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EGYPT 2024

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Our Expectation in PsA Management. Emerging Therapies and Research:

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PsA: Resetting Our Expectation in PsA Management

- Psoriatic Arthritis
  1. GRAPPA versus EULAR recommendations
  2. Axial PsA
  3. What to choose?
  4. New therapies
  5. Comorbidities

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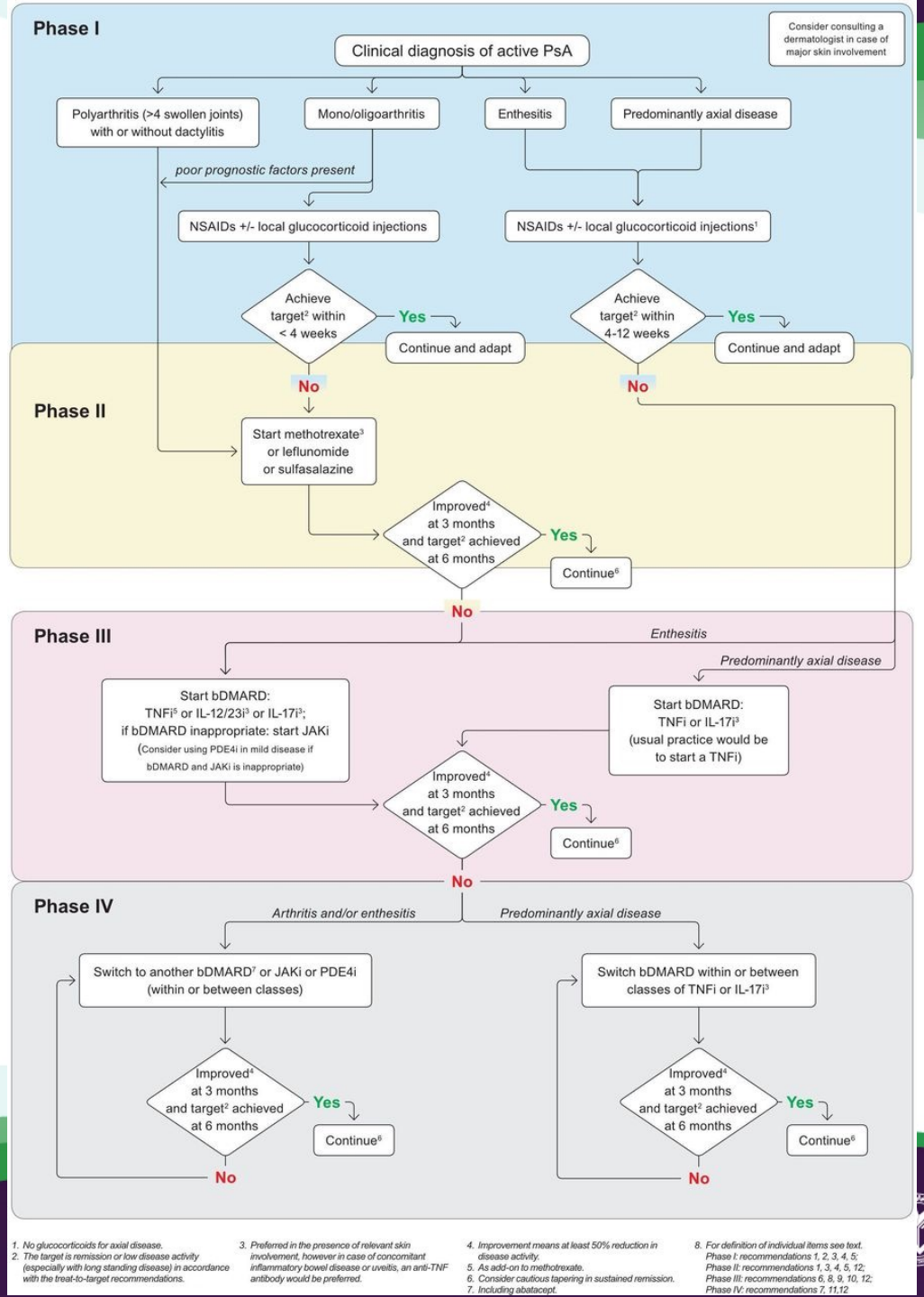
The EULAR 2019 algorithm for treatment of PsA with pharmacological non-topical treatments, bDMARDs, biological disease-modifying antirheumatic drugs



Laure Gossec et al. Ann Rheum Dis 2020;79:700-712

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2019 (current) version		Changes performed	2015 version
Recommendations			
4	In patients with polyarthritis, a csDMARD should be initiated rapidly, with **methotrexate preferred in those with relevant skin involvement.**	Modified	In patients with peripheral arthritis, particularly in those with many swollen joints, structural damage in the presence of inflammation, high ESR/CRP and/or clinically relevant extra-articular manifestations, csDMARDs should be considered at **an early stage**, with methotrexate preferred in those with relevant skin involvement.
6	In patients with peripheral arthritis and an inadequate response to at least one csDMARD, therapy with a bDMARD should be commenced; **when there is relevant skin involvement, an IL-17 inhibitor or IL-12/23 inhibitor may be preferred.**	Modified and merged	In patients with peripheral arthritis and an inadequate response to at least one csDMARD, therapy with a bDMARD, usually a TNF inhibitor, should be commenced. In patients with peripheral arthritis and an inadequate response to at least one csDMARD, in whom TNF inhibitors are not appropriate, bDMARDs targeting IL-12/23 or IL-17 pathways may be considered.
8	In patients with mild disease and an inadequate response to at least one csDMARD, **in whom neither a bDMARD nor a JAK inhibitor is appropriate**, a PDE4 inhibitor may be considered.	Modified	In patients with peripheral arthritis and an inadequate response to at least one csDMARD, in whom bDMARDs are not appropriate, a targeted synthetic DMARD such as a PDE4 inhibitor may be considered.
9	In patients with unequivocal enthesitis and insufficient response to NSAIDs or local glucocorticoid injections, therapy with a **bDMARD** should be considered.	Modified	In patients with active enthesitis and/or dactylitis and insufficient response to NSAIDs or local glucocorticoid injections, therapy with a bDMARD should be considered, which according to current practice is a TNF inhibitor.
10	In patients with predominantly axial disease which is active and has insufficient response to NSAIDs, therapy with a bDMARD should be considered, which according to current practice is a **TNF inhibitor; when there is relevant skin involvement, IL-17 inhibitor may be preferred.**	Modified	In patients with predominantly axial disease that is active and has insufficient response to NSAIDs, therapy with a bDMARD should be considered, which according to current practice is a TNF inhibitor.
11	In patients who fail to respond adequately to, or are intolerant of a bDMARD, switching **to another bDMARD or tsDMARD** should be considered*, including one switch within a class†.	Modified	In patients who fail to respond adequately to a bDMARD, switching to another bDMARD should be considered, including switching between TNF inhibitors.

Laure Gossec et al. Ann Rheum Dis 2020;79:700-712

2019 (current) version		Changes performed	2015 version
E	In managing patients with psoriatic arthritis, consideration should be given to each musculoskeletal manifestation and treatment decisions made accordingly.	New	Not applicable.
Recommendations			
5	In patients with monoarthritis or oligoarthritis, particularly with poor prognostic factors such as structural damage, high erythrocyte sedimentation rate/C reactive protein, dactylitis or nail involvement, a csDMARD should be considered.	New	Not applicable but partly covered in the recommendation above.
7	In patients with peripheral arthritis and an inadequate response to at least one csDMARD and at least one bDMARD, or when a bDMARD is not appropriate, **a JAK inhibitor may** be considered.	New	Not applicable.
12	In patients in sustained remission, **cautious tapering** of DMARDs may be considered.	New	Not applicable.

Laure Gossec et al. Ann Rheum Dis 2020;79:700-712

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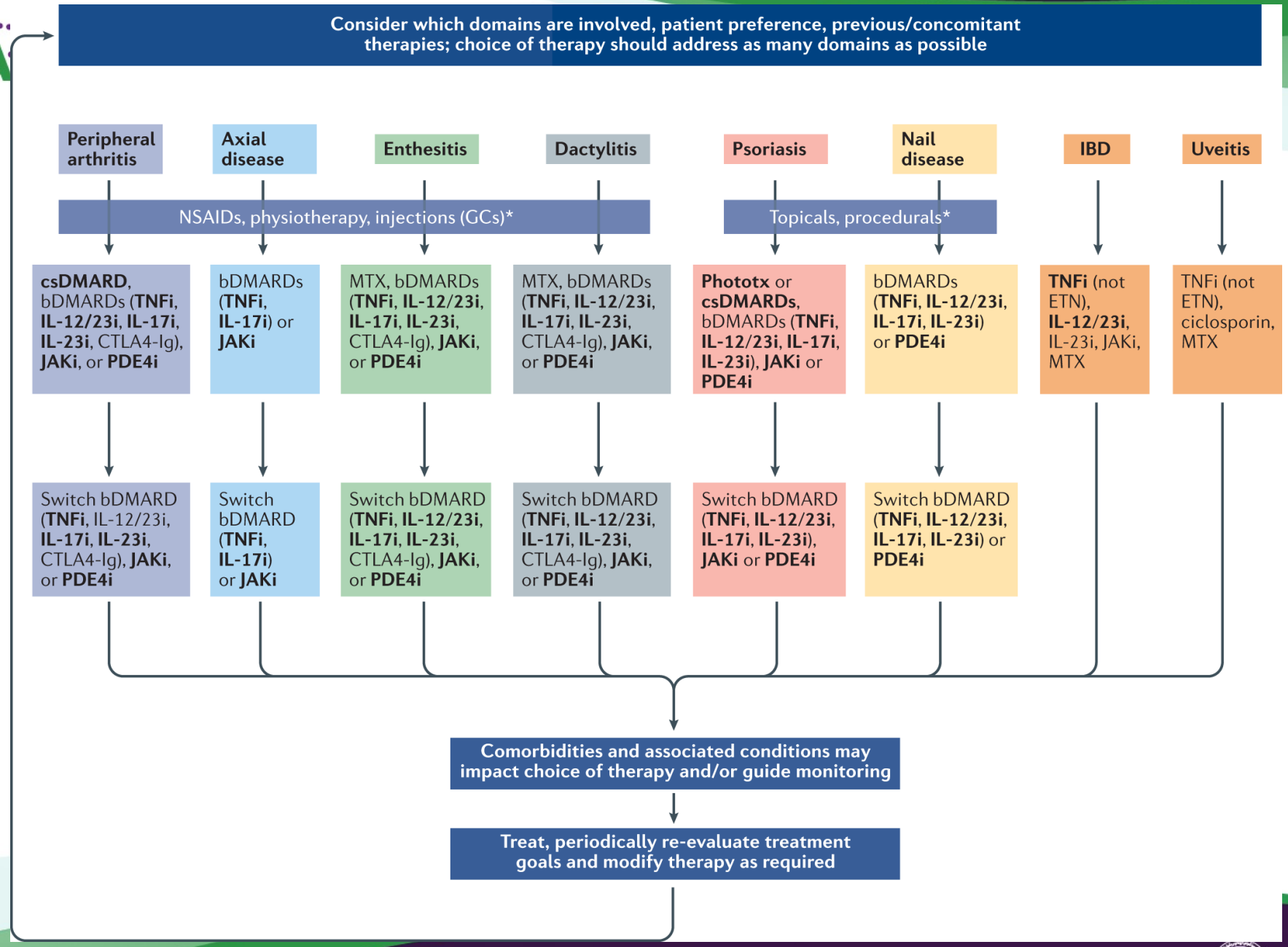

