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Difficult to treat PsA:but why?

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The D2T concept – Is there a standard definition?

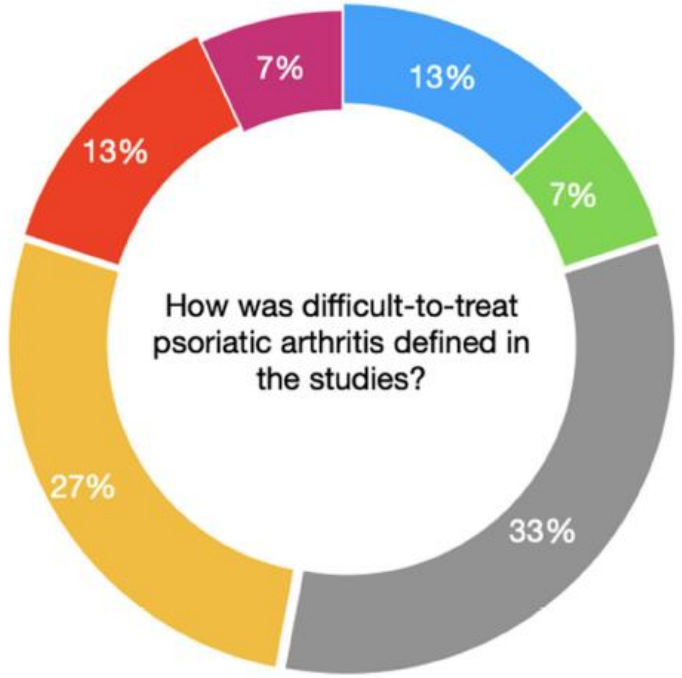
- No official definition suggested by EULAR
- EULAR survey: D2T status should be defined as failure of at least 2 bDMARDs with different mechanism of action (1)

D2T PsA should be defined as failure of*:

	%	n.
≥2 bDMARDs with ≥2 MOA	35.0%	85
≥3 bDMARDs with ≥3 MOA	23.5%	57
≥3 bDMARDs with ≥2 MOA	16.0%	39
≥2 bDMARDs, any class	13.6%	33

(1) Marzo-Ortega H. et al.. Ann Rheum Dis. 2023

GRAPPA Scope literature review



Psoriatic arthritis

RMD Open
Rheumatic & Musculoskeletal Diseases

ORIGINAL RESEARCH

Difficult-to-treat psoriatic arthritis (D2T PsA): a scoping literature review informing a GRAPPA research project

Shikha Singla,[1] Andre Ribeiro ,[2] Murat Torgutalp ,[3] Philip J Mease ,[4] Fabian Proft [5]

(2) Singla S et al. RMD Open. 2024

D2T PsA

- Despite the availability of numerous therapeutic options, many patients with PsA display residual disease activity and fail to achieve remission or at least low disease activity.
- In cross-sectional studies, the overall prevalence of MDA was 35% (95% CI: 30%–41%)
- Should we define D2T Psoriatic arthritis?

Zardin-Moraes M et al. J Rheum 2020

The D2T concept – Borrowing from D2T Rheumatoid Arthritis

- RA EULAR definition can be used. But is it "transferable"? RA differs considerably from PsA
  - In terms of phenotype
  - Also in terms of treatment (e.g steroids are not classically used in PsA- was not considered as therapeutic option in our study)

Box 1 EULAR definition of difficult-to-treat RA

1. Treatment according to European League Against Rheumatism recommendation and failure of ≥2 b/tsDMARDs (with different mechanisms of action)* after failing csDMARD therapy (unless contraindicated).†
2. Signs suggestive of active/progressive disease, defined as ≥1 of:
   a. At least moderate disease activity (according to validated composite measures including joint counts, for example, DAS28-ESR>3.2 or CDAI>10).
   b. Signs (including acute phase reactants and imaging) and/or symptoms suggestive of active disease (joint related or other).
   c. Inability to taper glucocorticoid treatment (below 7.5 mg/day prednisone or equivalent).
   d. Rapid radiographic progression (with or without signs of active disease).‡
   e. Well-controlled disease according to above standards, but still having RA symptoms that are causing a reduction in quality of life.
3. The management of signs and/or symptoms is perceived as problematic by the rheumatologist and/or the patient.

