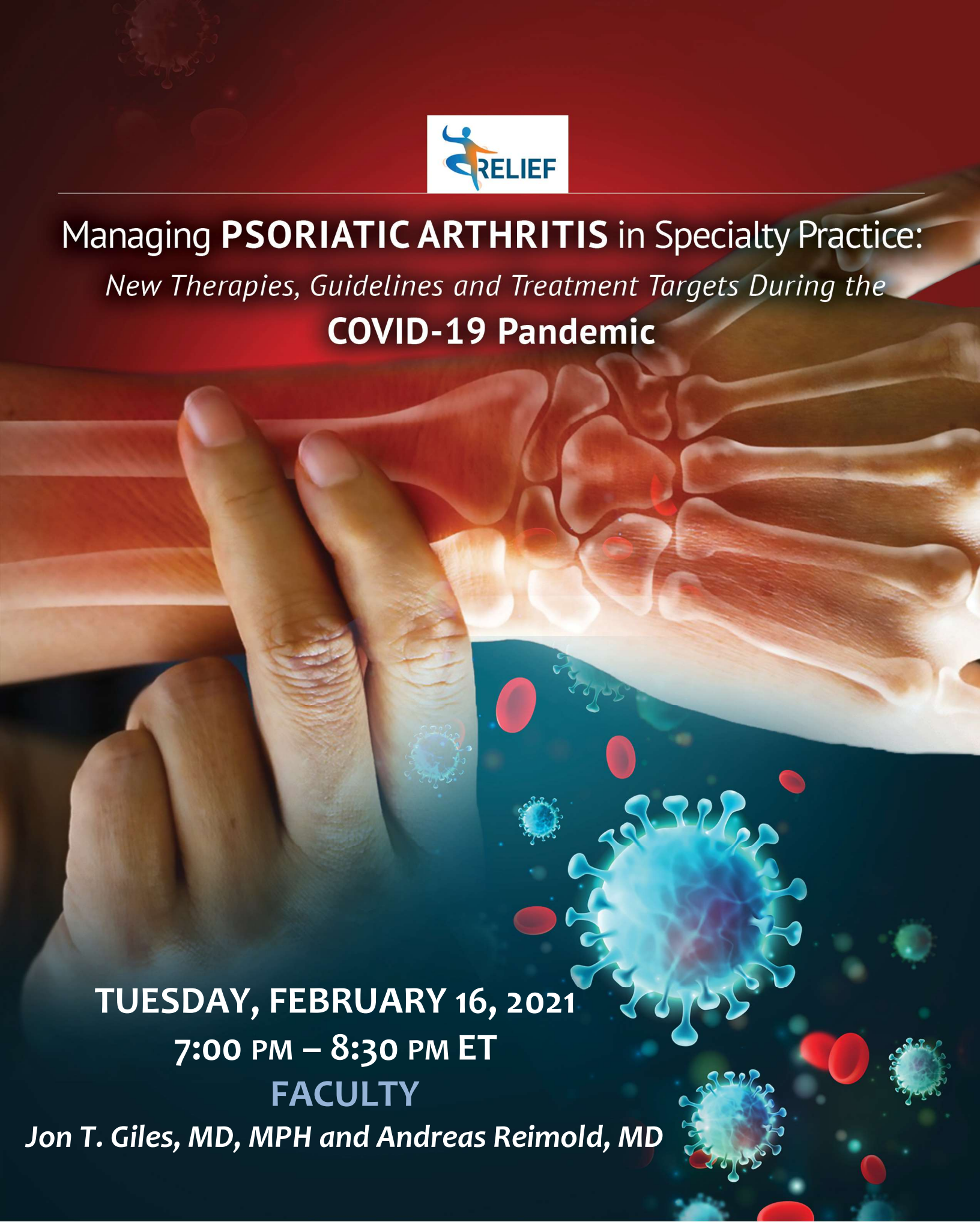
RELIEF

Managing **PSORIATIC ARTHRITIS** in Specialty Practice:

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



TUESDAY, FEBRUARY 16, 2021

7:00 PM – 8:30 PM ET

FACULTY

Jon T. Giles, MD, MPH and Andreas Reimold, MD

This activity is provided by Med Learning Group.
This activity is co-provided by Ultimate Medical Academy/Complete Conference Management (CCM).
This activity is supported by an educational grant from Lilly.

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

FACULTY

Jon T. Giles, MD, MPH
Associate Professor of Medicine
Columbia University, Vagelos School of Physicians & Surgeons
New York, NY

Andreas Reimold, MD
Professor of Internal Medicine
University of Texas Southwestern Medical Center
Dallas, TX

PROGRAM OVERVIEW
This case-based live virtual activity will cover the treatment and management of patients with psoriatic arthritis.

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
- 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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CREDIT DESIGNATION STATEMENT
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NURSING CREDIT INFORMATION
Purpose: This program would be beneficial for nurses involved in the care of patients with psoriatic arthritis.
CNE Credits: 1.5 ANCC Contact Hours.

CNE ACCREDITATION STATEMENT
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Andreas Reimold, MD has participated in a clinical trial sponsored by Pfizer.

CME Content Review
The content of this activity was independently peer-reviewed.
The reviewer of this activity has nothing to disclose.

CNE Content Review
The content of this activity was peer-reviewed by a nurse reviewer.
The reviewer of this activity has nothing to disclose.

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1. Read the CME/CNE information and faculty disclosures.
2. Participate in the live virtual activity.
3. Submit the evaluation form to Med Learning Group.

You will receive your certificate upon completion as a downloadable file.

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AGENDA

Introduction to Psoriatic Arthritis

a. Disease domains and joint manifestations
b. Identification and diagnosis
c. Differential diagnosis
d. Identifying severe disease

Telemedicine and Patient Considerations in the COVID-19 Pandemic

a. Risk of SARS-CoV-2 infection and severe COVID-19 complications in rheumatic patients
    i. Impact of comorbidities on risk
b. Treatment modifications in patients with COVID-19
    i. When to hold therapy
    ii. When to reinitiate therapy
c. Corticosteroid use in PsA patients during the COVID-19 pandemic
d. Strategies to incorporate telehealth into clinical practice
e. Infographic Case Study: Selecting a second-line agent

Medical Management of PsA in the COVID-19 Era

a. 2019 ACR guidelines and their application to practice
b. Therapeutic considerations in COVID-19
c. Conventional agents
d. Biologics, small molecules:
    a. Inhibitors of TNF, IL-12/23, IL-17A, IL-23, phosphodiesterase 4, T cell costimulation, and Janus kinases
e. Evolving standards of treatment in the COVID-19 era
f. Treating-to-target: establishing goals of therapy
g. Infographic Case Study: Managing a patient before and after a COVID-19 diagnosis

