Psoriatic Arthritis Management Update

Faculty

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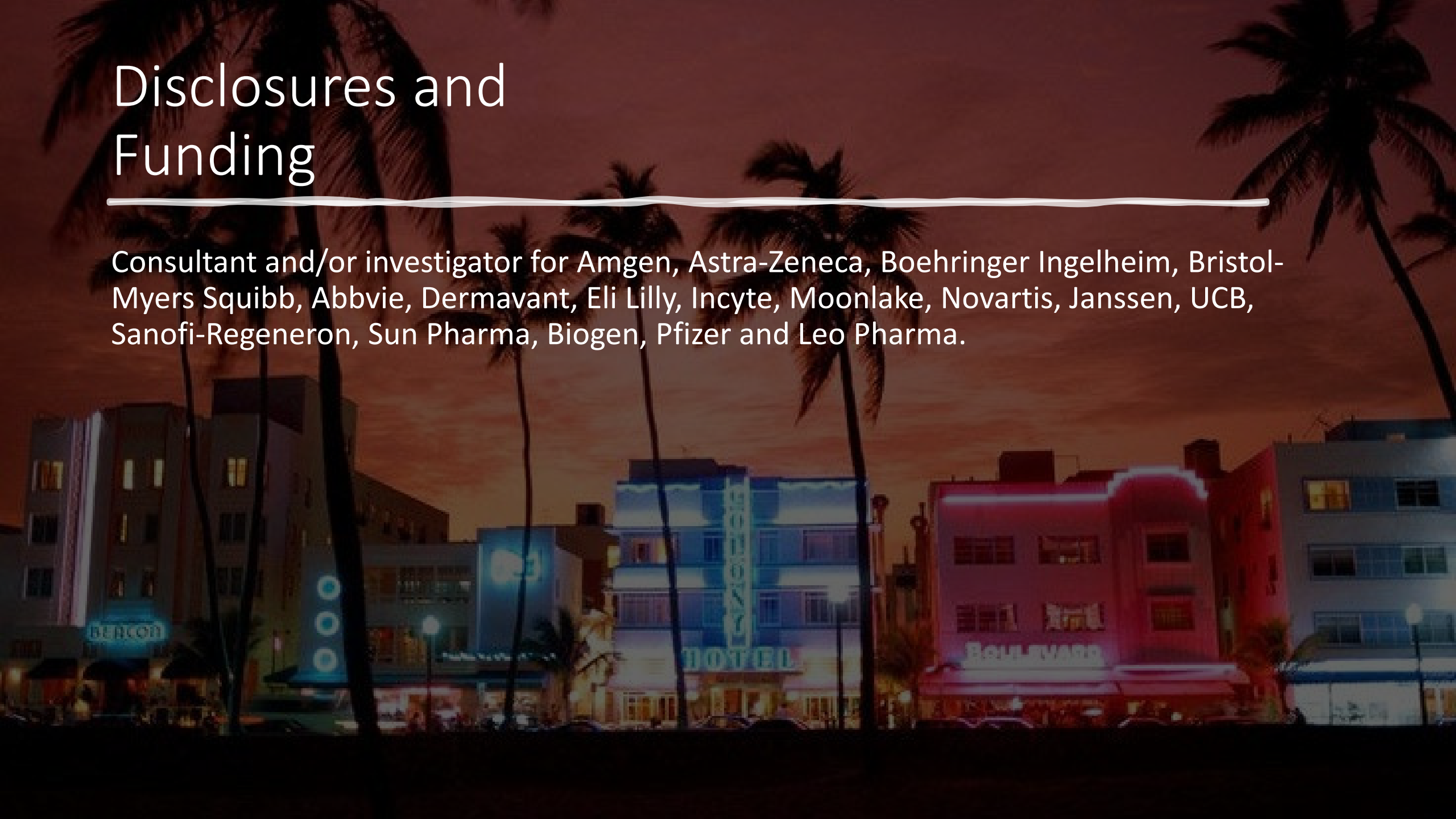
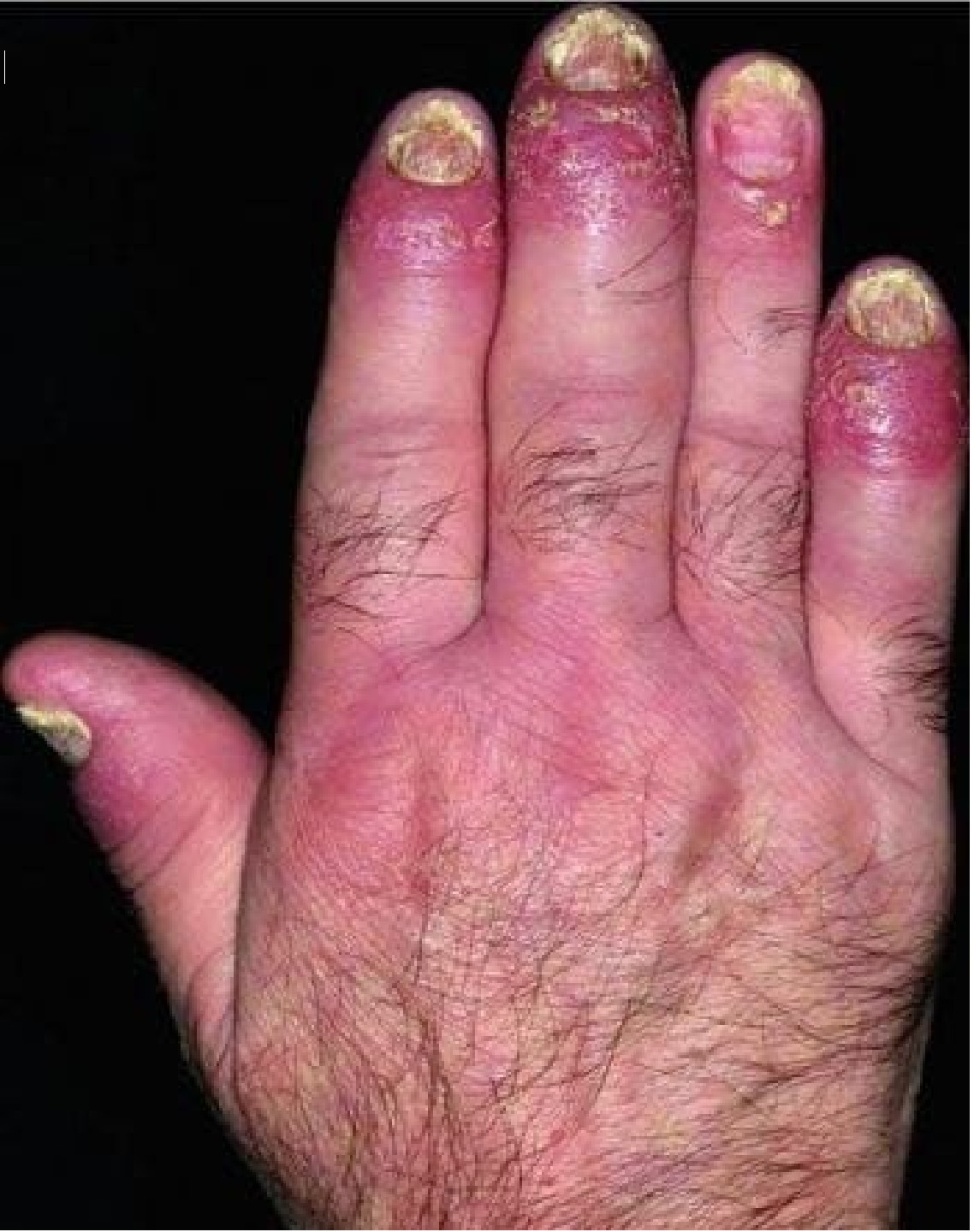
Disclosures and Funding



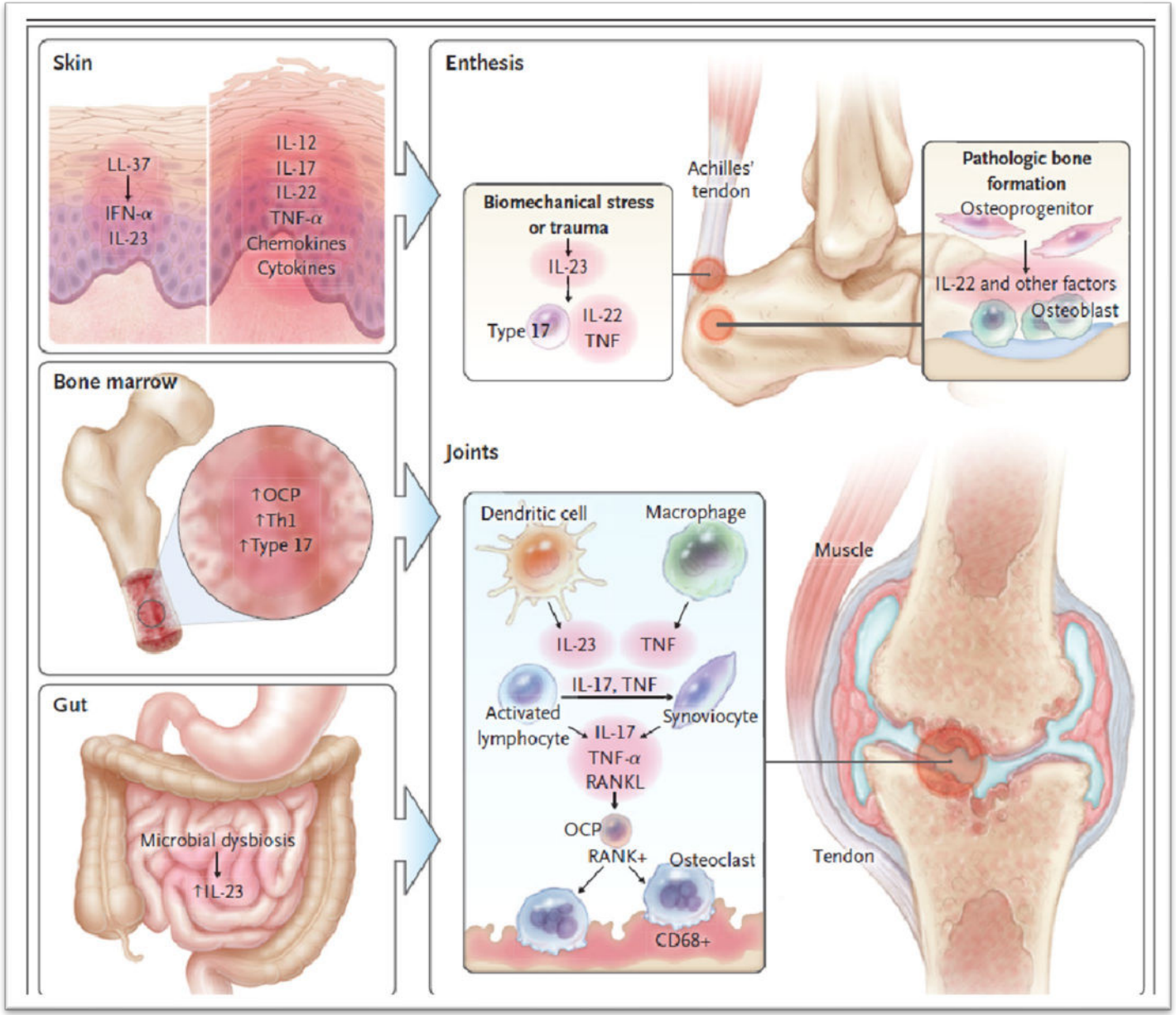
Consultant and/or investigator for Amgen, Astra-Zeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Abbvie, Dermavant, Eli Lilly, Incyte, Moonlake, Novartis, Janssen, UCB, Sanofi-Regeneron, Sun Pharma, Biogen, Pfizer and Leo Pharma.



Reasons Why PsA Is SO Important to Diagnose and Treat

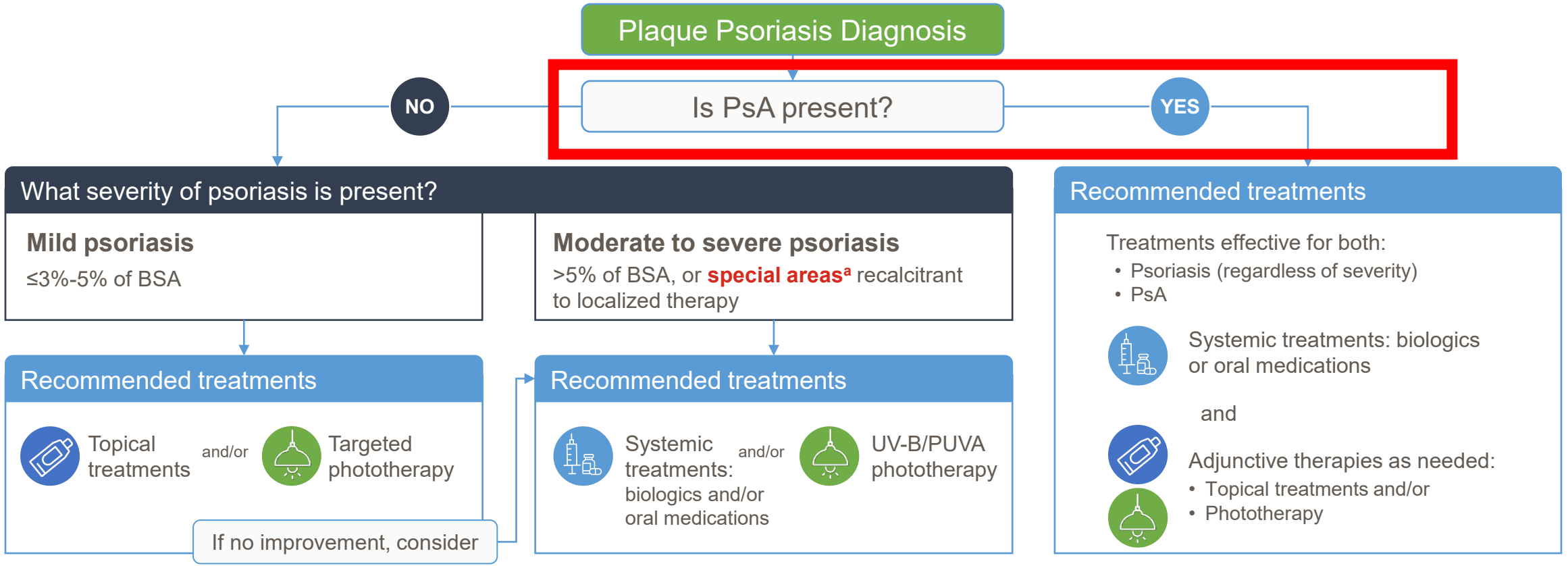
- PsA is common – up to a third or more of psoriasis patients
- PsA is disabling
- PsA frequently goes undiagnosed (up to 41%)
- Cutaneous disease can precede arthritis by 10-12 years
- Dermatologists can be the first to detect arthritis and MUST screen for PsA
- Dermatologists can prevent disability by initiating treatment early on (and/or referring)
- It is essential in the treatment of psoriasis to know first if the patient also has PsA

PsA: A Shared Pathogenesis



Ritchlin C, et al. *N Engl J Med*. 2017;376(10):957-970.