All three criteria need to be present in D2T RA.
b, biological; CDAI, clinical disease activity index; cs, conventional synthetic; DAS28-ESR, disease activity score assessing 28 joints using erythrocyte sedimentation rate; DMARD, disease-modifying antirheumatic drug; mg, milligram; RA, rheumatoid arthritis; ts, targeted synthetic.
*Unless restricted by access to treatment due to socioeconomic factors.
†If csDMARD treatment is contraindicated, failure of ≥2 b/tsDMARDs with different mechanisms of action is sufficient.
‡Rapid radiographic progression: change in van der Heijde-modified Sharp score ≥5 points at 1 year.[16]

Clinical case

- Male 23 years old
- Normal BMI
- No past medical history

Clinical case

- Tender joins: 6
- Swollen joints: 3
- Psoriasis: BSA 3%

Clinical case

- CRP:15 mg/l
- DAPSA: 21.1

Clinical case

- Initially treated with methotrexate 17.5 mg/week
- After 1 month LFT values were abnormal
- MTX discontinued and then reinitiated on 12.5 mg/week

Clinical case

- Not significant improvement both for skin and joint involvement

- What should we do next?

EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2023 update

Laure Gossec [1,2] Andreas Kerschbaumer [3] Ricardo J O Ferreira [4,5] Daniel Aletaha [3] Xenofon Baraliakos [6] Heidi Bertheussen,[7] Wolf-Henning Boehncke,[8] Bente Appel Esbensen [9,10] Iain B McInnes,[11] Dennis McGonagle,[12,13] Kevin L Winthrop [14] Andra Balanescu,[15] Peter V Balint,[16] Gerd R Burmester [17] Juan D Cañete [18,19] Pascal Claudepierre,[20,21] Lihi Eder [22] Merete Lund Hetland [23,24] Annamaria Iagnocco [25] Lars Erik Kristensen,[26,27] Rik Lories,[28,29] Rubén Queiro [30,31] Daniele Mauro [32] Helena Marzo-Ortega [12,13] Philip J Mease [33,34] Peter Nash [35] Wendy Wagenaar,[36,37] Laura Savage,[38] Georg Schett [39] Stephanie J W Shoop-Worrall [40] Yoshiya Tanaka [41] Filip E Van den Bosch [42] Annette van der Helm-van Mil,[43] Alen Zabotti [44] Désirée van der Heijde [43] Josef S Smolen[3]

EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2023 update

- MTX starting dose should be above 15 mg/week

- Efficacy-safety balance should be kept in mind due to metabolic comorbidities in PsA patients