Decision Aid Case Study

Post-test Questions

Q&A

Post-program moderator notes

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

Jon T. Giles, MD, MPH
Associate Professor of Medicine
Columbia University, Vagelos School of Physicians & Surgeons
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Psoriatic Arthritis

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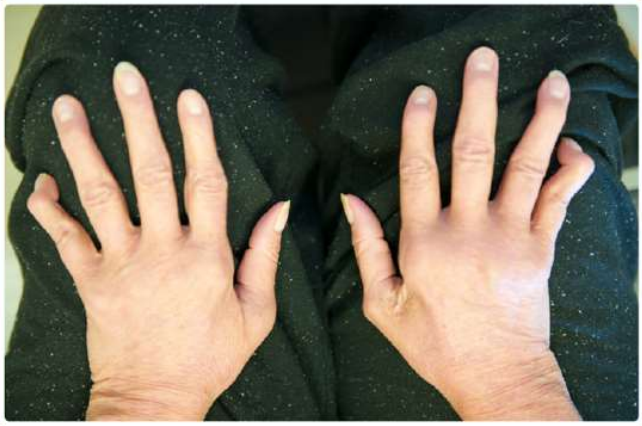
Psoriatic Arthritis Manifestations

PsA is a chronic, inflammatory musculoskeletal disease associated with psoriasis.

Symptoms include fatigue and joint pain, swelling, and stiffness.

Other disease manifestations include:

Spondylitis	Urethritis
Enthesitis	Nail disease
Dactylitis	Other extra-articular features (such as inflammatory bowel disease)
Iritis	
Conjunctivitis	



Lloyd P, et al. *Arthritis.* 2012;2012:176298. Boyd T, et al. *Rheum Dis Clin North Am.* 2015;41:739-754.

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CASPAR Classification Criteria for PsA

- To meet CASPAR criteria, a patient must have inflammatory articular disease (joint, spine, entheseal) with ≥3 total points from any of the following 5 categories.

Criterion	Points
1. Psoriasis (psoriatic skin or scalp disease)	2
• Current psoriasis on examination OR	
• Personal history OR	
• Family history in first- or second-degree relative	
2. Psoriatic nail dystrophy (eg, onycholysis, pitting, hyperkeratosis) on examination	1
3. Negative test for rheumatoid factor	1
4. Dactylitis (inflammatory swelling of an entire finger or toe)	
• Current dactylitis on examination OR	1
• Personal history in first- or second-degree relative	1
5. Juxta-articular new bone formation on plain radiographs of hands or feet	1

98.7% specificity, 91.4% sensitivity

Taylor W, et al. *Arthritis Rheum.* 2006;54:2665-2673.

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Differentiating PsA from Other Forms of Inflammatory Arthritis

Variable	PsA	RA	Gout	Osteoarthritis
Joint distribution at onset	Asymmetric	Symmetric	Asymmetric	Asymmetric
No. of affected joints	Oligoarticular	Polyarticular	Monoarticular or oligoarticular	Monoarticular or oligoarticular
Sites of hands or feet involved	Distal	Proximal	Distal	Distal
Areas involved	All joints of a digit	Same joint across digits	Usually monoarticular	Same joint across digits
Tenderness (kg on dolorimeter)	7	4	NA	NA
Purplish discoloration	Yes	No	Yes	No
Spinal involvement	Possible	Uncommon	Absent	Non-inflammatory
Sacroiliitis	Possible	Absent	Absent	Absent

Ritchlin CT, et al. *N Engl J Med.* 2017;376:957-970.

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Does Your Patient Have Severe Disease?

- No widely agreed-upon definitions of disease severity in PsA or psoriasis
- Severity should be judged on case-by-case basis
- ACR/NPF suggest the presence of ≥1 of the following qualifies as severe disease:

Severe Psoriatic Arthritis	Severe Psoriasis
• Erosive disease • Elevated markers of inflammation (ESR, CRP) attributable to PsA • Long-term damage that interferes with function (i.e. joint deformities) • Highly active disease that causes a major impairment in quality of life • Active PsA at many sites including dactylitis, enthesitis • Function-limiting PsA at a few sites • Rapidly progressive disease	• PASI of 12 or more • BSA of 5-10% or more • Significant involvement in specific areas (e.g., face, hands or feet, nails, intertriginous areas, scalp) where the burden of the disease causes significant disability • Impairment of physical or mental functioning can warrant a designation of moderate-to-severe disease despite the lower amount of surface area of skin involved

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

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New Treatment Paradigm

Patients with PsA are at increased risk of a host of comorbidities, including CV disease, metabolic syndrome, obesity, diabetes, dyslipidemia, IBD, and others.

The management of patients with PsA should be holistic and include:

BMI, vitals	Examination of dentition
Assessment of alcohol intake	Fasting lipids and CMP
Sleep problems	Fasting sugars and HbA1c
Skin involvement, with patient input	Diet/exercise and weight-loss program
Monitoring for inflammatory arthritis	Smoking cessation

Wollina U, et al. *Dermatol Ther.* 2020;33:e13743.

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Psoriatic Arthritis and COVID-19

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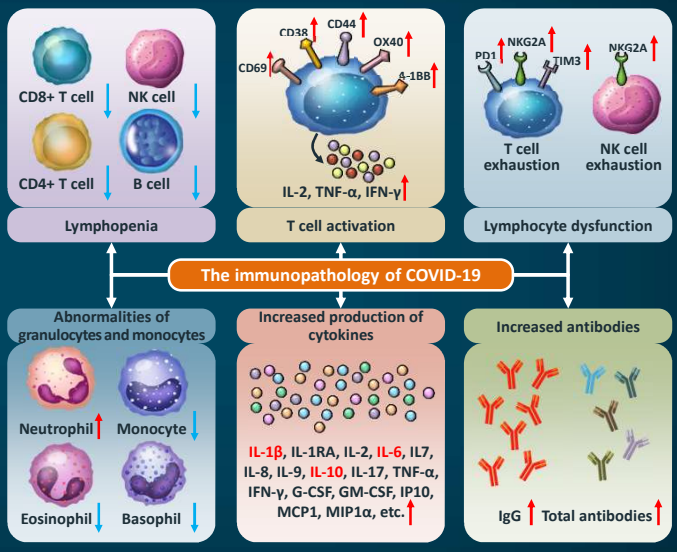
COVID-19-associated Hyperinflammation

- Clinical deterioration in COVID-19 often occurs 7-10 days after symptom onset when viral titres decline
  - Pathology likely driven by inflammation rather than direct viral injury
- 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.