Overall Treatment Approach for Plaque Psoriasis



[a]Special areas include the scalp, palms, soles, genitalia, and nails.

1. Armstrong AW, et al. *JAMA*. 2020;323(19):1945-1960. 2. Menter A, et al. *J Am Acad Dermatol*. 2019;80(4):1029-1072. 3. Smith CH, et al. *Br J Dermatol*. 2009;161(5):987-1019. 4. Menter A, et al. *J Am Acad Dermatol*. 2011;65(1):137-174.

PsA Treatment Options: 2024

Traditional DMARDs
- Methotrexate
- Leflunomide
- Sulfasalazine
- Cyclosporine

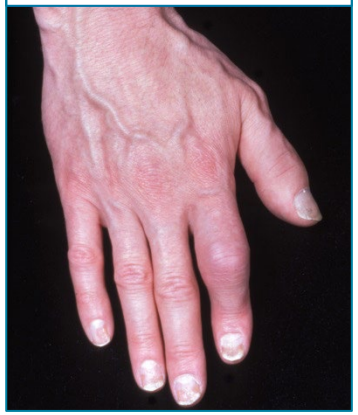
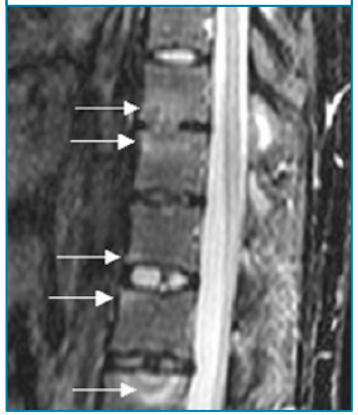
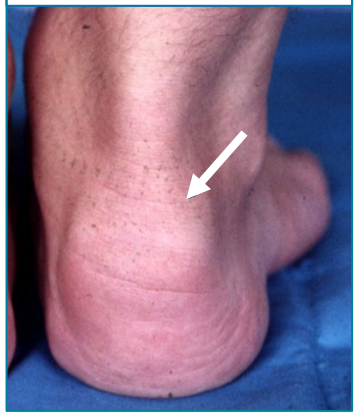
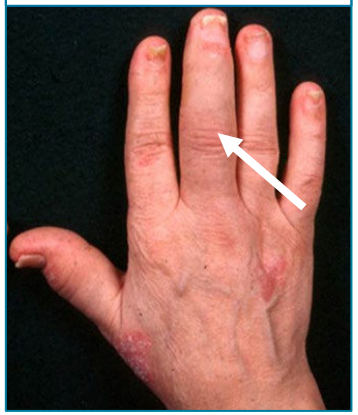
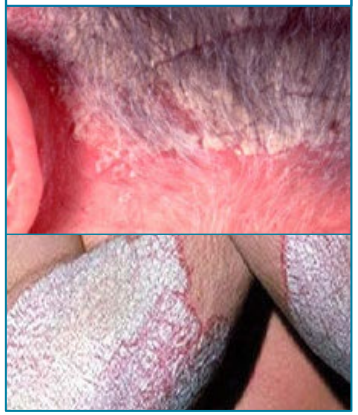
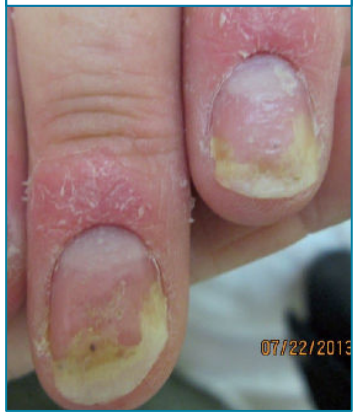
Anti-TNFa
- Adalimumab
- Etanercept
- Infliximab
- Golimumab
- Certolizumab

Other targeted therapies
- Secukinumab (IL17A)
- Ixekizumab (IL17A)
- Ustekinumab (IL12/23)
- Tofacitinib (JAK)
- Abatacept (CTLA4-Ig)
- Apremilast (PDE4)
- Risankizumab (IL23)
- Upadacitinib (JAK)
- Guselkumab (IL23)

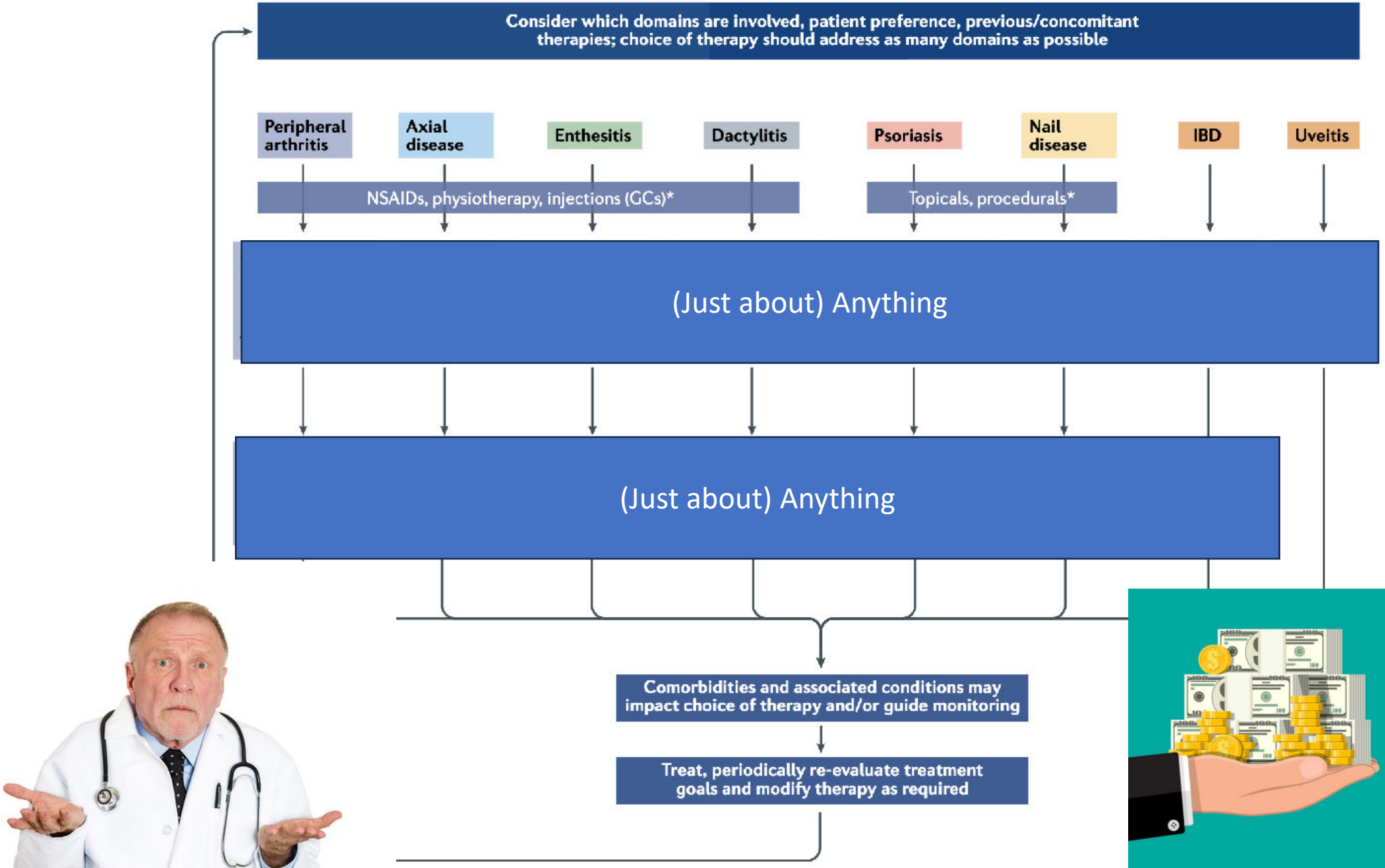
In development
- Bimekizumab (IL17A/F)
- Brodalumab (IL17R)
- Tildrakizumab (IL23)
- Deucravacitinib (TYK2)
- Sonelokimab (IL17A/F nanobody)

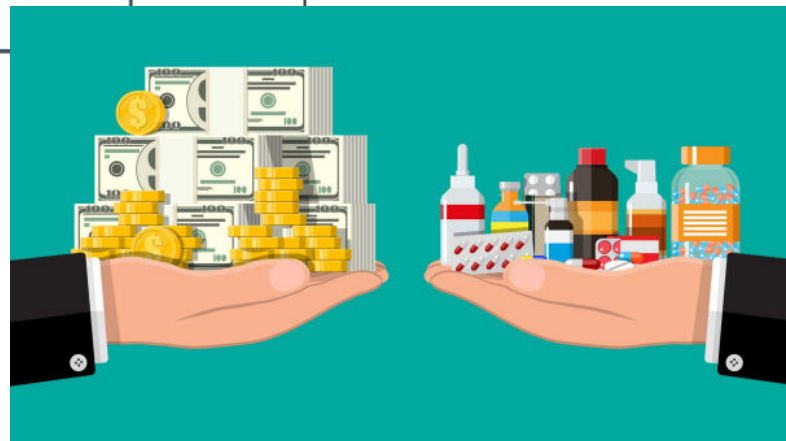
Other
- NSAIDs
- Corticosteroid injections
- Corticosteroids (oral)

Domains of Psoriatic Arthritis

Peripheral arthritis	Axial disease	Enthesitis	Dactylitis	Skin	Nails
					

GRAPPA PsA Tx Recommendations 2021





Treatment by Domains of Disease

	Peripheral Arthritis	Skin and Nail Disease	Axial Disease*	Dactylitis	Enthesitis	IBD	Uveitis
NSAIDs	✓		✓				
Intra-articular steroids	✓						
Topicals		✓					
UV Therapy		✓					
csDMARDs (eg MTX)	✓	✓	X	-	-	+/-	✓
Apremilast	✓	✓	X	✓	✓	X	
Anti-TNF**	✓	+	✓	✓	✓	✓	✓
Anti-IL-12/23	✓	++	X	✓	✓	✓	
Anti-IL-23 (p19)	✓	+++	?	✓	✓	✓	
Anti-IL-17**	✓	+++	✓[2]	✓	✓	X	
JAK inhibitors**	✓	+/-	✓	✓	✓	✓	
TYK2 inhibitor	?	++					

*** Based on data from ankylosing spondylitis trials (used as surrogate for axial PsA). [2]Dedicated axial PsA study (MAXIMISE).**

**** ≥1 in class have inhibition of radiographic progression in label**

Prepared by and Courtesy of JF MEROLA

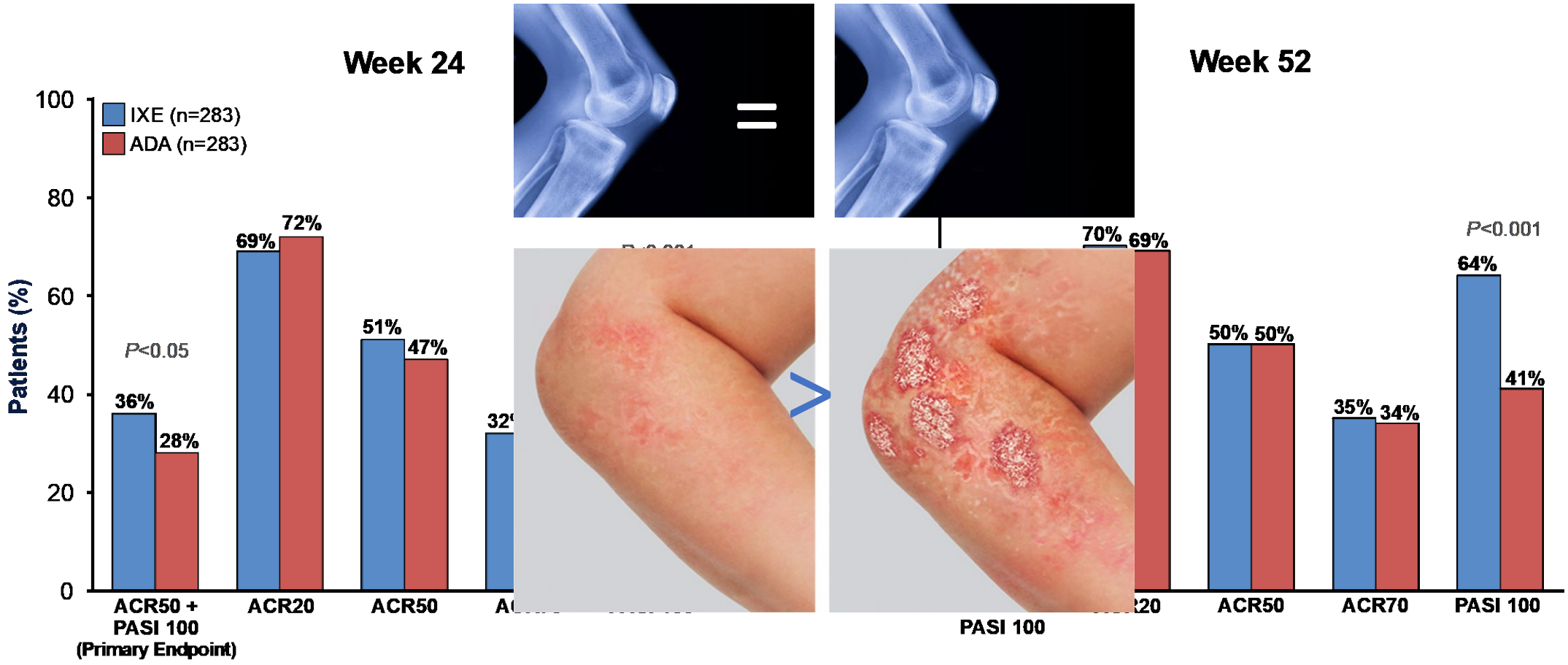
csDMARDs= conventional synthetic disease modifying anti-rheumatic drugs (such as MTX=methotrexate, sulfasalazine, leflunomide)
IBD=inflammatory bowel disease; UV=ultraviolet

Dethroned

Has the TNF-inhibitor been de-throned as king in PsA?