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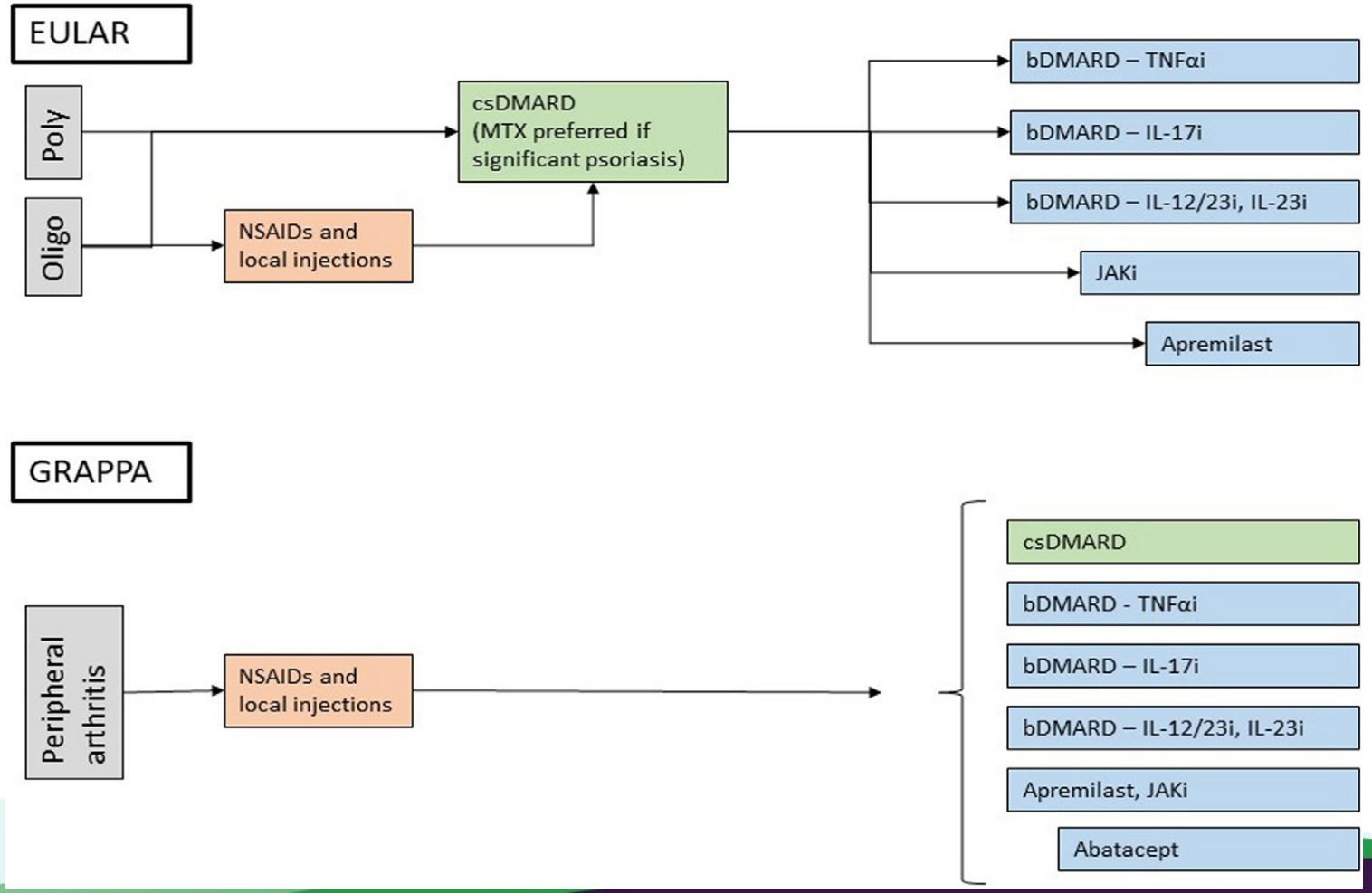
Coates, L.C., *Nat Rev Rheumatol* **18**, 465–479 (2022)c

Comorbidity	NSAIDs	GCs	MTX and/or LEF	TNF inhibitor	IL-17 inhibitor	IL-12/23 inhibitor, IL-23 inhibitor	JAK inhibitor	PDE4 inhibitor
Elevated risk of CVD	Caution	–	–	–	–	–	Caution	–
Congestive heart failure[a]	–	Caution	–	Avoid	–	–	–	–
Elevated risk for VTE	–	–	–	–	–	–	Caution	–
Obesity	–	–	Caution	–	–	–	–	–
Fatty liver disease	–	–	Avoid	–	–	–	–	–
Active hepatitis B or C	–	–	Avoid	Caution	Caution	Caution	Caution	Caution
HIV	–	–	–	Caution	Caution	Caution	Caution	Caution
Tuberculosis	–	–	–	Caution	Caution	Caution	Caution	Caution
History of recent malignancy	–	–	–	Caution	Caution	Caution	Caution	Caution
MS and/or demyelinating disease	–	–	–	Avoid	–	–	–	–
Depression and/or anxiety	–	–	–	–	–	–	–	Caution

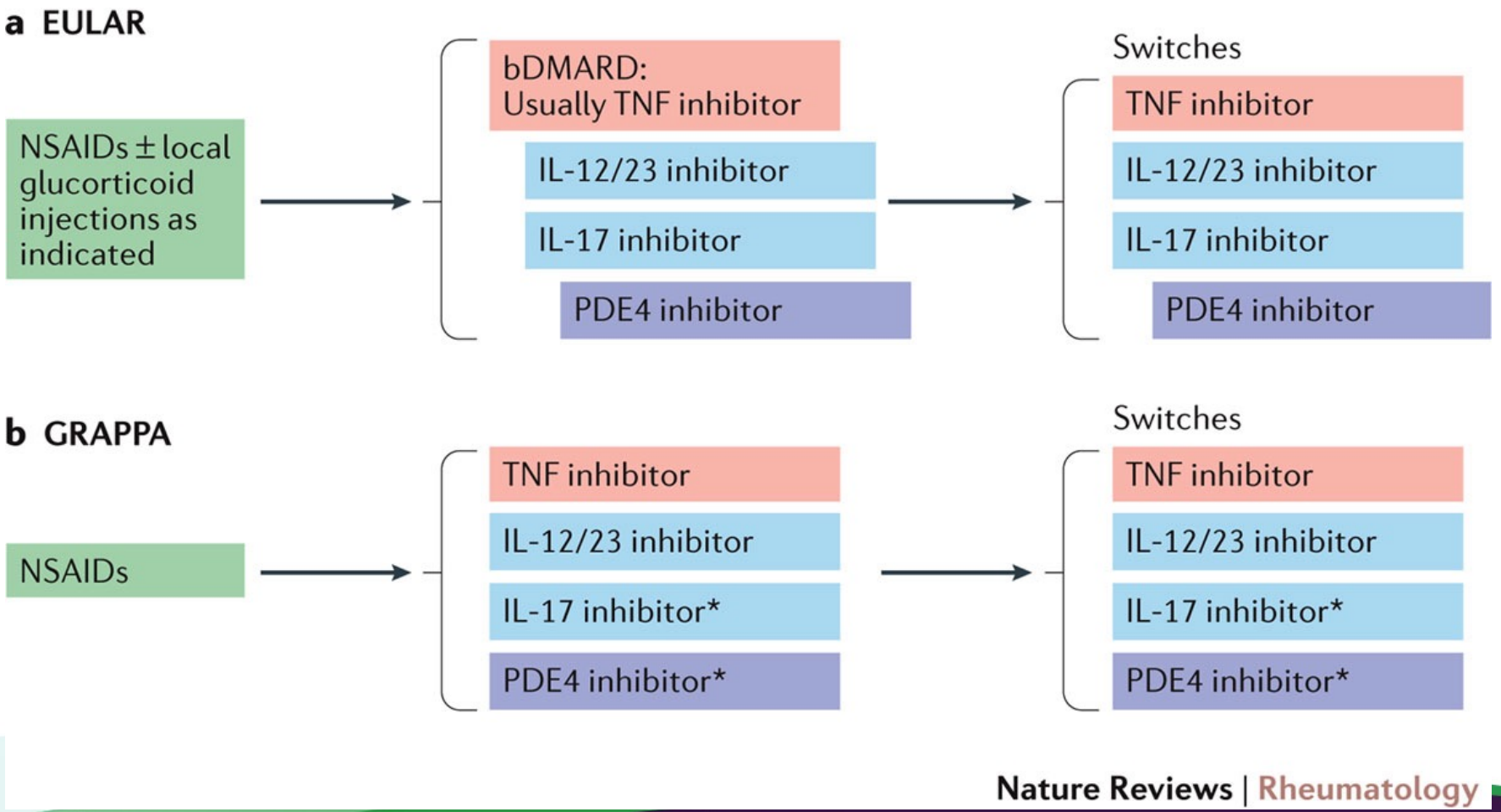
Coates, L.C., *Nat Rev Rheumatol* **18**, 465–479 (2022)

A comparison of drug algorithms for peripheral arthritis in the EULAR and GRAPPA recommendations



Coates L, Joint Bone Spine. 2023 Jan;90(1):105469.