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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.

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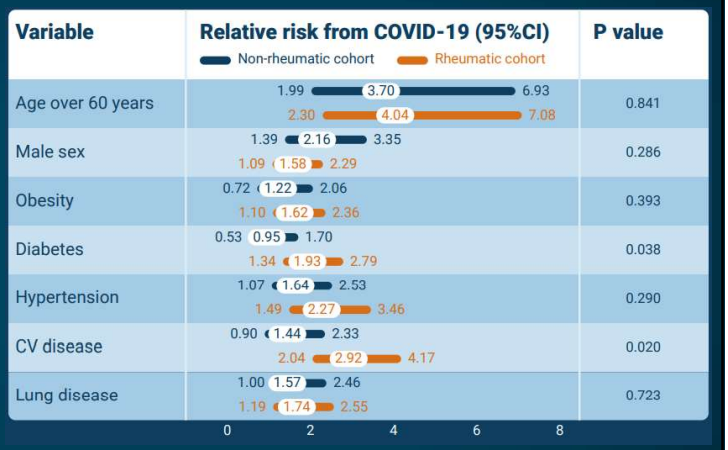
Impact of PsA Comorbidities on COVID-19 Outcomes

- PsA is associated with a higher incidence of CV disease, metabolic syndrome, obesity, diabetes, dyslipidemia, and inflammatory bowel disease
- Risk of poor outcomes for COVID-19 appears to be related to general risk factors such as older age, male sex, and comorbidities (obesity, diabetes, hypertension, CV or lung disease)



CV = cardiovascular; IBD = inflammatory bowel disease

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

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COVID-19 Treatment Modifications

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

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.

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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.

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ACR COVID-19 Vaccination Guidance for Rheumatic Patients

Medication	Timing Considerations for Immunomodulatory Therapy and Vaccination
Hydroxychloroquine; IVIG; glucocorticoids, prednisone-equivalent dose <20mg/day	No modifications to either immunomodulatory therapy or vaccination timing
SSZ; LEF; MMF; AZA; Cyclophosphamide (oral); TNFi; IL-6R; IL-1; IL-17; IL-12/23; IL-23; Belimumab; oral calcineurin inhibitors; Glucocorticoids, prednisone-equivalent dose ≥20mg/day	No modifications to either immunomodulatory therapy or vaccination timing
Methotrexate	Hold MTX 1 week after each vaccine dose, for those with well-controlled disease; no modifications to vaccination timing
JAKi	Hold JAKi for 1 week after each vaccine dose; no modification to vaccination timing
Abatacept SQ	Hold SQ abatacept both one week prior to and one week after the first COVID-19 vaccine dose (only); no interruption around the second vaccine dose
Abatacept IV	Time vaccine administration so that the first vaccination will occur four weeks after abatacept infusion (i.e., the entire dosing interval), and postpone the subsequent abatacept infusion by one week (i.e., a 5-week gap in total); no medication adjustment for the second vaccine dose
Cyclophosphamide IV	Time CYC administration so that it will occur ~1 week after each vaccine dose, when feasible
Rituximab	Assuming that patient's COVID-19 risk is low or is able to be mitigated by preventive health measures (e.g., self-isolation), schedule vaccination so that the vaccine series is initiated approximately 4 weeks prior to next scheduled rituximab cycle; after vaccination, delay RTX 2-4 weeks after 2nd vaccine dose, if disease activity allows

ACR COVID-19 Vaccine Clinical Guidance Summary. Available at: https://www.rheumatology.org/Portals/0/Files/COVID-19-Vaccine-Clinical-Guidance-Rheumatic-Diseases-Summary.pdf.

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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, 78.7% of these interruptions were NOT recommended by a physician.

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%)

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.

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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.

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Strategies to Increase Telehealth Uptake

- **Use technology** that allows you to send and receive patient-reported outcomes scales.

- **Prescreen patients with disease activity scales** and request in-person visit if scores are high.

- **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.

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Treatment Options for Psoriatic Arthritis

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Initiating Therapy

Treatment-naïve Active PsA

Discuss with the patient, since all recommendations are conditional based on low to very low quality evidence

Start TNFi biologic over OSM, IL-17i biologic or IL-12/23i biologic May consider alternative choices in some situations	Start OSM over IL-17i biologic or IL-12/23i biologic May consider alternative choices in some situations	Start MTX over NSAIDs May consider alternative choices in some situations	Start IL-17i biologic over IL-12/23i biologic May consider alternative choices in some situations

- 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; CSA = cyclosporine; IL = interleukin; LEF = leflunomide; MTX = methotrexate; NSAID = nonsteroidal anti-inflammatory drug; OSM = oral small molecule; SSZ = sulfasalazine; TNFi = tumor necrosis factor-alpha inhibitor.

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

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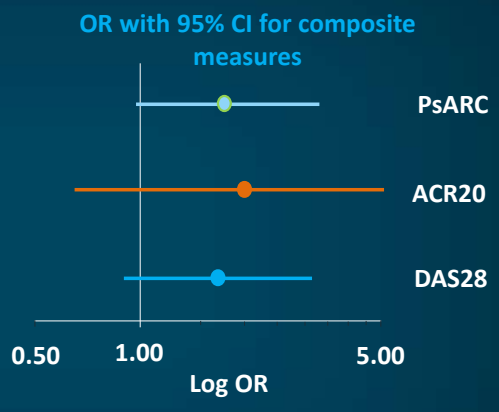
Methotrexate Is Not a DMARD in PsA

- 6-month DBRCT of MTX 15 mg/week vs PBO
- Primary outcome: PsARC
  Secondary outcomes: ACR20, DAS28, global and skin scores
- 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)



Despite issues with study design, MTX does not have disease-remitting properties.

CRP = C-reactive protein; DBRCT = double-blind, randomized controlled trial; ESR = erythrocyte sedimentation rate; MTX = methotrexate; PBO = placebo; PsARC = PsA response criteria; DAS = Disease Activity Score; SJC = swollen joint count; TJC = tender joint count.

Kingsley GH, et al. *Rheumatology (Oxford).* 2012;51:1368-1377.

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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 Cyclosporin 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.

