RhAPP

RHEUMATOLOGY ADVANCED PRACTICE PROVIDERS

RHAPP NATIONAL CONFERENCE

SEPTEMBER 8-10, 2022

Psoriatic Arthritis Advanced Track

Katie Springer PA-C

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Faculty Disclosures

- Speaker: Amgen

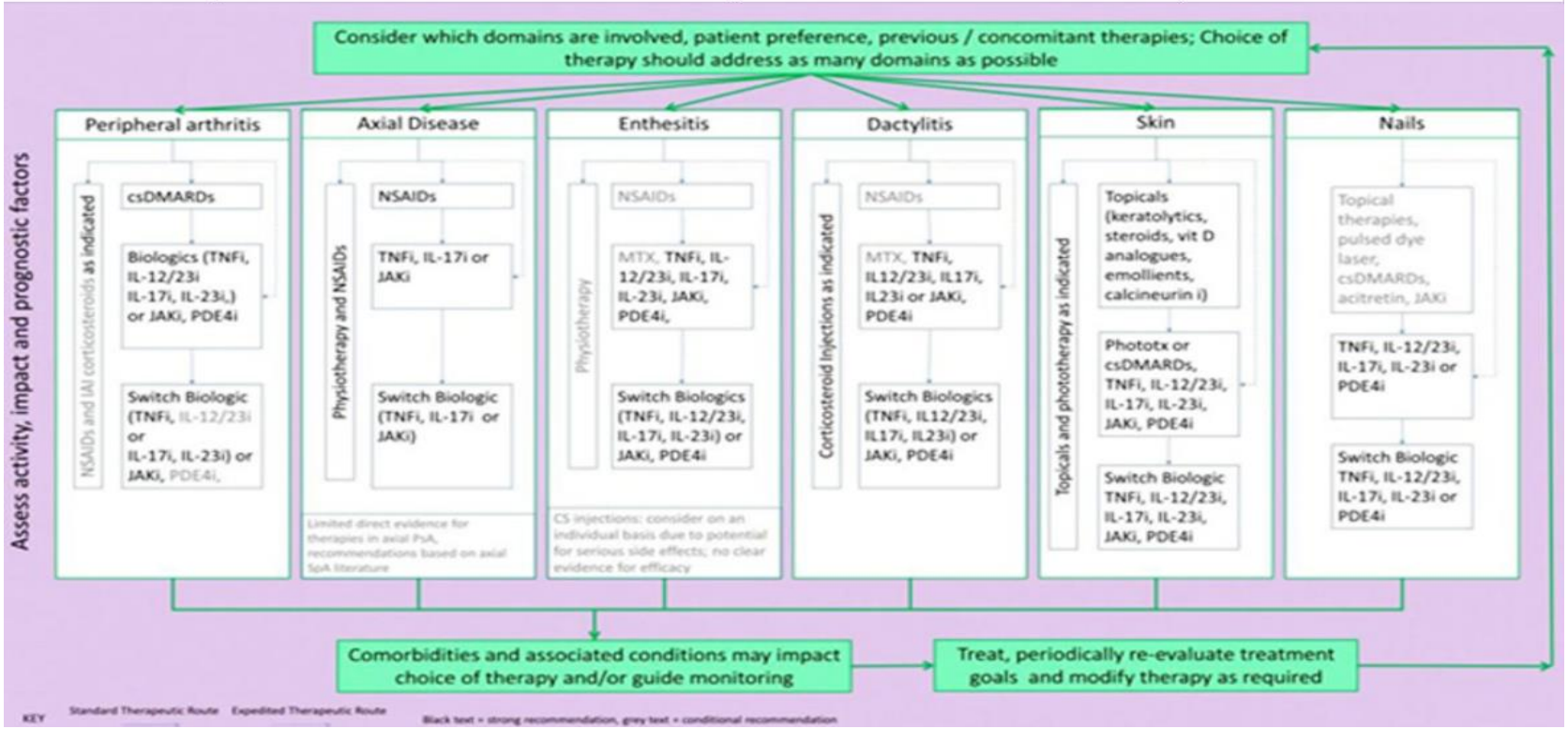
Potpourri of topics in 30 minutes (or less!)

GRAPPA Treatment Recommendations: 2021 Update

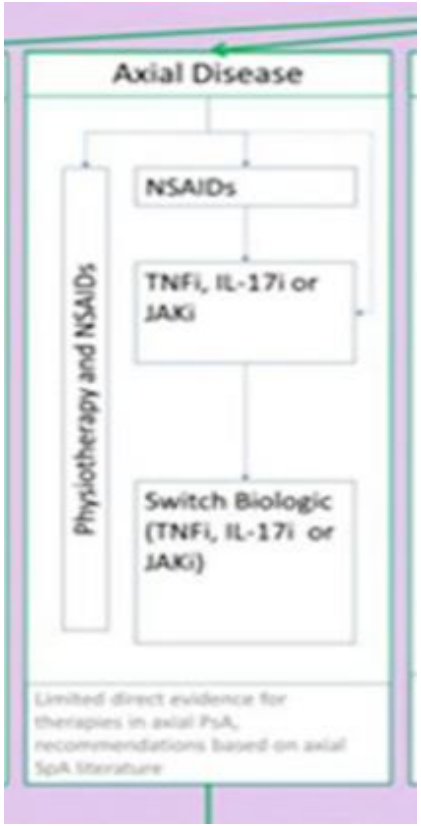
Laura C. Coates, Nadia Corp, Danielle A. van der Windt, Denis O'Sullivan, Enrique R. Soriano and Arthur Kavanaugh

The Journal of Rheumatology March 2022, jrheum.211331; DOI: https://doi.org/10.3899/jrheum.211331

Coates L, et al. J Rheumatol. 2022 Mar 15;jrheum.211331. doi: 10.3899/jrheum.211331.



