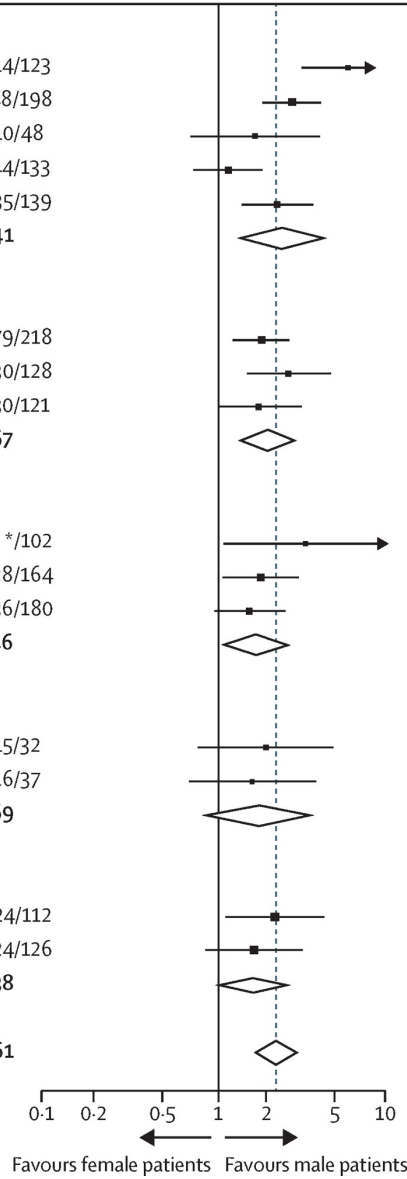


USZ Universitäts Spital Zürich

Reich K, Conrad C, Kristensen LE, Smith SD, Puig L, Rich P, Sapin C, Holzkaemper T, Koppelhus U, Schuster C. Network meta-analysis comparing the efficacy of biologic treatments for achieving complete resolution of nail psoriasis. J Dermatolog Treat. 2022 May;33(3):1652-1660. doi: 10.1080/09546634.2021.1892024. Epub 2021 Mar 1. PMID: 33641593.

