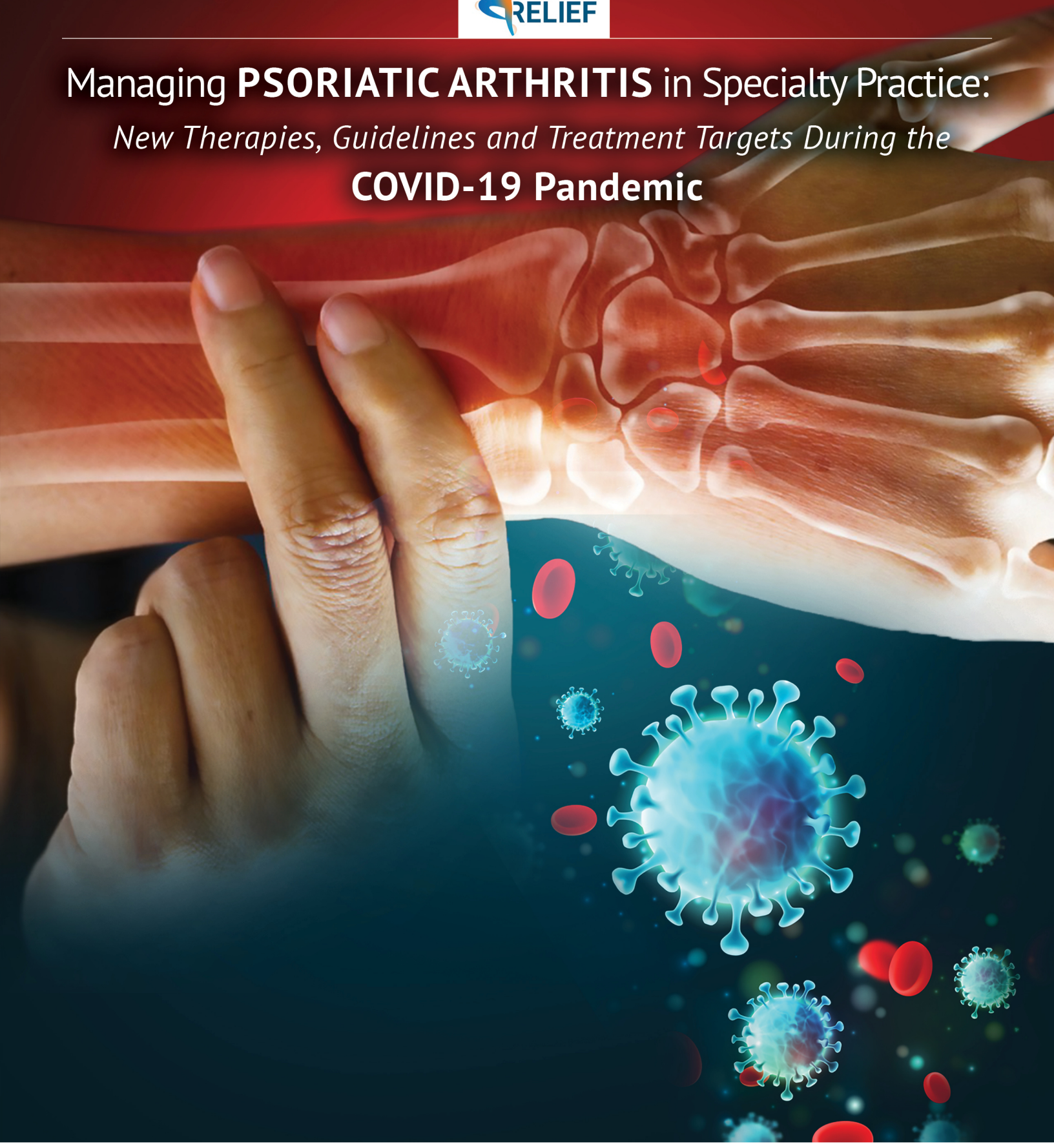
RELIEF

Managing **PSORIATIC ARTHRITIS** in Specialty Practice:

New Therapies, Guidelines and Treatment Targets During the **COVID-19 Pandemic**



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This activity is supported by an educational grant from Lilly.

Managing Psoriatic Arthritis in Specialty Practice: New Therapies, Guidelines and Treatment Targets During the COVID-19 Pandemic

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Andreas Reimold, MD Professor UT Southwestern Medical Center Dallas, TX	**Elaine Tozman, MD** Associate Professor of Clinical Medicine Rheumatology and Immunology University of Miami - Miller School of Medicine Miami, FL	

PROGRAM OVERVIEW
This activity will cover the treatment and management of patients with psoriatic arthritis during the COVID-19 pandemic.

TARGET AUDIENCE
This activity is intended for rheumatologists and rheumatology advanced practice providers (NPs and PAs) who are involved in the care and treatment of patients with psoriatic arthritis.

LEARNING OBJECTIVES
On completing the program, attendees should be able to:

- Identify the risk of COVID-19-related infections in PsA, along with their impact on therapeutic choice
- Pursue strategies to optimize PsA therapy in the COVID-19 era while minimizing risks and adverse events
- Assess methods for better evaluating and communicating with patients through telemedicine and virtual platforms
- Apply new ways to initiate and manage PsA treatment, monitor PsA disease progression and address adverse events via virtual communication

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Purpose: This program would be beneficial for nurses involved and/or interested in the therapeutic management of patients with psoriatic arthritis.

CNE Credits: 1.0 ANCC Contact Hour.

CNE ACCREDITATION STATEMENT
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Daniel George Arkfeld, MD	Dr. Arkfeld reports that he is on the speakers bureau for BMS, Amgen, and GSK. He also serves as a consultant for UCB.
Mohamad Bittar, MD	Dr. Bittar reports that he has no relevant relationships with a commercial entity or manufacturer.
Jon T Giles, MD, MPH	Dr. Giles reports that he serves as a consultant for Gilead, Eli Lilly, Bristol Myers Squibb, AbbVie, and UCB; and discloses a relationship with Pfizer.
Andreas Reimold, MD	Dr. Reimold reports that he has participated in a clinical trial sponsored by Pfizer.
Elaine Tozman, MD	Dr. Tozman reports that she has no relevant relationships with a commercial entity or manufacturer.

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The reviewer of this activity has nothing to disclose.

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The content of this activity was independently peer reviewed.
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- Christina Gallo, SVP, Educational Development for Med Learning Group, has nothing to disclose.
- Lauren Bartunek, Program Manager for Med Learning Group, has nothing to disclose.
- Diana Tommasi, PharmD, Medical Director for Med Learning Group has nothing to disclose.
- Lauren Welch, MA, VP, Accreditation and Outcomes for Med Learning Group, has nothing to disclose.
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2. Participate in the live virtual activity
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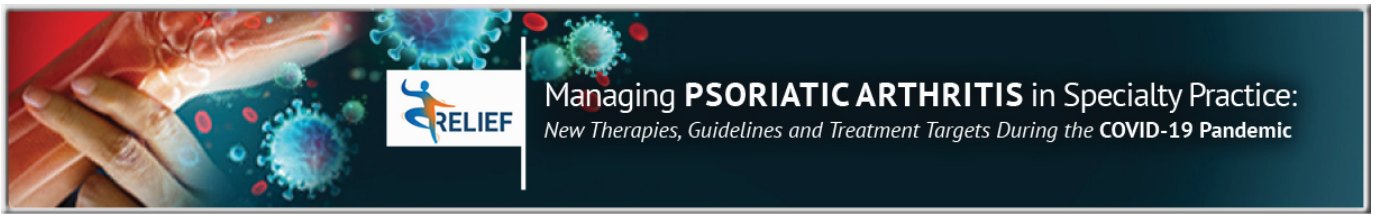

Program Agenda

Managing Psoriatic Arthritis (PsA) During the COVID-19 Pandemic

1. Immune dysregulation and hyperinflammation in COVID-19
2. ***Whiteboard animation: Inflammatory mediators in psoriatic arthritis***
3. Risk of severe COVID-19-associated complications in rheumatic patients
4. Impact of PsA comorbidities on COVID-19 outcomes
5. Managing patients with PsA and COVID-19
6. Need for continuity of care during the COVID-19 pandemic
7. Strategies to increase telehealth uptake

Treatment Options for PsA During the COVID-19 Era

1. ***Case #1: Treatment-naïve patient***
2. 2019 ACR guidelines and their application to practice
3. ***Whiteboard animation: Mechanism of action of biologic treatment options***
4. ***Case #2: Active PsA despite anti-TNF therapy***
5. Evolving standards of treatment in the COVID-19 era
6. Managing PsA and psoriasis
7. ***Case #3: Comorbidities that impact treatment options***
8. Clinical trial data on the efficacy and safety of biologic treatment options
9. Therapeutic considerations in COVID-19
10. ***Case #4: Patient with PsA and COVID-19***
11. Risks and benefits of altering therapy in patients with COVID-19

Conclusions and Q/A

Managing Psoriatic Arthritis in Specialty Practice: New Therapies, Guidelines and Treatment Targets During the COVID-19 Pandemic

PROGRAM CHAIR:

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University of California in Los Angeles

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Disclosures

- Please see Program Overview for specific speaker disclosure information
- During the course of this lecture, the presenter will discuss the use of medications for both FDA-approved and non-approved indications

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Managing PsA During the COVID-19 Pandemic

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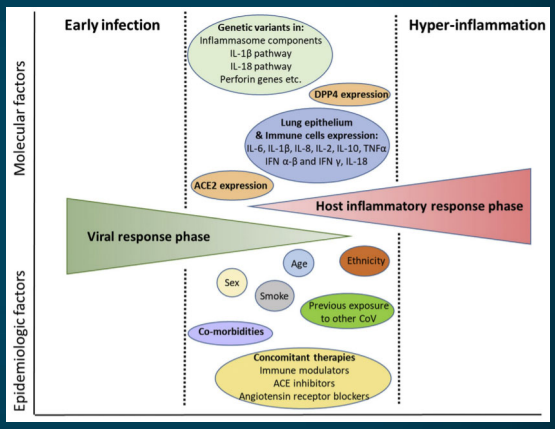
Managing PsA During the COVID-19 Pandemic

Role of Inflammation in COVID-19

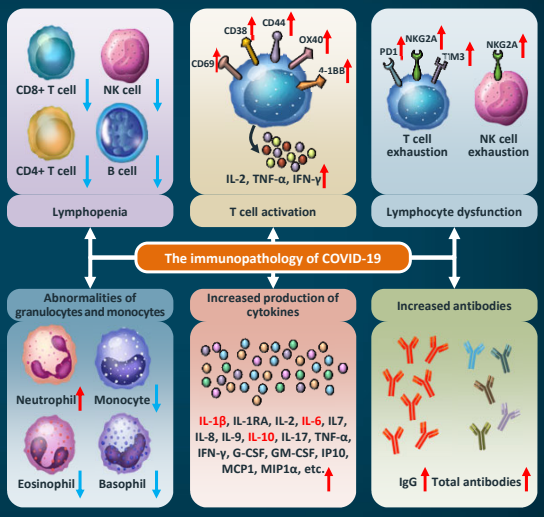
- COVID-19 is caused by infection with the SARS-CoV-2 virus, and may lead to ARDS, blood clots, and multiorgan failure
- Clinical deterioration in COVID-19 often occurs 7-10 days after symptom onset when viral titers decline
  - Pathology likely driven by inflammation rather than direct viral injury



Colafrancesco S, et al. *Autoimmunity Rev.* 2020;19:102573. Manson JJ, et al. *Lancet Rheumatol.* 2020;2:e594-e602. Yang L, et al. *Signal Transduct Target Ther.* 2020;5:128.