Head-to-Head in PsA
TNF vs IL-17

SPIRIT H2H Study:
Key Outcomes at Week 24 and 52 (NRI)

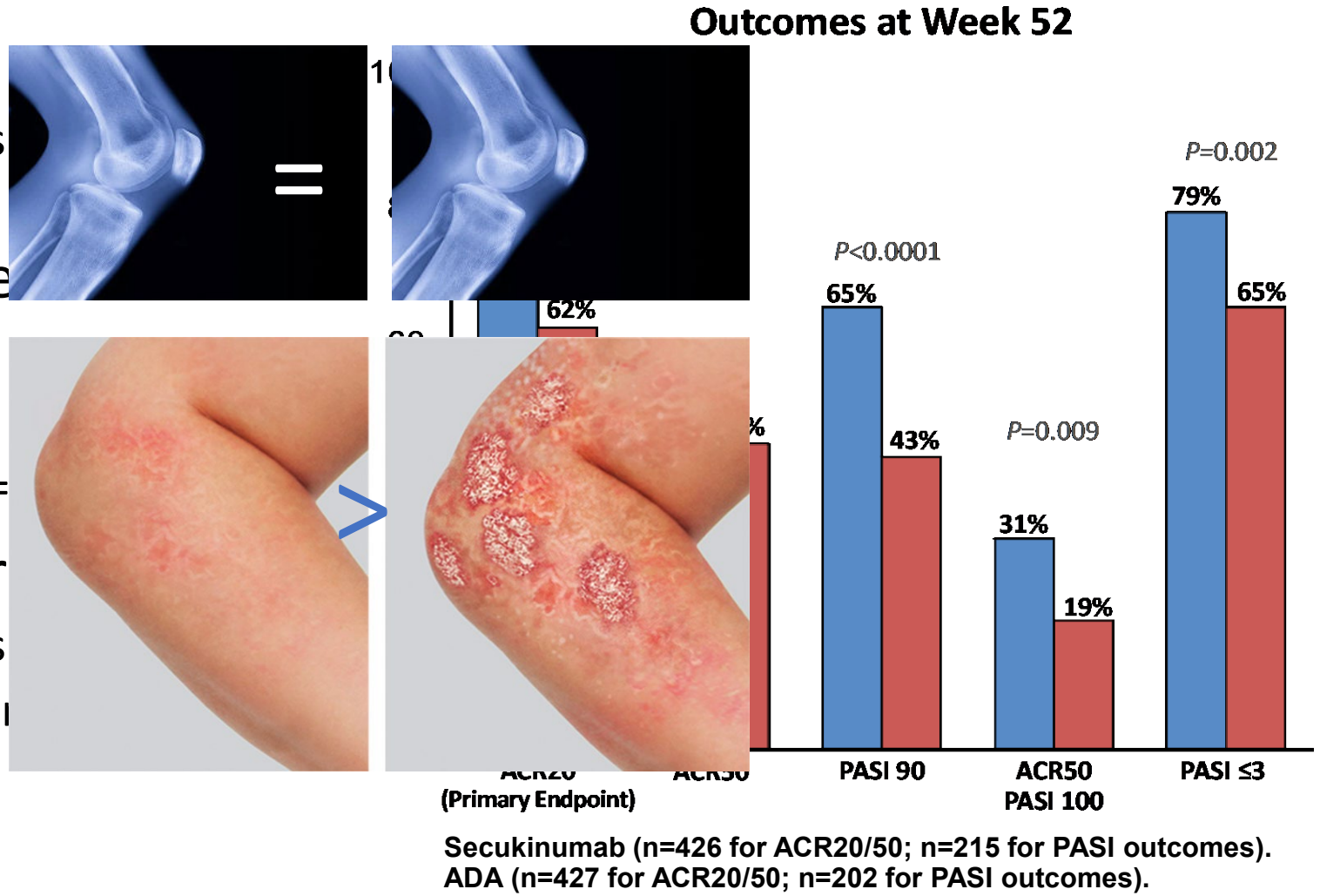


NRI = non-responder imputation method; ADA = adalimumab.

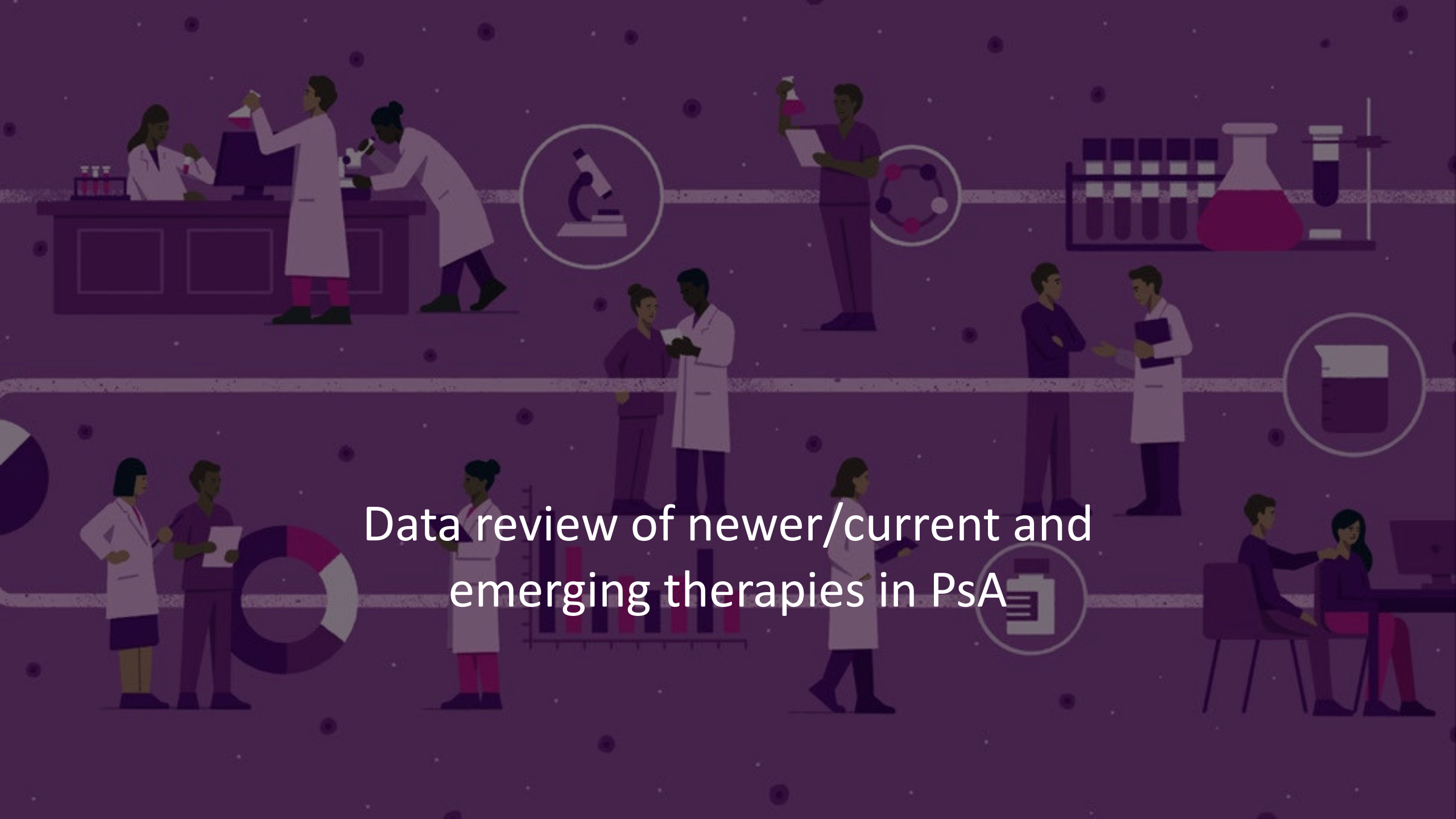
Mease PJ, et al. *Ann Rheum Dis*. 2020;79:123-131. Smollen JS, et al. *Ann Rheum Dis*. 2020;79:1310-1319.

EXCEED Trial: Key Outcomes at Week 52

- Primary endpoint (ACR20)
  - Superiority of secukinumab was established
- Secukinumab showed highe responses vs adalimumab
  - PASI 75/90/100 (*P*<0.001)
  - Combined ACR50 + PASI 100 (*P*=
- Similar outcomes in both gr
  - Improvements in HAQ-DI scores
  - Proportion achieving enthesitis

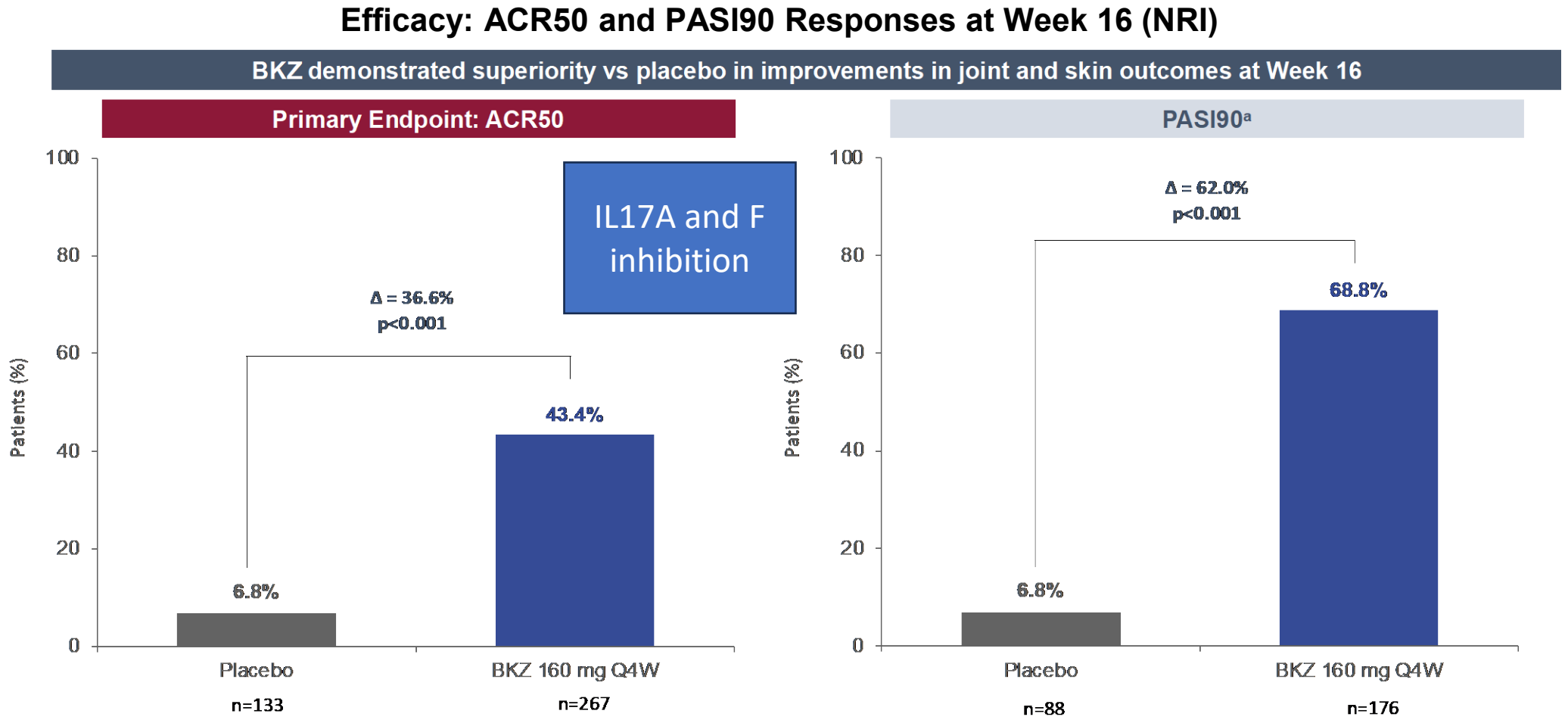


McInnes IB, et al. *Lancet*. 2020;395(10235):1496-1505.