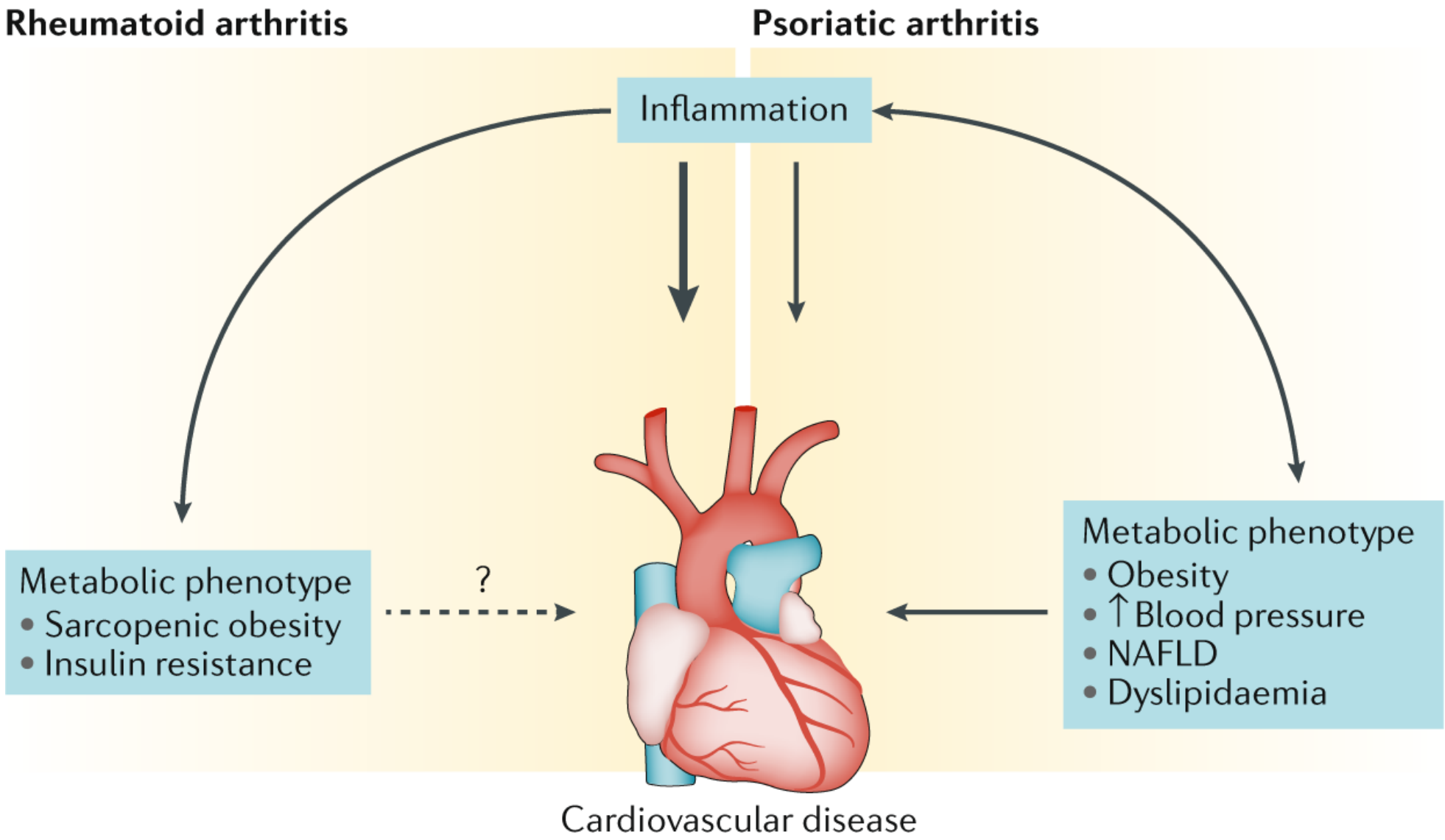
Sex differences – MDA from RCTs

	Medication (dose, interval)	Male patients, events/total	Female patients, events/total	OR (95% CI)	Relative weight, %
TNF inhibitor					
CONTROL[28]	Adalimumab (40 mg once every 2 weeks)	57/122	14/123	6·83 (3·53–13·22)	6·0
EXCEED[49]	Adalimumab (40 mg once every 2 weeks)	114/229	48/198	3·10 (2·04–4·69)	9·4
OPAL Broaden[74]	Adalimumab (40 mg once every 2 weeks)	17/52	10/48	1·85 (0·75–4·57)	3·9
SEAM-PsA[31]	Etanercept (50 mg once weekly)	58/151	44/133	1·26 (0·77–2·05)	8·2
SEAM-PsA[31]	Etanercept (50 mg once weekly) + methotrexate	66/144	35/139	2·51 (1·52–4·16)	8·0
Total TNF inhibitor		**698**	**641**	**2·62 (1·54–4·44)**	**35·5**
Heterogeneity: τ^2=0·30; χ^2=17·87; df=4 (p<0·01); I^2=78%					
IL-17 inhibitor					
EXCEED[49]	Secukinumab (300 mg once every 4 weeks)	106/208	79/218	1·83 (1·24–2·69)	9·9
SPIRIT P1+P2[46]	Ixekizumab (80 mg once every 2 weeks)	44/98	30/128	2·66 (1·50–4·71)	7·1
SPIRIT P1+P2[46]	Ixekizumab (80 mg once every 4 weeks)	40/108	30/121	1·78 (1·01–3·15)	7·1
Total IL-17 inhibitor		**414**	**467**	**1·99 (1·50–2·63)**	**24·1**
Heterogeneity: τ^2=0; χ^2=1·32; df=2 (p=0·52); I^2=0%					
IL-23 inhibitor					