COVID-19-associated Hyperinflammation

- Elevated inflammatory markers in COVID-19 patients are significantly associated with risk of next-day escalation of respiratory support or death (HR, 2.24)



Manson JJ, et al. *Lancet Rheumatol.* 2020;2:e594-e602. Yang L, et al. *Signal Transduct Target Ther.* 2020;5:128.

Whiteboard Presentation

Inflammatory Mediators in Psoriatic Arthritis

https://youtu.be/l65uHkKXJvU

Concerns During the COVID-19 Pandemic

- Patients with PsA are not at increased risk of death, invasive ventilation, ICU admission, or serious complications from COVID-19
  - Impact of PsA therapies on COVID-19 disease severity is unknown
- Risk of poor outcomes from COVID-19 appears to be related primarily to general risk factors such as age and comorbidities

Mortality in an Observational Study of COVID-19 Cases in China (n = 72,314)	
Characteristics	**Deaths (%)**
All confirmed cases	2.3
• Critical cases	49.0
• ≥80 years of age	14.8
• Cardiovascular disease	10.5
• 70-79 years of age	8.0
• Diabetes	9.2
• Chronic respiratory disease	8.0
• Hypertension	6.0
• Cancer	7.6

Mikuls TR, et al. *Arthritis Rheumatol*. 2020;72:1241-1251. Pablos JL, et al. *Ann Rheum Dis*. 2020;79:1544-1549. Wu Z, et al. *JAMA*. 2020;323:1239-1242. Wollina U, et al. *Dermatol Ther*. 2020;33:e13743.

Impact of PsA Comorbidities on COVID-19 Outcomes

- PsA is associated with a higher incidence of CV disease, metabolic syndrome, obesity, diabetes, dyslipidemia, and IBD
- Older age, male sex, and previous comorbidity increased the risk of severe COVID-19 in patients with rheumatic disease and nonrheumatic disease
  - Diabetes and CV disease were associated with a significantly increased risk of severe COVID-19 in rheumatic patients compared to nonrheumatic patients

Variable	Relative risk (95% CI)		P value
	Non-rheumatic cohort	Rheumatic cohort	
Age over 60 years	3.70 (1.99 to 6.93)	4.04 (2.30 to 7.08)	0.841
Male sex	2.16 (1.39 to 3.35)	1.58 (1.09 to 2.29)	0.286
Obesity	1.22 (0.72 to 2.06)	1.62 (1.10 to 2.36)	0.393
Diabetes	0.95 (0.53 to 1.70)	**1.93 (1.34 to 2.79)**	0.038
Hypertension	1.64 (1.07 to 2.53)	2.27 (1.49 to 3.46)	0.290
CV disease	1.44 (0.90 to 2.33)	**2.92 (2.04 to 4.17)**	0.020
Lung disease	1.57 (1.00 to 2.46)	1.74 (1.19 to 2.55)	0.723

CV = cardiovascular; IBD = inflammatory bowel disease.

Pablos JL, et al. *Ann Rheum Dis*. 2020;79:1544-1549.

ACR Recommendations: Managing PsA and COVID-19

Treatment of Rheumatic Disease in the Absence of COVID-19 Infection or Exposure	
HCQ/CQ, SSZ, MTX, LEF, immunosuppressants (tacrolimus, CSA, MMF, AZA), biologics, JAK inhibitors, NSAIDs	Continue therapy
Low-dose corticosteroids	May be started if clinically indicated (<10 mg prednisone equivalent/day)
Following SARS-CoV-2 Exposure	
HCQ/CQ, SSZ, NSAIDs	May be continued
Immunosuppressants (tacrolimus, CSA, MMF, AZA), non-IL-6 biologics, JAK inhibitors	Stop therapy temporarily, pending a negative COVID-19 test or 2 weeks of symptom-free observation
IL-6 inhibitors	May be continued in select circumstances
Documented or presumptive COVID-19	
HCQ/CQ	May be continued
SSZ, MTX, LEF, non-IL-6 biologics, immunosuppressants, and JAK inhibitors	Withhold or stop therapy
NSAIDs	Should be stopped in patients with severe respiratory symptoms

- All recommendations based on very low quality of evidence and moderate to high consensus
- Recommendations are for rheumatic disease in general and are not subdivided by patient disease. There are no specific recommendations for PsA.
  - May reinitiate therapy within 7-14 days of symptom resolution for those with mild COVID-19
  - Consider reinitiating therapy in 10-17 days after positive PCR results if asymptomatic COVID-19
  - Timing of reinitiating therapy after severe COVID-19 should be made on case-by-case basis

ACR = American College of Rheumatology; AZA = azathioprine; CSA = cyclosporine A; CQ = cloroquine; HCQ = hydroxychloroquine; IL = interleukin; JAK = Janus kinase; LEF = leflunomide; MMF = mycophenolate mofetil; MTX = methotrexate; NSAID = nonsteroidal anti-inflammatory drug; SSZ = sulfasalazine.

Mikuls TR, et al. *Arthritis Rheumatol*. 2020;72:1241-1251.

Corticosteroid Use During the COVID-19 Pandemic

- A case series of 600 patients found prednisone ≥10 mg/day was associated with increased odds of hospitalization (OR, 2.05)
- A study in patients with inflammatory bowel disease and COVID-19 found steroids increase the risk of severe COVID-19 (aOR, 6.0)

Glucocorticoids should be used at the lowest possible dose to control rheumatic disease, regardless of exposure or infection status

Glucocorticoids should not be abruptly stopped, regardless of exposure or infection status

OR = odds ratio; aOR = adjusted odds ratio.

Gianfrancesco M, et al. *Ann Rheum Dis*. 2020;79:859-866. Brenner EJ, et al. *Gastroenterology*. 2020;159:481-491. Mikuls TR, et al. *Arthritis Rheumatol*. 2020;72:1241-1251.

Need for Continuity of Care During the COVID-19 Pandemic

- In a study of 1,517 patients in the US with PsA, RA, SpA, or SLE, 14.9% stopped using their DMARD between March-May 2020
- Of the patients who stopped their DMARDs, what percentage of these interruptions were NOT recommended by a physician? → **78.7%**
- 29.5% of patients used telehealth services
  - Treatment interruption was more common among patients who reported that telehealth was not available (25.4% vs 13.1%, respectively)

DMARD = disease-modifying anti-rheumatic drug; RA = rheumatoid arthritis; SLE = systemic lupus erythematosus; SpA = spondyloarthritis.

George M, et al. *J Rheumatol*. 2020. doi:10.3899/jrheum.201017.

Incorporating Telehealth into Your Practice

- **Schedule enough time**. Telehealth consults often take longer than expected to find the required information
- **Train staff in triaging symptom burden**. Identify patients with unstable symptoms who require an in-person appointment
- **Educate on self-management**. Patients may not come in for a follow-up appointment for weeks or months.
  - Teach about warning signs that require prompt evaluation
  - Educate about how to manage symptoms remotely
  - Ensure patients have enough medication
- **Clarify expectations** of what can or cannot be done remotely
  - Recognize patients who require in-person evaluation

Centers for Disease Control and Prevention website (https://www.cdc.gov/coronavirus/2019-ncov/hcp/telehealth.html). Landewe RBM, et al. *Ann Rheum Dis*. 2020;79:851-858.

Strategies to Increase Telehealth Uptake

- **Prescreen patients with disease activity scales** and request in-person visit if scores are high
- **Use technology** that allows you to send and receive patient-reported outcomes scales
- **Offer flexibility** in platforms that can be used for video consultation, and non-video options to serve patients with limited technology and connectivity
- **Postpone** regular blood monitoring and face-to-face consultations in patients with stable disease and therapy without signs of drug toxicity
- **Communicate with insurers/payers** to understand availability of covered telehealth services

Centers for Disease Control and Prevention website (https://www.cdc.gov/coronavirus/2019-ncov/hcp/telehealth.html). Landewe RBM, et al. *Ann Rheum Dis*. 2020;79:851-858.

Treatment Options for PsA

Case Study 1: Samuel

- Samuel is a 48-year old man who presents with 8 months of pain in bilateral 5 DIPs, left knee, and left ankle.
  - He has pain in his right Achilles insertion and just below the right elbow on pressure, indicative of enthesitis
  - His left knee is swollen
  - CDAI: 16
- He has a five year history of psoriasis.
  - Plaques found on his scalp, shins, elbows (PASI: 9)
  - Pitting nails
  - Moderate lower back pain

CDAI = Clinical Disease Activity Index; DIP = distal interphalangeal.

Case Study 1: Lab Results

- CBC and CMP are normal
- ESR = 22 mm/hr
- MRI reveals sacroiliac erosions on the left and some classical psoriatic DIP erosions

How would you manage Samuel?

A. Methotrexate
B. Cyclosporine A
C. Adalimumab
D. Sulfasalazine

CBC = complete blood count; CMP = comprehensive metabolic panel; ESR = erythrocyte sedimentation rate; MRI = magnetic resonance imaging.

Would MTX, CSA, or SSZ be appropriate for this patient?

Drug	RCTs (N)	Patients in RCTs (N)	Other studies (N)	Main results
Methotrexate (MTX)	3	93	7	Some efficacy with skin lesions and globals X-rays: no data
Sulfasalazine (SSZ)	7	666	2	Some efficacy on joints Skin: no efficacy X-rays: no data
Leflunomide (LEF)	1	190	3	Mild efficacy on joints Skin: limited efficacy X-rays: no data
Cyclosporine (CSA)	3	206	6	Efficacy on joints and skin X-rays: no data

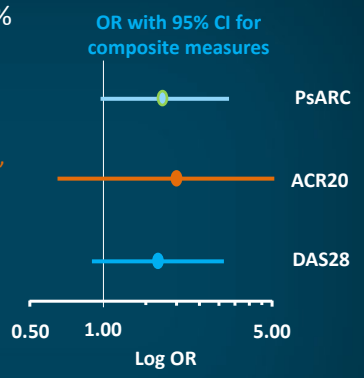
Not FDA approved for PsA.

RCT = randomized controlled trial.

Ash Z, et al. *Ann Rheum Dis.* 2012;71:319-26. Mease P. *Ann Rheum Dis*. 2011;70(1):i77-i84. Wilsdon TD, et al. *Cochrane Database Syst Rev*. 2019; CD012722.

MTX in Psoriasis and PsA

- In **psoriasis**, PASI75 achieved in 35-42%
- In **PsA**, no difference in SJC, TJC, CRP/ESR, PsARC, ACR20, DAS28 at 3 and 6 months
  - Patient, MD global, and skin scores significantly improved at 6 months (*P*=0.01, 0.02, 0.02)
- AEs: GI upset, oral ulcers, hair shedding, fatigue >>> marrow suppression, hepatic fibrosis, pulmonary fibrosis
- Pregnancy category: X



ACR =American College of Rheumatology; CRP = C reactive protein; ESR = erythrocyte sedimentation rate; DAS = Disease Activity Score; OR = odds ratio; PBO = placebo; PsARC = PsA response criteria; SJC = swollen joint count; TJC = tender joint count.