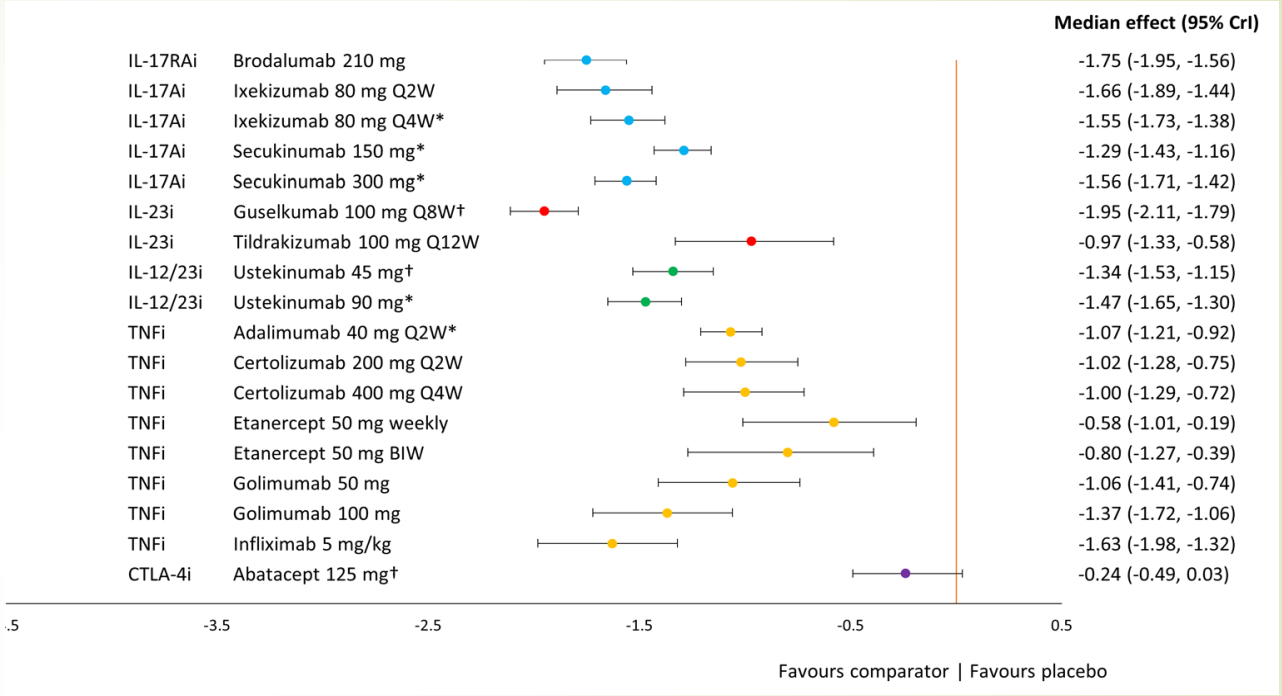
Clinical case

- Started upadacitinib 15mg/day
- Joint involvement was improved, but skin involvement wasn't improved
  BSA: 3%
- DAPSA: 8

Clinical case

- Started Guselkumab
- After 6 months, skin and joint involvement were improved
- DAPSA: 3, BSA 0%

- Skin
  - Anti-IL-23/-17 class > anti-TNF in PASI75
    - head-to-head in psoriasis
      - Ustekinumab, Ixekizumab >> Etanercept
      - Guselkumab > Adalimumab
      - Tildrakizumab > Etanercept



Gordon K et al Lancet 2018
Reich K et al Lancet 2017
Lin VW et al Arch Derm 2012
Griffiths CE et al NEJM 2010
Griffiths CE et al Lancet 2015
Blauvelt et al J Am Acad Dermatol 2017
Paul J et al Blauvelt et al J Am Acad Dermatol 2018

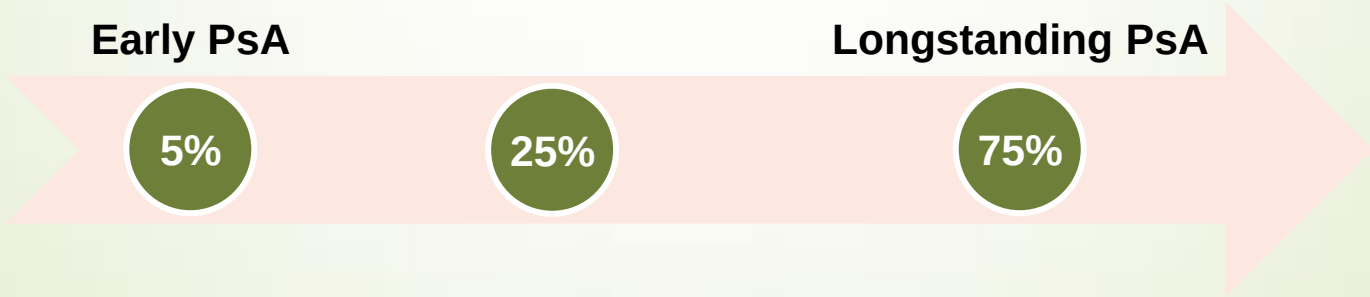
Clinical case

- After 6 months on guselkumab he developed axial symptomatology
- MRI SJ: unilateral sacroilitis
- Guselkumab was discontinued and started secukinumab

Axial PsA Frequency

- 2–5% of PsA patients have **ONLY** axial disease
- About 20–30% of PsA patients have subclinical axial disease (radiologic but not clinical)
- 15% of PsA patients without axial disease at diagnosis, developed within the first 10 years

Prevalence of axial disease in PsA varies (depends on disease duration)
In **25–70%** of patients with PsA **and in 5–28%** within the first year of diagnosis**.**



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Axial-PsA
Trying to define…

› Ther Adv Musculoskelet Dis. 2021 Dec 18;13:1759720X211057975.
doi: 10.1177/1759720X211057975. eCollection 2021.