COSMOS[58]	Guselkumab (100 mg once every 8 weeks)	*/85	*/102	3·33 (1·10–10·04)	3·0
DISCOVER-1+2[61]	Guselkumab (100 mg once every 4 weeks)	57/209	28/164	1·82 (1·10–3·03)	8·4
DISCOVER-1+2[61]	Guselkumab (100 mg once every 8 weeks)	55/195	36/180	1·57 (0·97–2·54)	7·9
Total IL-23 inhibitor		**489**	**446**	**1·79 (1·29–2·50)**	**19·3**
Heterogeneity: τ^2=0; χ^2=1·78; df=2 (p=0·41); I^2=0%					
IL-12/23i					
MUST[71]	Ustekinumab (45 mg every 12 weeks)	30/47	15/32	2·00 (0·80–4·99)	3·8
MUST[71]	Ustekinumab (45 mg every 12 weeks) + methotrexate (15 mg weekly)	28/50	16/37	1·67 (0·71–3·94)	4·2
Total IL-12/23i		**97**	**69**	**1·82 (0·97–3·40)**	**8·1**
Heterogeneity: τ^2=0; χ^2=0·08; df=1 (p=0·78); I^2=0%					
JAK or TYK2 inhibitor					
OPAL Bro+Bey[74]	Tofacitinib (5 mg twice daily)	34/114	24/112	2·03 (1·09–3·76)	6·6
OPAL Bro+Bey[74]	Tofacitinib (10 mg twice daily)	31/96	24/126	1·56 (0·85–2·85)	6·5
Total JAK or TYK2 inhibitor		**210**	**238**	**1·77 (1·15–2·73)**	**13·1**
Heterogeneity: τ^2=0; χ^2=0·36; df=1 (p=0·55); I^2=0%					
Total random effects for ACR20 (95% CI)		**1908**	**1861**	**2·12 (1·73–2·60)**	**100**
Heterogeneity: τ^2=0·03; χ^2=26·7, df=14 (p=0·02); I^2=47%					