Kingsley GH et al. *Rheumatology (Oxford).* 2012;51:1368-1377. Barker, et al. *Br J Dermatol.* 2011;165(5):1109-17.Saurat, et al. *Br J Dermatol.* 2008;158:558-566.

CSA in Psoriasis and PsA

- CSA 2.5-5 mg/kg/day yielded PASI75 response in 28% to 97% of patients
- Remission could be maintained at CSA dose of at least 3mg/kg/day
- More than 50% of patients treated with CSA may have an increase in serum creatinine value >30% of baseline if treatment is prolonged for 2 years

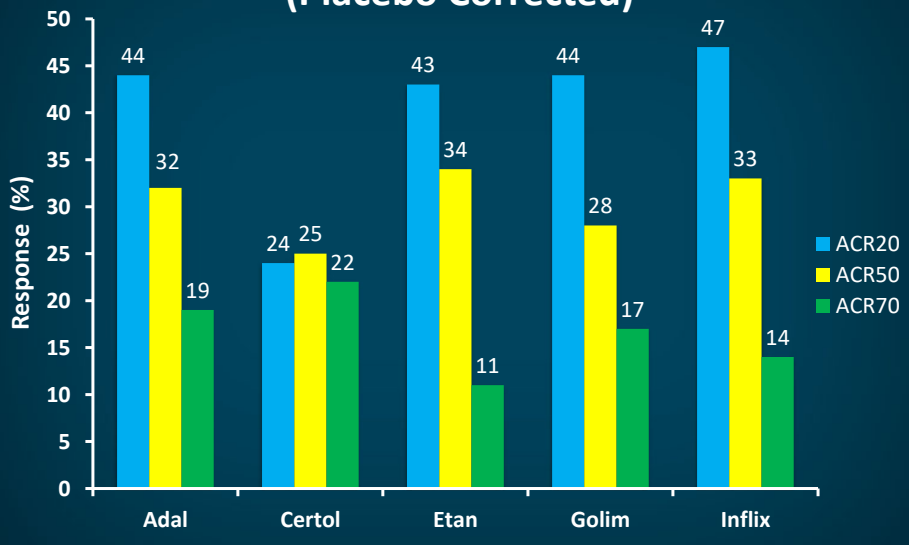
24 Week Randomized, Open NSAID* Controlled Study of Cyclosporine A in PsA (N=99)

	P-value	Significance CSA vs NSAID*
ACR50	0.02	+
ACR70	0.05	+
Swollen Joint Count	0.05	+
Tender Joint Count	0.01	+
Pain	0.002	+
Patient Global improved ≥1 point	0.04	+
MD Global improved ≥1 point	0.01	+

*NSAID +/- prednisone 5 mg daily +/- analgesics

Salvanarani C, et al. *J Rheum.* 2001;28:2274-2282. Maza J-H, et al. *JEADV.* 2011;25(2):19-27.

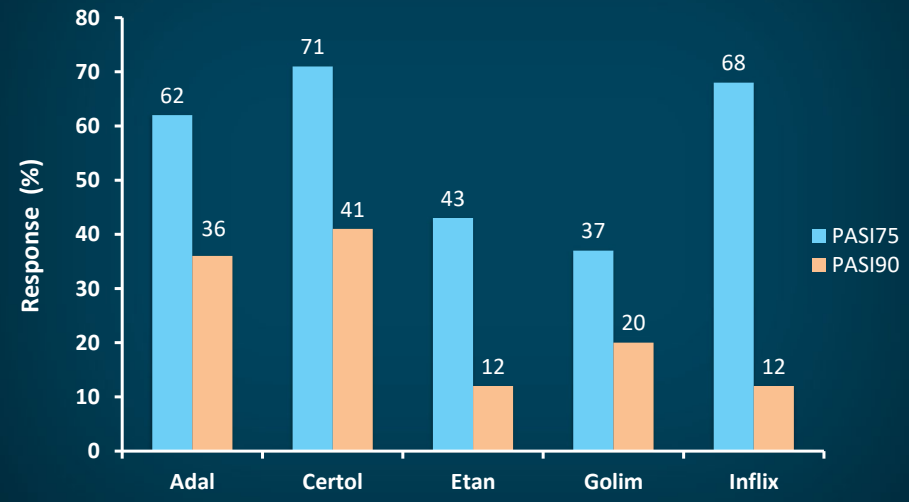
TNFi Response in Psoriatic Arthritis in 12 Week Trials (Placebo Corrected)



Adal = adalimumab; Certol = certolizumab; Etan = etanercept; Golim = golimumab; Inflix = infliximab.

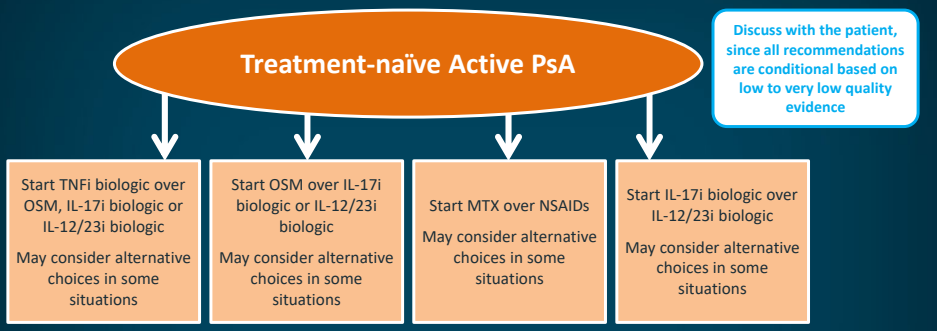
Mease PJ, et al. *Rheum Dis N Am.* 2015;4:723-738.

TNFi Response in Psoriasis in 12 Week Trials (Placebo Corrected)



Mease PJ, et al. *Rheum Dis Clin N Am.* 2015;4:723-738. Yang H, et al. *Health Tech Assess.* 2011;15(1):87-95. Reich K, et al. *Br J Derm.* 2012;167:180-190.

Initiating Therapy



- Contraindications to TNFi include congestive heart failure, previous serious infection, recurrent infections, or demyelinating disease
- An OSM (MTX, SSZ, LEF, CSA, or APR) may be considered if disease is not severe, oral therapy is preferred, or patient does not want to start a biologic

APR = apremilast; IL = interleukin; OSM = oral small molecule; TNFi = tumor necrosis factor-alpha inhibitor.

Singh JA, et al. *Arthritis Rheumatol*. 2019;71:5-32.

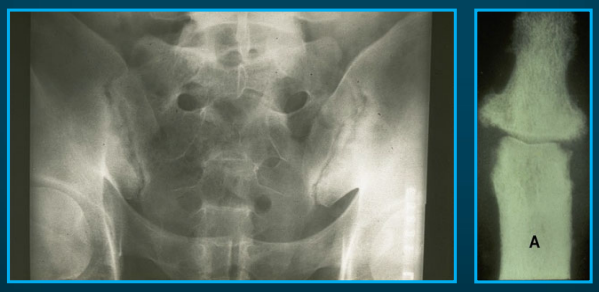
Whiteboard Presentation

Mechanism of Action of Biologic Treatment Options

https://youtu.be/AY0FTSkM-Sk

Patient 2: Linda's Presentation

- Linda is a 34-year old woman who presents simultaneously with:
  - Mild psoriasis involving the scalp, elbows, and knees (PASI: 8)
  - Pain in her wrist, right hand, right knee, and lower back (CDAI: 16)
- X-ray shows sacroiliac joint lesions on both sides of joint and DIP joint narrowing with erosion



Case Study 2: Linda

- Normal lab results: CBC, CMP, ESR (16 mm/hr), and CRP 0.6 mg/dL
- Patient is prescribed:
  - Diclofenac 150 mg QD for 6 weeks
  - Adalimumab 40 mg Q2W for 12 weeks
- After 12 weeks, CDAI increased from 16 to 20 and PASI increased from 8 to 10

Case Study 2: Linda

- How would you manage Linda?
  - A. Infliximab
  - B. IL-17i (Secukinumab or ixekizumab)
  - C. Ustekinumab
  - D. Guselkumab

Is infliximab an option for this patient?

- Enthesitis → ~60–75% improvement
- Dactylitis → ~60% improvement
- Function
  - Significant improvement achieved as assessed by HAQ
- QoL
  - Significant improvements in SF-36, PsAQoL, DLQI, EQ-5D
- Fatigue
  - Significant improvement observed, eg, with FACIT

Conclusion: TNFi work in multiple aspects of PsA. Infliximab has an ACR20 of 40-45%.

MASES = Maastricht Enthesitis Index; HAQ = Health Assessment Questionnaire; SPARCC = Spondyloarthritis Research Consortium of Canada; PsAQoL = PsA quality of life; DLQI = Dermatology Life Quality Index; EQ-5D = EuroQol 5-domain; FACIT = Functional Assessment of Chronic Illness Therapy.

Mease PJ. *Ann Rheum Dis.* 2011;70(Suppl 1):i77-i84. Mease PJ. *Arthritis Care Res (Hoboken)*. 2011:63(Suppl 11):S64-S85.

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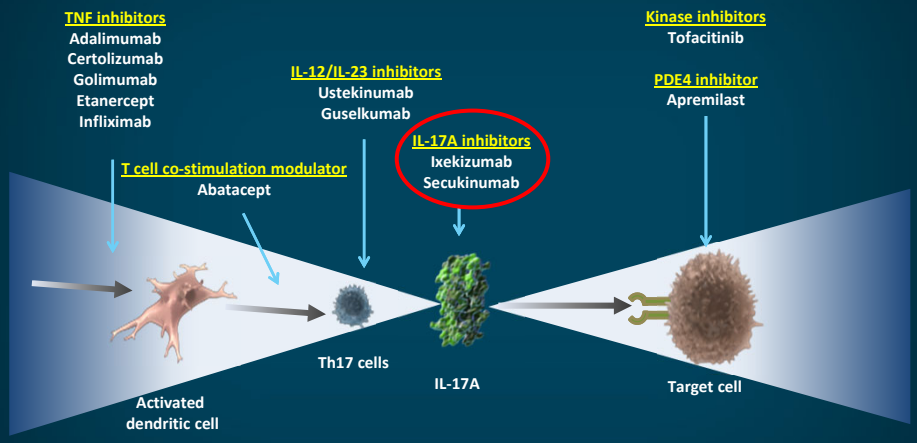
  - Significant improvement observed, eg, with FACIT

Conclusion: TNFi work in multiple aspects of PsA. Infliximab has an ACR20 of 40-45%.

MASES = Maastricht Enthesitis Index; HAQ = Health Assessment Questionnaire; SPARCC = Spondyloarthritis Research Consortium of Canada; PsAQoL = PsA quality of life; DLQI = Dermatology Life Quality Index; EQ-5D = EuroQol 5-domain; FACIT = Functional Assessment of Chronic Illness Therapy.

Mease PJ. *Ann Rheum Dis.* 2011;70(Suppl 1):i77-i84. Mease PJ. *Arthritis Care Res (Hoboken)*. 2011:63(Suppl 11):S64-S85.