Axial Involvement in Psoriatic Arthritis cohort (AXIS): the protocol of a joint project of the Assessment of SpondyloArthritis international Society (ASAS) and the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA)

Denis Poddubnyy [1], Xenofon Baraliakos [2], Filip Van den Bosch [3], Jürgen Braun [2], Laura C Coates [4], Vinod Chandran [5], Torsten Diekhoff [6], Floris A van Gaalen [7], Lianne S Gensler [8], Niti Goel [9], Alice B Gottlieb [10], Désirée van der Heijde [7], Philip S Helliwell [11], Kay Geert A Hermann [6], Deepak Jadon [12], Robert G Lambert [13], Walter P Maksymowych [14], Philip Mease [15], Peter Nash [16], Fabian Proft [17], Mikhail Protopopov [17], Joachim Sieper [17], Murat Torgutalp [17], Dafna D Gladman [5]

Affiliations + expand

PMID: 34987619 PMCID: PMC8721378 DOI: 10.1177/1759720X211057975

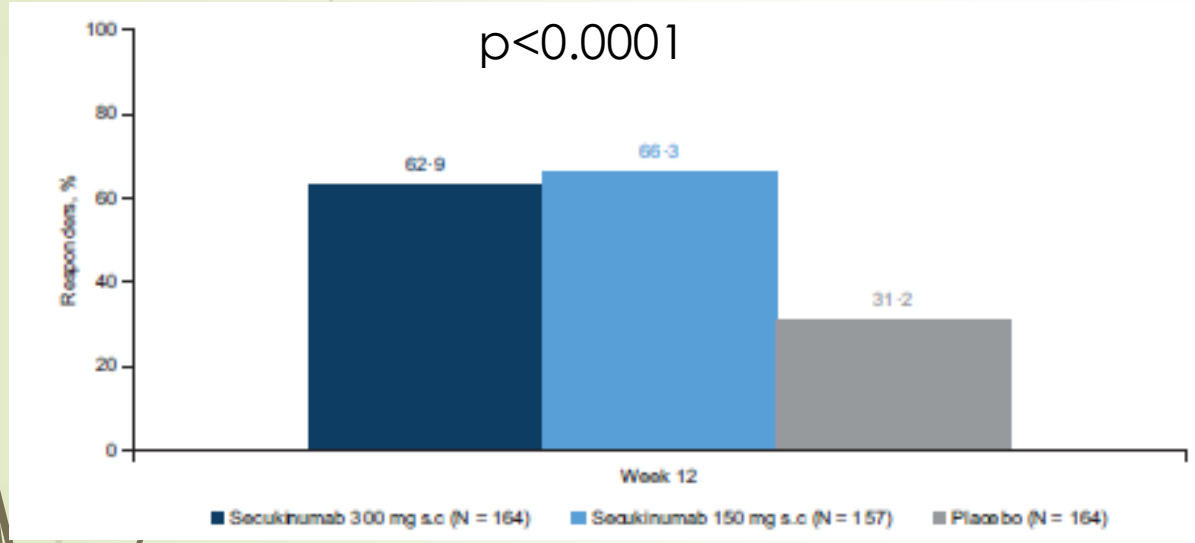
Free PMC article

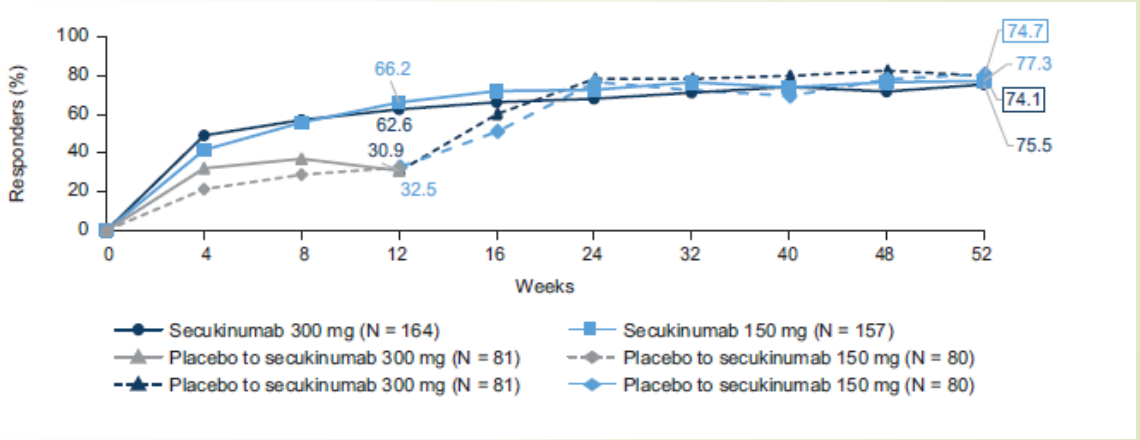
Psoriatic arthritis
Axial disease

- cDMARDs
  - Not effective for axial disease
- bDMARDs/tsDMARDs
  - Anti-IL-17
  - JAK-inhibitors
  - Anti-TNF
  - Anti-IL-23 ???