Simplified EULAR and GRAPPA treatment algorithms for predominant entheseal psoriatic arthritis



Nature Reviews | Rheumatology

Gossec, L. *et al.* (2016)*Nat. Rev. Rheumatol.*.2016.183

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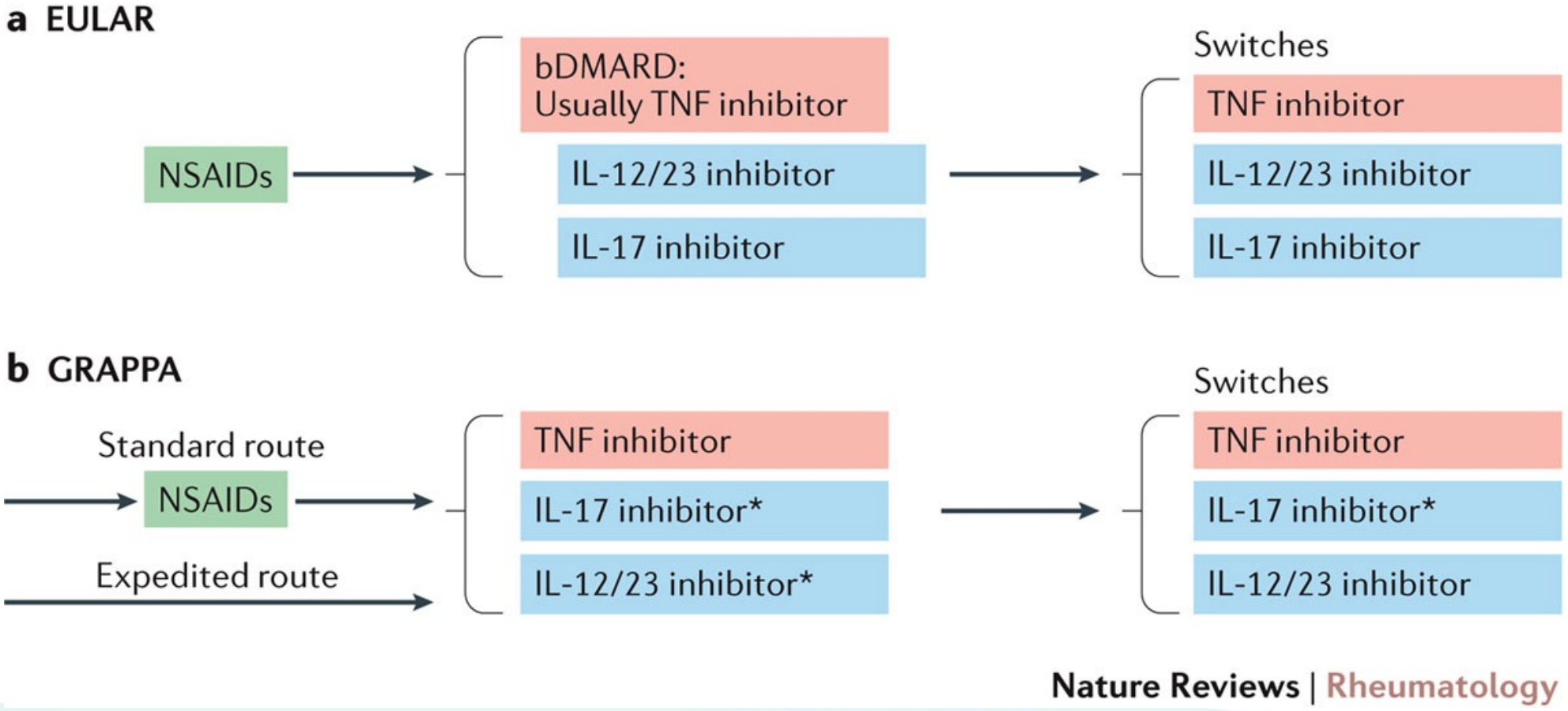
Simplified EULAR and GRAPPA treatment algorithms for predominant axial psoriatic arthritis



Gossec, L. *et al.* (2016)*Nat. Rev. Rheumatol.*.2016.183

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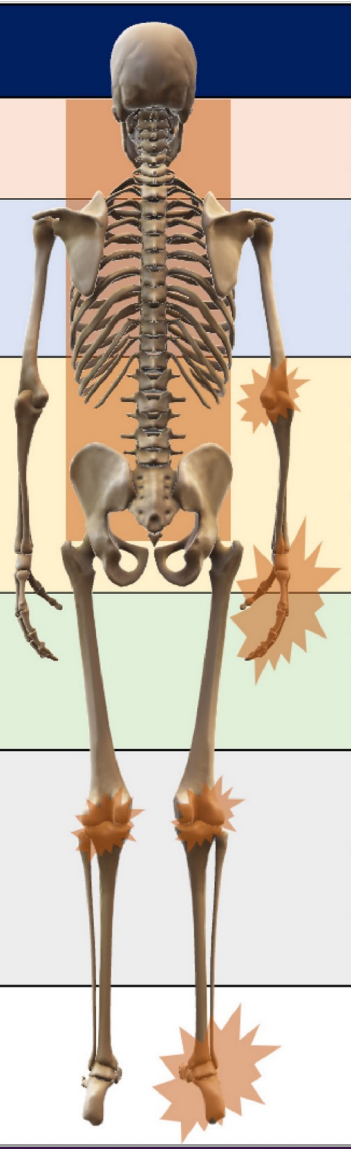
AXIAL PsA : does it exist?

Main features of axial PsA vs AxSpa

	AxSpA	Axial PsA
Demographic	• More frequently male • Younger age at onset	• Similar frequency in males and females • Older age at onset
Clinical	• Back pain has inflammatory character in the majority of patients • Peripheral involvement in approximately 15%-30% of patients	• Inflammatory back pain is less frequent than in axSpA • Peripheral involvement in most patients • Can be asymptomatic
Imaging	• Symmetrical sacroiliitis • Classical symmetrical and marginal syndesmophytes • More frequent fusion of lumbar facet joints	• More frequent involvement of cervical spine • More frequent fusion of facet joints in cervical spine • Less severe sacroiliitis and frequently asymmetrical • Non-marginal syndesmophytes and paravertebral ossifications • Less syndesmophyte symmetry
Genetic	• Higher proportion of HLA-B27–positive patients (90%)	• Only 14% to 44% of patients are HLA-B27 positive • More frequently associated with HLA-B08 and HLA-B38
Treatment Response	• NSAIDs, TNFis, and IL-17 inhibitors are effective treatment options; lack of efficacy of IL-23 inhibitors	• Positive data from one randomized controlled trial with an IL-17 inhibitor (secukinumab) • Data from post hoc analyses of IL-23 inhibitor (guselkumab) and IL-12/23 inhibitor (ustekinumab) • Efficacy of NSAIDs and TNFis is assumed based on axSpA data



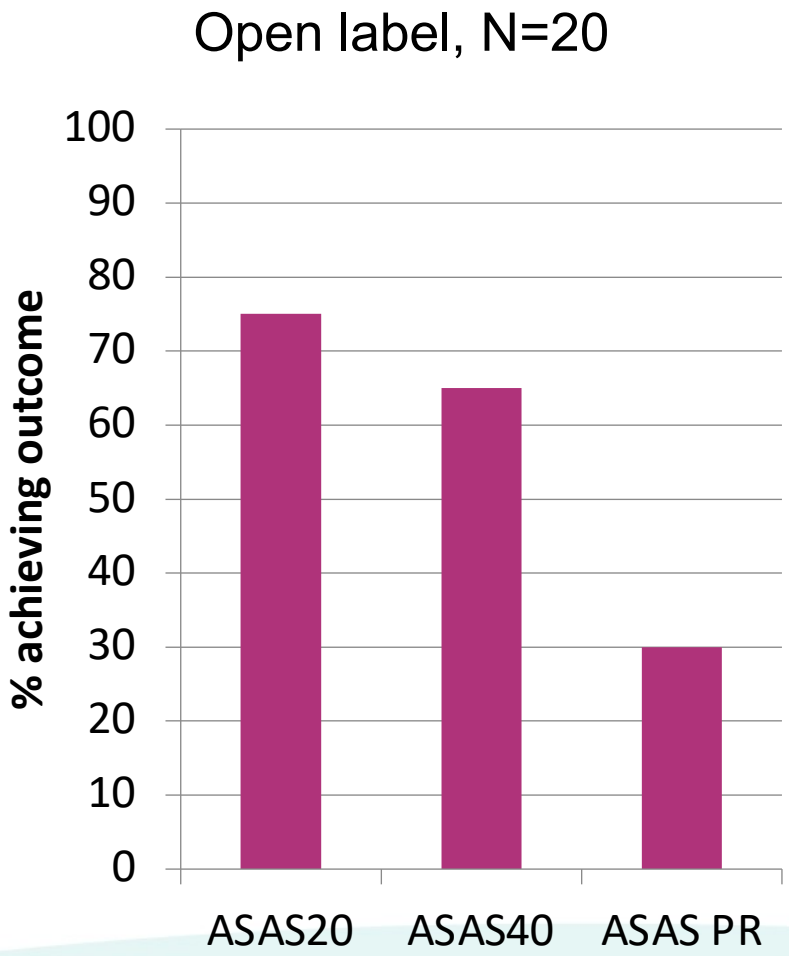
Poddubny D Sem Arthritis Rheum 2021, 880