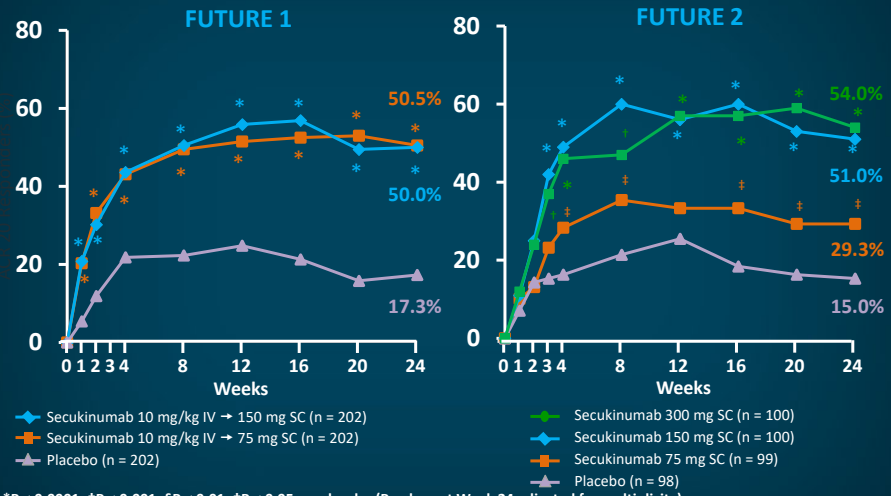
Current and Novel Treatment Options for PsA Treatment



Adapted from Nestle FO, et al. *N Engl J Med*. 2009;361:496-509. Kopf M, et al. *Nat Rev Drug Discov*. 2010;9:703-718. Garber K. *Nat Biotechnol*. 2011;29:563-566. Thanks to Iain McInnes.

Is this patient a candidate for an IL-17i?

Secukinumab in PsA: ACR20



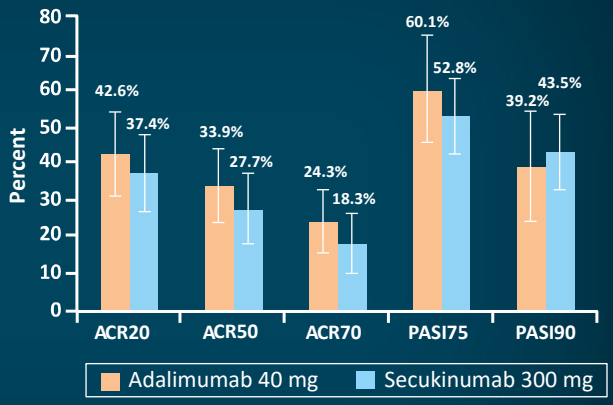
*P < 0.0001; †P < 0.001; §P < 0.01; ‡P < 0.05 vs. placebo (P-values at Week 24 adjusted for multiplicity).
Missing values imputed as nonresponse (nonresponder imputation).

IV =intravenous; SC = subcutaneous.

Mease PJ, et al. *N Engl J Med*. 2015;373:1329-1339. McInnes IB, et al. *Lancet*. 2015;386:1137-1146.

Adalimumab vs Secukinumab in PsA:
Indirect Comparison

- 302 patients from ADEPT (ADA) and 2 PsA trials of SEC (FUTURE 1 & 2)
- Matching for age, weight, gender, race, MTX use, PASI, dactylitis, enthesitis, HAQ-DI
- Number needed to treat to achieve 1 additional PASI75 responder:
  - ADA 40 mg: 1.7
  - SEC 150 mg: 2.2
  - SEC 300 mg: 1.9

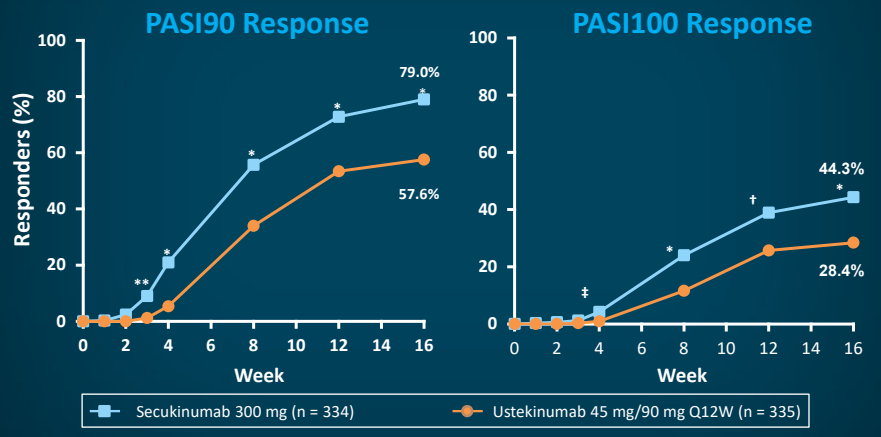


Conclusion: Secukinumab (anti-IL-17) was shown to be as effective or slightly less effective than adalimumab for PsA (numerical only).

ADA = adalimumab; SEC = secukinumab.

Betts KA, et al. *Arthritis Rheumatol.* 2015;67(10): Abstract 2868. Strand V. *Rheumatol Ther.* 2017;4:349-362.

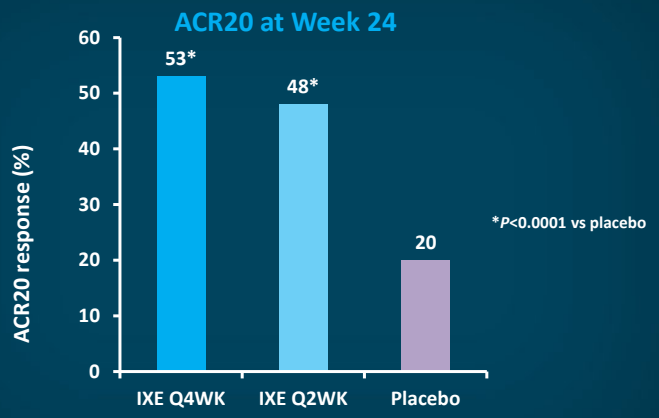
CLEAR Study: Secukinumab (aIL-17A) vs Ustekinumab (aIL-12/23) in Psoriasis



*P<0.0001; **P=0.0001; †P<0.001; ‡P<0.05

Thaci D, et al. *JAAD*. 2015;73(3):400-409.

SPIRIT-P2: Ixekizumab in Patients with Active PsA and an Inadequate Response to TNFi



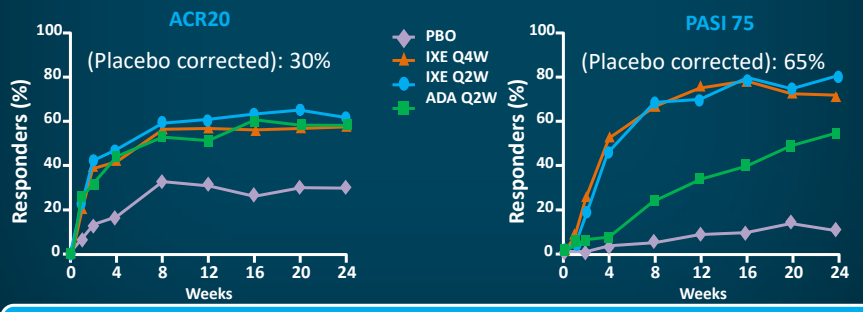
Both the 2-week and 4-week ixekizumab dosing regimens improved the signs and symptoms of patients with active PsA who had an inadequate response to TNFi therapy.

IXE = ixekizumab.

Nash P, et al. *Lancet*. 2017;389:2317-2327.

Ixekizumab vs Adalimumab for PsA

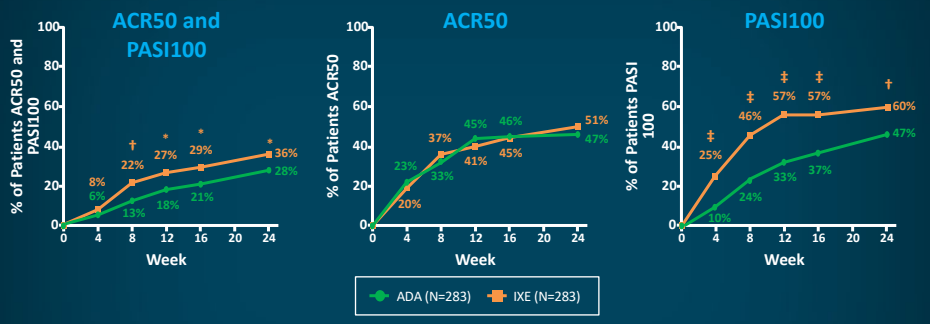
- Randomized, double-blind placebo-controlled trial in patients who were biologic DMARD naïve
- More patients achieved an ACR20 response with IXE Q2W (62.1%) or IXE Q4W (57.9%) than placebo (30.2%)
- Disease activity and functional disability were significantly improved with ixekizumab vs placebo (*P*< .01), and there was significantly less progression of structural damage at week 24 with ixekizumab (*P*<0.01)



Conclusion: Ixekizumab and adalimumab were both equally better than placebo in PsA. Ixekizumab was better than adalimumab for psoriasis.

Mease P, et al. *Ann Rheum Dis*. 2017;76:79-87.

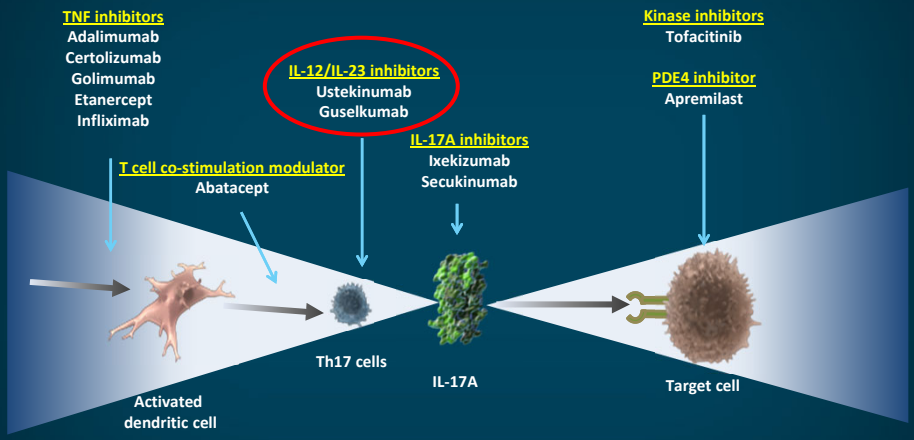
SPIRIT H2H: Head-to-Head Comparison of Ixekizumab and Adalimumab



- Ixekizumab was superior to adalimumab in achievement of simultaneous improvement in joint and skin disease (ACR50 and PASI100) in patients with active PsA and inadequate response to csDMARDs
- Ixekizumab was non-inferior to adalimumab for ACR50 response (IXE: 51%, ADA: 47%) but superior for PASI100 response (IXE: 60%, ADA:47%, *P*=0.001)

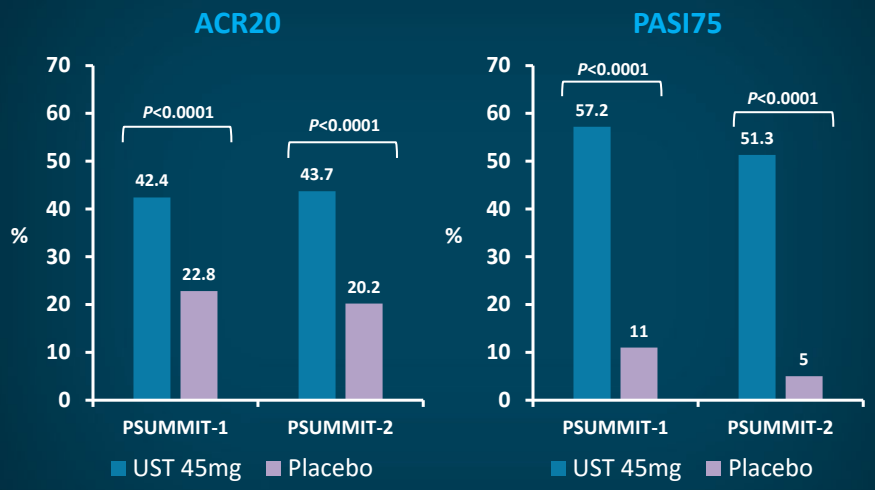
Mease PJ, et al. *Ann Rheum Dis.* 2020;79:123-131.