USZ Universitäts Spital Zürich

Eder L, Mylvaganam S, Pardo Pardo J, Petkovic J, Strand V, Mease P, Colaco K. Sex-related differences in patient characteristics, and efficacy and safety of advanced therapies in randomised clinical trials in psoriatic arthritis: a systematic literature review and meta-analysis. Lancet Rheumatol. 2023 Dec;5(12):e716-e727. doi: 10.1016/S2665-9913(23)00264-3. Epub 2023 Nov 14. PMID: 38251562.

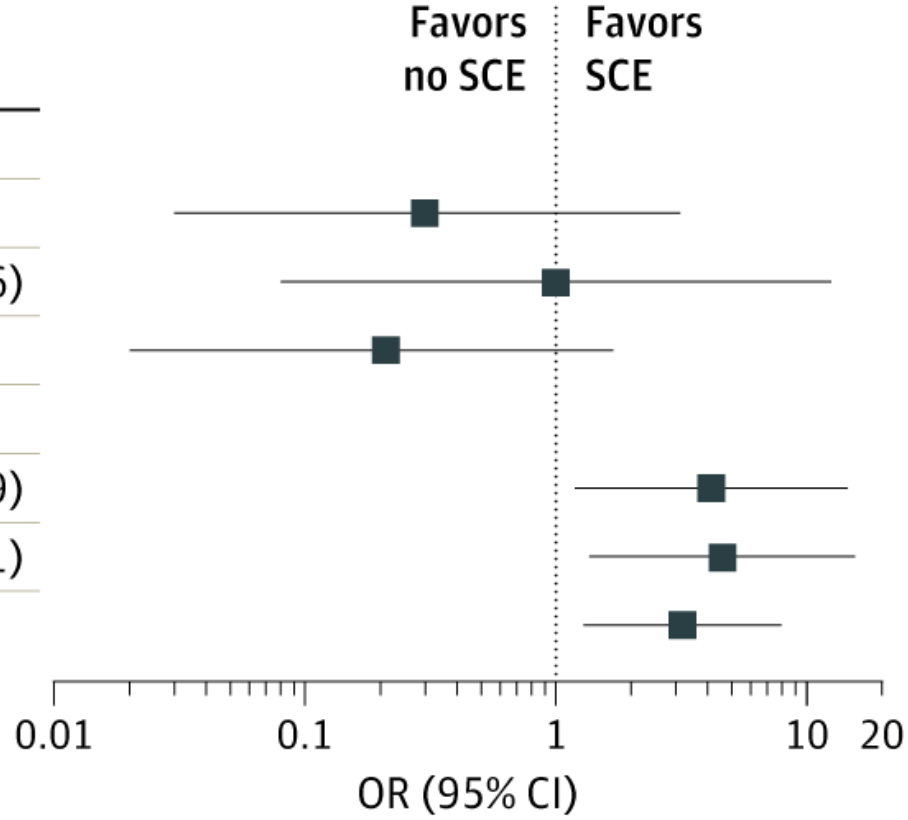


Ferguson LD, Siebert S, McInnes IB, Sattar N. Cardiometabolic comorbidities in RA and PsA: lessons learned and future directions. Nat Rev Rheumatol. 2019 Aug;15(8):461-474. doi: 10.1038/s41584-019-0256-0. Epub 2019 Jul 10. PMID: 31292564.

Kardiovaskuläres Risiko bei Psoriasis unter Ustekinumab

Association Between Ustekinumab Treatment Initiation and Severe Cardiovascular Events (SCEs) According to Cardiovascular Risk

Source	OR (95% CI)
Low cardiovascular risk (n = 22)[a]	
Main analysis[b]	0.30 (0.03-3.13)
Exposure including reinitiations and dose increases[c]	1.00 (0.08-12.56)
All cardiovascular events[d]	0.21 (0.02-1.69)
High cardiovascular risk (n = 76)[a]	
Main analysis[b]	4.17 (1.19-14.59)
Exposure including reinitiations and dose increases[c]	4.62 (1.36-15.61)
All cardiovascular events[d]	3.20 (1.29-7.92)



[b]Exposure: ustekinumab initiation; event: hospitalized in intensive care unit with acute coronary syndrome and stroke; 6-month periods.

USZ Universitäts Spital Zürich

Poizeau F, Nowak E, Kerbrat S, Le Nautout B, Droitcourt C, Drici MD, Sbidian E, Guillot B, Bachelez H, Ait-Oufella H, Happe A, Oger E, Dupuy A. Association Between Early Severe Cardiovascular Events and the Initiation of Treatment With the Anti-Interleukin 12/23p40 Antibody Ustekinumab. JAMA Dermatol. 2020 Nov 1;156(11):1208-1215. doi: 10.1001/jamadermatol.2020.2977. PMID: 32902568; PMCID: PMC7489429.