Kavanaugh A et al Ann Rheum Dis. 2018
Gossec L et al Ann Rheum Dis. 2018
Poddubny et al Ann Rheum Dis 2018

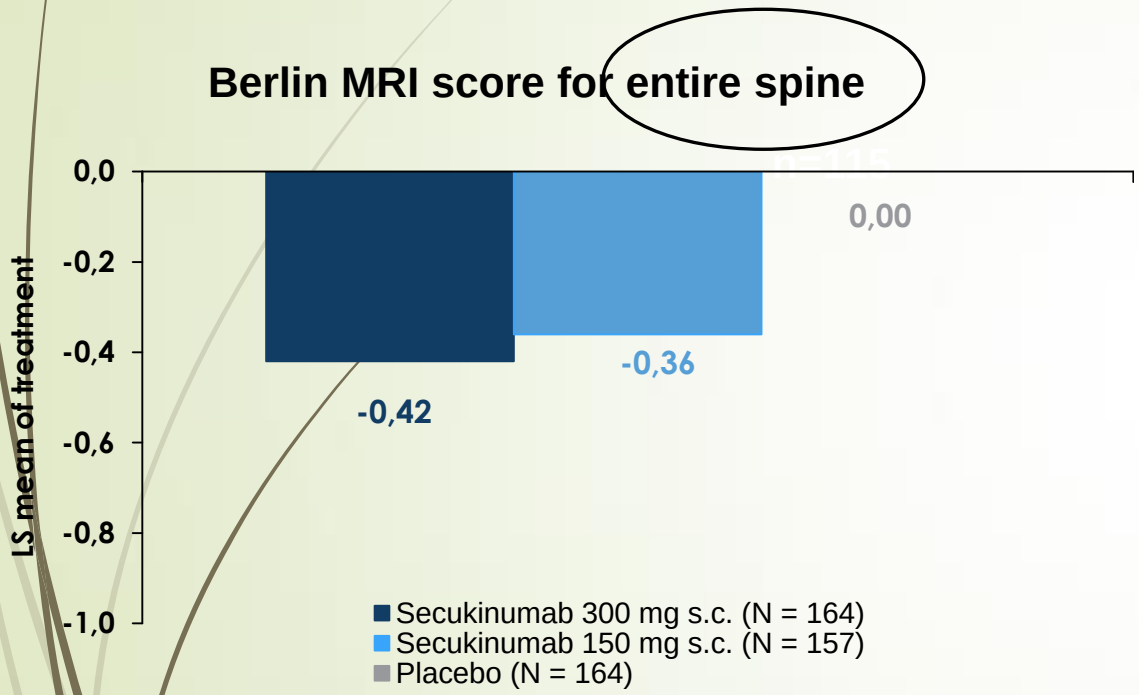
Axial-PsA (MAXIMISE)
ASAS20 (primary endpoint)





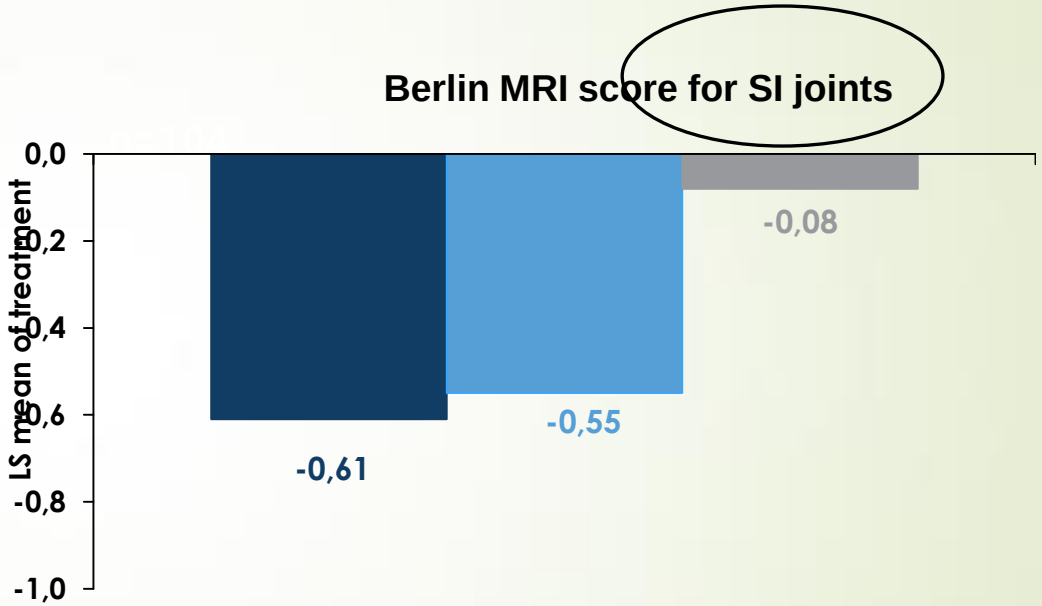
Baraliakos X, et al. Ann Rheum Dis. 2021