Current and Novel Treatment Options for PsA Treatment



Adapted from Nestle FO et al. *N Engl J Med.* 2009;361:496-509. Kopf M et al. *Nat Rev Drug Discov.* 2010;9:703-718. Garber K. *Nat Biotechnol.* 2011;29:563-566. Thanks to Iain McInnes.

Ustekinumab: Efficacy in PsA

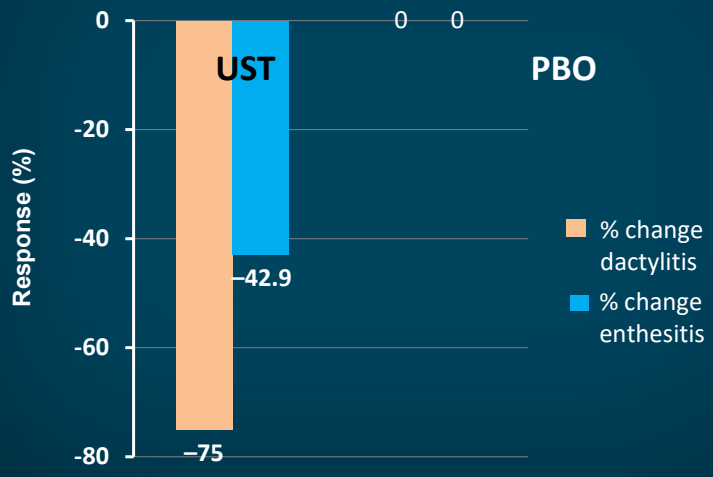


UST = ustekinumab.

McInnes IB et al. *Lancet.* 2013;382:780-789. Ritchlin C et al. *Ann Rheum Dis.* 2014;73:990-999.

Ustekinumab Is Effective in PsA

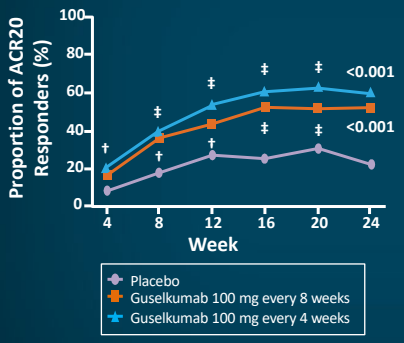
24-Week DBRCT
(PBO: n = 206; UST: n = 205; 45 mg IV at 0, 4, and every 12 weeks)



McInnes IB ,et al. *Ann Rheum Dis.* 2012;71(3):107. McInnes I. *Lancet.* 2013;382:780-789.

DISCOVER-1 Trial of Guselkumab

- Phase 3, placebo-controlled trial of guselkumab in 381 patients with active PsA who were biologic-naïve or had previously received a TNFi
- 31% of patients had been previously treated with ≤2 TNFi agents



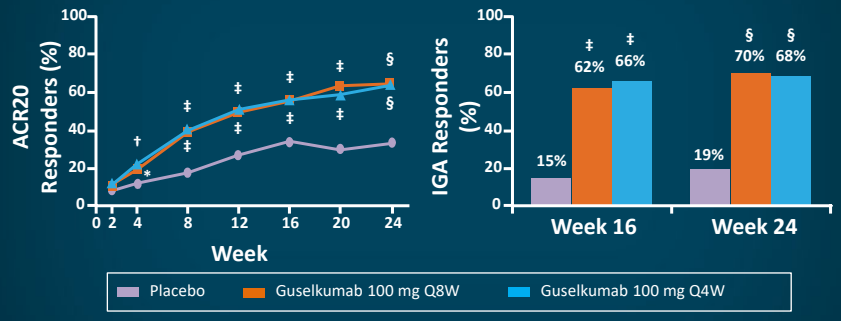
	Guselkumab 100 mg		Placebo
	Q4W	Q8W	
Number of patients	128	127	126
ACR20 response at Week 24, n/N (%)			
Patients with prior TNFi use	22/38 (57.9%)	23/41 (56.1%)	7/39 (17.9%)
% difference vs. placebo (95% CI)	40.0 (20.8, 59.2)	38.5 (19.3, 57.7)	
Unadjusted p value	<0.001	<0.001	
Patients without prior TNFi use	54/90 (60.0%)	43/86 (50.0%)	21/87 (24.1%)
% difference vs. placebo (95% CI)	35.9 (22.3, 49.4)	25.9 (12.0, 39.7)	
Unadjusted p value	<0.001	<0.001	

- ACR20 at week 24 was achieved by significantly greater proportions of patients in the guselkumab Q4W (59%) and Q8W (52%) groups than in the placebo group (22%)

Deodhar A, et al. *Lancet*. 2020;395:1115-1125.

DISCOVER-2 Trial of Guselkumab

- Phase 3 trial of 741 biologic-naïve patients with active PsA
- Patients randomized to guselkumab Q4W, Q8W, or placebo

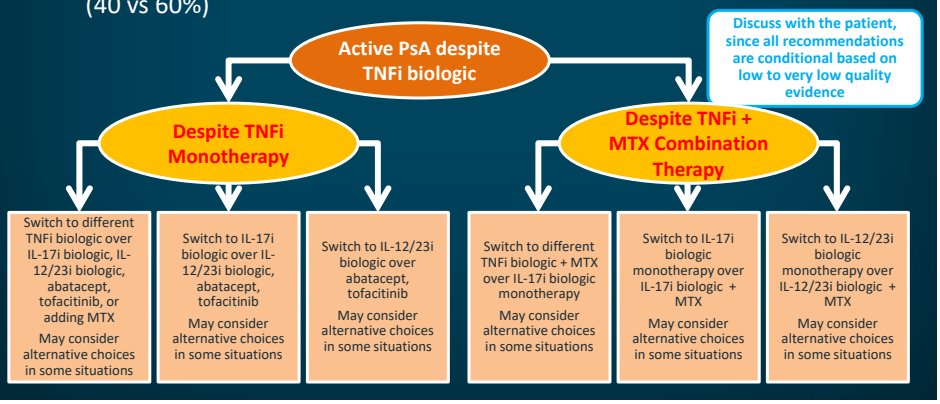


- Significantly greater proportions of patients in the guselkumab Q4W (64%) and Q8W (64%) groups achieved ACR20 at week 24 than placebo (33%)

Mease PJ, et al. *Lancet*. 2020;395:1126-1136.

Patient 2: Summary

- The best options for this patient are another TNFi inhibitor (if no contraindications) or an IL-17i (ixekizumab or secukinumab)
- In PsA, ixekizumab and secukinumab both have reasonable responses (30-35%)
  - Ixekizumab may have better results on skin lesions than secukinumab (40 vs 60%)



Patient 3: Tina

- Tina is a 47-year old woman who presents with swelling of her left wrist, and lower back pain, bilateral shoulder pain, left wrist and right elbow pain, bilateral 3 PIP and right 3, 4 DIP pain
  - CDAI: 18 (above TJC and SJC, patient global: 6.0, MD global: 5.0)
  - 2+ edema to mid-calf
- Significant skin involvement (PASI:14)

TJC = Tender Joint Count; SJC = Swollen Joint Count.

Patient 3: Tina's Past Medical History

- Congestive heart failure
- Obesity (BMI: 32)
- Hypertension (160/95 mmHg)
- History of MI three years ago
- Family history positive for MI

Case Study 3: Tina's Lab and Imaging Results

- Lab results:
  - Hemoglobin: **10.0 g/dL** (normal: 12-16)
  - WBC: 5.2 x 10^9/L (normal: 4.0-11.0)
  - Platelets: 285 x 10^9/L (normal: 150-400)
  - ESR: **32 mm/hr** (normal: 0-29 mm/hr)
  - Remainder of CBC and CMP are normal
- Imaging results:
  - Radiographs of the knees shows osteoarthritis on the right
  - Chest film shows cardiomegaly

How Would You Manage Tina?

A. Adalimumab or infliximab

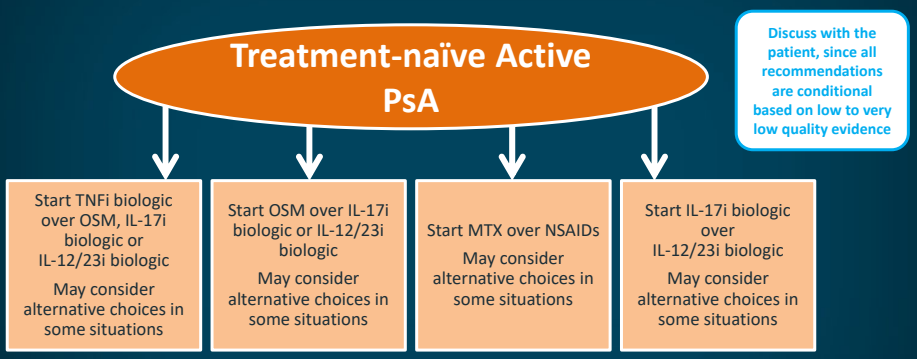
B. Secukinumab or ixekizumab

C. Ustekinumab

D. Methotrexate or cyclosporine

E. Apremilast

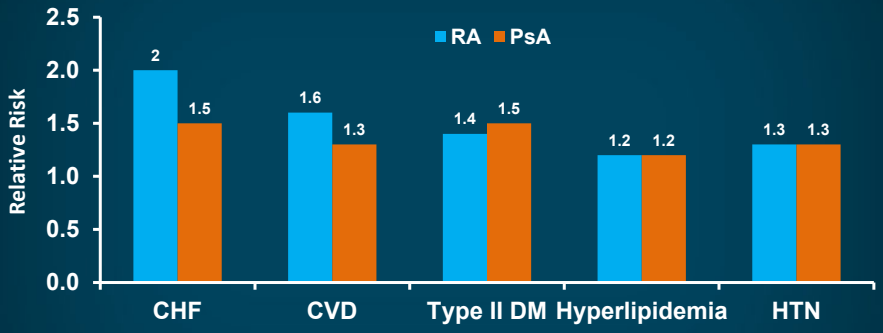
Treatment-naïve Patient



Singh JA, et al. *Arthritis Rheumatol.* 2019;71:5-32.