Focus on Axial manifestation

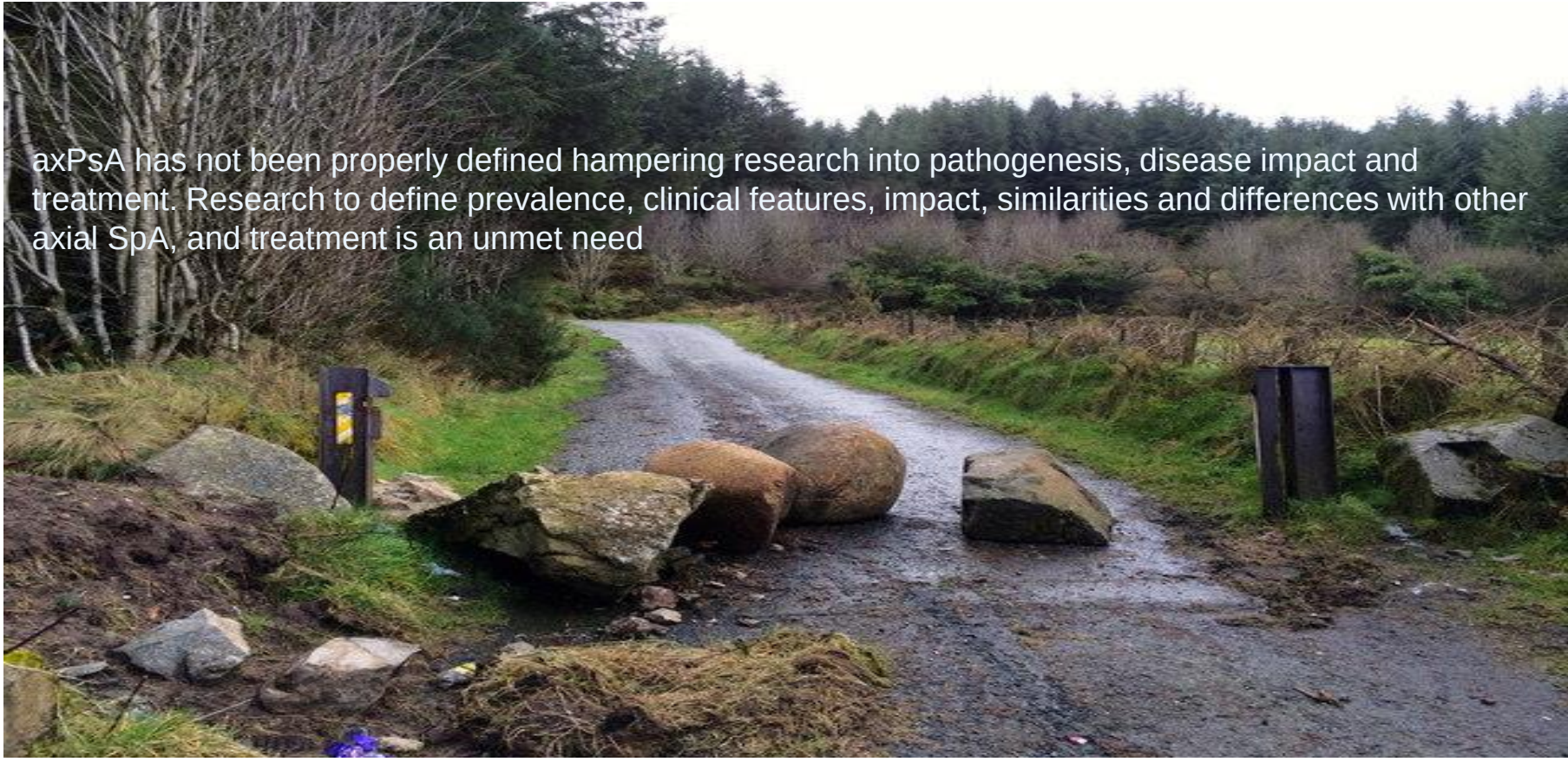


How do we know if it is PsA with axial disease or AS with psoriasis?

RABBIT-SpA

- 2017 - present German disease registry for axial spondyloarthritis and psoriatic arthritis
- axPsA
- older age at onset , more peripheral disease , less likely HLA B27 positive, less frequent uveitis, less likely have IBD

Roadblock



axPsA has not been properly defined hampering research into pathogenesis, disease impact and treatment. Research to define prevalence, clinical features, impact, similarities and differences with other axial SpA, and treatment is an unmet need

IL-17 axPsA

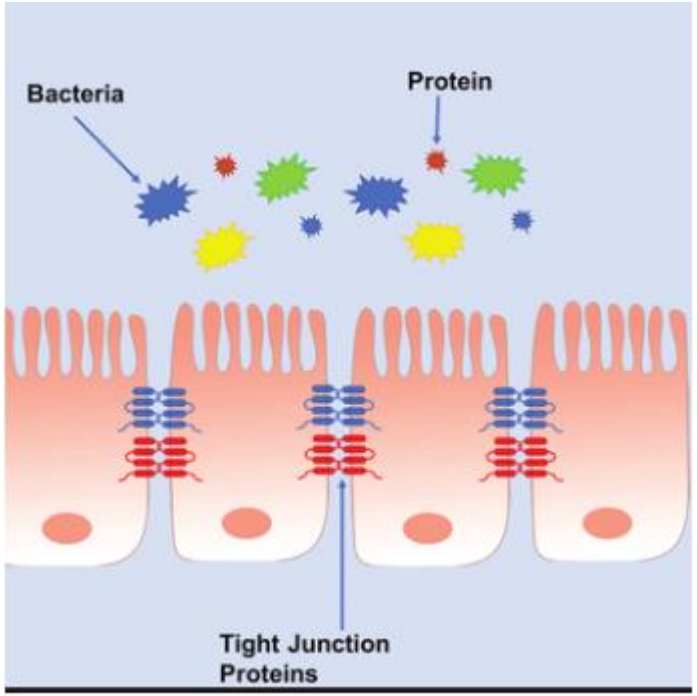
- Where does IL-17 fit in?
- Which one to use?

Why can IXE claim superiority to ADA but SEC can not?