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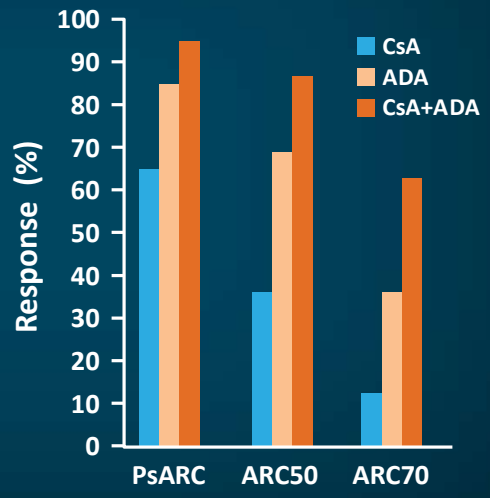
Adalimumab Or Cyclosporine as Monotherapy or Combination For Severe PsA: A Prospective, 12-month, Observational Study

- A 12-month, observational study of 170 TNFi- and cyclosporine-naïve patients
- Patients who received adalimumab (40mg Q2W) (n=57), cyclosporine (2.5-3.75 mg/kg/day) (n=58), or their combination (n=55)
- MTX-IR (25 mg weekly or less, for a minimum of 6 months)
- Assessments: 0.5, 1, 2, 3, 4, 5, 6, 8, 10, and 12 months
- Combination therapy improved PASI50 response rates but NOT beyond the effect of cyclosporine monotherapy (not shown)



MTX-IR = methotrexate inadequate response
Karanikolas GN, et al. *J Rheumatol*. 2011;38:2466-2474.

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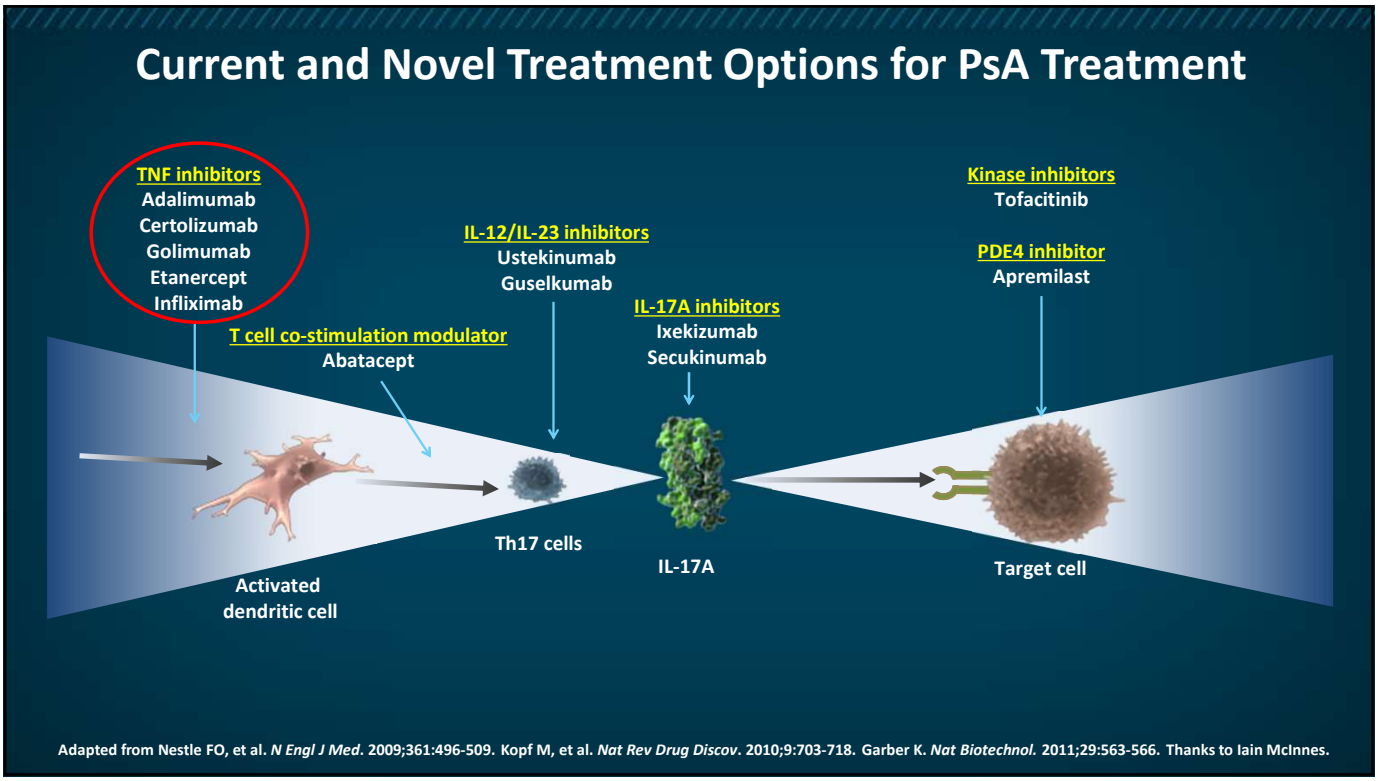
Current and Novel Treatment Options for PsA Treatment
TNF inhibitors
Adalimumab
Certolizumab
Golimumab
Etanercept
Infliximab
T cell co-stimulation modulator
Abatacept
IL-12/IL-23 inhibitors
Ustekinumab
Guselkumab
IL-17A inhibitors
Ixekizumab
Secukinumab
Kinase inhibitors
Tofacitinib
PDE4 inhibitor
Apremilast
Activated dendritic cell
Th17 cells
IL-17A
Target cell
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.