Kardiovaskuläres Risiko bei Psoriasis/Psoriasis-Arthritis

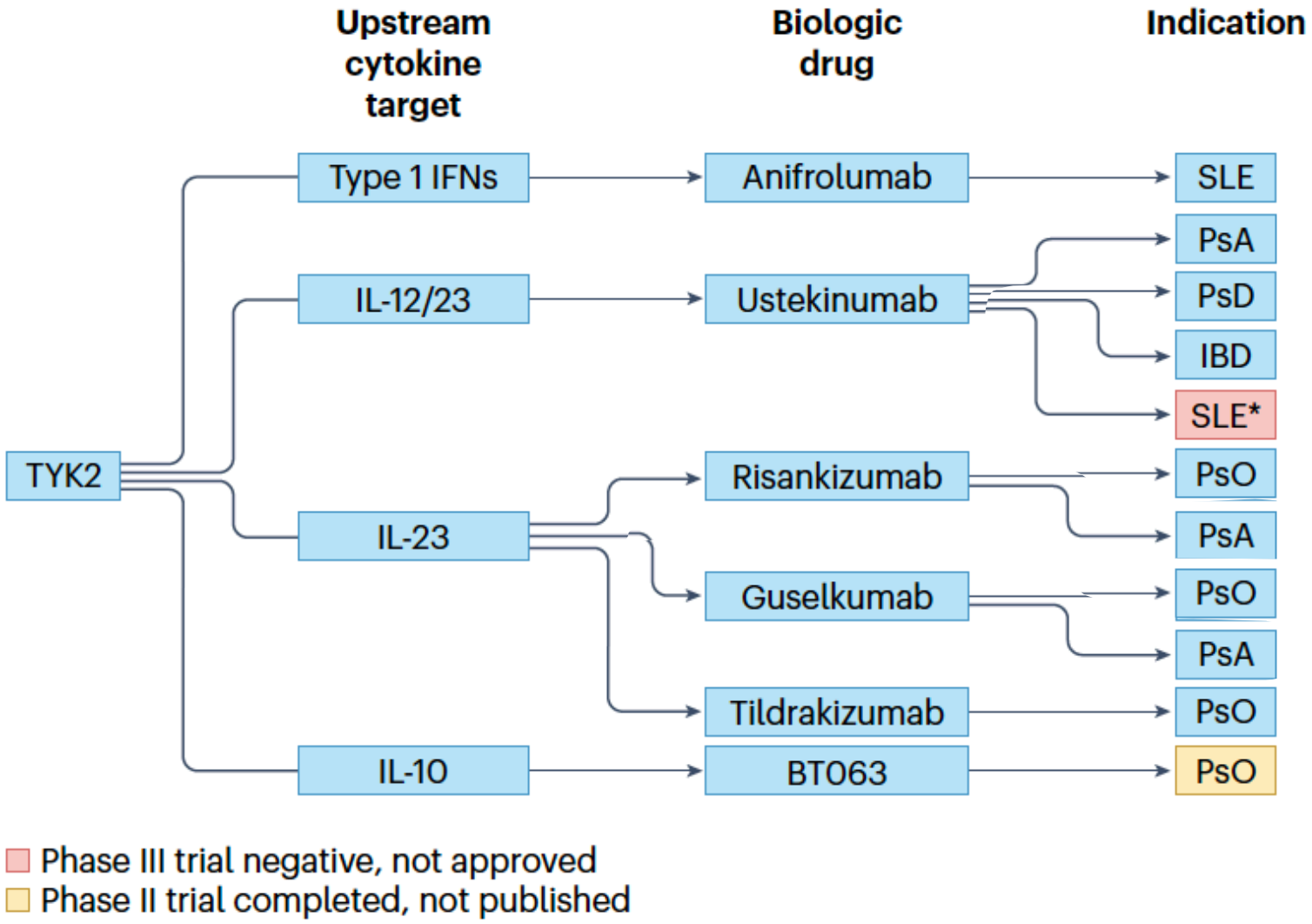
Target	IMID benefit	CVD benefit	Effect of IMID drug on CVD	Shared IMID–CVD target?
TNF	**In RA, PsA, AS** • Adalimumab • Certolizumab-pegol • Etanercept • Infliximab • Golimumab			Unclear
IL-17A/IL-17F	**In AS, PsA** • Secukinumab, ixekizumab • Bimekizumab	Preclinically tested		Unclear
IL-12 and IL-23p40	**In PsA** • Ustekinumab • Guselkumab • Risankizumab			No
T cell costimulation	**In RA** • Abatacept	Preclinically tested		Possibly according to preclinical data
JAK	**In RA, PsA** • Tofacitinib • Baricitinib • Upadacitinib • Filgotinib	**Preclinically tested (JAK2i)**		Unclear

Evidence of efficacy | Early evidence of efficacy | Under clinical evaluation | No evidence | Evidence of harm

USZ Universitäts Spital Zürich

Buch MH, Mallat Z, Dweck MR, Tarkin JM, O'Regan DP, Ferreira V, Youngstein T, Plein S. Current understanding and management of cardiovascular involvement in rheumatic immune-mediated inflammatory diseases. Nat Rev Rheumatol. 2024 Sep 2. doi: 10.1038/s41584-024-01149-x. Epub ahead of print. PMID: 39232242.