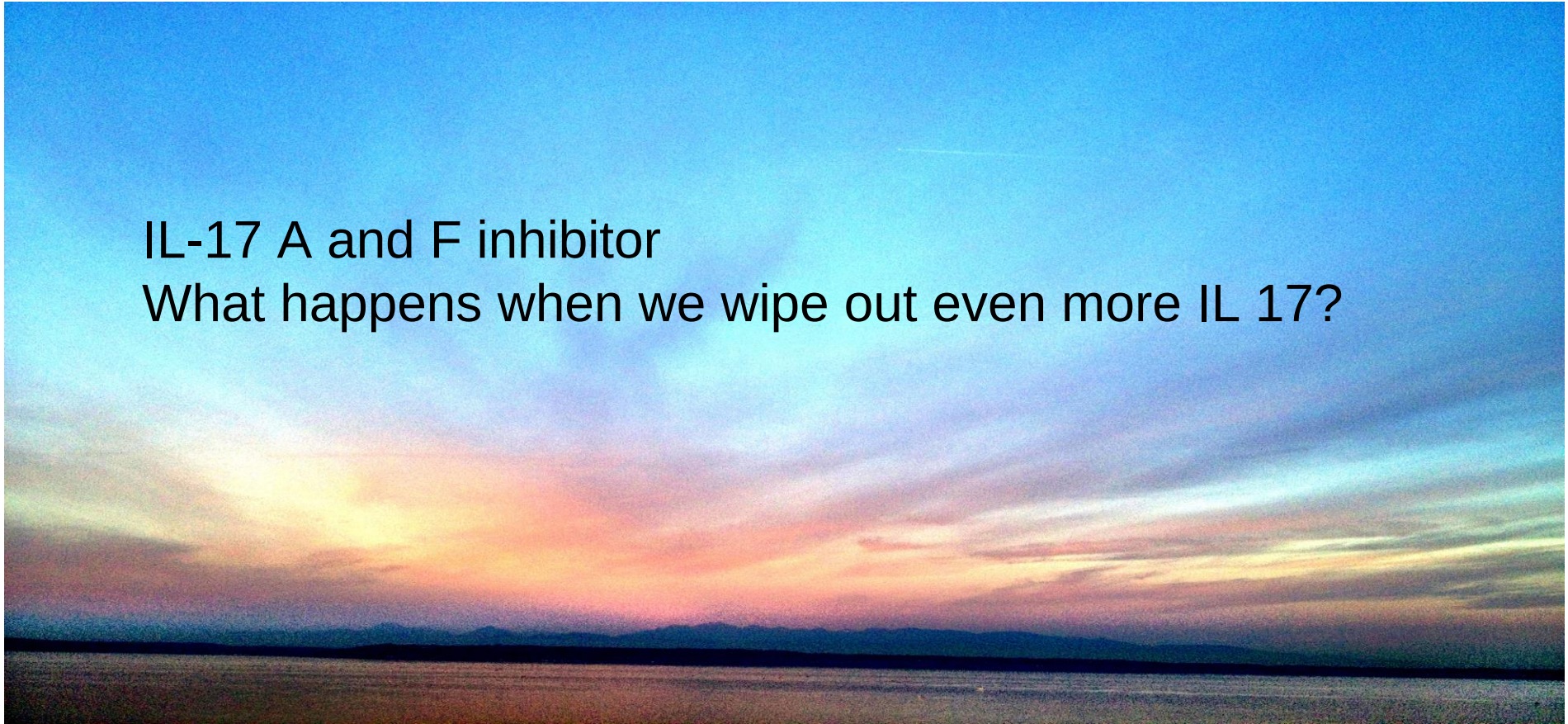
- Both IL-17A inhibitors
- The difference is study design
  - IXE study (SPIRIT) combined end point PASI and ACR score
  - SEC study (EXCEED) end point was ACR score only

Why does IL-17 affect the gut?

IL-17 is needed to maintain tight junctions in endothelial cells in our gut lining. When we inhibit IL-17, this allows bacteria to cross into gut lumen.



On the horizon: Bimekizumab

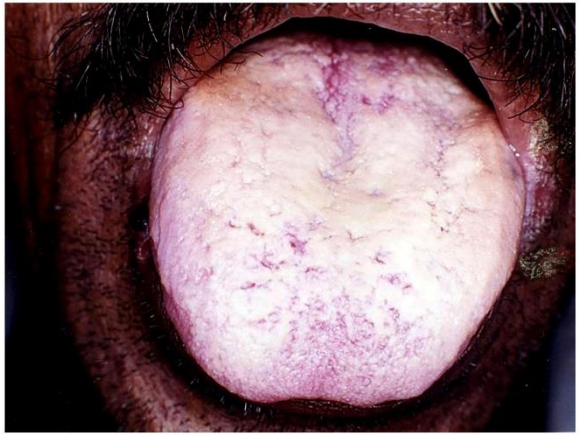


IL-17 A and F inhibitor

What happens when we wipe out even more IL 17?

bimekizumab safety

- oral candidiasis with drop outs due to severe thrush



JAKI axPsA

- Where do JAKI fit in?
- Oral Surveillance

JAKIs for axPsA: SELECT-PsA 1&2 trials
Upacitinib axial PsA data vs ADA and PBO

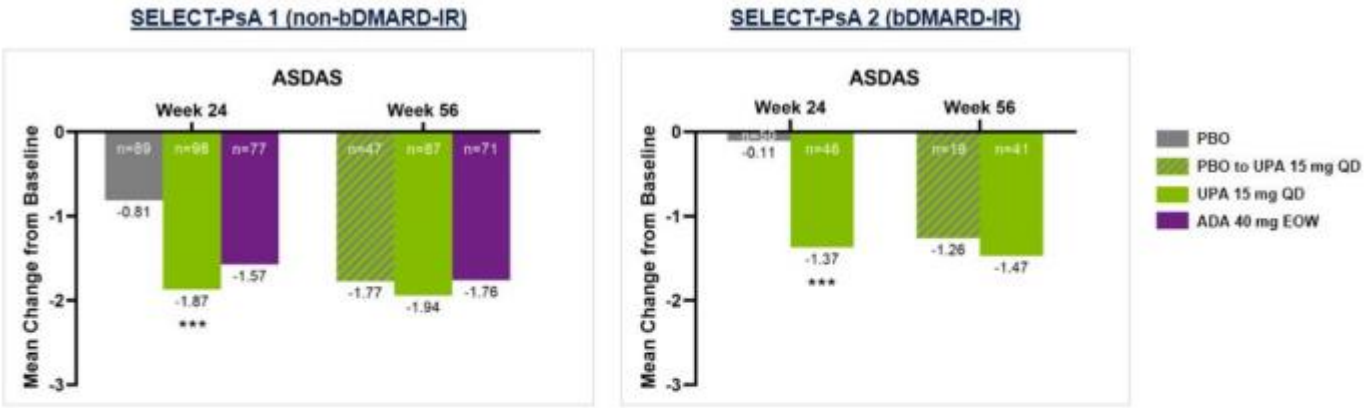


Figure 5. Mean Change from Baseline in ASDAS Scores at Weeks 24 and 56 (MMRM)

*** *P*<0.001, UPA vs PBO. Nominal *P*-values are shown and were not multiplicity controlled.

Source: Baraliakos, 2021.