Data review of newer/current and emerging therapies in PsA

Bimekizumab in Patients with Active PsA and an Inadequate Response to Tumor Necrosis Factor Inhibitors: 16-Week Efficacy and Safety from BE COMPLETE, a Phase 3, Multicenter, Randomized, Placebo-Controlled Study



Not FDA approved for PsA

Randomized set. *p*-values were obtained from logistic regression with treatment, prior TNF inhibitor exposure and region as factors. [a]In patients with PSO involving ≥3% BSA at baseline.

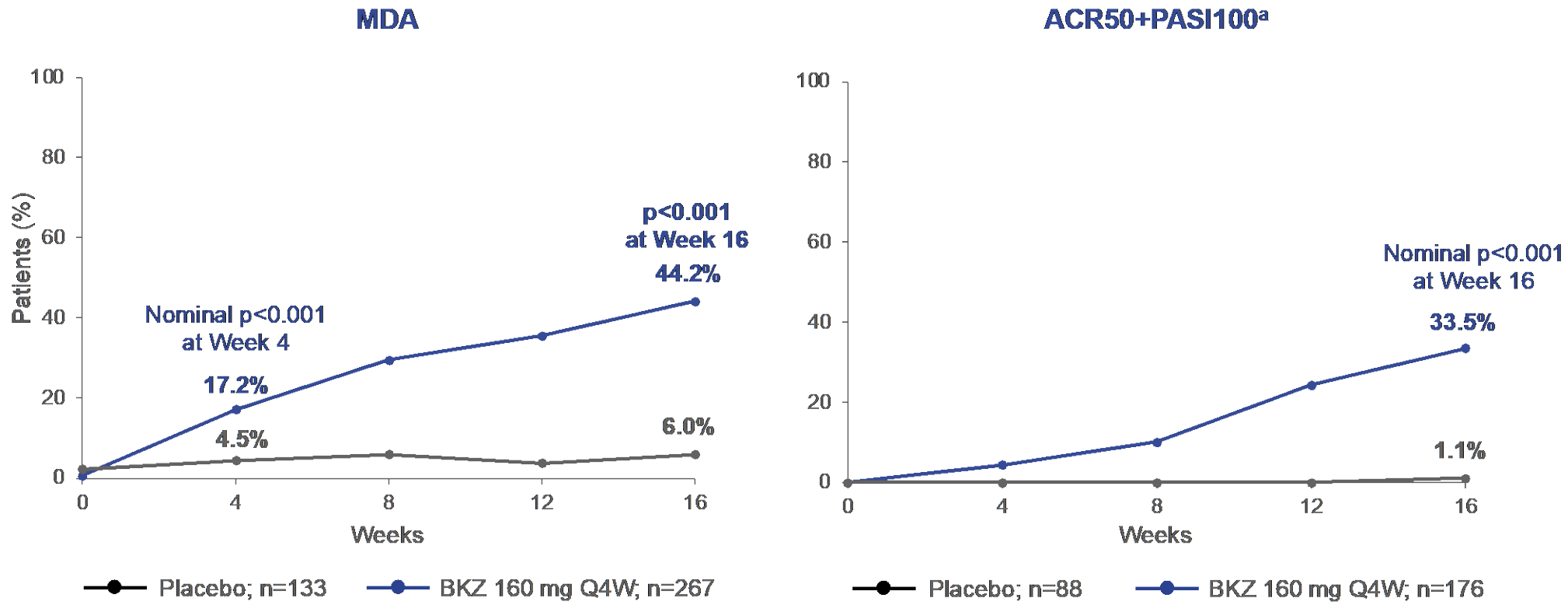
BKZ = bimekizumab.

Merola JF, et al. *Lancet*. 2023;401(10370):38-48.

Efficacy: Proportion of Patients Achieving MDA and ACR50+PASI100 (NRI)

IL17A and F inhibition

BKZ demonstrated superiority vs placebo in achievement of the MDA composite at Week 16



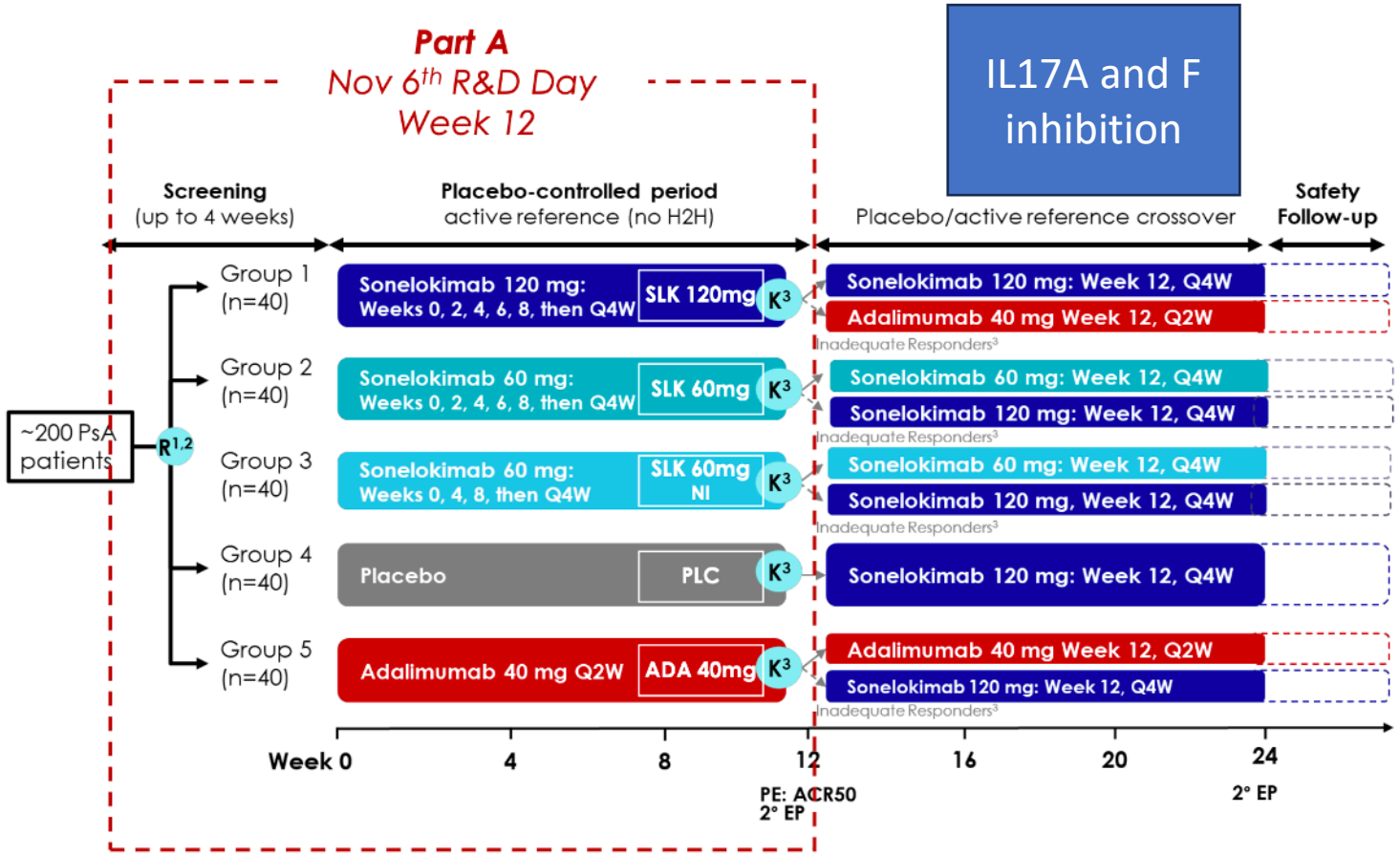
Randomized set. *p*-values obtained from logistic regression with treatment, prior TNFi exposure, and region as factors. Nominal *p* values were not powered or adjusted for multiplicity and should not be used to assess statistical significance. MDA response defined as achievement of at least five of the seven following criteria: TJC ≤1; SJC ≤1; PASI ≤1 or BSA ≤3%; Patient's Assessment of Arthritis Pain ≤15 mm; Patient's Global Assessment-PsA ≤20 mm; HAQ-DI ≤0.5; LEI ≤1. [a]In patients with PSO involving ≥3% of BSA at baseline.

MDA = minimal disease activity.

Merola JF, et al. *Lancet*. 2023;401(10370):38-48.

Sonelokimab: IL17A/F nanobody

ARGO: Phase 2 trial design



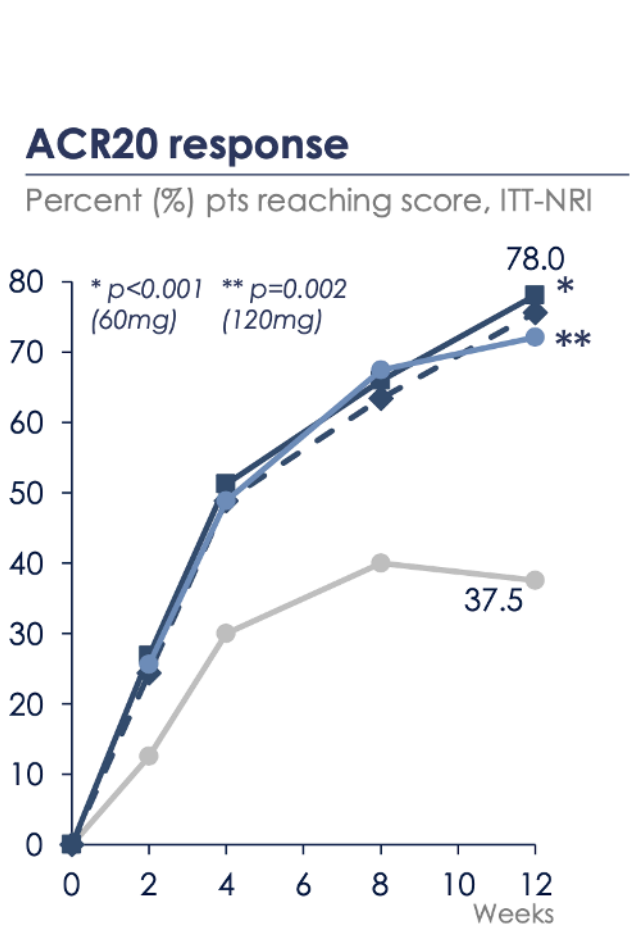
Key design elements of ARGO

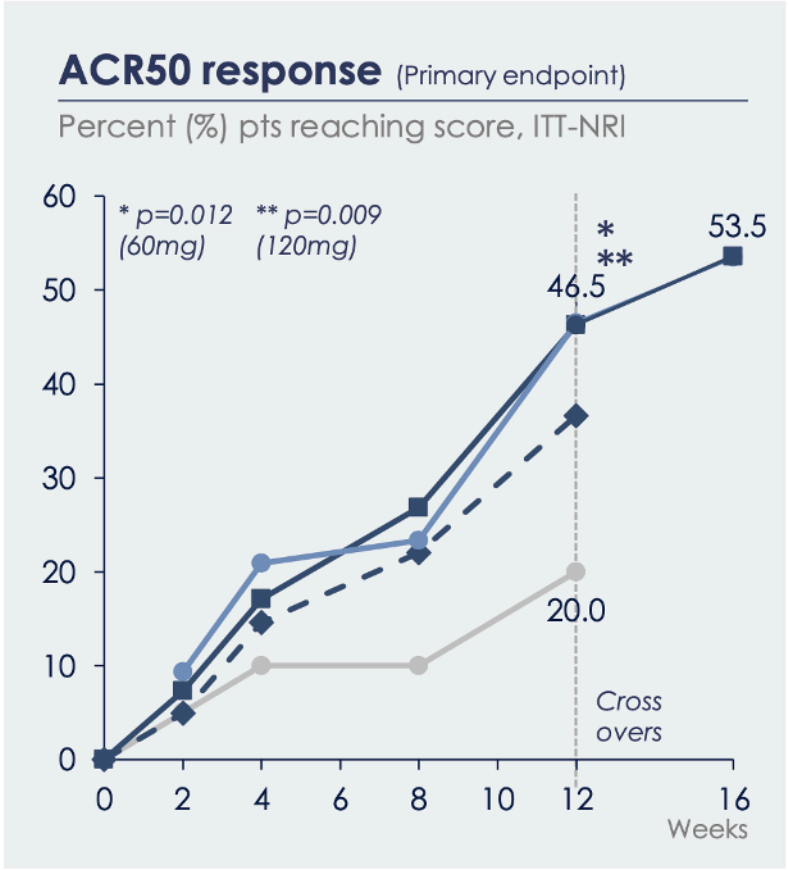
- Global study with approx. **50 sites**, with **207 patients** randomized
- **Double-blind, placebo-controlled, active reference arm**
- **Active PsA** (TJC68 ≥3, SJC≥3, current active PsO and/or confirmed PsO)
- **ACR50** as primary endpoint, PASI90 as key secondary endpoint
- **ITT-NRI** primary analysis; Stratification by sex, previous bio use
- Groups 1 (“**SLK 120mg**” with induction) and 2 (“**SLK 60mg**” with induction) are doses previously used in SLK trials
- Group 3 (“**SLK 60mg NI**”, no induction) was used to support requirement for induction dosing

Notes: 1 Randomization stratified by sex and prior exposure to biologics; 2 At Week 0/Day 1, all eligible participants were randomized 1:1:1:1:1; 3 In the cross-over period, starting at Week 12, participants on sonelokimab 120 mg who did not achieve an adequate response switched to adalimumab 40 mg Q2W until Week 24; participants on sonelokimab 60 mg (started at baseline Q2W or Q4W) who did not achieve an adequate response switched to sonelokimab 120 mg Q4W until week 24; participants on adalimumab who did not achieve an adequate response switched to sonelokimab 120 mg Q4W until Week 24; an adequate response is defined as a reduction of the tender and swollen joint count of ≥20%. Participants on placebo at Week 12 were switched to sonelokimab Q4W until Week 24