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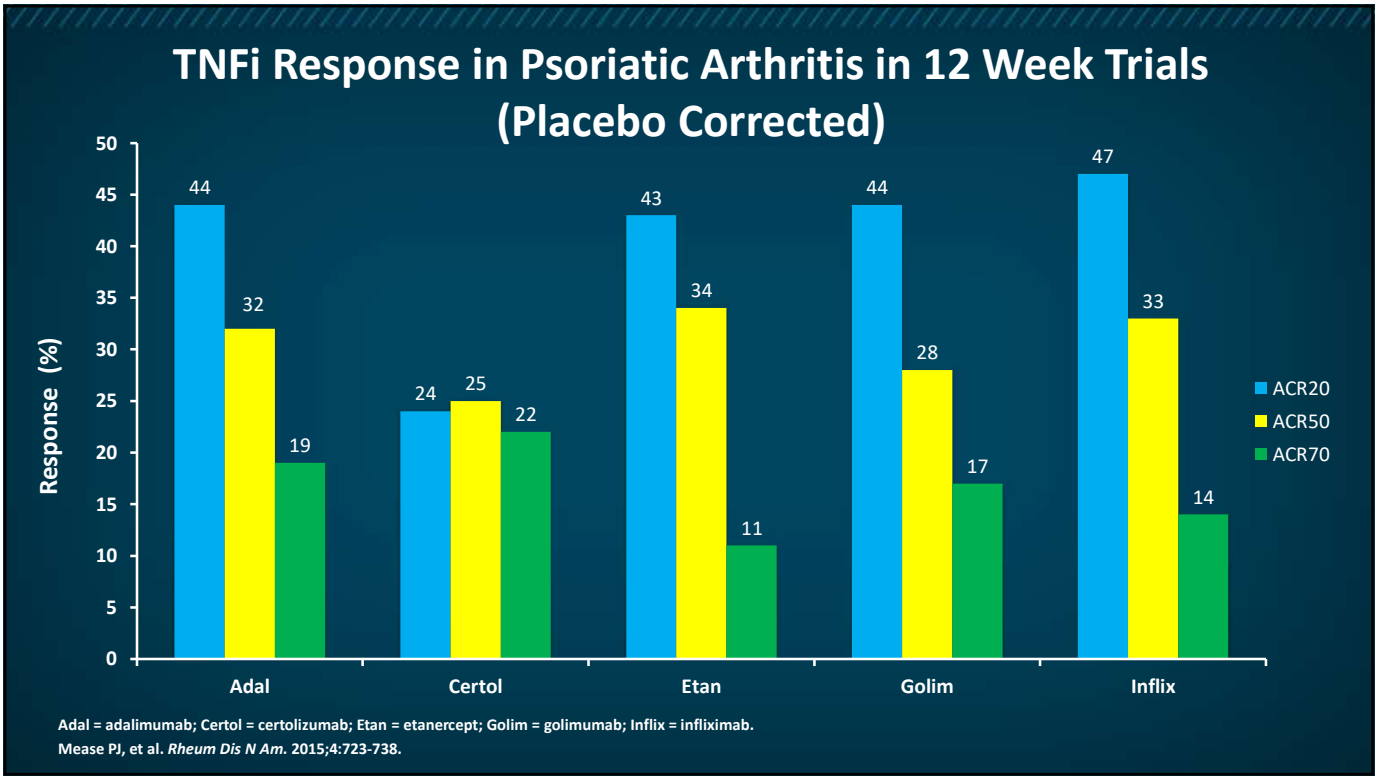
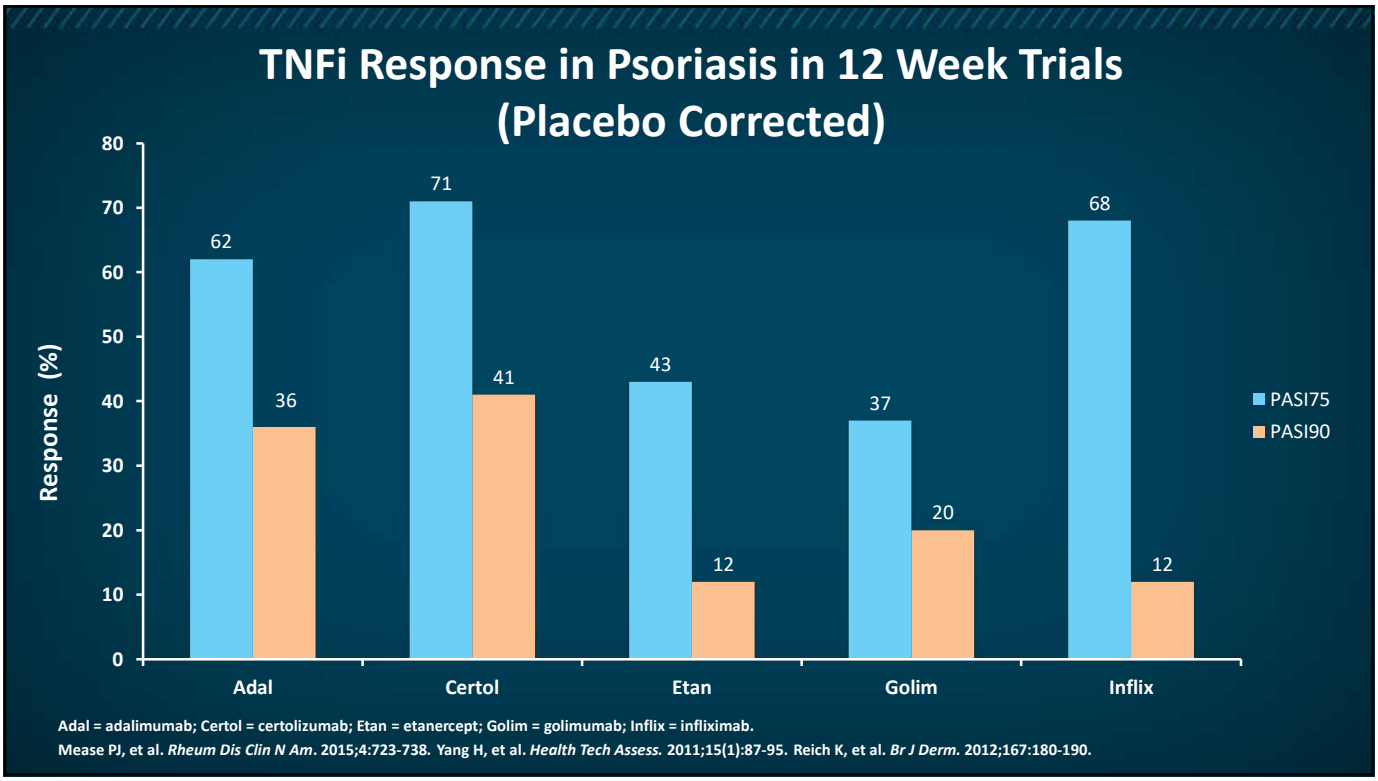
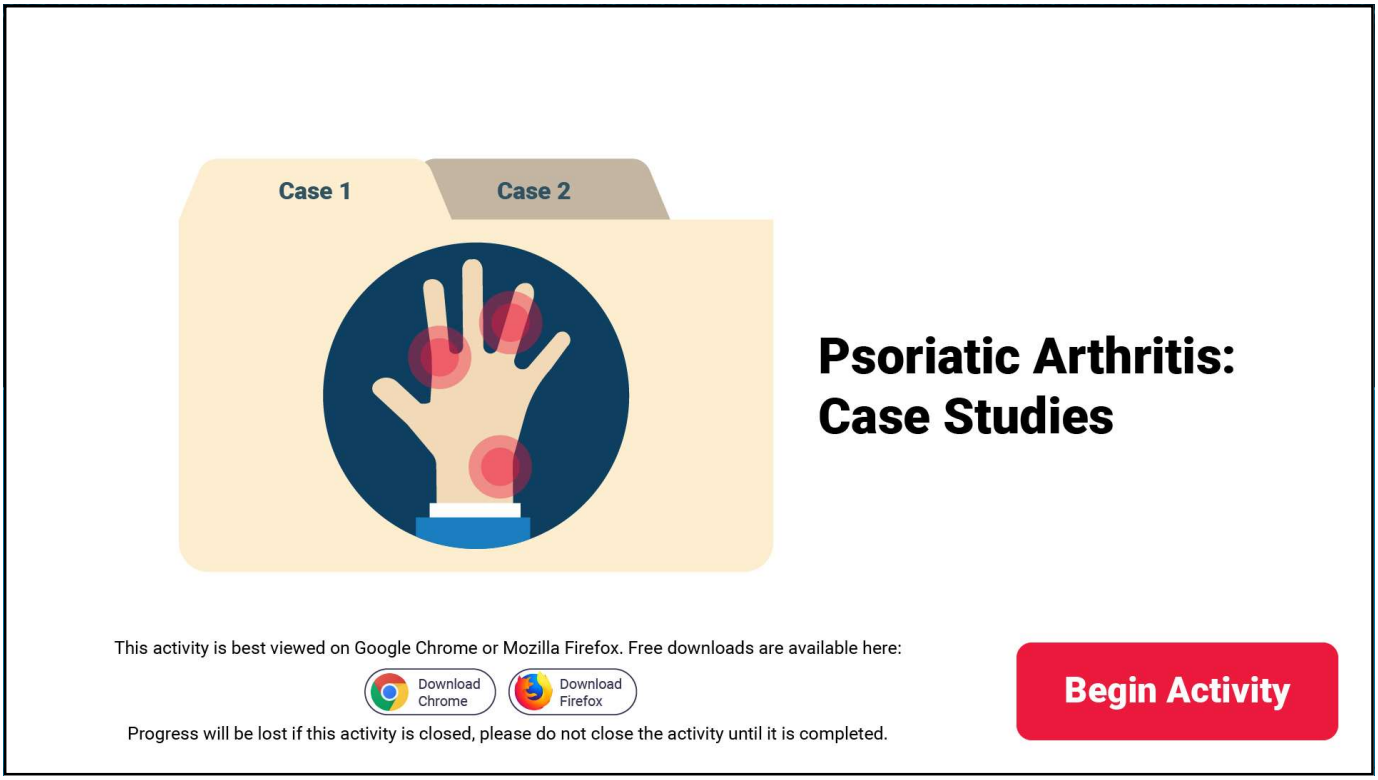