A significantly greater proportion of PsA patients with axial involvement treated with UPA vs PBO at week 24, and a numerically greater proportion of patients treated with UPA vs Humira at weeks 24 and 56, achieved ASDAS thresholds and maintained response over time (Figures 6 and 7). The proportion of patients achieving ASDAS CII was significantly greater with UPA vs Humira at week 24.

JAKIs for axPsA : PASTOR trial

- **Tofacitinib for Reduction of Spinal Inflammation in Patients With Psoriatic ArthritiS PresenTing With Axial InvOlvement (PASTOR)**
- **Prospective, PBO controlled**
- **MRI SI and whole spine at baseline and at week 12**

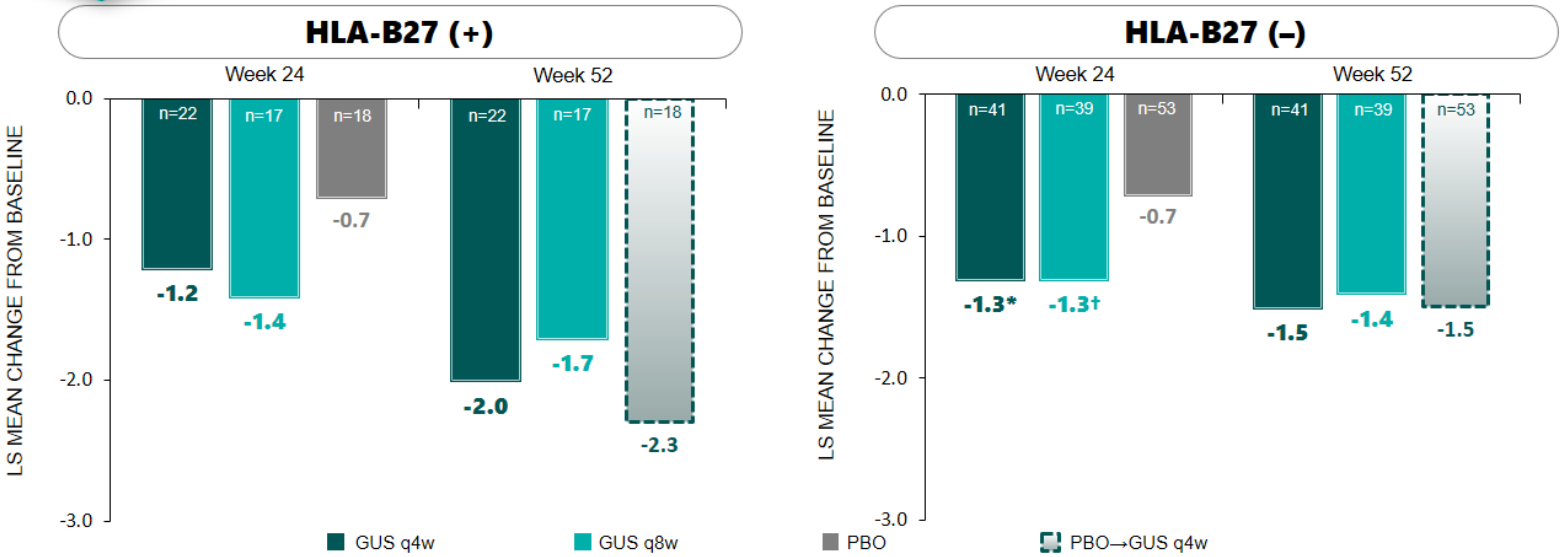
Case Study

- 40 year old female w/ psoriatic arthritis, NAFLD, personal h/o DVT on apixaban
- inflammatory back pain, MRI SI negative
- sister and maternal aunt have MS, avoided TNFI so far
- only partial response to trials of IXE and SEC
- What Now?
- IL-12 + IL-23
- or
- **IL-23**

IL-23 for axPsA

ASDAS Scores Improved at Week 24 With GUS vs. PBO and are Maintained Through Week 52 Irrespective of HLA-B27 Status (NRI)

DISCOVER 1 & 2



Unadjusted *p*-value vs. PBO *p<0·01. †p<0·05.

ASDAS=Ankylosing spondylitis disease activity score; GUS=Guselkumab; HLA=Human leukocyte antigen; NRI=Nonresponder imputation; PBO=Placebo; LS=Least squares; q4w=Every 4 weeks; q8w=Every 8 weeks.

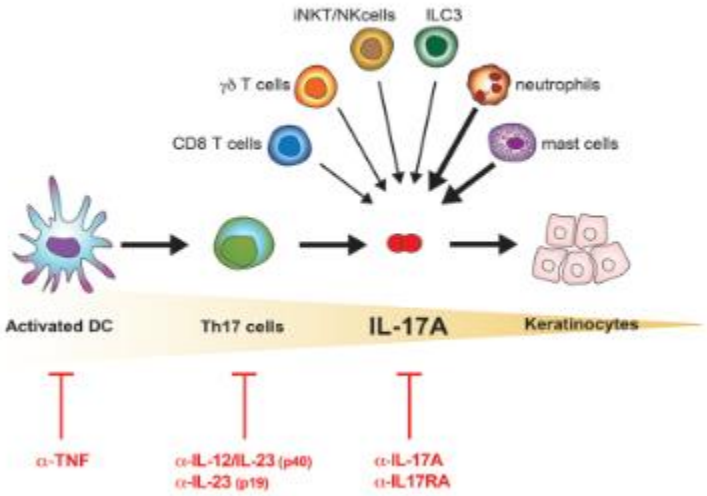
1. Mease P, et al. *Lancet Rheumatol*. 2021;73(4):604-616.