Source: MoonLake Clinical

Sonelokimab: IL17A/F nanobody





Primary endpoint met for 60mg and 120mg – SLK 60mg NI not significantly different from PLC

High response levels across all ACR levels measured

As expected, **60mg dose of SLK is sufficient** to drive promising ACR50 responses

Scores **increase over time** esp. for the higher scores

PLC higher vs. **4-13% in similar trials**[1], and **before control with the ADA active reference** arm

*, ** multiplicity-controlled p-values from a logistic regression with covariates for sex and prior biologic use. All patients have reached week 16, week 24 database to be locked in Q1 2024 1 Including comparable trials: ADEPT, DISCOVER 1 and 2, SPIRIT-P1, BE OPTIMAL (BKZ, 7%), FUTURE 2, KEEPsAKE 2, SELECT 1 (highest PLC, 13%)

Source: MoonLake Clinical

Sonelokimab: IL17A/F nanobody

Achievement of leading MDA responses **already at week 12** for SLK

Minimal Disease Activity (MDA) response in ARGO

Percent (%) of patients in each arm, ITT-NRI

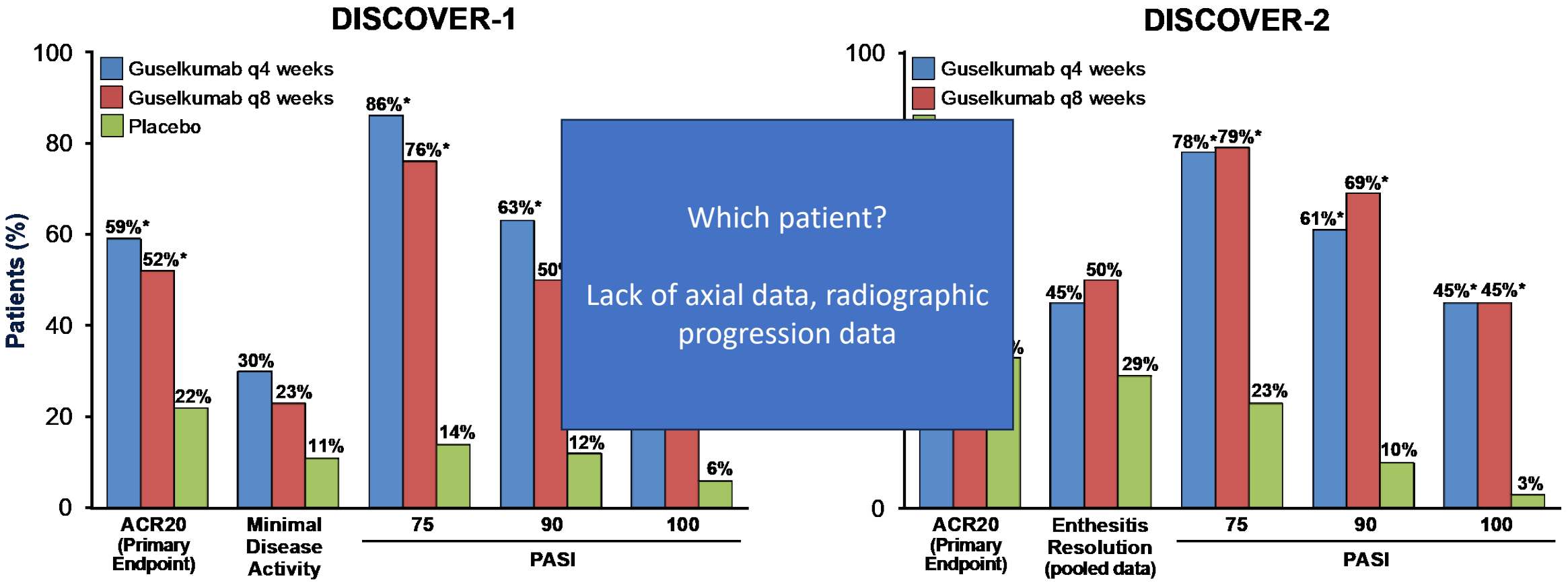
At week 12, MDA responses of SLK **already above what would was observed** in data from other products

At week 16, the ADA arm was similar to week 12 whereas **SLK responses keep increasing – 120 mg close to 50%**

Note: Comparisons across trials, with inherent limitations. No head-to-head trials. Nominal p-value from a logistic regression with covariates for sex and prior biologic use. All patients have reached week 16, week 24 database to be locked in Q1 2024 1 Estimated from data published for the respective study (Merola et al. Lancet. 2023;401:38–48 BE COMPLETE, McInnes et al. Lancet. 2023;401:25–37 BE OPTIMAL)

Source: MoonLake Clinical

DISCOVER-1 and -2: Key Outcomes with GUS at Week 24

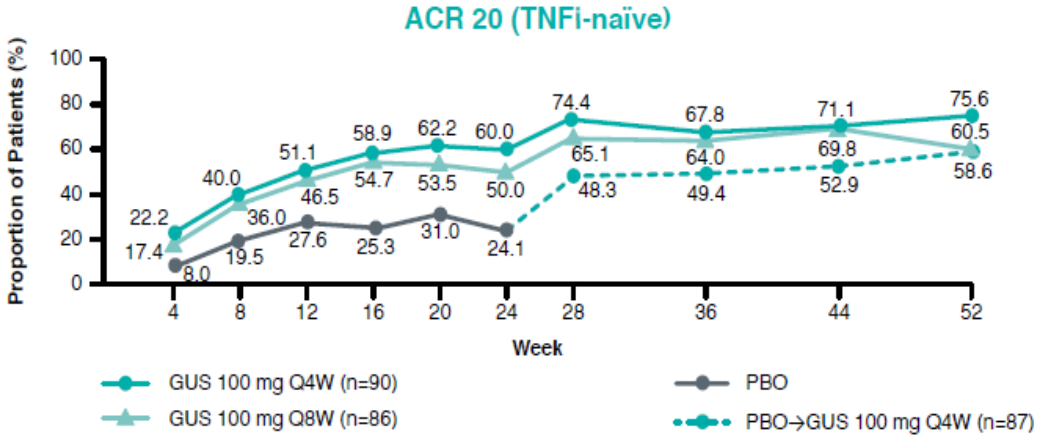


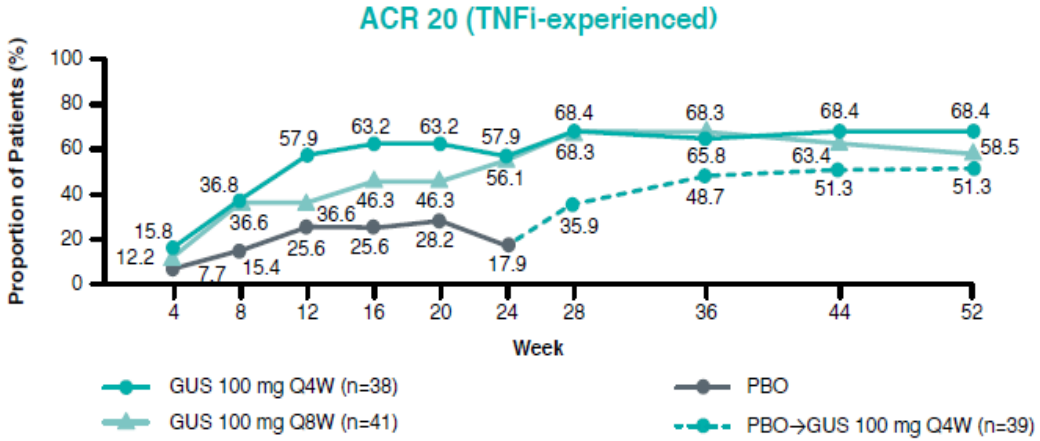
*P<0.001 vs placebo.

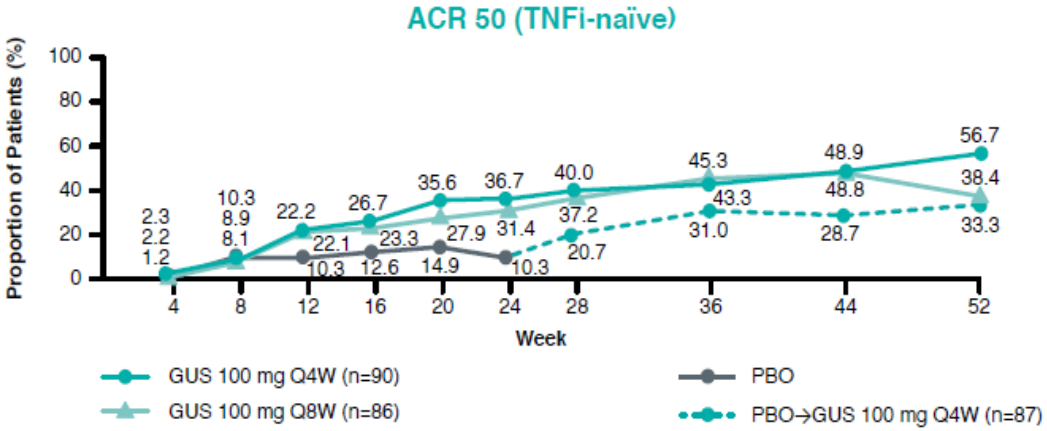
PASI data: Patients with BSA ≥3% and investigator's global assessment ≥2 at baseline; enthesitis (Leeds Enthesitis Index): Pooled data from both studies.

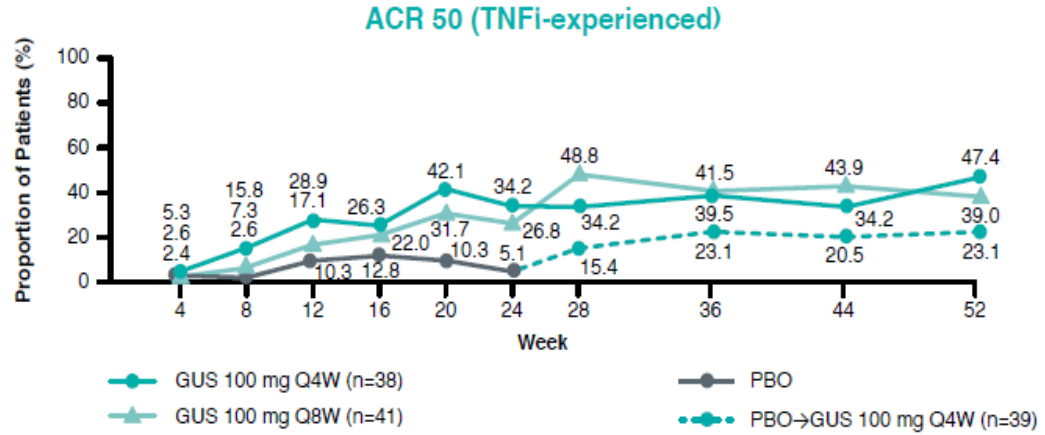
Deodhar A, et al. *Lancet*. 2020;395(10230):1115-1125. Mease PJ, et al. *Lancet*. 2020;395(10230):1126-1136.

DISCOVER-1: GUS Efficacy in TNF Inhibitor-Experienced and Naïve Patients with PsA through 52 Weeks







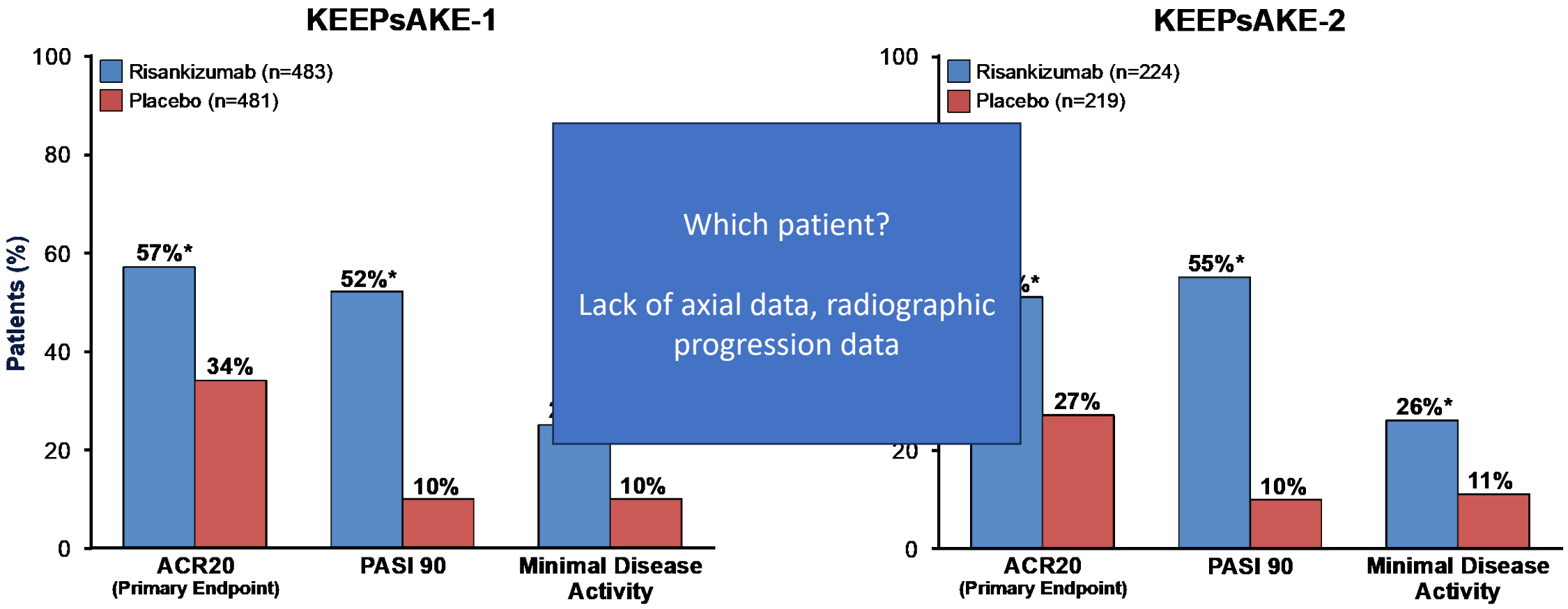


Following application of relevant treatment failure rules, patients with missing data were considered nonresponders through Week 52

PBO = placebo.