Comorbidities in Rheumatoid and Psoriatic Arthritis

Patients with PsA have an increased risk of cardiovascular complications. Tina has CHF, hypertension, a history of MI, and obesity.



- Managed care claims database of >2.7 million patients
- 28,200 patients had RA (1.02%), and 3,066 patients had PsA (0.11%)

CHF = congestive heart failure; CVD = cardiovascular disease; MI = myocardial infarction; DM = diabetes mellitus; HTN = hypertension.

Han C, et al. EULAR 2005. Abstract OP0160.

Is a TNFi an option for Tina?
TNFi Adverse Events

A TNFi is relatively contraindicated in patients with congestive heart failure. Therefore, a TNFi is not a good option for Tina.

INFECTIONS	Overall	Comment
Tuberculosis	Rare	IFX>ETA=Adal
Opportunistic	VR	IFX>ETA=Adal
Bacterial	UC	2.7/100 pt yrs
Hepatitis B	-	Not increased
Hepatitis C	-	Not increased

	Overall	Comment
Lymphoma	R	IFX>ETA=Adal (active disease)
CHF (EF <30)	R	OR: 1.26
Hematologic	VR	.0001 (.01%)
Hepatotoxicity	VR	IFX>ETA>Adal
AST/ALT >2x	UC	.006 (.6%)
Demyelinating disease	R	ETA>IFX=Adal
Antinuclear antibodies (ANA)	C	FDA PI

C = common ≥10%; UC = uncommon: OR : 2.3; R = rare ≤ 0.001 (0.1%); VR = very rare ≤ 0.0001 (0.01%); EF = ejection fraction, FDA PI = Food and Drug Administration prescribing information.

Khanna D, et al. *Drug Safety.* 2004;27(5):307-324. Calabrese L ,et al. *Ann Rheum Dis.* 2006;65(8):983-989. Baecklund E, et al. *Arthritis Rheum.* 2003;48(6):1543-1550. Krueger GG, et al. *N Eng J Med.* 2007;356:580-592. Lee WJ ,et al. *Rheum,* 2018;57(2):273-282. Cannizzaro MV, et al. *Psoriasis (Auckl).* 2017;7:35-60.

Is an IL-17i an option for Tina? Secukinumab: Adverse Events

Common Adverse Events[1]			
	SEC 300 mg	SEC 150 mg	Placebo
URI	4 (4%)	8 (8%)	7 (7%)
Nasopharyngitis	6 (6%)	4 (4%)	8 (8%)
Diarrhea	2 (2%)	2 (2%)	3 (3%)
Headache	7 (7%)	4 (4%)	4 (4%)
Nausea	3 (3%)	4 (4%)	4 (4%)
Sinusitis	1 (1%)	2 (2%)	1 (1%)
Psoriatic arthropathy	0	3 (3%)	2 (2%)
Urinary tract infection	2 (2%)	4 (4%)	4 (4%)
Hematuria	2 (2%)	3 (3%)	1 (1%)
Vomiting	2 (2%)	2 (2%)	1 (1%)

Warnings[2]

1. Infection
2. Tuberculosis
3. Hypersensitivity reactions
4. **New or worsening inflammatory bowel disease**

URI = upper respiratory tract infection.

1. McInnes IB et al. *Lancet*. 2015;386:1137-1146 2. Secukinumab (Cosentyx®) prescribing information (www.pharma.us.novartis.com/sites/ www.pharma.us.novartis.com/files/cosentyx.pdf).

Is an IL-17i an option for Tina? Ixekizumab: Adverse Events

Ixekizumab Adverse Events		
	IXE 80 mg (n=1167)	Placebo (n=791)
Injection site reactions	196 (17%)	26 (3%)
Upper Resp Infection	163 (14%)	101 (13%)
Nausea	23 (2%)	5 (1%)
Tinea Infections	17 (2%)	1 (<1%)

Warnings

1. Infection
2. Tuberculosis
3. Hypersensitivity reactions
4. Inflammatory bowel disease

Adverse events occurring in ≥ 1% of IXE group, and more frequently than placebo.

Ixekizumab and secukinumab are good options for Tina. An IL-17i or IL-12/23i may be used in patients with severe psoriasis, those who have contraindications or experience serious adverse events with a TNFi, or if TNFi therapy fails. An IL-17i is preferred over IL-12/23i unless the patient has inflammatory bowel disease.

Singh JA, et al. *Arthritis Rheumatol*. 2019;71:5-32. Ixekizumab (Taltz®) prescribing information (https://pi.lilly.com/us/taltz-uspi.pdf).

Is ustekinumab an Option for Tina?

- Meta-analysis of 30 RCT of 16 week duration in 9626 patients
- AEs and SAEs include infections, cough, headache, URI, nausea, ISR, CV event, cancer, death

Ustekinumab Adverse Events

Adverse events	UST	Placebo	P value
Infections	1210 (19.7%)	588 (17.1%)	<0.01
Nasopharyngitis	318 (5.2%)	162 (4.7%)	0.31
Cough	21 (2.3%)	25 (4.8%)	0.01
Upper respiratory tract infection	150 (3.2%)	201 (7.1%)	<0.001
Nausea	113 (4.8%)	58 (5.0%)	0.80
Headache	302 (6.1%)	141 (5.1%)	0.06
Infusion/Injection site reaction (ISR)	149 (3.9%)	44 (2.0%)	<0.001
Malignancy	3 (0.1%)	5 (0.2%)	0.16
Death	5 (0.1%)	1 (0.1%)	0.43
CV	7 (0.2%)	4 (0.2%)	1.00

Ustekinumab would be a safe and effective option for Tina. An IL-17i or IL-12/23i may be used in patients with severe psoriasis, those who have contraindications or experience serious adverse events with a TNFi, or if TNFi therapy fails. An IL-17i is preferred over IL-12/23i unless the patient has inflammatory bowel disease.

Rolston VS, Kimmel J et al *Drug Dis and Science.* 2020. Singh JA, et al. *Arthritis Rheumatol.* 2019;71:5-32.

Are Methotrexate or Cyclosporine Good Options for Tina?

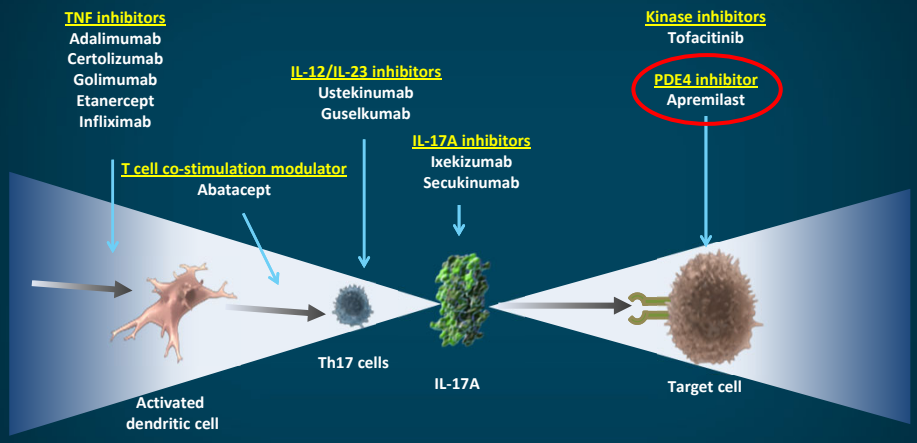
Limitations of Conventional Systemic Therapies

Agent	Safety
Methotrexate	Nausea, diarrhea, stomatitis, fatigue, elevated liver enzymes, myelosuppression, pneumonitis, increased risk of infection
Cyclosporine	Nausea, abdominal pain, nephrotoxicity, hypertension

Tina has hypertension and mild anemia. These agents are not good options for Tina given their toxicity profile and relatively poor comparative efficacy.

Cuchacovich R, et al. *Ther Adv Chronic Dis.* 2012;3:259-269.

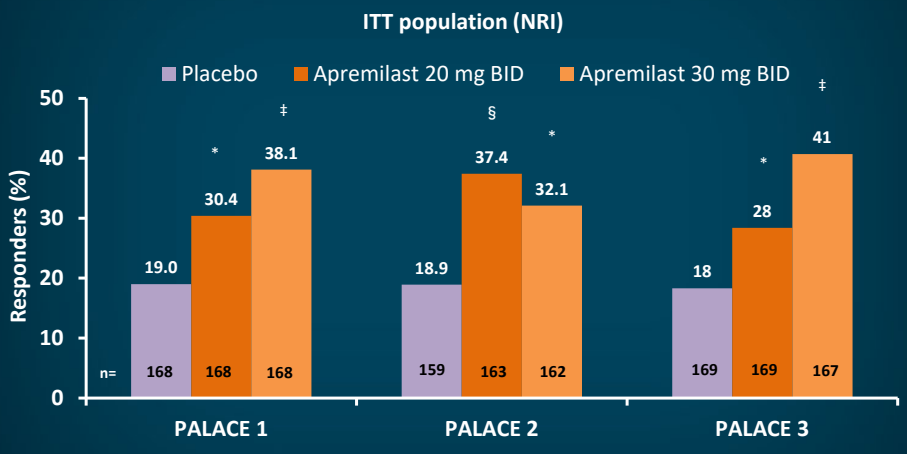
Current and Novel Treatment Options for PsA Treatment



Adapted from Nestle FO et al. *N Engl J Med*. 2009;361:496-509. Kopf M et al. *Nat Rev Drug Discov*. 2010;9:703-718. Garber K. *Nat Biotechnol*. 2011;29:563-566. Thanks to Iain McInnes.

Apremilast in PsA: PALACE 1, 2, and 3

Primary endpoint across studies: ACR20 response at week 16

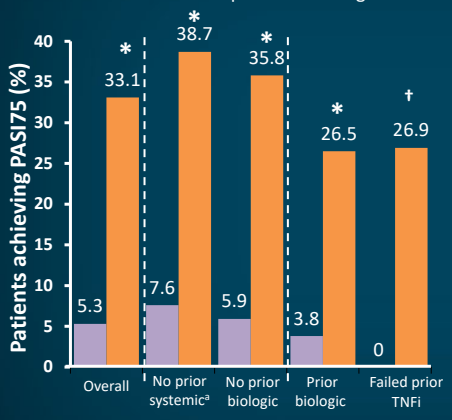


*P<0.05; §P<0.005; ‡P≤0.0001 vs placebo.
NRI = non-responder imputation.

Kavanaugh A, et al. *Ann Rheum Dis*. 2014;73:1020-1026. Cutolo M, et al. *J Rheumatol*. 2016;43:1724-1734. Edwards CJ, et al. *Ann Rheum Dis*. 2016;75:1065-1073.