The IL-17 and IL-23 connection

- Inhibiting IL-23 , inhibits some sources of IL-17, but not ALL sources of IL-17. IL-17 is still made by some resident cells

Sources of IL-17

Figure 1



Goldilocks phenomenon

On the horizon

VEGA trial : guselkumab + TNFI
TNFI IR→ changing to golimumab and adding guselkumab in IBD

AFFINITY trial in PsA (no data readout yet)

axPsA treatment considerations

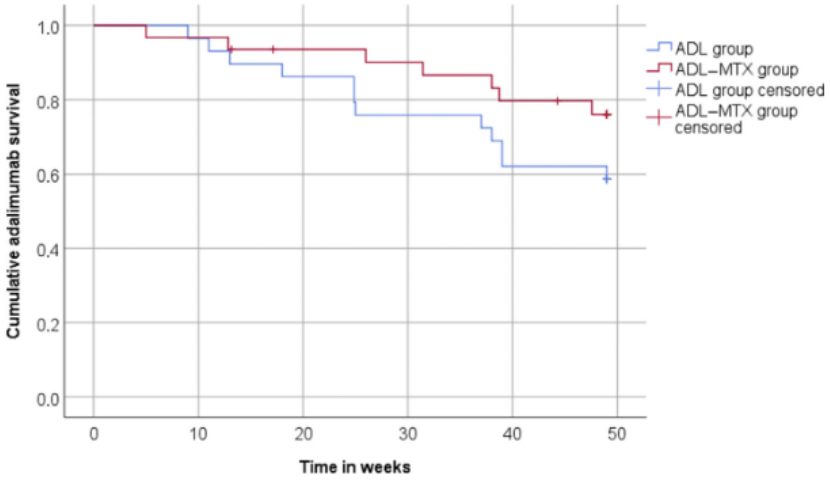
- Are they able to take MTX with the bDMARD?

adalimumab +/- MTX

G van der Kraaij et al.

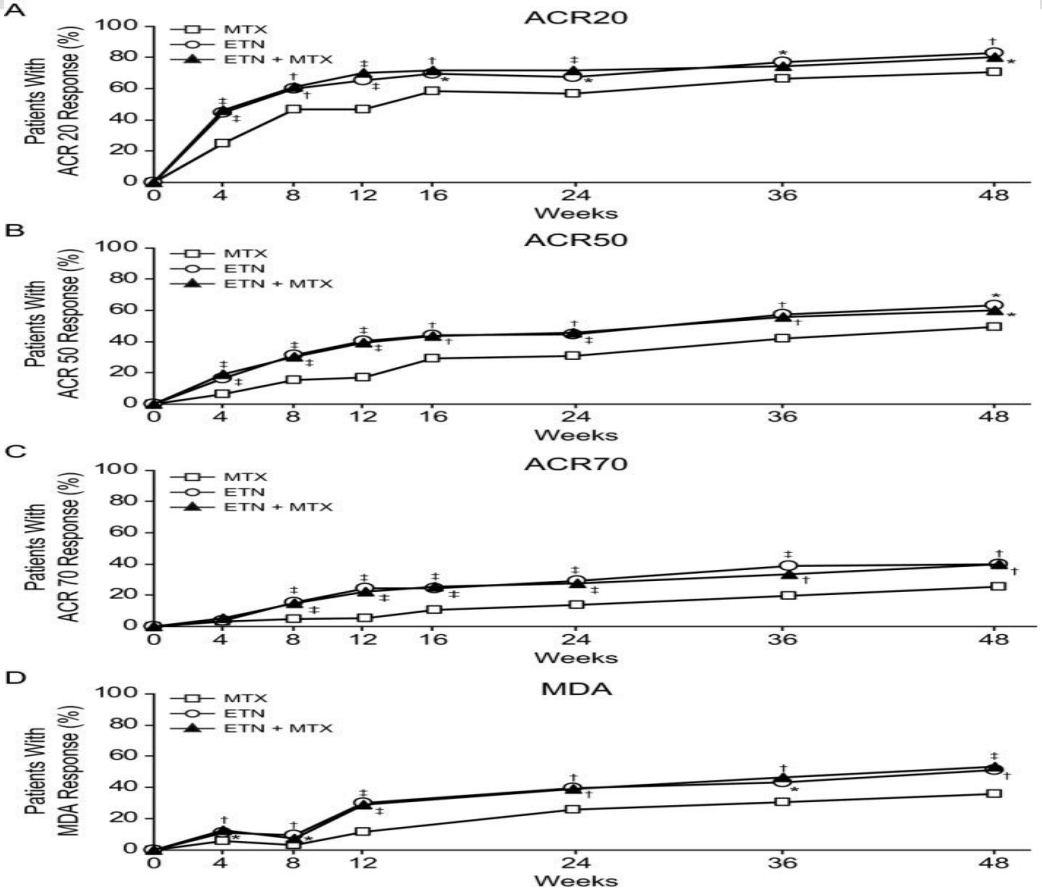
Adalimumab with Methotrexate vs. Adalimumab Monotherapy in Psoriasis

Figure 2. Kaplan–Meier curves of adalimumab drug survival in the ADL–MTX group and ADL group during the first year. At week 49, the cumulative survival was 74.2% in the ADL–MTX group and 58.6% in the ADL group ($P = 0.15$). ADL, adalimumab monotherapy; ADL–MTX, adalimumab with methotrexate.



Journal of Investigative Dermatology (2022) ■, ■–■; doi:10.1016/j.jid.2022.01.033

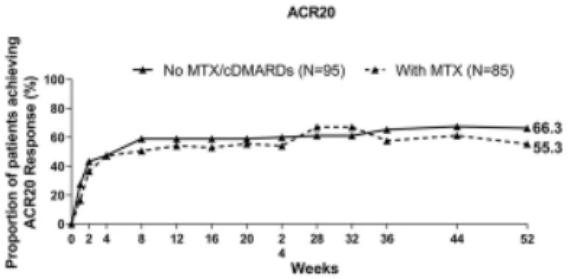
etanercept +/- MTX no difference

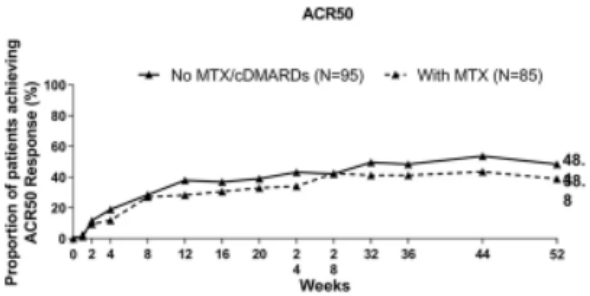


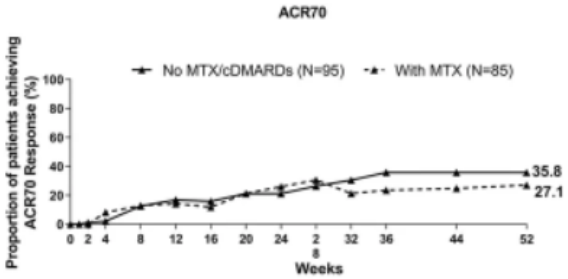
Ixekizumab +/- MTX no difference

From: Ixekizumab, with or without concomitant methotrexate, improves signs and symptoms of PsA: week 52 results from Spirit-P1 and Spirit-P2 studies