Ritchlin CT, et al. Presented at AAD VMX 2021. April 23-25, 2021 Virtual. P27847.

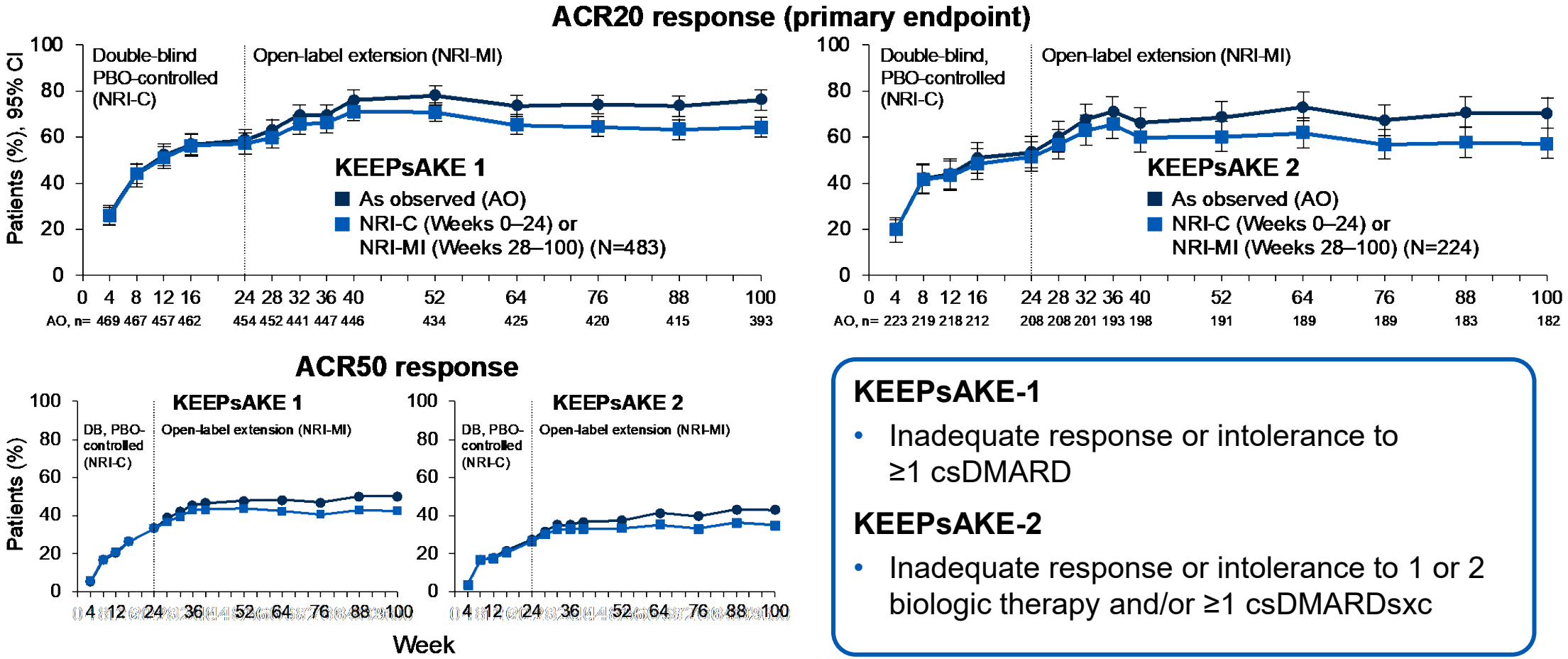
KEEPsAKE-1 and -2: Key Outcomes with Risankizumab at Week 24



*P<0.001 vs placebo.

Kristensen LE, et al. *Ann Rheum Dis*. 2022;81:225-231. Östör A, et al. *Ann Rheum Dis*. 2022;81:351-358.

KEEPsAKE 1 and 2: 100-Week Efficacy and Safety of RZB for Active PsA in Patients Originally Randomized to RZB



KEEPsAKE-1

- Inadequate response or intolerance to ≥1 csDMARD

KEEPsAKE-2

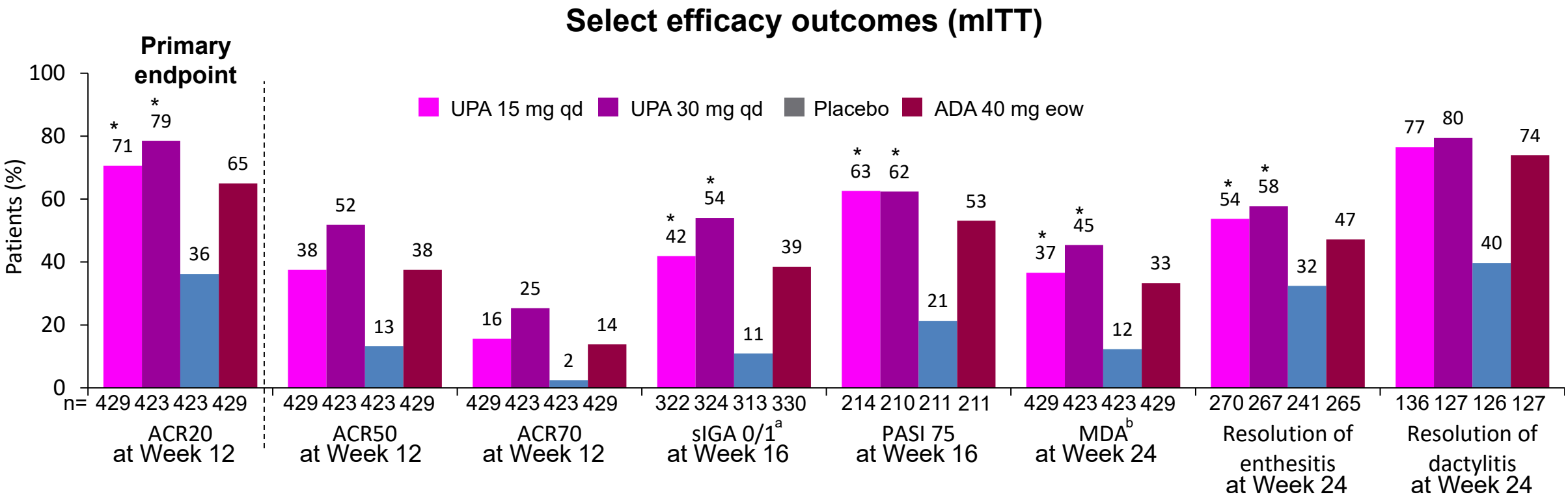
- Inadequate response or intolerance to 1 or 2 biologic therapy and/or ≥1 csDMARDsxc

NRI-C incorporating multiple imputation to handle missing data due to COVID-19; NRI-MI, as observed with missing data imputed as nonresponders except those missing due to COVID-19 or geopolitical conflict in Ukraine and Russia, which are imputed by multiple imputation.

RZB = risankizumab.

Kristensen LE, et al. Presented at: European Academy of Dermatology and Venereology (EADV) 2022, May 12-14. Ljubljana, Slovenia. D3T01.1D.

SELECT-PsA 1: Key Outcomes after Treatment with Upadacitinib vs Placebo and Adalimumab among Adults with Psoriatic Arthritis

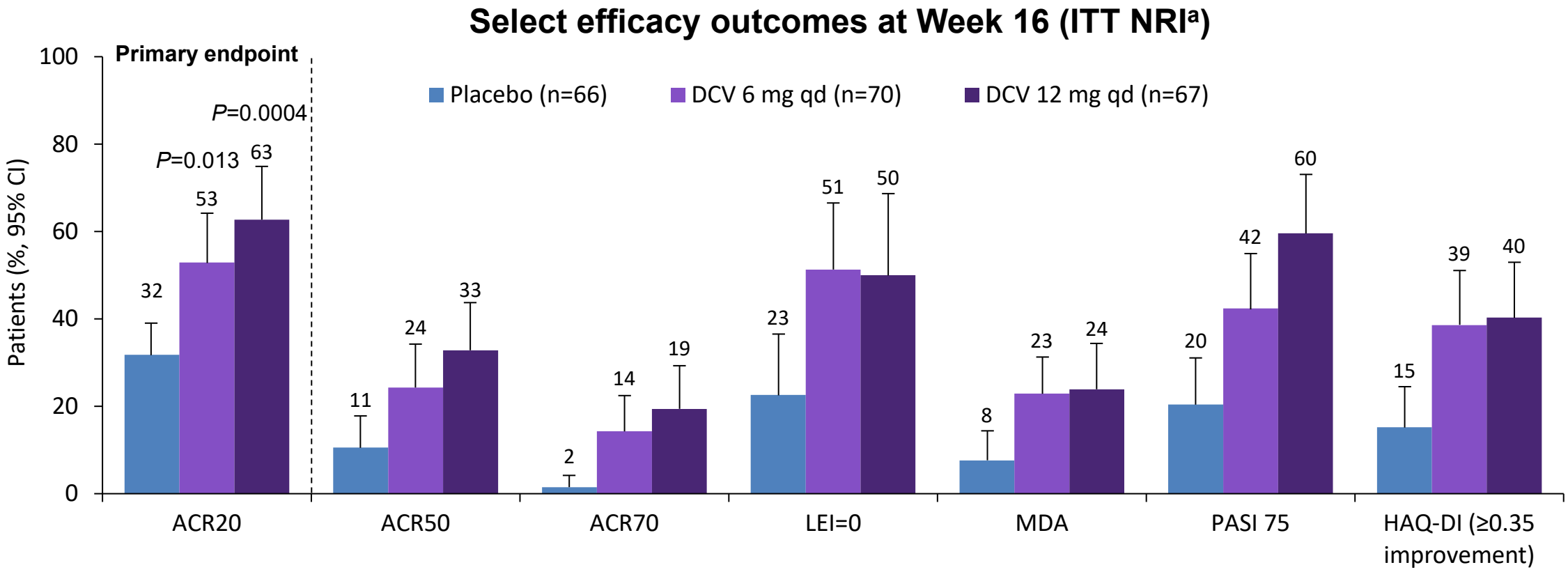


***P<0.001 vs placebo (controlled for multiplicity).**
For binary endpoints, NRI was used to handle missing data.
[a]Plus ≥2-point decrease from baseline; [b]MDA determined as fulfilment of 5 of 7 criteria: Tender joint count ≤1, swollen joint count ≤1, PASI score ≤1 or ≤3% BSA involvement, patient pain NRS ≤1.5, PtGA-disease activity NRS ≤2.0, HAQ-DI score ≤0.5, Leeds Enthesitis Index ≤1.

Bio-naïve population

McInnes IB, Anderson JK, Magrey M, Merola JF, Liu Y, Kishimoto M, Jeka S, Pacheco-Tena C, Wang X, Chen L, Zueger P, Liu J, Pangan AL, Behrens F.*N Engl J Med*. 2021;384:1227-1239.

Phase 2 Trial: ACR Responses and Other Outcomes after 16 Weeks of Treatment with Deucravacitinib among Patients with Active PsA



- [a]Modified baseline observation carried forward used to impute data for PASI 75 and HAQ-DI responses.
  LEI (Leeds Enthesitis Index) assessed among patients with enthesitis at baseline (LEI ≥1, N=96, 46%).
  MDA (Minimal Disease Activity) response defined as patients achieving 5/7 of the following: Tender joint count ≤1, swollen joint count ≤1, PASI ≤1 or ≤3% BSA affected, Patient Global Assessment (PtGA) of pain ≤15, PtGA of disease activity ≤20, HAQ-DI ≤0.5, tender entheseal points ≤1.
  Mease PJ, et al. Presented at: ACR Convergence 2020; Maui Derm for Dermatologists 2021.

Not FDA approved for PsA

Tx Options: How Do We Decide in 2023?

Domain of disease

Co-morbidities

Shared decision making around treatment goals

Patient preferences (topical, oral/injectable, etc.)

Access / insurance

Comorbidities/Co-Prevalent Disease in Psoriatic Disease

- Uveitis
- Renal disease
- Hepatosteatosis
- COPD
- Sleep apnea
- Depression
- Alcoholism
- Smoking
- Diabetes
- Dyslipidemia
- Obesity
- Peripheral vascular disease
- Myocardial infarction
- Stroke
- Cardiovascular death
- Gout

Jamnitski A, et al. *Ann Rheum Dis*. 2013;72(2):211-216. Yeung H, et al. *JAMA Dermatol*. 2013;149(10):1173-1179.