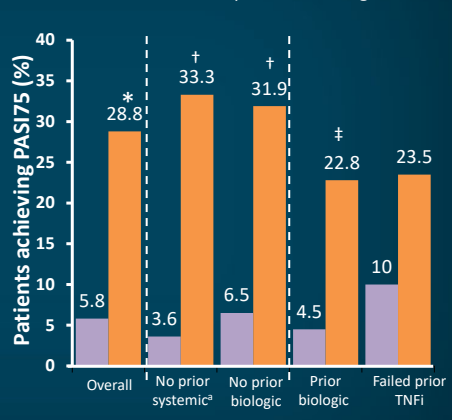
Apremilast in Moderate-to-Severe Psoriasis

ESTEEM 1: PASI75 by prior treatment at week 16 (LOCF, full analysis set; N = 844)



*P<0.0001; †P=0.0273 vs PBO; [a]Conventional ± biologics

ESTEEM 2: PASI75 by prior treatment at Week 16 (LOCF, full analysis set; N = 411)



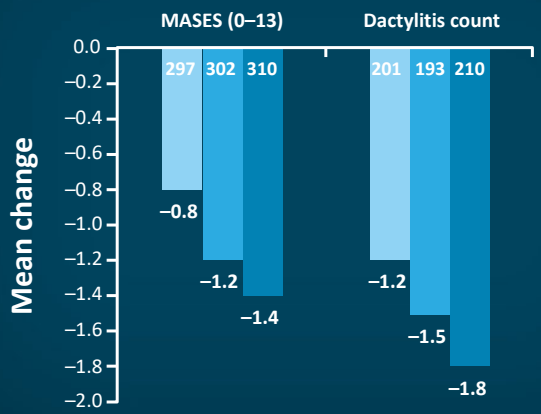
*P<0.0001; †P<0.001, ‡P=0.0069 vs PBO

LOCF = last observation carried forward.

Paul C et al. *J Am Acad Dermatol.* 2014;70(5):AB164 (abstract P8412). Papp K et al. *J Am Acad Dermatol.* 2015;73:37-49. Reich K et al. AAD 2013, Late breaker. Paul C et al. *Br J Dermatol.* 2015;173:1387-1399.

Apremilast Effects on Enthesitis and Dactylitis

Data pooled from PALACE 1–3, week 24



Gladman DD, et al. *Arthritis Rheum.* 2013;65(10 suppl): S347 (abstract 816).

PALACE 2: 52-Week Safety of Apremilast[1]

Adverse Events	Placebo (N = 159)	APR 30 BID (24 weeks) (N = 162)	APR 30 BID (52 weeks) (N = 234)
Diarrhea	8 (5.0)	24 (14.8)	32 (13.7)
Nausea	3 (1.9)	26 (16.0)	32 (13.7)
Headache	7 (4.4)	19 (11.7)	23 (9.8)
URI	6 (3.8)	11 (6.8)	22 (9.4)
Nasopharyngitis	6 (3.8)	8 (4.9)	10 (4.3)
Hypertension	7 (4.4)	5 (3.1)	13 (5.6)
Laboratory values			
ALT >150 u/L	1/158 (0.6)	2/160 (1.3)	3/230 (1.3)
Creatinine elevation	0/158 (0.0)	1/160 (0.6)	2/230 (0.9)

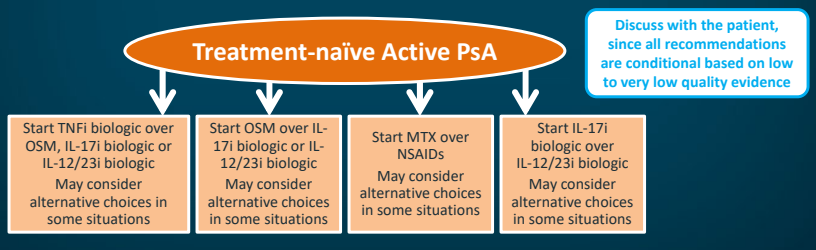
Warnings for[2]:
1. Depression and suicidal behavior
2. Weight loss

APR = apremilast; ALT = alanine aminotransferase.

1. Cutolo M, et al. *J Rheumatol.* 2016;43:1724-1734.
2. Apremilast (Otezla ®) PI (http://media.celgene.com/content/uploads/otezla-pi.pdf).

Case Study 3: Summary

- A TNFi is recommended as a first-line option in treatment-naïve patients. Contraindications to TNFi therapy include congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease
- An OSM may be used in patients without severe PsA or severe psoriasis
- IL-17i or IL-12/23i biologics may be used in patients with severe psoriasis or contraindications to TNFi agents. An IL-17i is recommended over an IL-12/23i, unless the patient has concomitant IBD or prefers less frequent dosing



Singh JA, et al. *Arthritis Rheumatol.* 2019;71:5-32.

Case Study 4: Teresa

- A 43-year-old overweight woman presents with a 6-year history of PsA principally involving the back. She has difficulty carrying groceries up one flight of stairs due to her back pain. She reports morning stiffness lasting up to 1 hour.
- She also complains of joint pain in her right ankle, right knee, left DIP, and left shoulder.
- Her past medical history is significant for:
  - Type 2 diabetes. HbA1c of 7.6 despite long acting insulin and metformin therapy.
  - Hypertension. Blood pressure of 152/92 mmHg despite lisinopril and furosemide.

Case Study 4: Teresa's Examination

- Patient pain today: 4.5; Patient global today: 5.0; MD global: 5.0

- Tender bilateral SI joints. **Bilateral Achilles insertional pain**. **Bilateral talocalcaneal pain. L23 and 34 pain.** Pain of both shoulders, both wrists, right 3 PIP, bilateral 2 – 4 DIP pain with mild swelling, right knee, right talus pain for a **joint tenderness count of 6/28 and 13/68.** Swelling of right wrist and right knee for a **joint swelling count of 2/28 and 2/66. CDAI:18**.

- Scaling and mild erythema posterior scalp, thick scaling with mild erythema of both elbows, right intertriginous area and both knees for a **PASI: 8**.

Case Study 4: Prior Treatment

- Teresa is prescribed secukinumab
  - CDAI improved from 18 to 8
  - Mild pain noted in left wrist, DIPs, and right knee only
  - Dactylitis of the right toes
  - PASI improved from 8 to 3
  - Scalp and elbow lesions remain
- Lab results show neutropenia with WBC of 1.4 and PMNs of 0.9
  - Her secukinumab therapy is stopped
  - Within 3 weeks, her WBC is 3.2 and PMNs are 2.0

WBC = white blood cell count; PMN = polymorphonuclear cells

How Would You Manage Teresa?

A. Ixekizumab

B. Ustekizumab

C. Tofacitinib

D. Guselkumab

Long-term Safety of Secukinumab

- Pooled data from 18 RCTs and post-marketing safety surveillance data of secukinumab in psoriasis and PsA

Exposure Adjusted Incidence Rate

	Psoriasis	PsA
No. of patients, N	5181	1380
No. of RCT, N	15	3
Upper respiratory tract infection	1.4%	1.9%
Inflammatory bowel disease	0.01%	0.05%
MACE	0.3%	0.4%
Neutropenia	0.3%	0.2%

- Given the development of neutropenia with secukinumab, switching to a non-IL-17i should be considered

MACE = major adverse cardiovascular events

Deodhar A, et al. *Arthritis Res Ther*. 2019;21.

Ustekinumab Adverse Events

- Meta-analysis of 9626 patients in 30 RCT of 16 weeks duration
- AEs and SAEs include infections, cough, headache, upper respiratory tract infection, nausea, injection site reactions, CV event, cancer, and death

Adverse events	UST	Placebo	P value
Infections	1210 (19.7%)	588 (17.1%)	<0.01
Nasopharyngitis	318 (5.2%)	162 (4.7%)	0.31
Cough	21 (2.3%)	25 (4.8%)	0.01
Upper respiratory tract infection	150 (3.2%)	201 (7.1%)	<0.001
Nausea	113 (4.8%)	58 (5.0%)	0.80
Headache	302 (6.1%)	141 (5.1%)	0.06
Infusion/Injection site reaction	149 (3.9%)	44 (2.0%)	<0.001
Malignancy	3 (0.1%)	5 (0.2%)	0.16
Death	5 (0.1%)	1 (0.1%)	0.43
CV	7 (0.2%)	4 (0.2%)	1.00

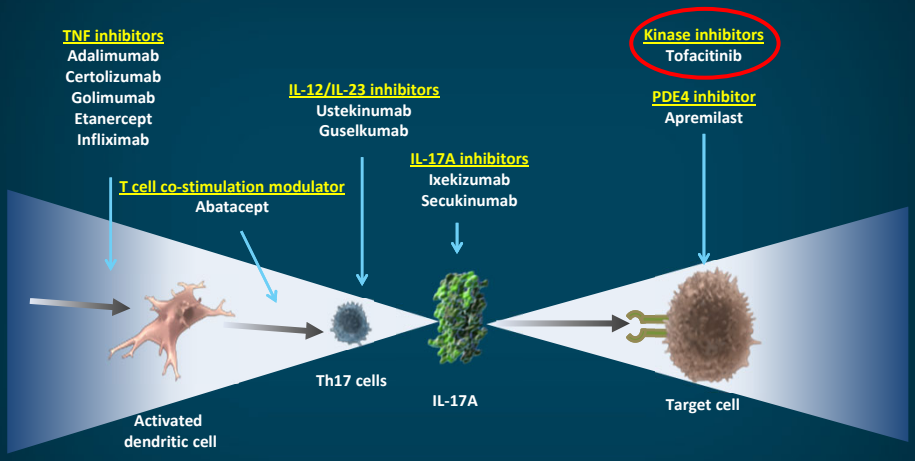
Rolston VS, et al. *Dig Dis Sci*. 2020. doi:10.1007/s10620-020-06344-w.

Guselkumab Adverse Events

	PBO	GUS	
		100 mg Q8W	100 mg Q4W
Patients with ≥1 AE (%)	60%	54%	55%
SAE (%)	4%	3%	0%
Discontinuation due to AE (%)	2%	2%	1%
Infections (%)	25%	26%	24%
Alanine aminotransferase increase	2%	6%	4%
Aspartate aminotransferase increase	2%	7%	2%
Nasopharyngitis	6%	13%	5%
Upper respiratory tract infection	6%	6%	9%

Deodhar A, et al. *Lancet*. 2020;395:1115-1125.

Current and Novel Treatment Options for PsA Treatment

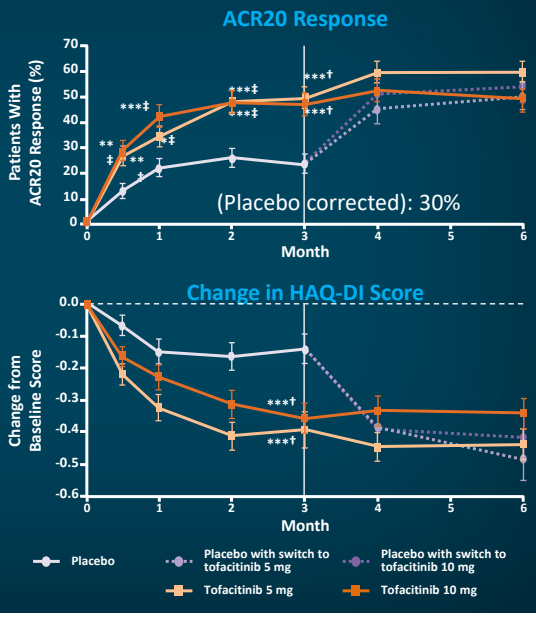


Adapted from Nestle FO et al. *N Engl J Med*. 2009;361:496-509. Kopf M et al. *Nat Rev Drug Discov*. 2010;9:703-718. Garber K. *Nat Biotechnol*. 2011;29:563-566. Thanks to Iain McInnes.