TNFi Response in Psoriatic Arthritis in 12 Week Trials (Placebo Corrected)
Response (%)
50
45
40
35
30
25
20
15
10
5
0
44
32
19
24
25
22
43
34
11
44
28
17
47
33
14
Adal
Certol
Etan
Golim
Inflix
ACR20
ACR50
ACR70
Adal = adalimumab; Certol = certolizumab; Etan = etanercept; Golim = golimumab; Inflix = infliximab.
Mease PJ, et al. Rheum Dis N Am. 2015;4:723-738.

29


TNFi Response in Psoriasis in 12 Week Trials
(Placebo Corrected)
Response (%)
80
70
60
50
40
30
20
10
0
62
36
71
41
43
12
37
20
68
12
Adal
Certol
Etan
Golim
Inflix
PASI75
PASI90
Adal = adalimumab; Certol = certolizumab; Etan = etanercept; Golim = golimumab; Inflix = infliximab.
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.

30


Case 1
Case 2
Psoriatic Arthritis:
Case Studies
This activity is best viewed on Google Chrome or Mozilla Firefox. Free downloads are available here:
Download Chrome
Download Firefox
Progress will be lost if this activity is closed, please do not close the activity until it is completed.
Begin Activity

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Case Study 1: Lindsey
Case Study 2: Tina
Case Study 1: Lindsay
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All definitions are defined in the glossary.