Treatment by Domains of Disease

	Peripheral Arthritis	Skin and Nail Disease	Axial Disease*	Dactylitis	Enthesitis	IBD	Uveitis
NSAIDs	✓		✓				
Intra-articular steroids	✓						
Topicals		✓					
UV Therapy		✓					
csDMARDs (eg MTX)	✓	✓	X	-	-	+/-	✓
Apremilast	✓	✓	X	✓	✓	X	
Anti-TNF**	✓	+	✓	✓	✓	✓	✓
Anti-IL-12/23	✓	++	X	✓	✓	✓	
Anti-IL-23 (p19)	✓	+++	?	✓	✓	✓	
Anti-IL-17**	✓	+++	✓[2]	✓	✓	X	
JAK inhibitors**	✓	+/-	✓	✓	✓	✓	
TYK2 inhibitor	?	++					

*** Based on data from ankylosing spondylitis trials (used as surrogate for axial PsA). [2]Dedicated axial PsA study (MAXIMISE).**

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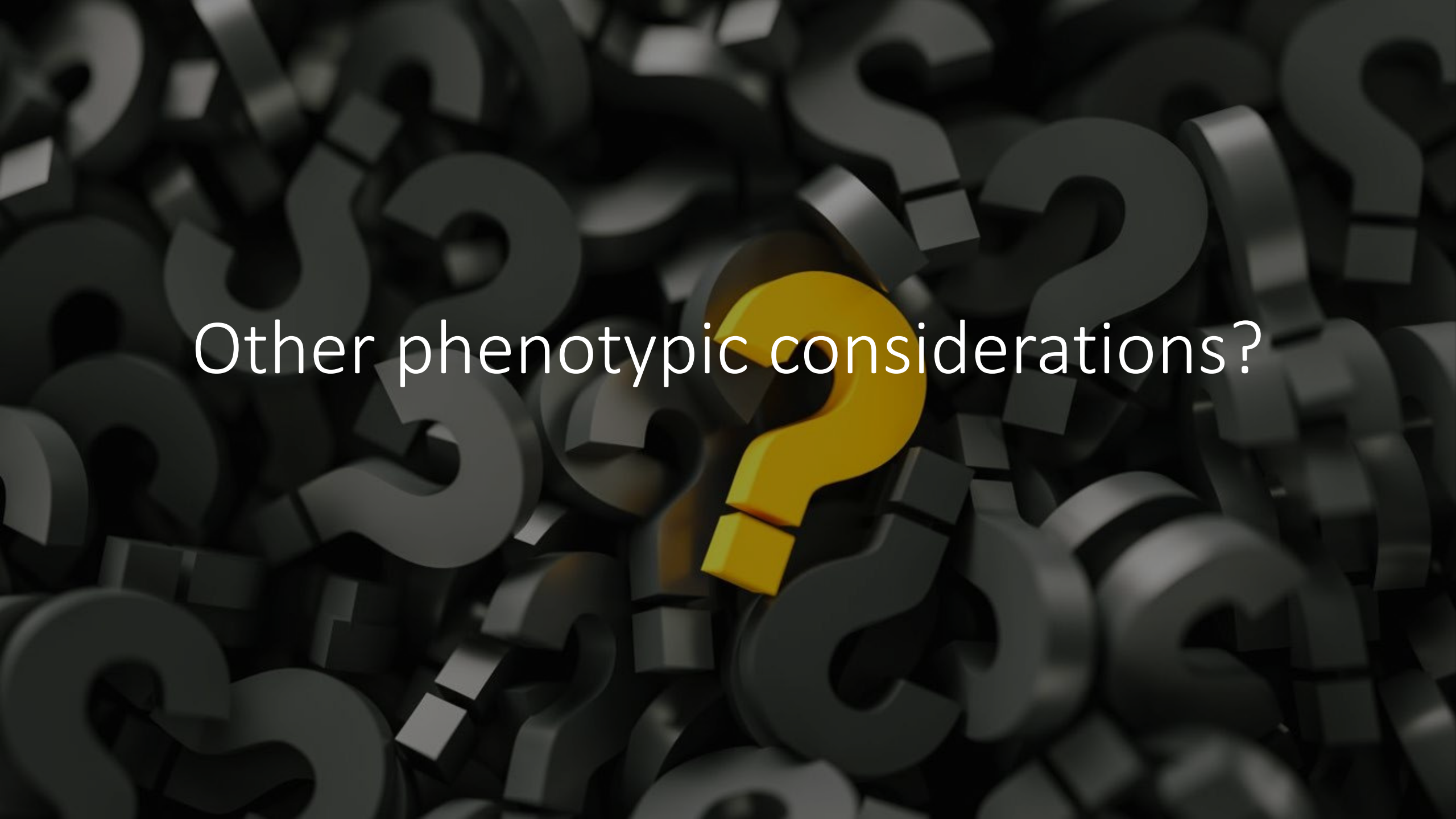
csDMARDs= conventional synthetic disease modifying anti-rheumatic drugs (such as MTX=methotrexate, sulfasalazine, leflunomide)
IBD=inflammatory bowel disease; UV=ultraviolet


Other phenotypic considerations?

FOREMOST: Phase 4, randomized, placebo-controlled trial of apremilast for patients with early oligoarticular psoriatic arthritis

Patient eligibility

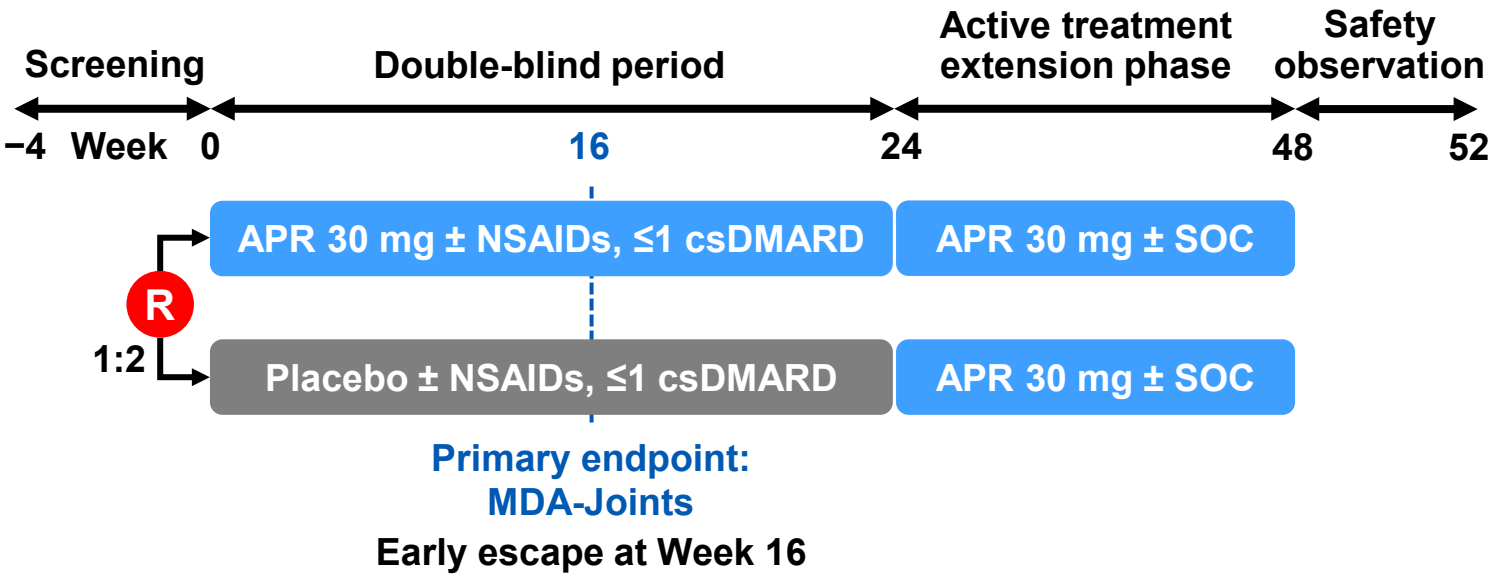
- PsA duration ≤5 years
- >1 to ≤4 swollen and >1 to ≤4 tender joints despite treatments with NSAIDs and/or ≤2 csDMARDs

Primary endpoint: MDA-Joints at Week 16[1]

- Minimal disease activity (MDA)-Joints was defined as a composite of:
  - **Two** mandatory cutoffs:
    - TJC ≤1 and SJC ≤1
  - **AND any three** of the following:
    - Psoriasis-involved BSA ≤3%
    - Patient pain VAS ≤15
    - PtGA VAS ≤20
    - HAQ-DI ≤0.05
    - Enthesitis count ≤1 based on LEI

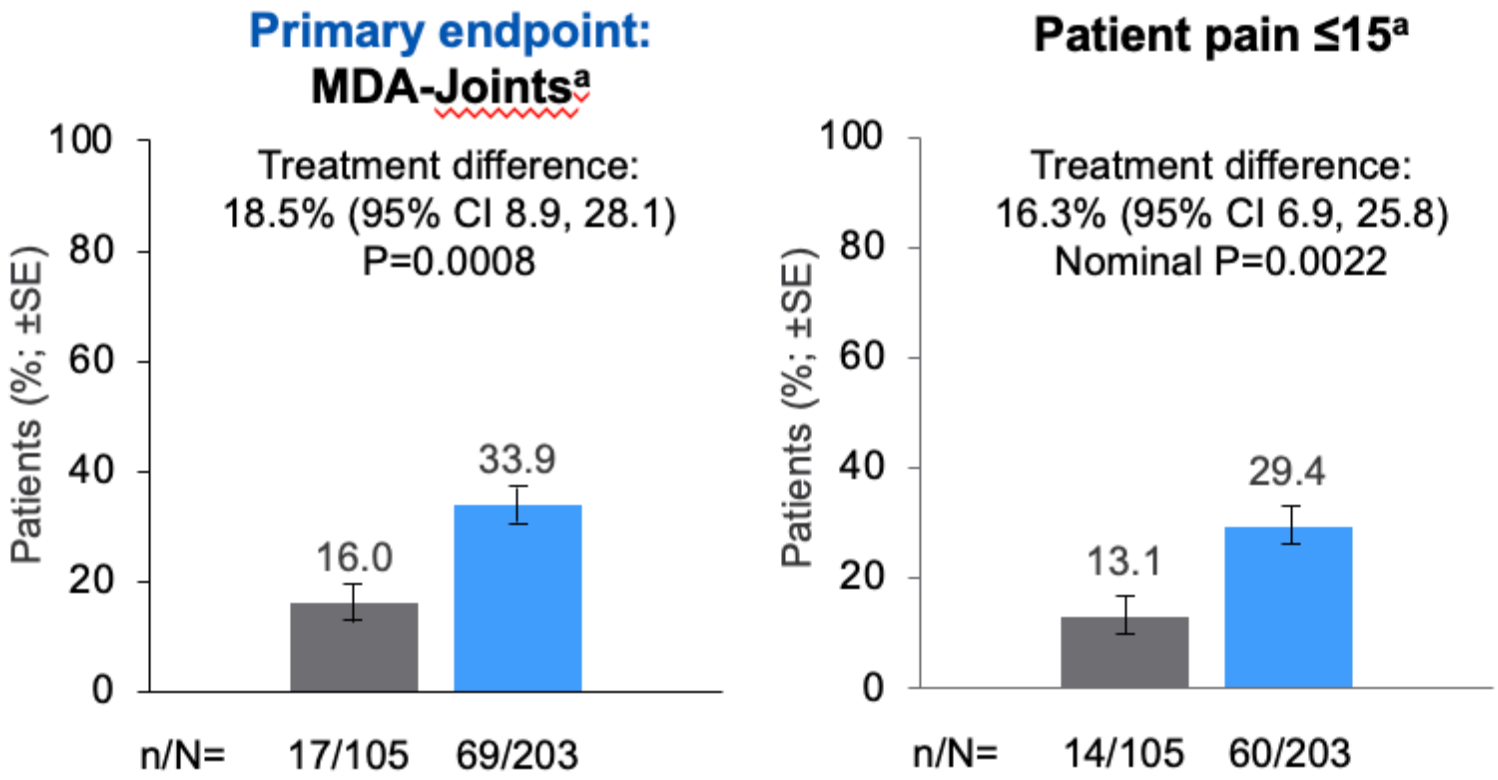
Exploratory endpoints (Week 16)

- Nail VAS = 0
- BSA = 0



1. Coates LC, Helliwell PS. J Rheumatol 2016;5:311–16
Gossec L, et al. EADV 2023, P2574. Sponsored by Amgen Inc.

FOREMOST: Effect of apremilast on disease outcomes at Week 16 among patients with early oligoarticular psoriatic arthritis



[a]Patients who discontinued the study prior to Week 16 due to AEs or lack of efficacy were imputed as non-responders. Remaining missing values at Week 16 were imputed by multiple imputation. The number of responders was rounded based on the value given by multiple imputations; [b]Patients with non-missing data. Based on a mixed model for repeated measures of the change prior/concomitant use of csDMARD (naïve, prior use only both prior and concomitant use) and baseline glucocorticosteroids use (yes/no) per interactive web response system data as factors, and baseline value as a covariate.