Axial-PsA (MAXIMISE)
Secukinumab reduced total berlin MRI score for the entire spine at Week 12*



300 mg vs placebo ***P*=0.0031**

150 mg vs placebo: ***P*=0.0127**

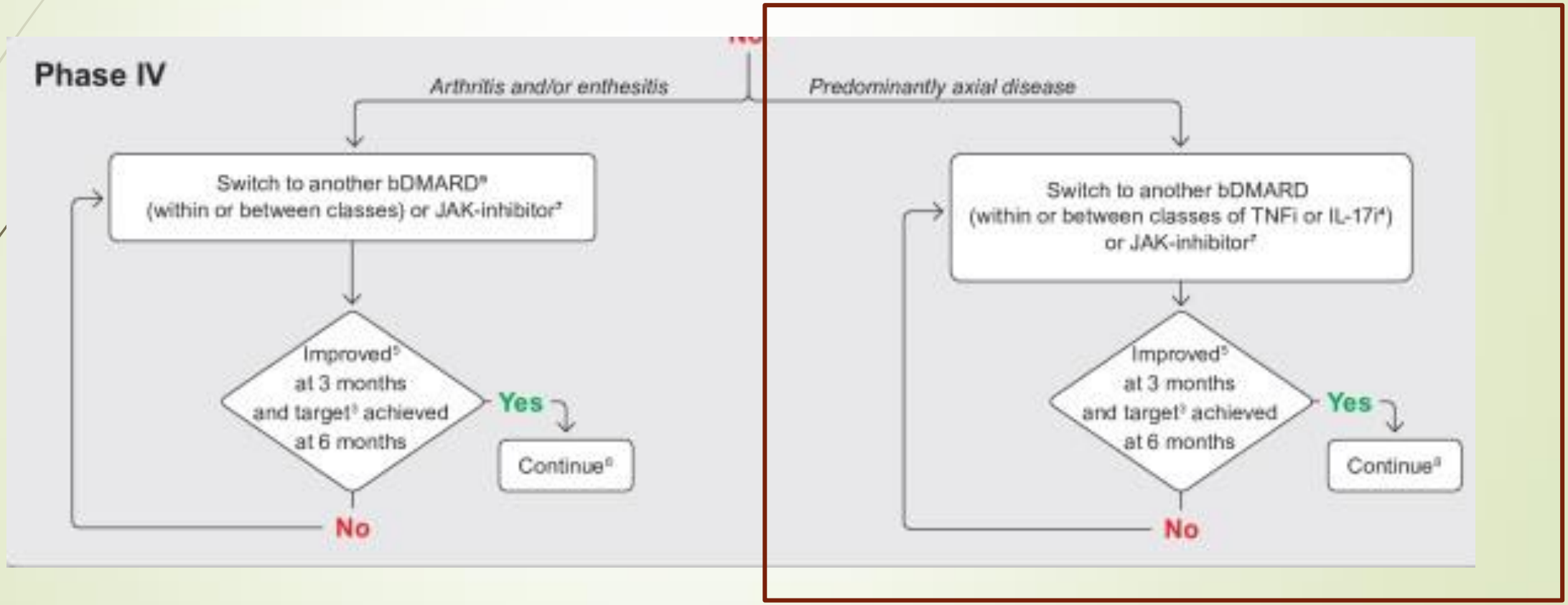


300 mg vs placebo: ***P*=0.0034**

150 mg vs placebo: ***P*=0.0091**

Baraliakos X, et al. Ann Rheum Dis. 20

EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2023 update



In conclusion: D2T PsA case

- Failure of MTX
- Failure of upadacitinib and guselkumab
- Why: skin+axial+periperal disease

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Thank you for your attention