Neue Therapien: TYK2 Inhibitoren



Morand E, Merola JF, Tanaka Y, Gladman D, Fleischmann R. TYK2: an emerging therapeutic target in rheumatic disease. Nat Rev Rheumatol. 2024 Apr;20(4):232-240. doi: 10.1038/s41584-024-01093-w. Epub 2024 Mar 11. PMID: 38467779.

Neue Therapien: TYK2 Inhibitoren

Compound	Indication	Trial phase	Primary end point	Dosing regimen	Efficacy results (versus placebo)	Ref.
Deucravacitinib	Psoriasis	Phase III	PASI 75 at week 16	6 mg/day	58.4% versus 12.7%; *P*<0.0001	33
	Psoriasis	Phase III	PASI 75 at week 16	6 mg/day	53.0% versus 9.4%; *P*<0.0001	34
	PsA	Phase II	ACR20 at week 16	6 mg/day	52.9% versus 31.8%; *P*=0.0134	35[b]
				12 mg/day	62.7% versus 31.8%; *P*=0.0004	
	SLE	Phase II	SRI-4 at week 32	3 mg twice daily	58% versus 34%; *P*<0.001	38
				6 mg twice daily	49.5% versus 34.4%; *P*=0.02	
				12 mg/day	44.9% versus 34.4%; *P*=0.08	
Brepocitinib	Psoriasis	Phase II	Mean change in PASI at week 12	30 mg/day	−17.3% versus 7%; *P*<0.0001	61[a]
	PsA	Phase II	ACR20 at week 16	10 mg/day	64.5% versus 44.3%; (did not reach statistical significance)	62[b]
				30 mg/day	66.7% versus 44.3%; *P*=0.0197	
				60 mg/day	74.6% versus 44.3%; *P*=0.0006	
	IBD	Phase II	Total Mayo Score at week 8	10 mg/day	6.1 versus 7.9; *P*=0.009	63
				30 mg/day	5.6 versus 7.9; *P*=0.001	
				60 mg/day	4.7 versus 7.9; *P*<0.001	
Ropsacitinib	Psoriasis	Phase II	PASI 90 at week 16	400 mg/day	Risk difference 46.5%; *P*<0.0001	60[b,c]

IBD, inflammatory bowel disease; PASI, psoriasis area and severity index; PsA, psoriatic arthritis; SLE, systemic lupus erythematosus; SRI-4, SLE responder index 4. [a]This study assessed 4-week induction therapy with 30 mg/day or 60 mg/day brepocitinib or placebo, followed by 10 mg/day, 30 mg/day or 100 mg/day brepocitinib or placebo for 8 weeks. Only the 30 mg/day continuous treatment group, which showed the greatest change from baseline, is shown for simplicity. [b]Absolute responder and non-responder numbers were not reported for these studies. [c]This study also assessed 50 mg/day and 100 mg/day ropsacitinib, but the primary end point was not met for these doses and the risk difference was not reported.

Morand E, Merola JF, Tanaka Y, Gladman D, Fleischmann R. TYK2: an emerging therapeutic target in rheumatic disease. Nat Rev Rheumatol. 2024 Apr;20(4):232-240. doi: 10.1038/s41584-024-01093-w. Epub 2024 Mar 11. PMID: 38467779.

USZ Universitäts Spital Zürich

Psoriasis: von der Haut zum Gelenk

PD Dr. med. Raphael Micheroli MPH
Leitender Arzt
Klinik für Rheumatologie
UniversitätsSpital Zürich