IXE Q4W





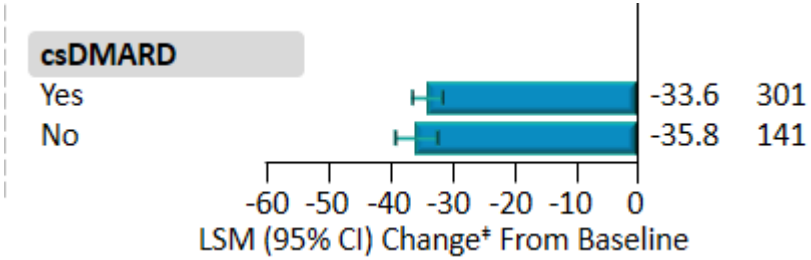


IXE Q2W

Guselkumab +/- MTX, no difference

DAPSA score improvement to week 100
Guselkumab with csDMARD (MTX) and w/o csDMARD

DISCOVER 2 McInnes IB, et al. EULAR 2022. Poster #POS0072.




New Oral Agent

New tyrosine kinase 2 (TYK2) inhibitor

- deucravacitinib (doo-krav-a-**sih**-ti-nib)
- PsO –applied for FDA approval- PDUFA date SEPT 10 (p*ositive results from the pivotal Phase III POETYK-PSO clinical trial program demonstrating superior efficacy of deucravacitinib over* Otezla® (apremilast) *and placebo in treating adults with moderate to severe plaque psoriasis)*
- PsA- Phase II, Mease trial ACR 20 , 6 mg vs PBO (52.9% vs 31.8%) at week 12
- IBD
- SLE

Deucravacitinib

- selectively target TYK2, thereby inhibiting signaling of interleukin (IL)-23, IL-12 and Type 1 interferon (IFN)

- Is it an "*oral IL-12 and 23 inhibitor*?"

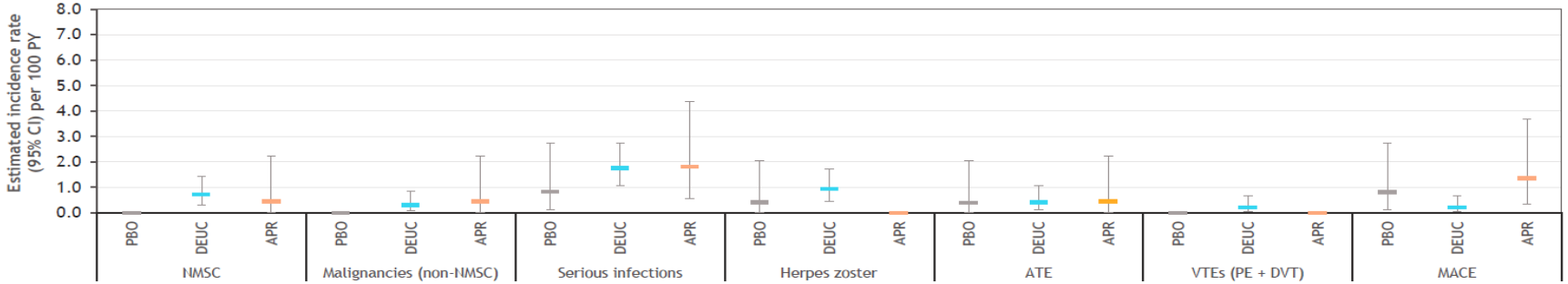
How might Tyk2 differ from other JAKI?

- Across both Phase 3 trials (**POETYK PSO-1 and POETYK PSO-2)***No clinically meaningful changes were observed in multiple laboratory parameters (including anemia, blood cells, lipids and liver enzymes) over 52 weeks.*
- *No “downstream” or “Stat” effects of Jak 1,2,3 inhibition*

Deucravacitinib safety

Phase 3 POETYK PSO-1 and POETYK PSO-2 (integrated)

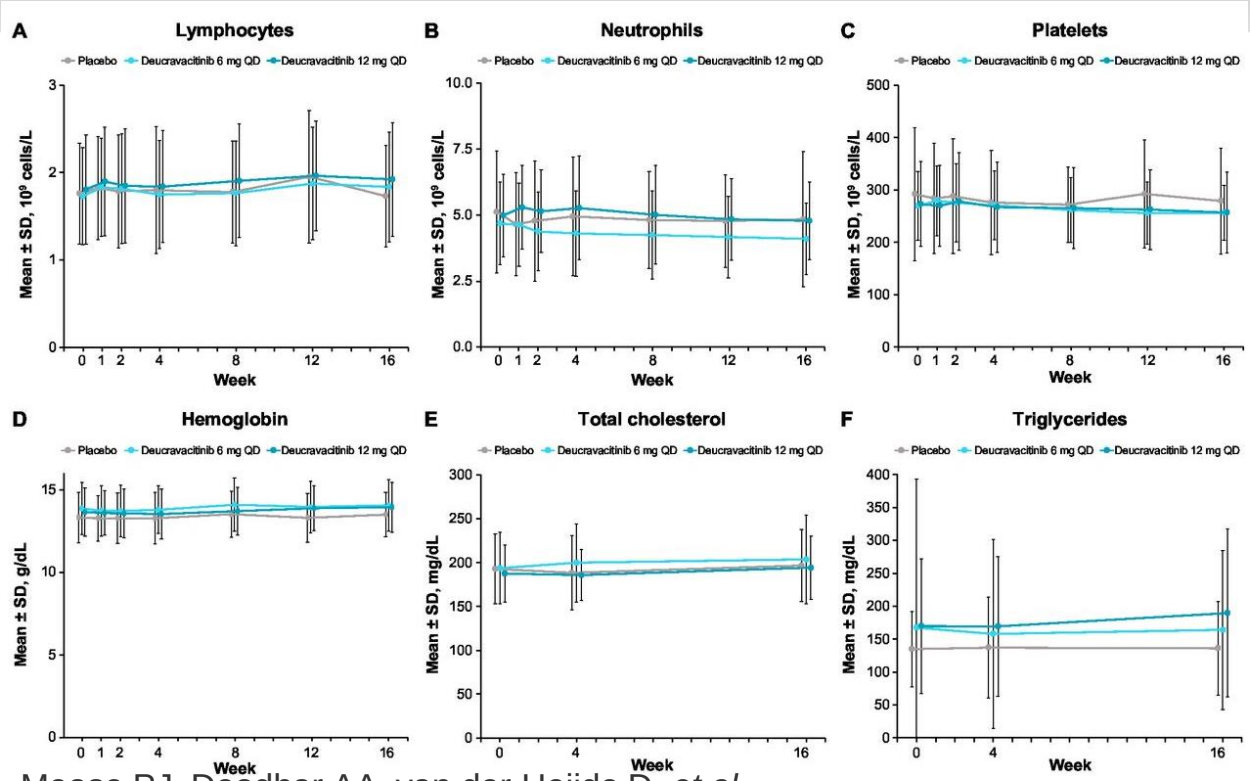
AEs of interest (integrated): Weeks 0-52