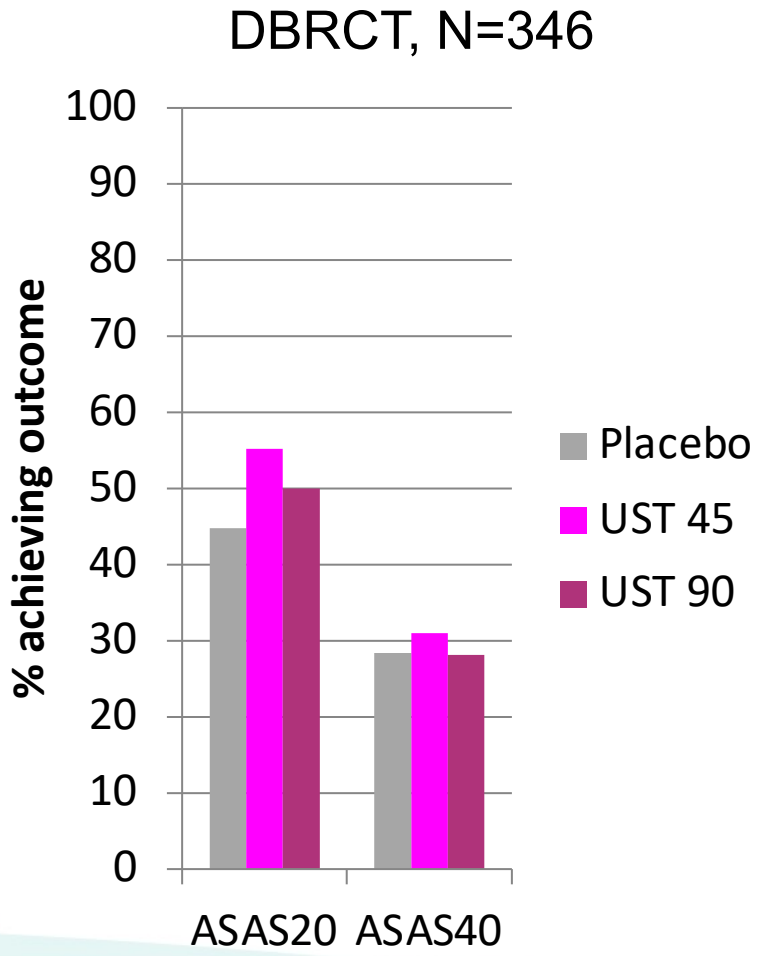
Similar to mSASSS, patients with SpA had more syndesmophytes compared with patients with PsA

	Patients with axSpA, n=176	Patients with SpA,* n=213	Patients with PsA, n=312	P value
mSASSS, mean±SD min, 0.25, median, 0.75, max	10.7±15.2 1-2-**6**-13-64	10.3±14.91 1-2-**5**-13-64	4.5±4.24 1-2-**3**-6-21	0.014
Erosions ≥1, n (%)	3 (1.7)	4 (1.9)	13 (4.2)	0.146
Erosions (spine), mean±SD min, 0.25, median, 0.75, max	1±0.0 1-1-**1**-1-1	1±0.0 1-1-**1**-1-1	1.5±1.39 1-1-**1**-1-6	0.770
Syndesmophytes (total spine) ≥1, n (%)	13 (7.4)	14 (6.6)	33 (10.6)	0.115
Syndesmophytes (total spine), mean±SD min, 0.25, median, 0.75, max	5.5±5.90 1-1-**4**-5-22	4.9±5.78 1-1-**3.5**-5-22	2.0±1.45 1-1-**2**-2-8	0.005
Syndesmophytes (cervical spine) ≥1, n (%)	8 (4.5)	9 (3.5)	24 (7.7)	0.048
Syndesmophytes (cervical spine), mean±SD min, 0.25, median, 0.75, max	3.1±3.00 1-1-**2.5**–3.5-10	2.9±2.89 1-1-**2**-3-10	1.8±1.32 1-1-**1**-2-7	0.070

de Hooge M, *RMD Open* 2023

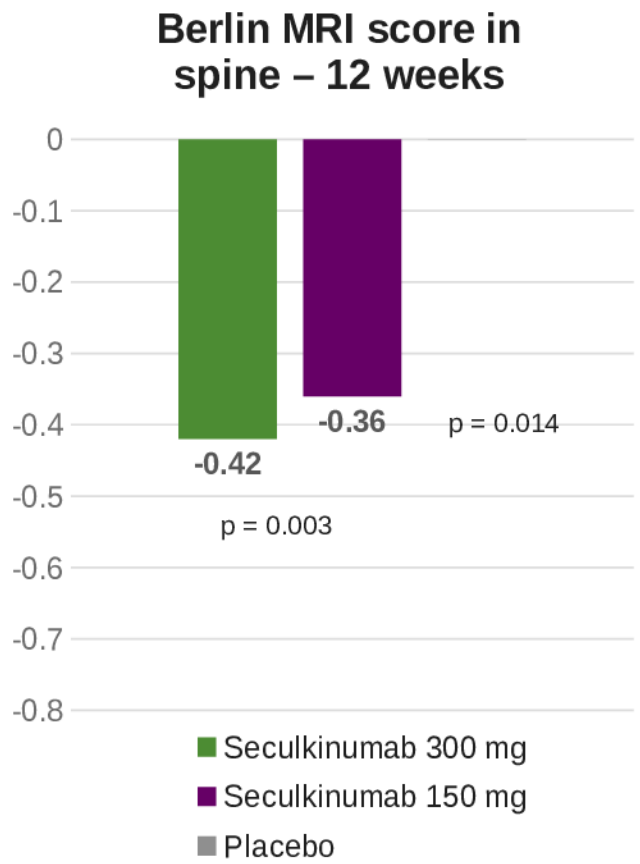
Ustekinumab

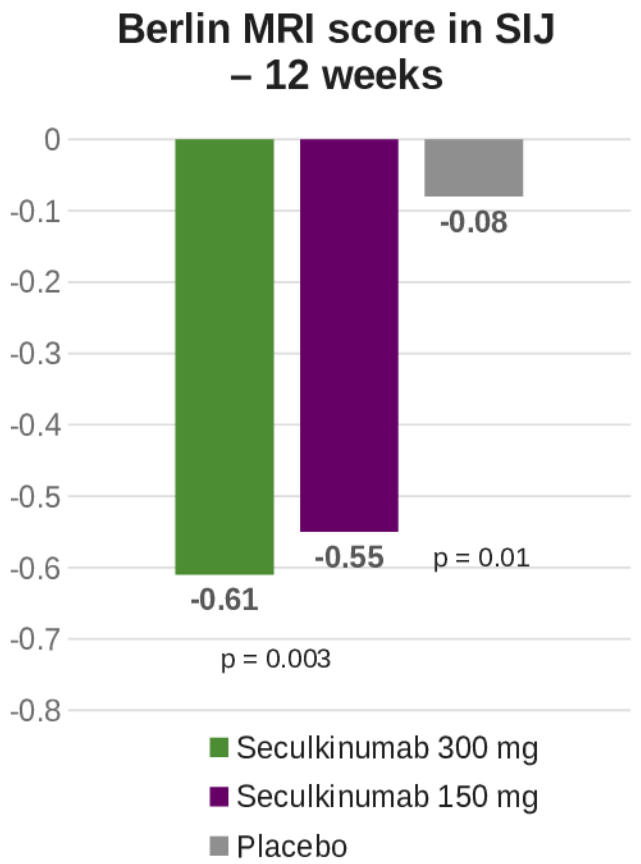


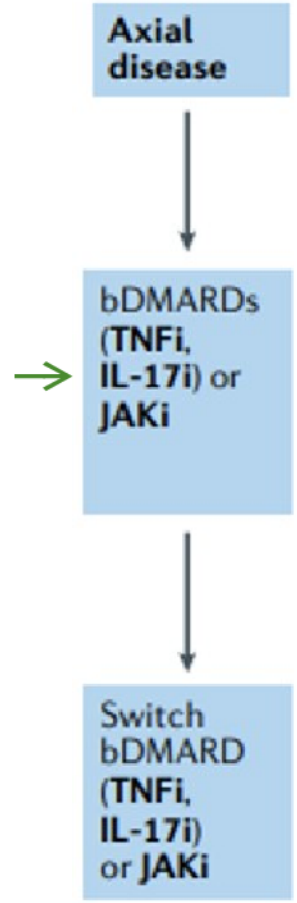


Poddubnyy D, et al. Ann Rheum Dis 2014;73:817, Deodhar et al Arthritis Rheumatol. 2019 Feb;71(2):258-270.

Axial Disease – Secukinumab in axial PsA: MAXIMISE trial







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Baraliakos X, Gossec L, Pournara E, et al. Annals of the Rheumatic Diseases 2020;79:35-36.
Coates LC, Soriano ER, Corp N, et al. Nat Rev Rheumatol. 2022;18:465–479.