Efficacy of Tofacitinib in PsA

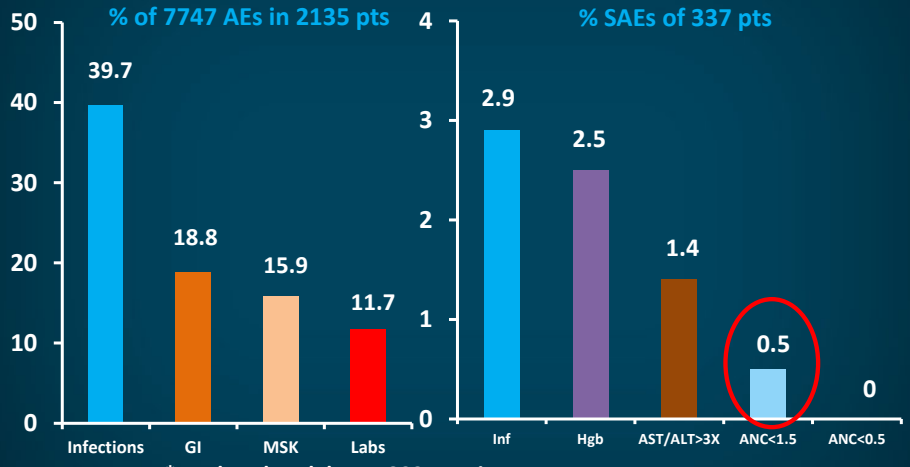
- 395 patients with active PsA and an inadequate response to TNFi were randomized to:
  - Tofacitinib 5 mg BID
  - Tofacitinib 10 mg BID
  - Placebo, with a switch to 5 mg or 10 mg tofacitinib BID at 3 months
- No efficacy noted on Leeds Enthesitis Index, Dactylitis Severity Score, FACIT-F total score, and SF-36 physical functioning

Conclusion: Tofacitinib has some efficacy in PsA, but no efficacy noted in some symptoms



Gladman D, et al. *N Eng J Med*. 2017;377:1525-1536.

Adverse Events in 3118 Patient-Years in Tofacitinib Open-Label, Long-Term Extension Study of Therapy for RA*

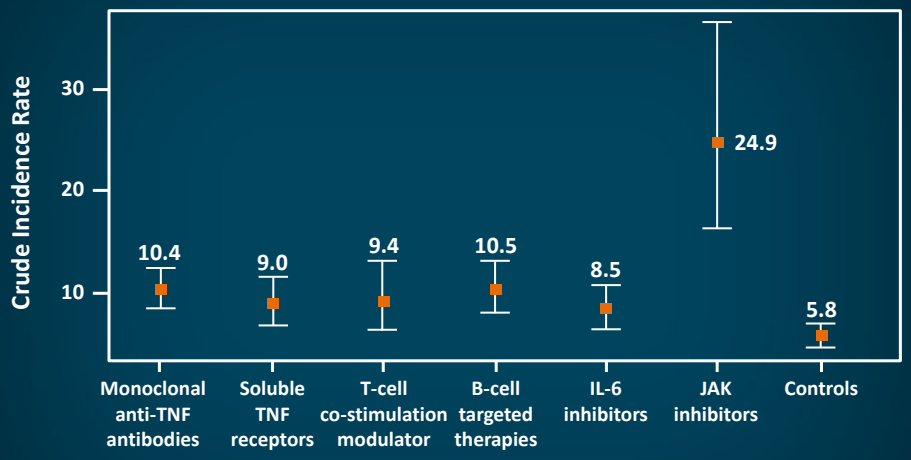


*No dose breakdown; 3227 pts in Treatment Emergent AEs

GI = gastrointestinal disorders; MSK = musculoskeletal and connective tissue disorders; Inf = infections; HGB = decreased hemoglobin; AST/ALT = aspartate/alanine; ANC = absolute neutrophil count.

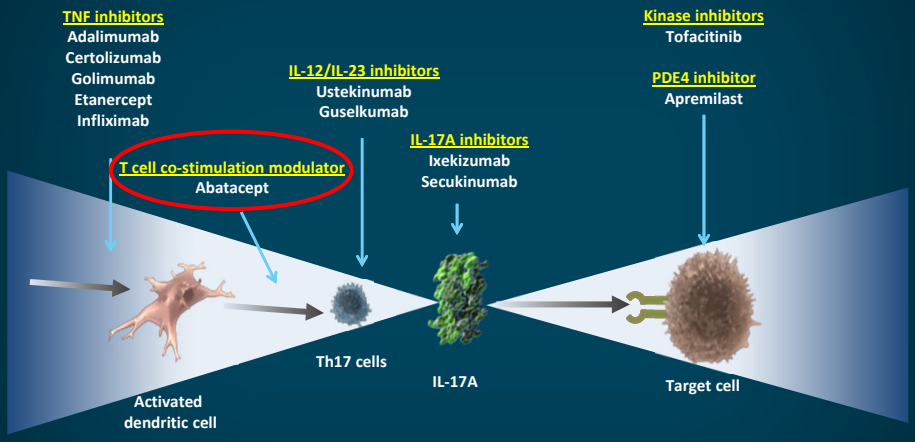
Wollenhaupt J ,et al. ACR 2011. Abstract 407.

Incident Rates of Herpes Zoster in RA Patients



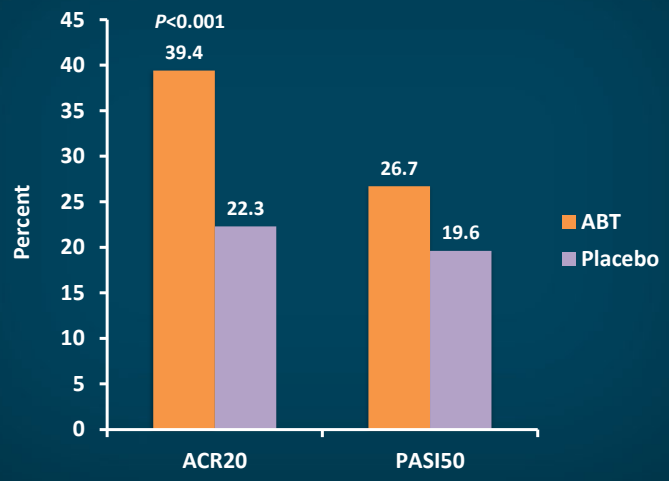
Strangfeld A, et al. EULAR 2020. Abstract OP0238.

Current and Novel Treatment Options for PsA Treatment



Adapted from Nestle FO et al. *N Engl J Med*. 2009;361:496-509. Kopf M et al. *Nat Rev Drug Discov*. 2010;9:703-718. Garber K. *Nat Biotechnol*. 2011;29:563-566. Thanks to Iain McInnes.

Abatacept: Phase III Trial



ABT = abatacept.

Mease PJ, et al. *Ann Rheum Dis*. 2017;76:1550-1558.

Case Study 4: Teresa's COVID-19 Diagnosis

- Teresa's therapy is switched to ustekinumab. Three weeks later, she schedules a telemedicine appointment and reports her recent COVID-19 diagnosis. She experiences shortness of breath, fever, and cough. She would like to know if she should continue taking her PsA medications.
- How would you manage Teresa's PsA?
  - A. Decrease the frequency of ustekinumab dosing
  - B. Initiate prednisone
  - C. Switch to adalimumab
  - D. Consider holding PsA therapy and reinitiating 7-14 days after symptom resolution
  - E. Stop therapy and reinitiate 1 month after negative COVID-19 test

ACR Recommendations: Managing PsA and COVID-19

Treatment of Rheumatic Disease During the COVID-19 Pandemic[8]	
Treatment of Rheumatic Disease in the Absence of COVID-19 Infection or Exposure	
HCQ/CQ, SSZ, MTX, LEF, immunosuppressants (tacrolimus, CSA, MMF, AZA), biologics, JAK inhibitors, NSAIDs	Continue therapy
Low-dose corticosteroids	May be started if clinically indicated (<10 mg prednisone equivalent/day)
Following SARS-CoV-2 Exposure	
HCQ/CQ, SSZ, NSAIDs	May be continued
Immunosuppressants (tacrolimus, CSA, MMF, AZA), non-IL-6 biologics, JAK inhibitors	Stop therapy temporarily, pending a negative COVID-19 test or 2 weeks of symptom-free observation
IL-6 inhibitors	May be continued in select circumstances
Documented or presumptive COVID-19	
HCQ/CQ	May be continued
SSZ, MTX, LEF, immunosuppressants, non-IL-6 biologics, and JAK inhibitors	Withhold or stop therapy
NSAIDs	Should be stopped in patients with severe respiratory symptoms

Mikuls TR, et al. *Arthritis Rheumatol*. 2020;72:e1-e12.

- All recommendations are based on very low quality of evidence and moderate to high consensus.
- The recommendations are for rheumatic disease patients in general and are not subdivided by patient disease. There are no specific recommendations for PsA
  - Mild COVID-19 symptoms: reinitiate therapy in 7-14 days
  - Asymptomatic COVID-19: reinitiate therapy in 10-17 days
  - Severe COVID-19: reinitiating therapy is dependent on a case-by-case review

Final Remarks

- Pharmacologic treatment of PsA is only 1 part of the picture. Other factors to consider include:
  - Patient goals
    - Improve quality of life, function, and social participation
    - Control symptoms and inflammation (enthesitis, dactylitis, joint pain)
    - Prevent joint damage
  - Starting treatment early
  - Minimizing associated comorbidities.
  - Multidisciplinary care:
    - Physical therapy, occupational therapy, management of comorbidities by dermatologists, endocrinologists, cardiologists, etc.

Perez-Chada LM, et al. *Clin Immunol*. 2020;108397.

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Resource	Address
Manson JJ, et al. **COVID-19-associated hyperinflammation and escalation of patient care: A retrospective longitudinal cohort study.** *Lancet Rheumatol*. 2020;2:e594-e602.	https://pubmed.ncbi.nlm.nih.gov/32864628/
Mikuls TR, et al. **American College of Rheumatology Guidance for the Management of Rheumatic Disease in Adult Patients During the COVID-19 Pandemic: Version 1.** *Arthritis Rheumatol*. 2020;72:1241-1251.	https://pubmed.ncbi.nlm.nih.gov/32349183/
Pablos JL, et al. **Clinical outcomes of hospitalised patients with COVID-19 and chronic inflammatory and autoimmune rheumatic diseases: A multicentric matched cohort study.** *Ann Rheum Dis*. 2020;79:1544-1549.	https://pubmed.ncbi.nlm.nih.gov/32796045/
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Nash P, et al. **Ixekizumab for the treatment of patients with active psoriatic arthritis and an inadequate response to tumour necrosis factor inhibitors: Results from the 24-week randomised, double-blind, placebo-controlled period of the SPIRIT-P2 phase 3 trial.** *Lancet*. 2017;389:2317-2327.	https://pubmed.ncbi.nlm.nih.gov/28551073/
Mease PJ, et al. **Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naive patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebo-controlled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1.** *Ann Rheum Dis*. 2017;76:79-87.	https://pubmed.ncbi.nlm.nih.gov/27553214/
Mease PJ, et al. **A head-to-head comparison of the efficacy and safety of ixekizumab and adalimumab in biological-naïve patients with active psoriatic arthritis: 24-week results of a randomised, open-label, blinded-assessor trial.** *Ann Rheum Dis.* 2020;79:123-131.	https://pubmed.ncbi.nlm.nih.gov/31563894/
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