- None of the serious infections with deucravacitinib led to discontinuation[1]
- No cases of herpes zoster with deucravacitinib were serious, were systemic, or led to discontinuation[1]
- No tuberculosis events and no opportunistic systemic infections were reported with deucravacitinib[1]
- There were 2 cases of VTE in the deucravacitinib group, with an EAIR of 0.2 per 100 PY[1-3]
  - 1 SAE adjudicated as a VTE occurred in a patient receiving deucravacitinib who had an aortic dissection complicated by a PE and was determined to be unrelated to deucravacitinib. The patient resumed deucravacitinib and is enrolled in the LTE study
  - Another case of VTE was non-serious and was related to IV cannulation with minor thrombosis occurring thereafter

Reproduced with permission from Armstrong AW.[1]
Total exposure: deucravacitinib, 969.0 PY; placebo, 240.9 PY; apremilast, 221.1 PY. Most placebo-related data were obtained during Weeks 0-16.
AE, adverse event; APR, apremilast; ATE, arterial thromboembolic event; DEUC, deucravacitinib; DVT, deep vein thrombosis; EAIR, exposure-adjusted incidence rate; IV, intravenous; LTE, long-term extension; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer; PBO, placebo; PE, pulmonary embolism; PY, patient-years; SAE, serious adverse event; VTE, venous thromboembolism.
1. Armstrong A et al. Oral presentation at AAD VMX; April 23-25, 2021; Virtual. 2. MS events and presentations. Accessed September 2021.
https://players.brightcove.net/1892432924001/zW6RyBjSF_default/index.html?videoId=6250560405001 3. Warren R et al. Poster presented at San Diego Dermatology Symposium; March 11-13, 2022; San Diego CA.

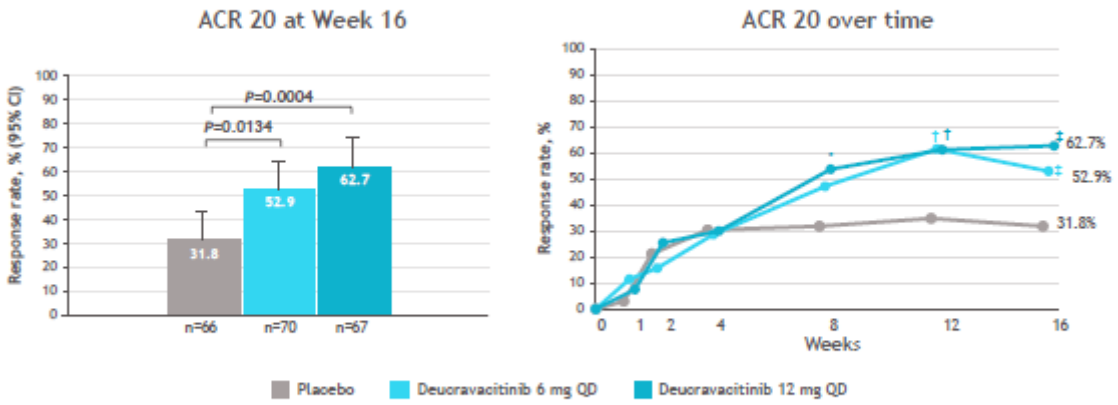
Deucravacitinib safety



Mease PJ, Deodhar AA, van der Heijde D*, et al*
Efficacy and safety of selective TYK2 inhibitor, deucravacitinib, in a phase II trial in psoriatic arthritis
Annals of the Rheumatic Diseases 2022;**81:**815-822.

Deucravacitinib efficacy

Figure 3. ACR 20 responses (ITT, NRI)



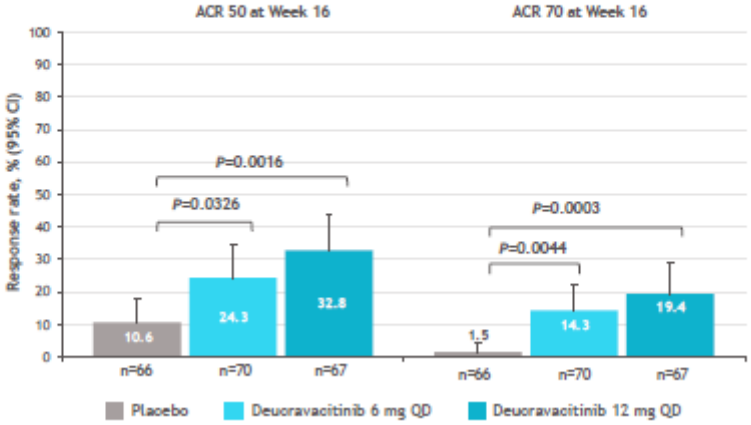
Nominal *P* values for pairwise comparison versus placebo. *P* values in time course are for odds ratios obtained using a stratified Cochran-Mantel-Haenszel (CMH) test with stratification factors (body weight and prior TNFI use) per randomization. Missing data were reported using NRI.

*P=0.0108 (12mg); †P=0.0021 (6 mg); *P*=0.0021 (12 mg); ‡P=0.0134 (6 mg); *P*=0.0004 (12 mg).