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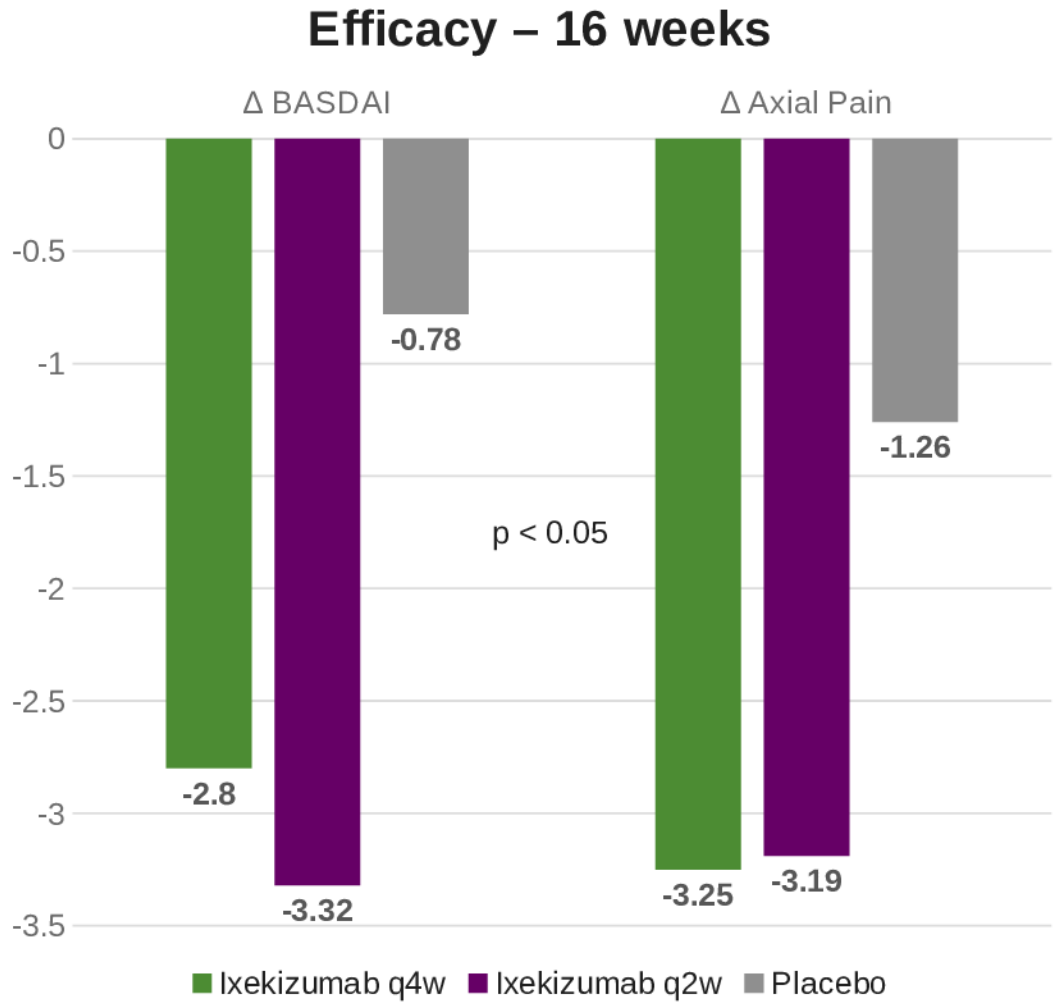
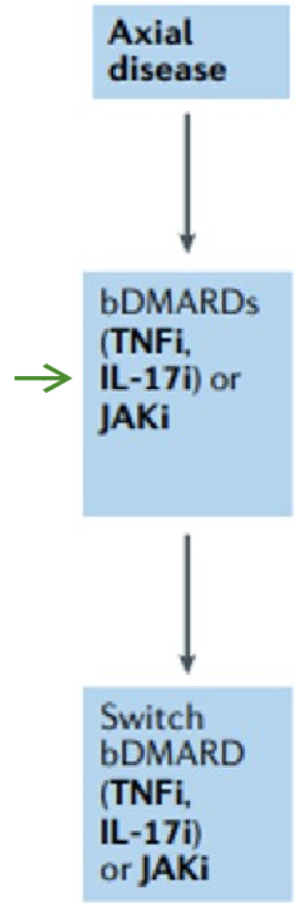
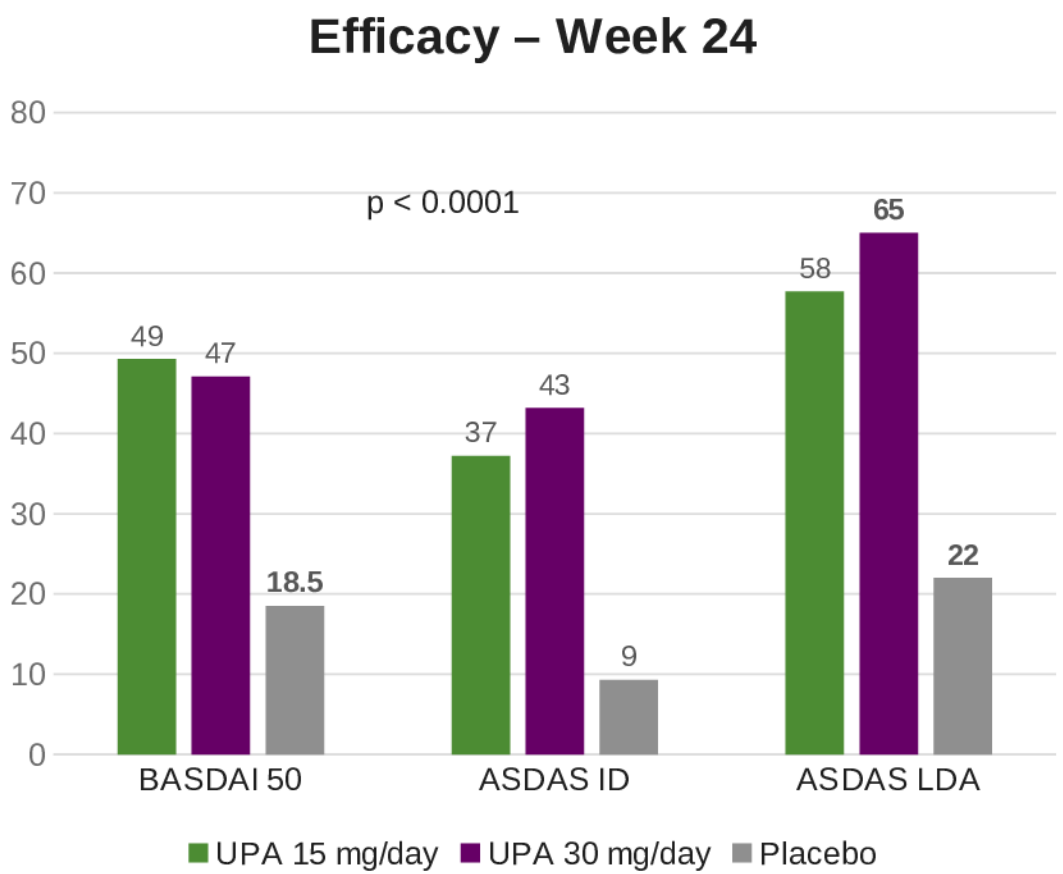
Axial Disease – Ixekizumab in axial PsA: Post-hoc analysis of SPIRIT-P1 and SPIRIT-P2 trials

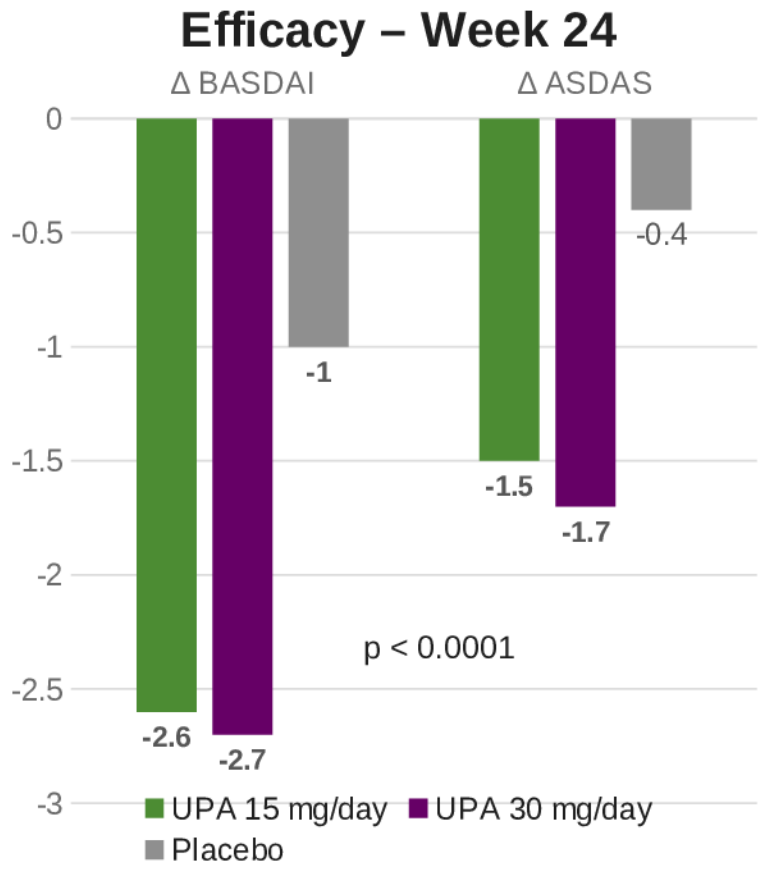


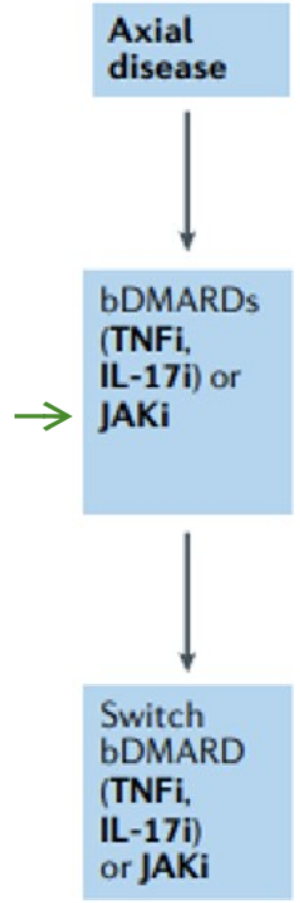


Deodhar A, Ogdie A, Muram T, et al. Ann Rheum Dis. 2019;78:1838.
Coates LC, Soriano ER, Corp N, et al. Nat Rev Rheumatol. 2022;18:465–479.

Axial Disease – Upadacitinib in axial PsA: Post-hoc of SELECT-PsA-1 and SELECT-PsA-2 trials







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Deodhar A, Ranza R, Ganz F, et al. Arthritis Rheumatol. 2020;72(suppl 10).
Coates LC, Soriano ER, Corp N, et al. Nat Rev Rheumatol. 2022;18:465–479.

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What should be used as outcome measure in axial PsA is BASDAI enough? Should we use ASDAS?