Gossec L, et al. EADV 2023, P2574. Sponsored by Amgen, Inc


Future considerations

Arthritis & Rheumatology

AN OFFICIAL JOURNAL OF THE AMERICAN COLLEGE OF RHEUMATOLOGY

American College of Rheumatology

NOTES FROM THE FIELD

Moving the Goalpost Towards Remission: The Case for Combination Immunomodulatory Therapies in Psoriatic Arthritis

Jose U. Scher ✉, Alexis Ogdie, Joseph F. Merola, Christopher Ritchlin ✉

First published: 12 April 2021 | https://doi.org/10.1002/art.41765

Rheum-Derm-GI/IBD Interface

A Study of Guselkumab and Golimumab Combination Therapy in Participants With Active Psoriatic Arthritis (AFFINITY)

https://clinicaltrials.gov/ct2/show/NCT05071664

VEGA Phase 2a Study:

Results of Novel Clinical Study Show Adults with Moderately to Severely Active Ulcerative Colitis Achieved Higher Rates of Clinical Response, Clinical Remission, and Endoscopic Improvement at 12 Weeks with Guselkumab and Golimumab Combination Therapy Versus Either Monotherapy Alone

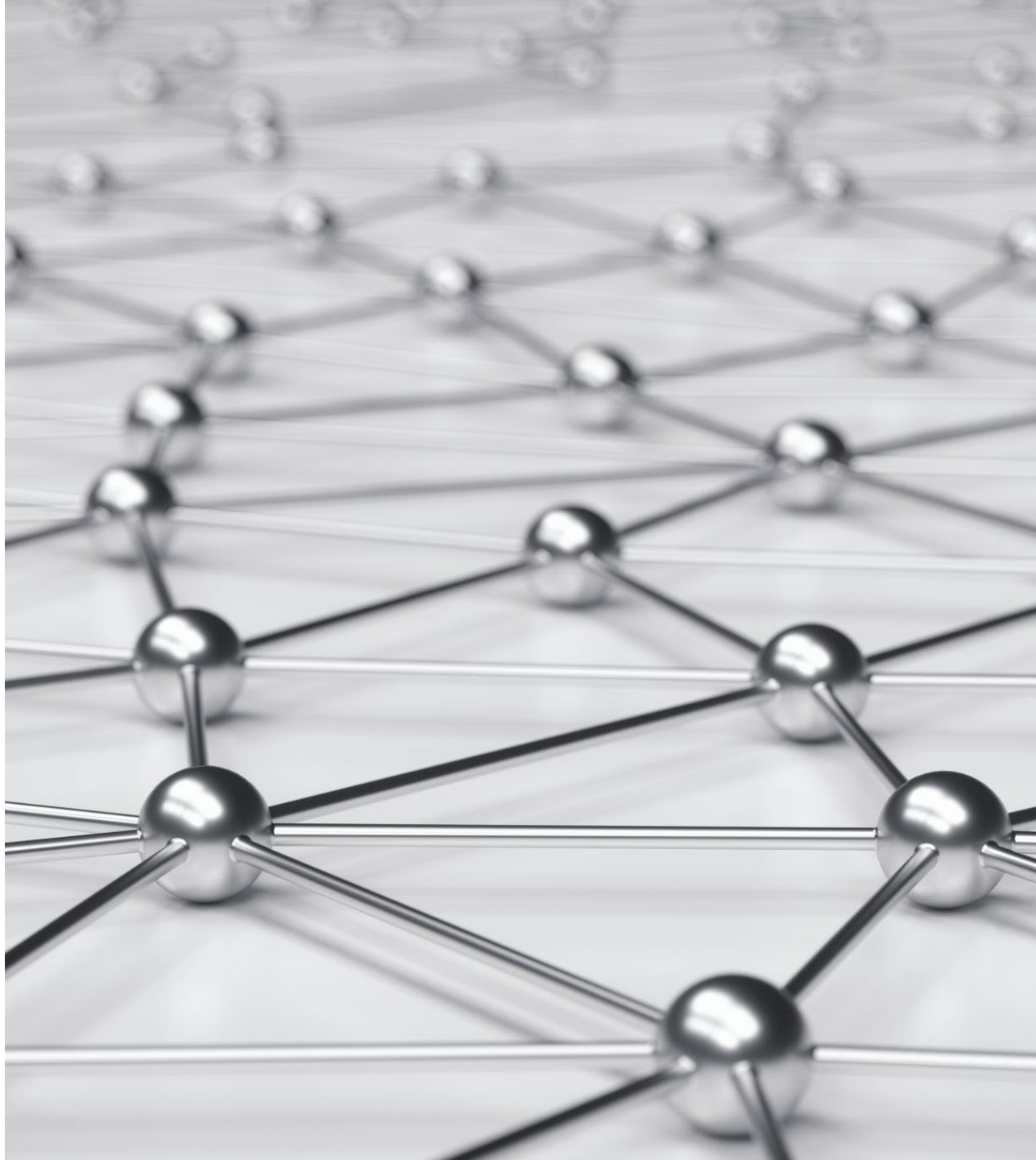
Embarking on a novel combination therapy trial

- Multi-center partnership
- Interventional study
- Practical, clinically relevant study design

Mount Sinai

UT Southwestern Medical Center

NYU Langone Health




Prevention?

nature REVIEWS RHEUMATOLOGY

REVIEWS

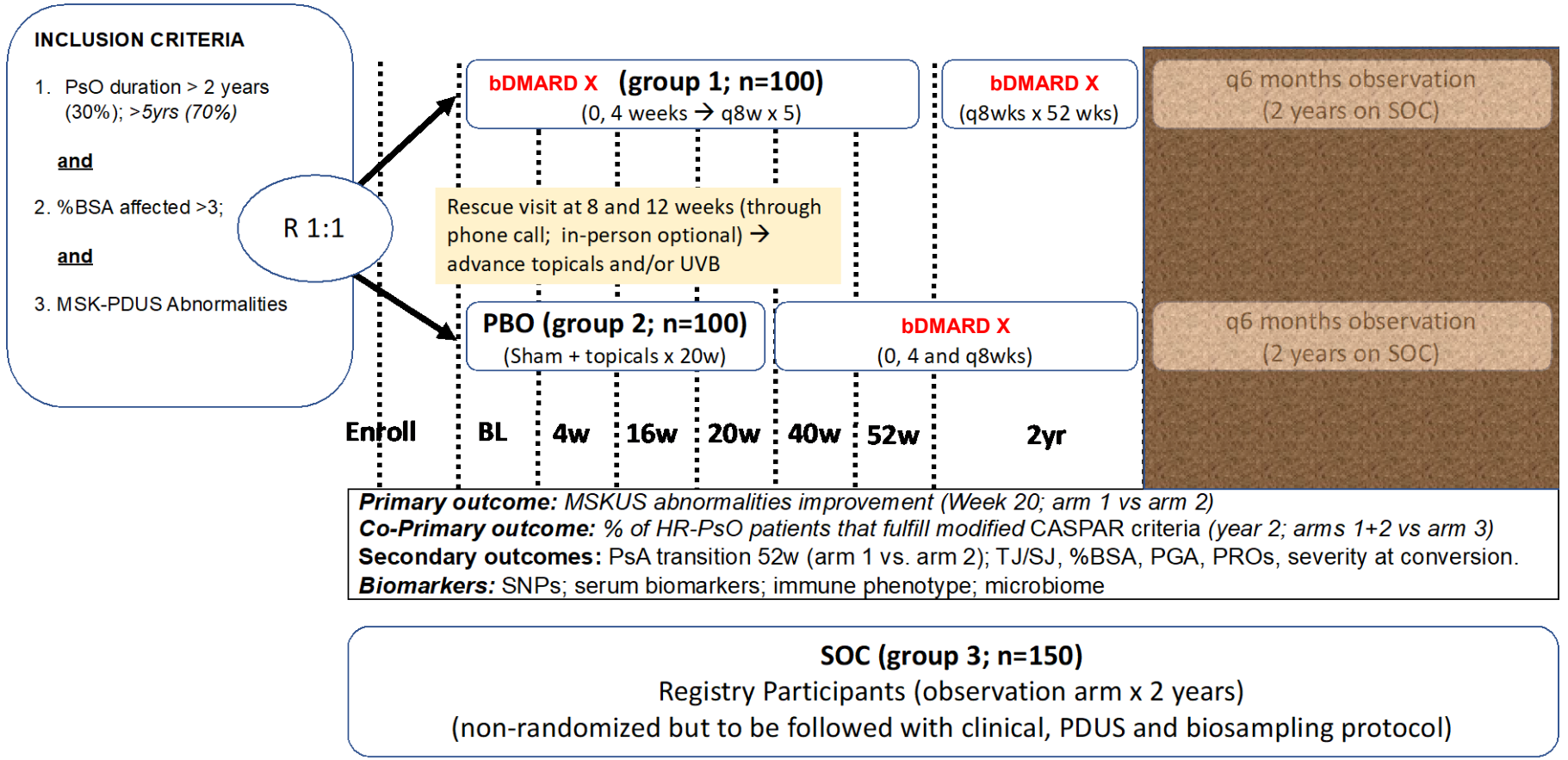
Preventing psoriatic arthritis: focusing on patients with psoriasis at increased risk of transition

Jose U. Scher[1]*, *Alexis Ogdie*[2], *Joseph F. Merola*[3] and *Christopher Ritchlin*[4]*

Nature Reviews Rheumatology **volume 15**, pages153–166 (2019)

Prevention of PsA

PAMPA trial: An investigator-initiated, multicenter study



Scher JU, Ogdie A, Merola JF, Ritchlin C. *Nat Rev Rheumatol*. 2019;15(3):153-166.

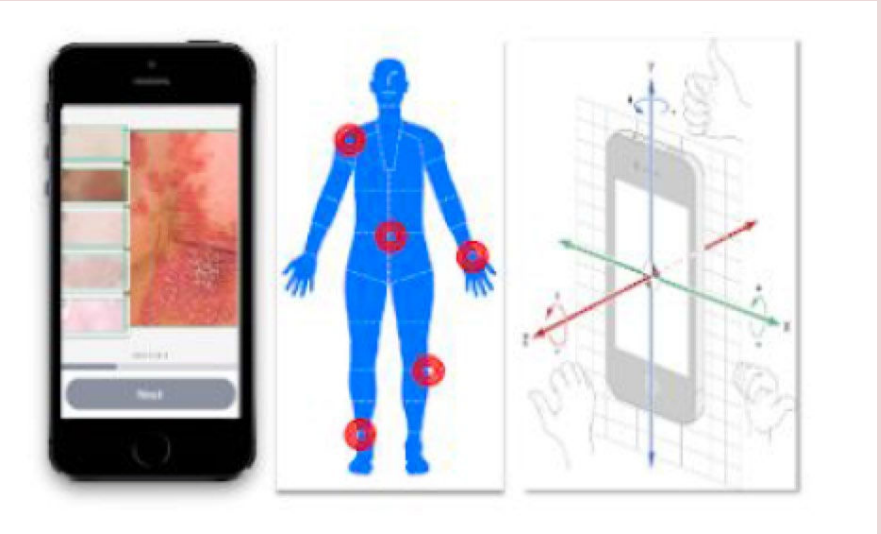
SAGE-PPACMAN PSORCAST Digital Biomarker Project

- SAGE Bionetworks has successfully developed disease monitoring apps launched in Parkinson's, RA, others

- Novel digital biomarker in PsO/PsA
- >$1.5M in funding to date for PSORCAST

Passive and active data capture, biometric data; biospecimen component

- 1) PsO and PsA measurement with emphasis on transition to PsA
- 2) PsO and PsA disease activity measurement / remote symptom tracking



SageBionetworks

PPACMAN
Psoriasis & Psoriatic Arthritis Clinics Multicenter Advancement Network

Psorcast

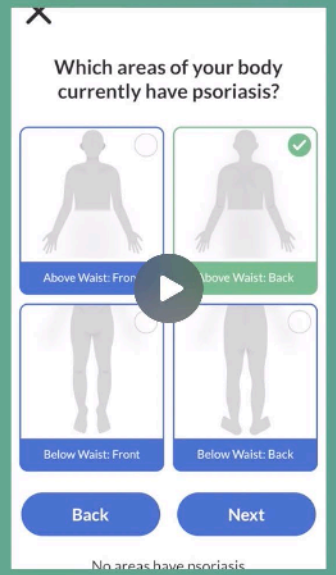
Download on the App Store

Predicting treatment response, psoriatic arthritis risk, and flares

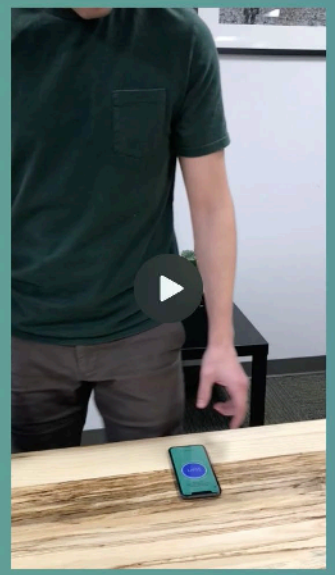
In the Psorcast Research Study, we hope to forecast which drugs might work best for certain people, who is at greatest risk of developing psoriatic arthritis, and flare/remission cycles.

How will I measure my symptoms with my phone?

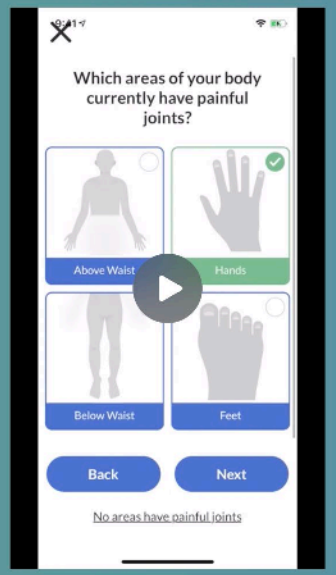
Psoriasis Draw



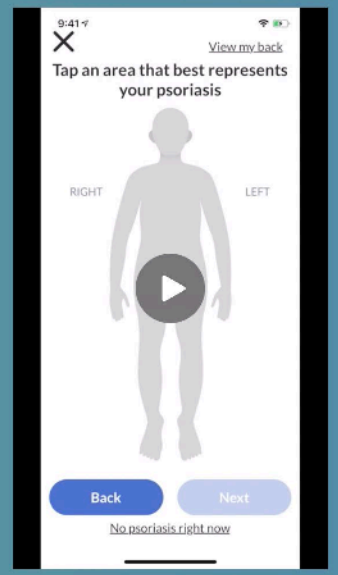
Digital Jar Open



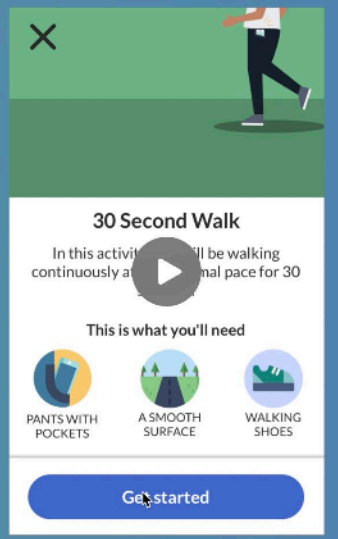
Painful Joint Count



Psoriasis Area Photo



30-Second Walk



www.Psorcast.org


THANK YOU