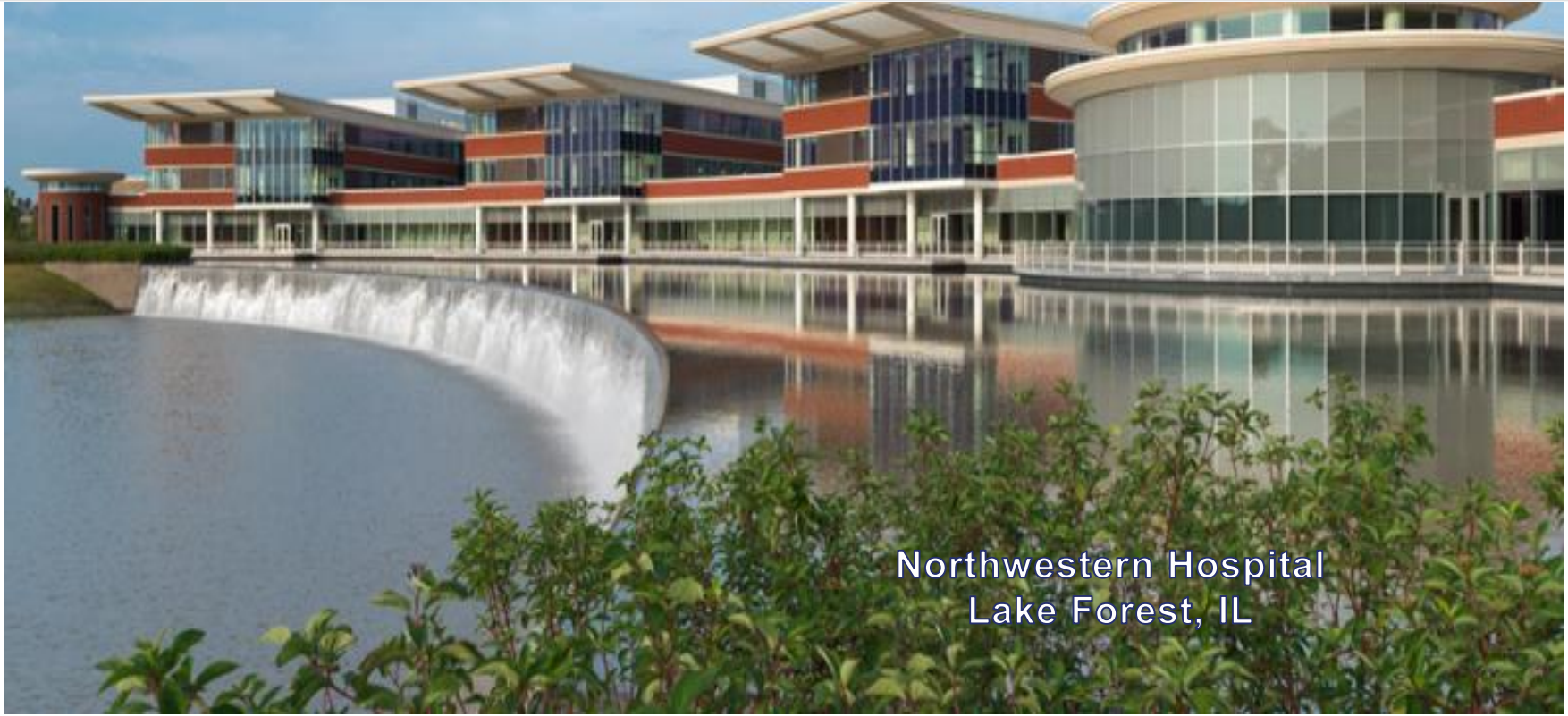
ACR 20, 20% improvement in American College of Rheumatology criteria; CMH, Cochran-Mantel-Haenszel; ITT, intent-to-treat; NRI, nonresponder imputation; QD, once daily; TNFI, tumour necrosis factor inhibitor.

Deucravacitinib

Figure 3. ACR 50 and ACR 70 responses (ITT, NRI)



Thank you!



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AB0556 COMPARING EFFICACY OF GUSELKUMAB VERSUS USTEKINUMAB IN PATIENTS WITH PSORIASIS ARTHRITIS: AN ADJUSTED COMPARISON USING INDIVIDUAL PATIENT DATA FROM DISCOVER 1&2 AND PSUMMIT TRIALS J. Diels P. Thilakarathne A. Schubert F. Hassan S. Peterson W. Noel1

Risankizumab versus Ustekinumab for Moderate-to-Severe Plaque Psoriasis Author**:** Kim A. Papp, Andrew Blauvelt, Michael Bukhalo, et al **Publication:** The New England Journal of Medicine **Publisher:** Massachusetts Medical Society **Date:** Apr 20, 2017

Mease P, Deodhar A, van der Heijde D, et al. Efficacy and Safety of Deucravacitinib, an Oral, Selective Tyrosine Kinase 2 Inhibitor, in Patients With Active Psoriatic Arthritis: Results From a Phase 2, Randomized, Double-Blind, Placebo-Controlled Trial. Oral presentation at the Annual European League of Associations for Rheumatology (EULAR) Congress; June 12-15 2021; Virtual Congress

Mease PJ, Deodhar AA, van der Heijde D, et al. Efficacy and safety of selective TYK2 inhibitor, deucravacitinib, in a phase II trial in psoriatic arthritis. *Ann Rheum Dis.* Published online March 3, 2022. doi:10.1136/annrheumdis-2021-221664

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LB0001 BIMEKIZUMAB IN BDMARD-NAIVE PATIENTS WITH PSORIATIC ARTHRITIS: 24-WEEK EFFICACY & SAFETY FROM BE OPTIMAL, A PHASE 3, MULTICENTRE, RANDOMISED, PLACEBO-CONTROLLED, ACTIVE REFERENCE STUDY

OP0255 BIMEKIZUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND AN INADEQUATE RESPONSE TO TUMOUR NECROSIS FACTOR INHIBITORS: 16-WEEK EFFICACY & SAFETY FROM BE COMPLETE, A PHASE 3, MULTICENTRE, RANDOMISED PLACEBO-CONTROLLED STUDY

- 17th Congress of ECCO (VEGA trial info) : DOI: https://doi.org/10.1016/S2468-1253(22)00059-0 The Lancet published April 2022