Areas covered by the different tools to assess axial involvement in PsA

Items	ASDAS-B	ASDAS-C	BASDAI	mBASDAI**
Back pain	+	+	+*	+*
Morning Stiffness duration	+	+	+	+
Patient Global	+	+	-	-
Peripheral pain/swelling	+	+	+	-
Fatigue	-	-	+	+
Neck/back/hip pain	-	-	+	+
Tender areas	-	-	+	+
Morning stiffness level	+	+	+	+
ESR	+	-	-	-
CRP	-	+	-	-

Eder L, ARD 2010

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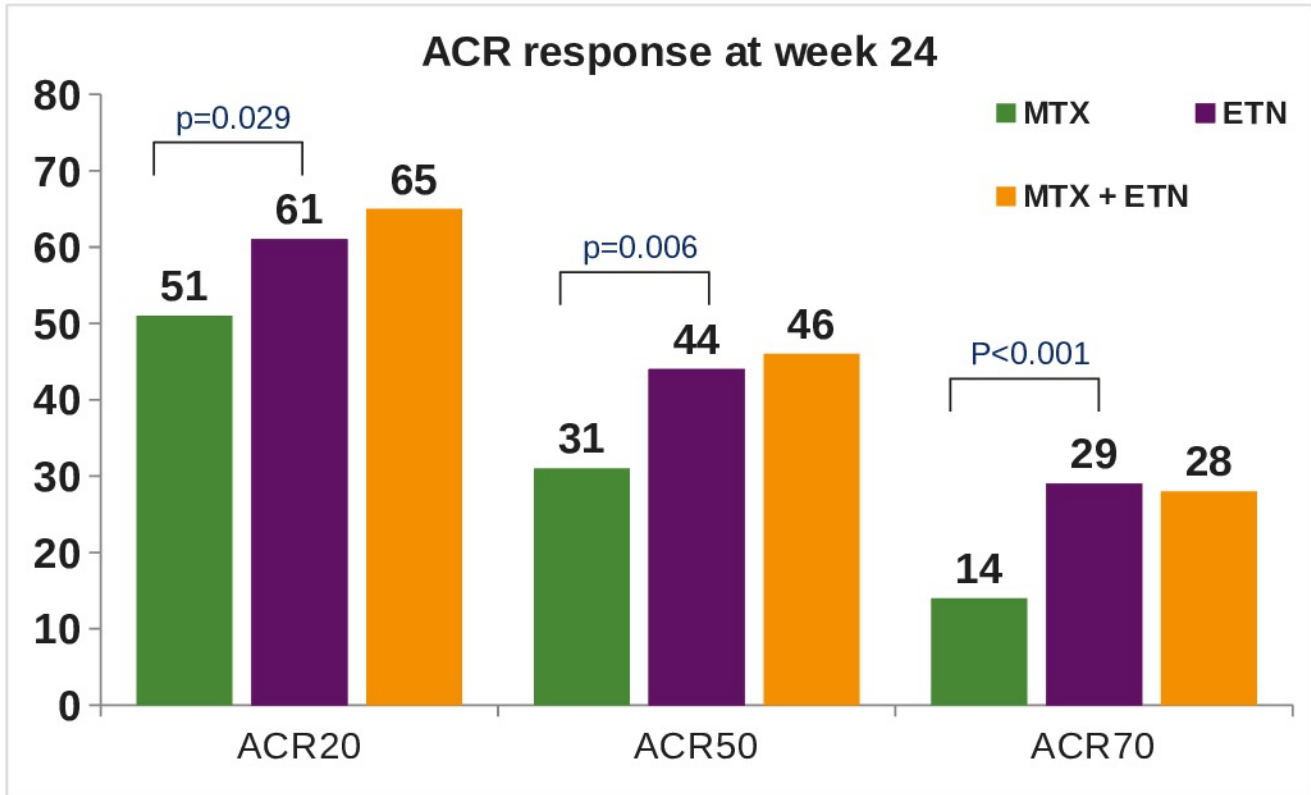
What to choose?

MTX vs ETN: the SEAM trial



Peripheral arthritis

→ csDMARD
bDMARDs
TNFi
IL-12/23i
IL-17i
IL-23i
CTLA4-Ig
JAKi
PDE4i

**The SEAM trial is not a placebo-controlled study and thus offers limited quality of evidence for MTX use, especially because the primary outcome was designed to assess TNF superiority to MTX, not MTX efficacy itself

Mease PJ, Gladman DD, Collier DH, Ritchlin CT, Helliwell PS, Liu L, Kricorian G, Chung JB. Arthritis Rheumatol. 2019;71:1112-1124.

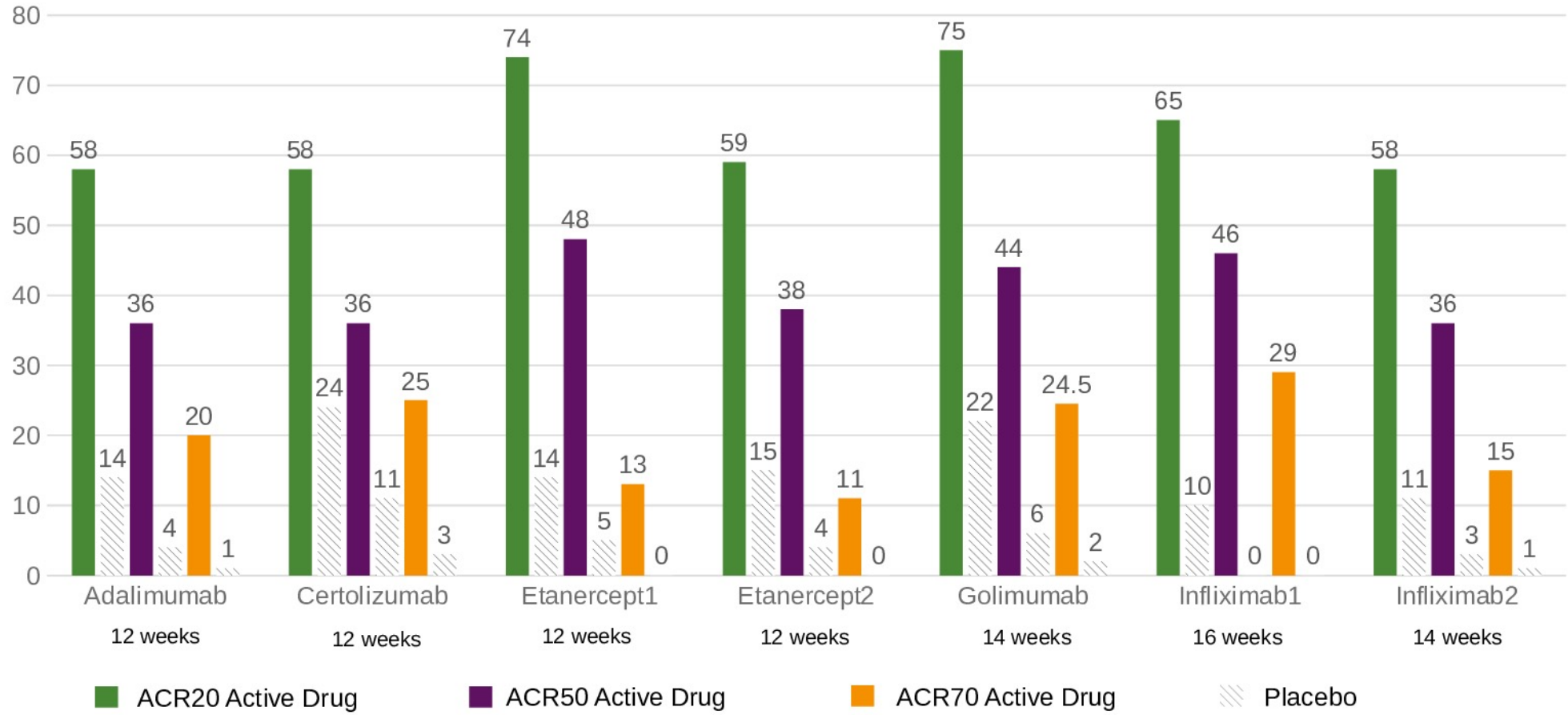
Coates LC, Soriano ER, Corp N, et al. Nat Rev Rheumatol. 2022;18:465–479.

TNFi therapies in PsA: ACR responses

Peripheral arthritis

csDMARD
bDMARDs
TNFi
IL-12/23i
IL-17i
IL-23i
CTLA4-Ig
JAKi
PDE4i

ACR20, -50, -70 Responses in Phase 2 & Phase 3 Trials

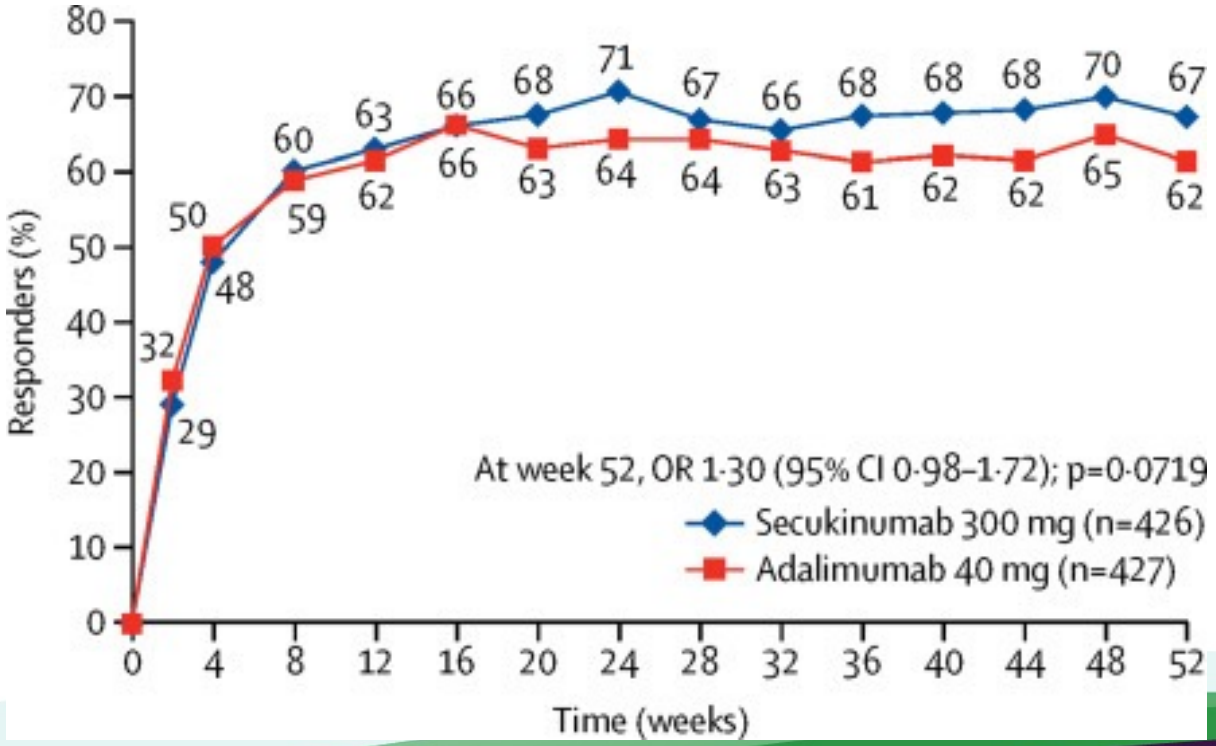


Mease et al, ARD 2005; 52:3279; Mease et al, ARD 2014; **73:**48-55; Mease et al. Lancet 2000;356:385-90; Mease et al. A&R 2004;50:2264-72; Kavanaugh et al. Arthritis Rheum 2017; Antoni et al, A8R 2005; 52:1227; Antoni et al. ARD 2005; 64:1150.