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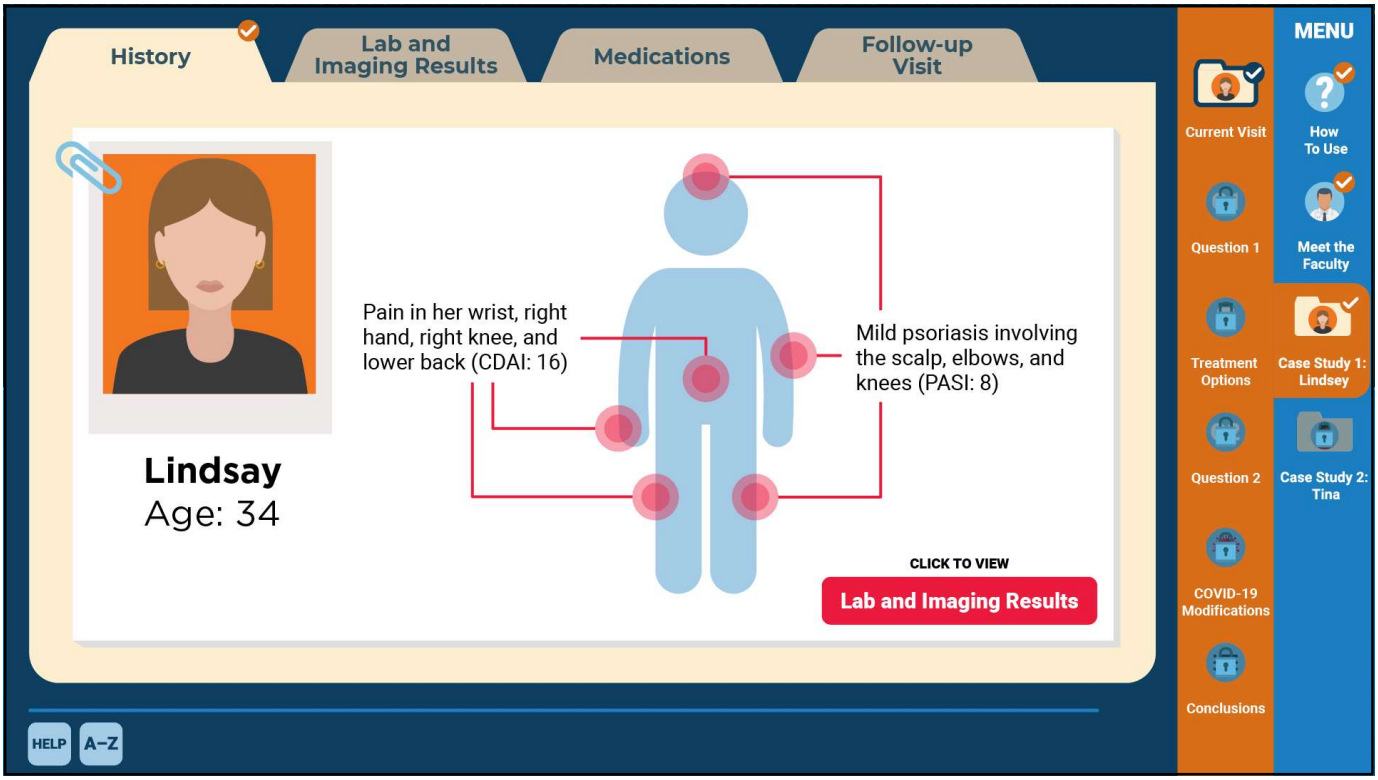
History
Lab and Imaging Results
Medications
Follow-up Visit
Lindsay
Age: 34
Pain in her wrist, right hand, right knee, and lower back (CDAI: 16)
Mild psoriasis involving the scalp, elbows, and knees (PASI: 8)
CLICK TO VIEW
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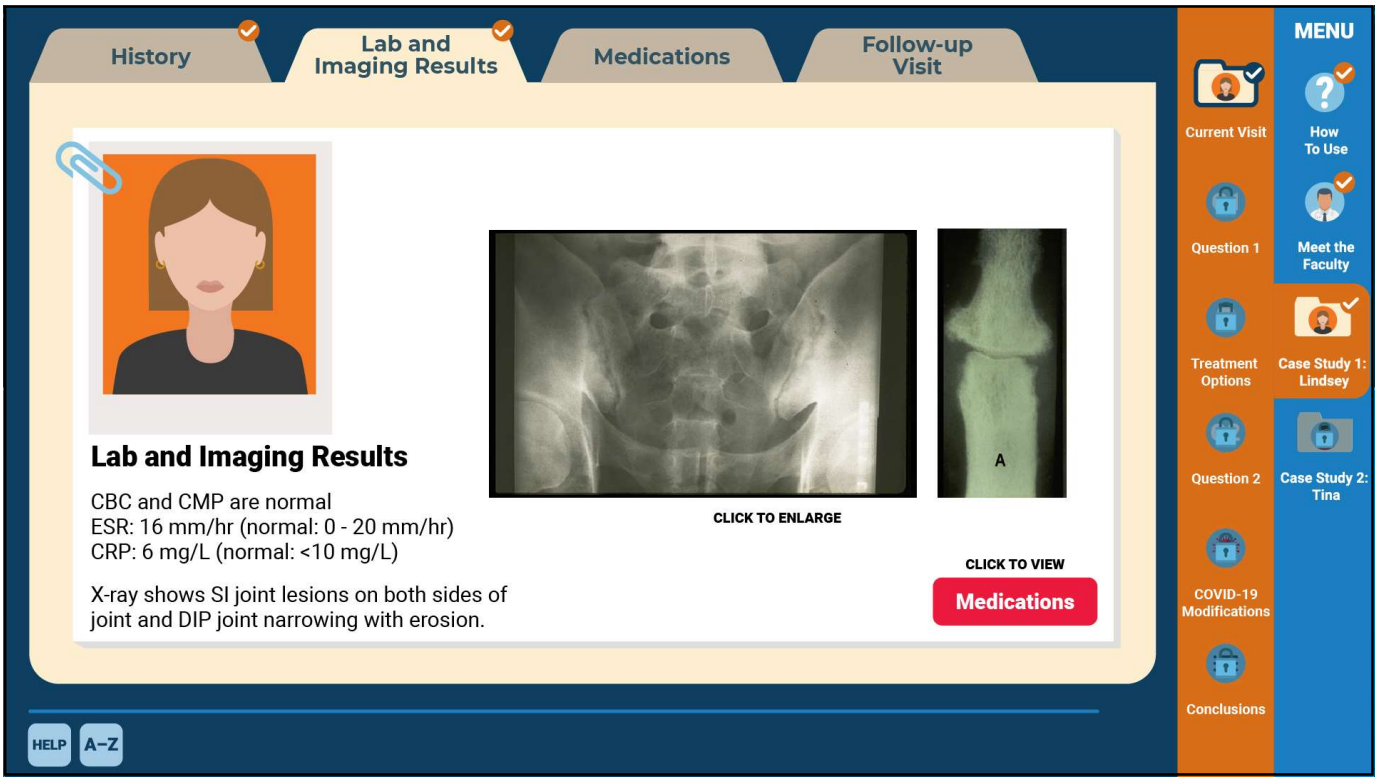
History
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Lab and Imaging Results
CBC and CMP are normal
ESR: 16 mm/hr (normal: 0 - 20 mm/hr)
CRP: 6 mg/L (normal: <10 mg/L)
X-ray shows SI joint lesions on both sides of joint and DIP joint narrowing with erosion.
A
CLICK TO ENLARGE
CLICK TO VIEW
Medications
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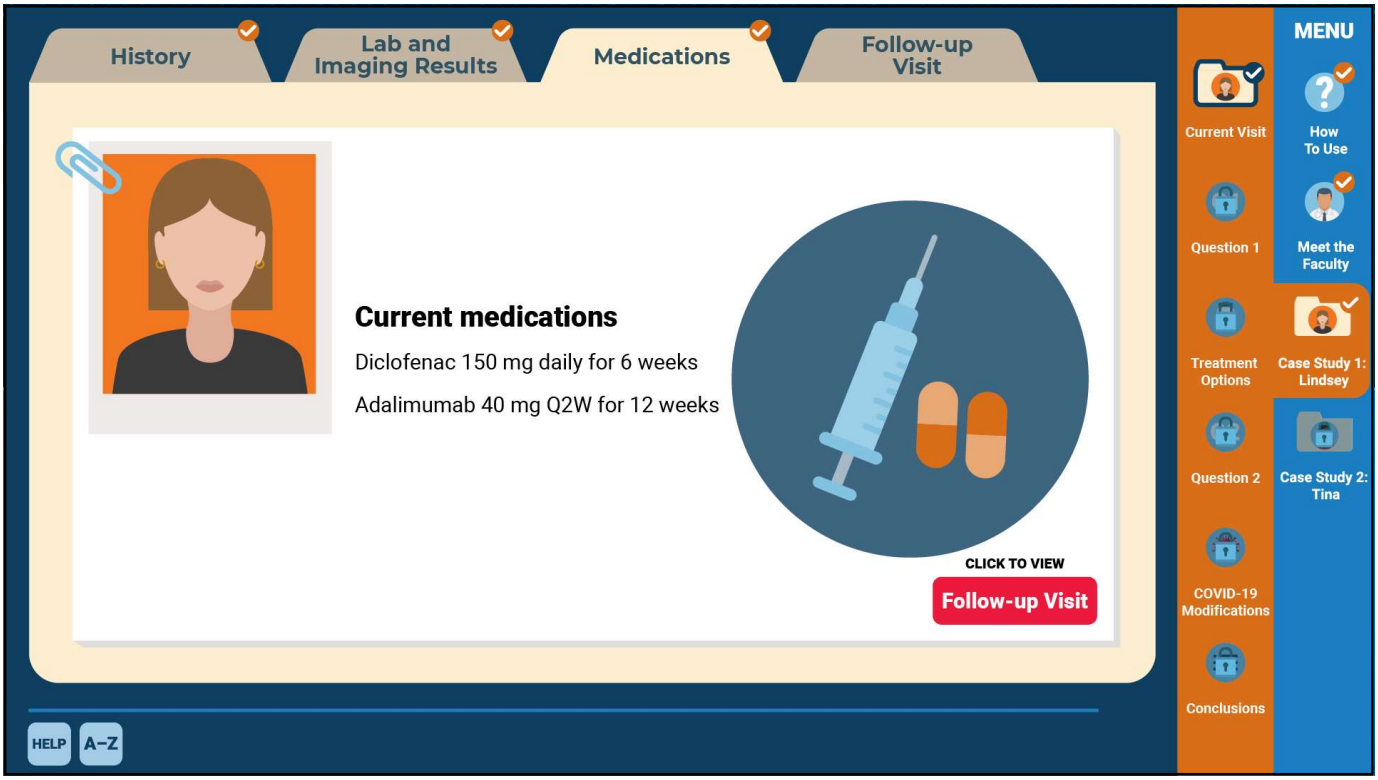
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Current medications
Diclofenac 150 mg daily for 6 weeks
Adalimumab 40 mg Q2W for 12 weeks
CLICK TO VIEW