26.09.2024

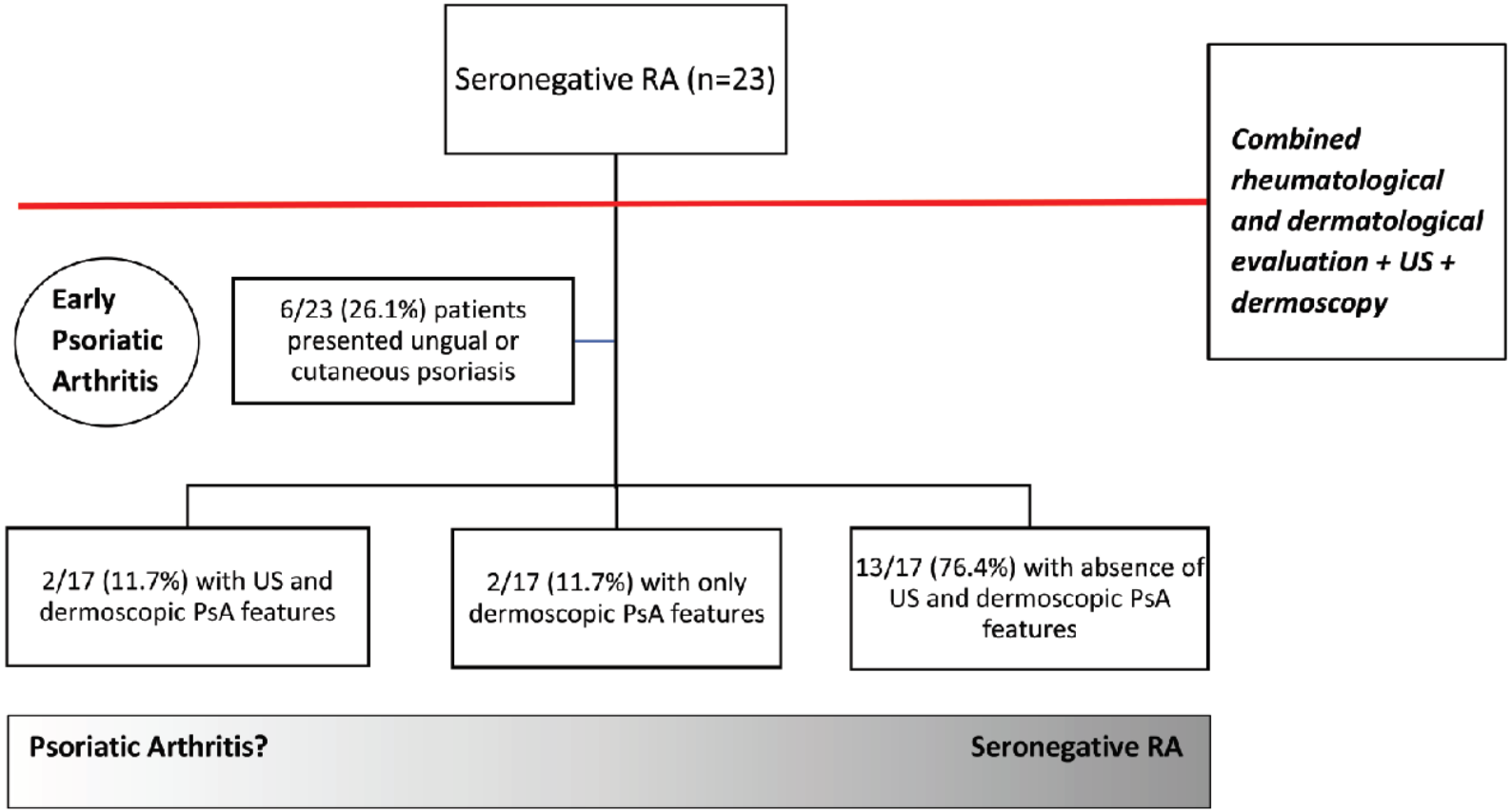
USZ Universitäts Spital Zürich

Psoriasis: vom Gelenk zur Haut

PD Dr. med. Raphael Micheroli MPH
Leitender Arzt
Klinik für Rheumatologie
UniversitätsSpital Zürich

26.09.2024

Patients with “undifferentiated arthritis”



Zabotti et al. Early Psoriatic Arthritis Versus Early Seronegative Rheumatoid Arthritis: Role of Dermoscopy Combined with Ultrasonography for Differential Diagnosis. J Rheumatol. 2018 May;45(5):648-654.

USZ Universitäts Spital Zürich

Vielen Dank für Ihre Aufmerksamkeit!

Raphael.Micheroli@usz.ch