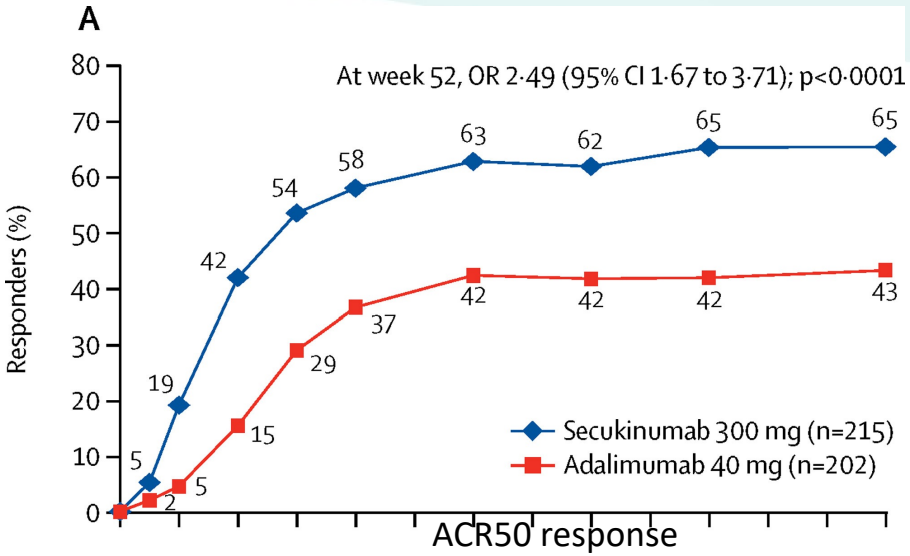
Coates LC, Soriano ER, Corp N, et al. Nat Rev Rheumatol. 2022;18:465–479.

Secukinumab versus adalimumab for treatment of active psoriatic arthritis (EXCEED)

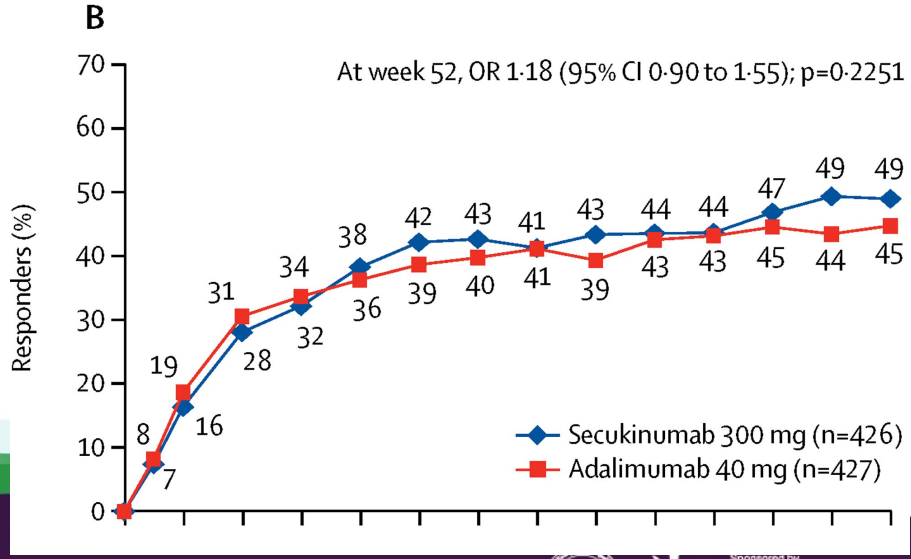
ACR20 response



PASI 90

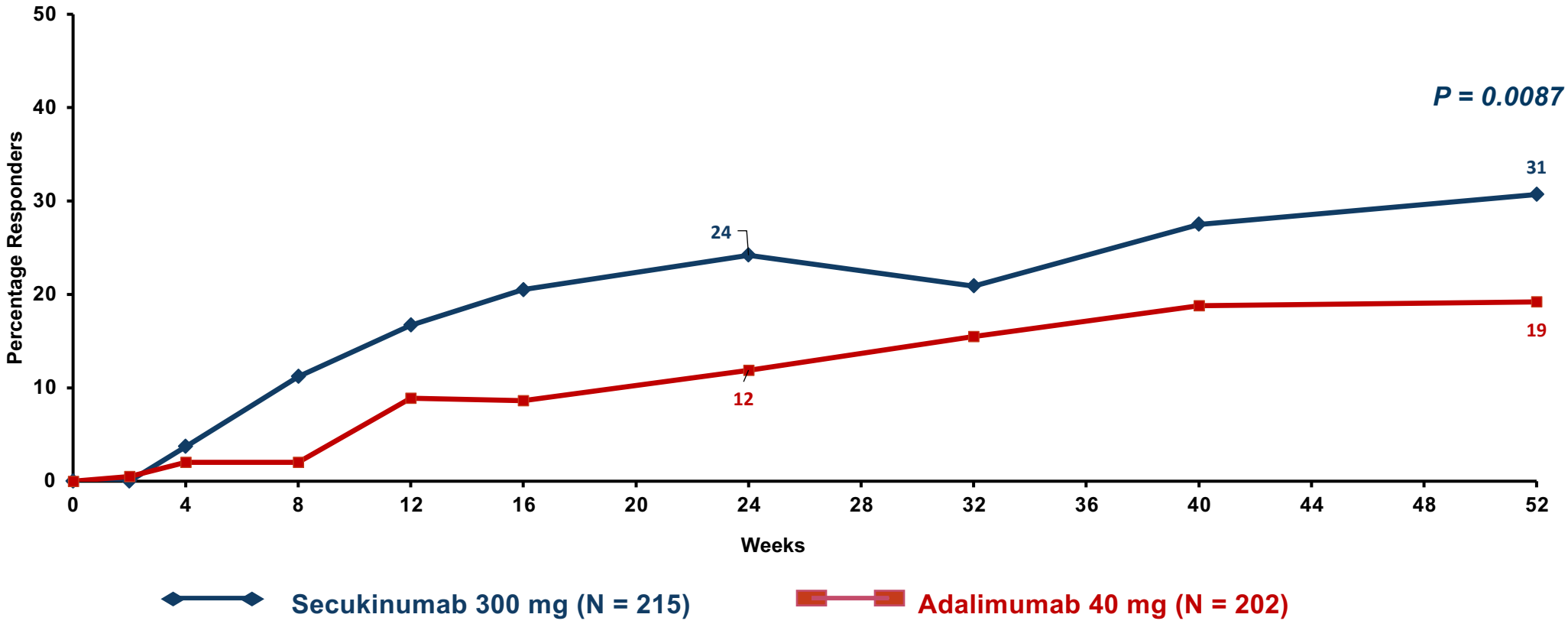


ACR50 response



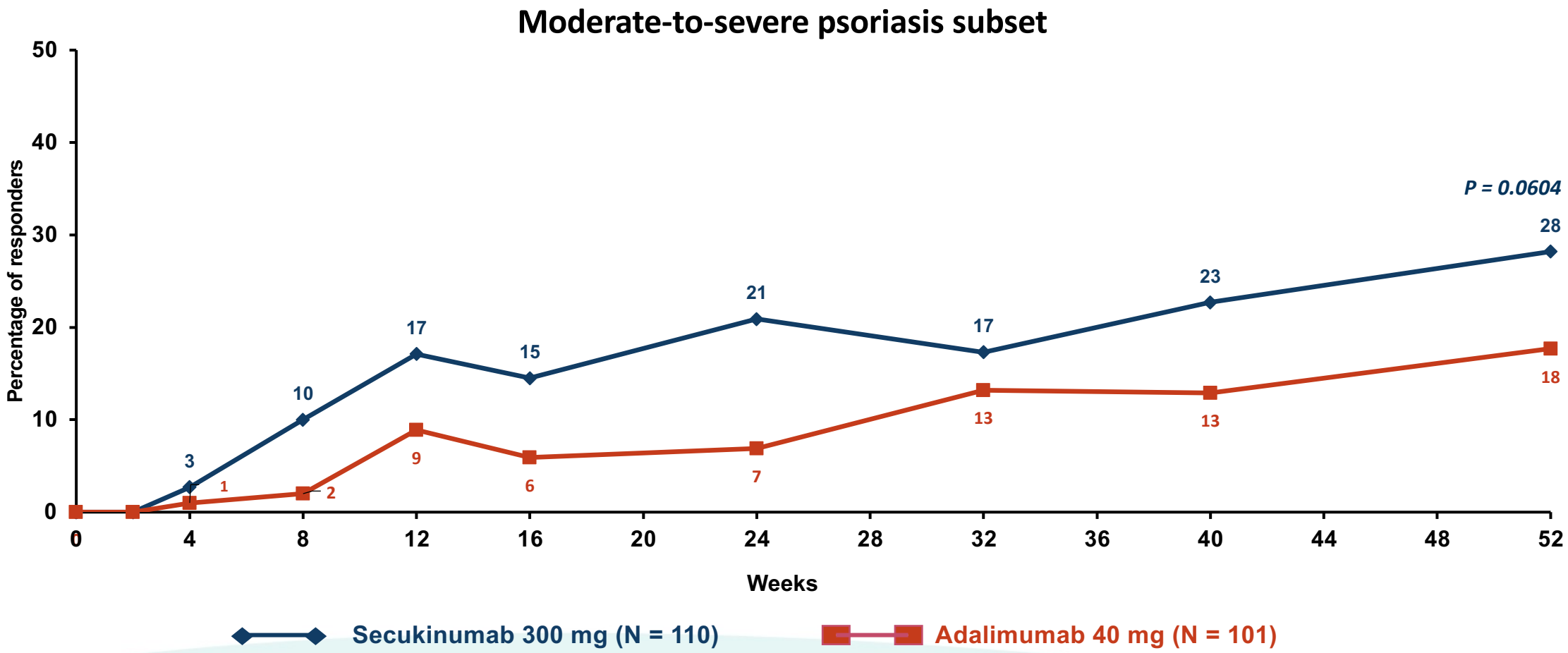
McInnes IB, Lancet 2020

Simultaneous ACR50 and PASI 100 Responses up to Week 52



Patients with PsO having ≥ 3% BSA affected at baseline:
P versus adalimumab; Non-adjusted p-value is reported at Week 52; N, Number of available patients; Patients who discontinued study treatment before or at Week 50 or took csDMARDs after Week 36 are considered non-responders for the visits after discontinuation or taking csDMARDs. ACR, American college of rheumatology; PASI, psoriasis area severity index;

ACR50 and PASI 100 response up to week 52

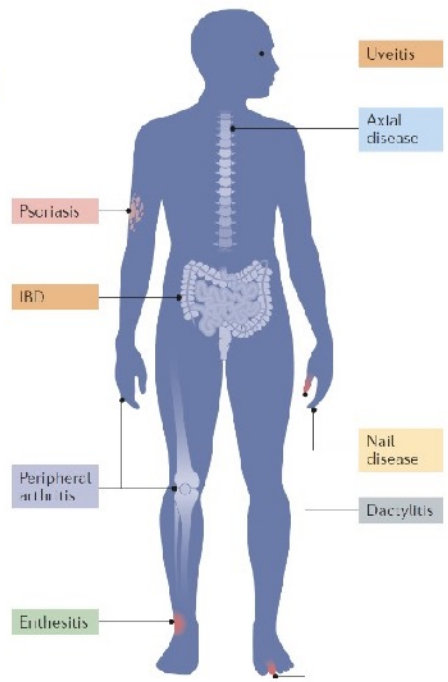


Comparison of Biologic Drugs

IL 12/23i
Severe skin
Mild/moderate joint
IBD
*Not for axial disease

TNFi
Cover all 6 domains
Mild/moderate skin
Moderate/severe joint
IBD / Uveitis

IL 17i
Cover all 6 domains
Severe skin
Moderate/severe joint
*Not for IBD / Uveitis



JAKi
Cover all 6 domains
Moderate/severe joint
Mild/moderate skin
IBD

IL 23i
Severe skin
Moderate/severe joint
IBD
*Not for axial disease

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Higher Risk for comorbidities in PsA vs pSPA

1.35

1.60

1.81

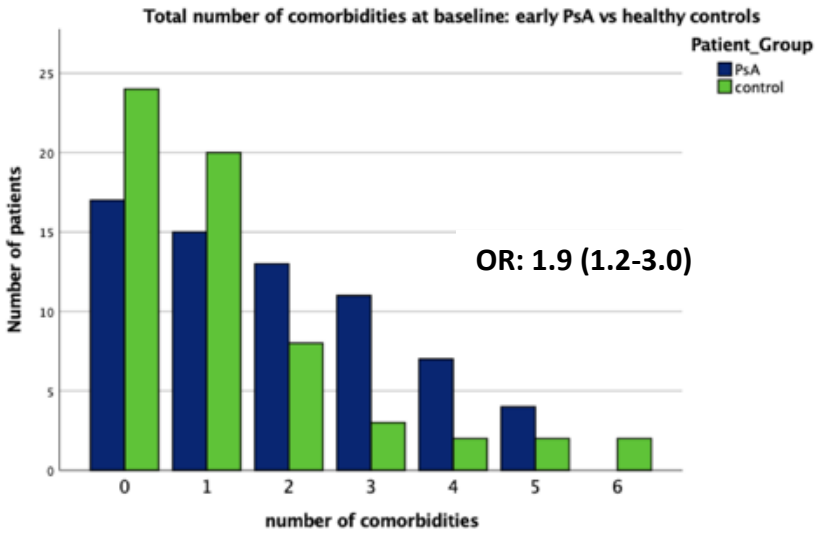
1.39

1.58

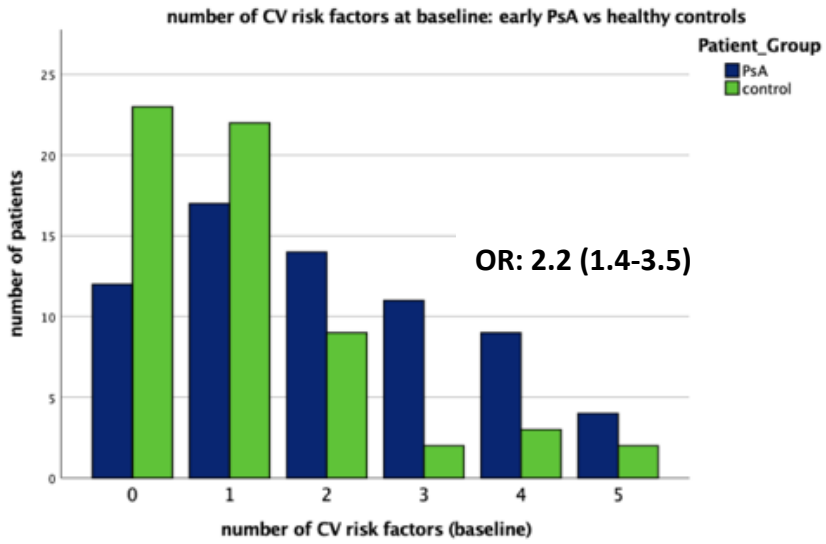
Haque, de Vlam 2015

Controlled for age, gender, disease duration and medication. controlling for age, gender, disease duration and medication. Risk expressed as Odd's Ratio (OR)

Multiple Comorbidities in early PsA



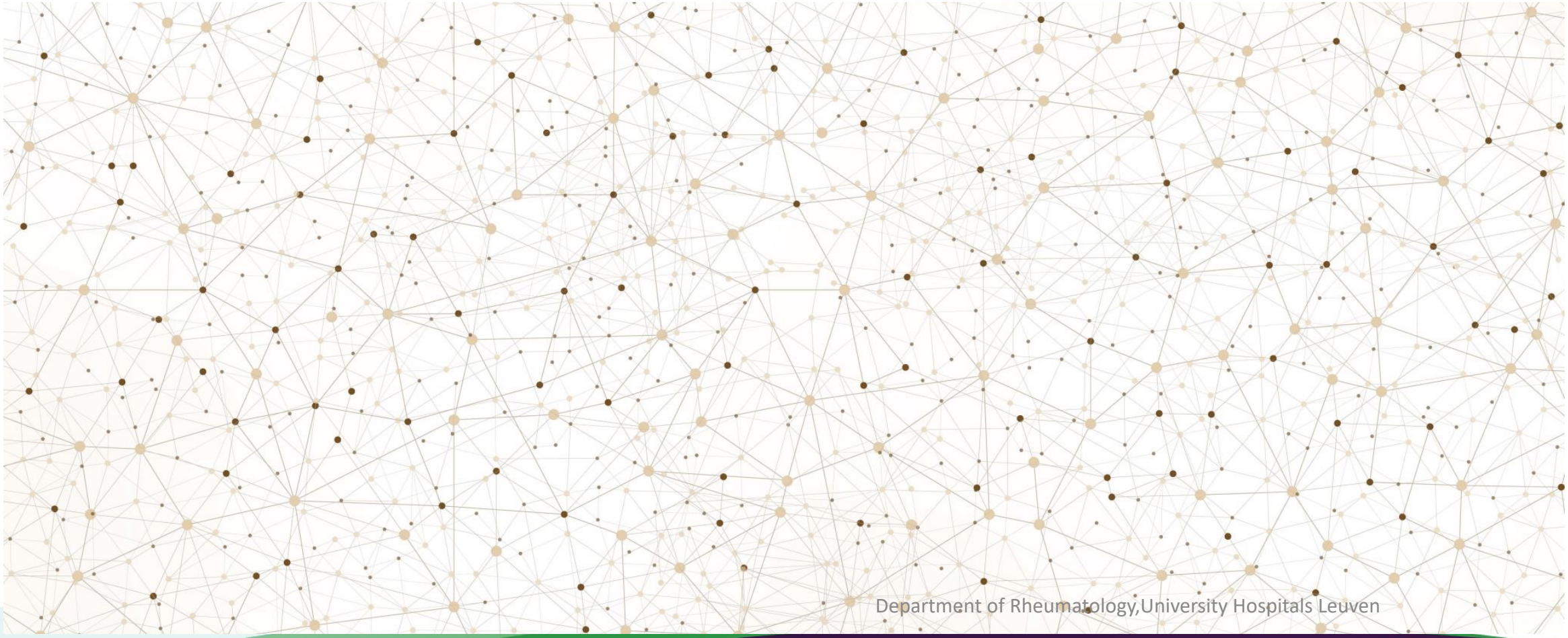
A. Comparison of overall comorbidities in early PsA and matched controls at baseline. Number of comorbidities is significantly higher in early PsA (p= 0.045, chi-sq test).



B. Comparison of cardiovascular risk factors (CV RF) in early PsA and matched controls at baseline. Number of CV RF is significantly higher in early PsA than in controls (p= 0.011, chi-sq test).

Ishchenko, de Vlam 2022

Thank you for your attention !



I am happy to take questions

Department of Rheumatology,University Hospitals Leuven

Skeletal Biology and Engineering Research Center (SBE),Dept Development and Regeneration, KULeuven

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Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

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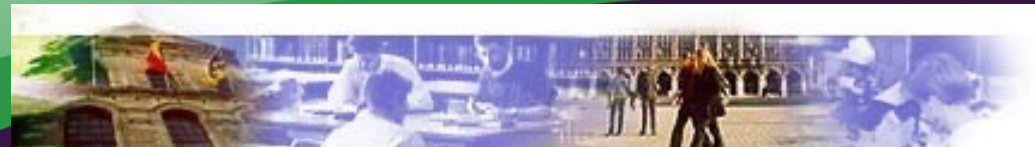

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