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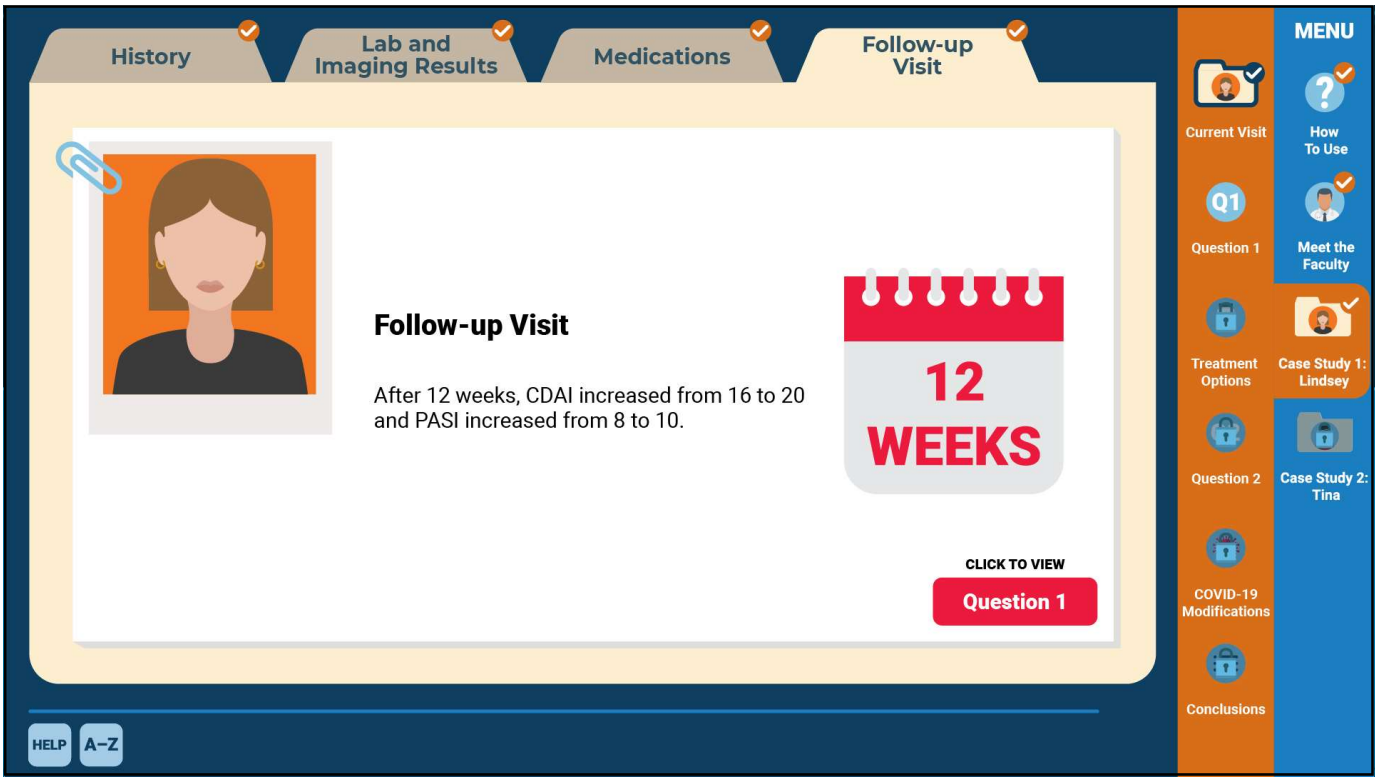
History
Lab and Imaging Results
Medications
Follow-up Visit
Follow-up Visit
After 12 weeks, CDAI increased from 16 to 20 and PASI increased from 8 to 10.
12 WEEKS
CLICK TO VIEW
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Question 1
Which of the following is the best treatment option for Lindsay?
Please select all appropriate choices.
A Ixekizumab
B Infliximab
C Guselkumab
D Ustekinumab
Submit
ACR guideline recommendations
Active PsA despite TNFi monotherapy
Switch to different TNFi biologic over IL-17i biologic, IL-12/23i biologic, abatacept, tofacitinib or adding MTX.
May consider alternative choices in some situations.
Switch to IL-17i biologic over IL-12/23i biologic, abatacept, or tofacitinib.
May consider alternative choices in some situations.
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Medical Management of PsA in the COVID-19 Era

Dr. Jon Giles

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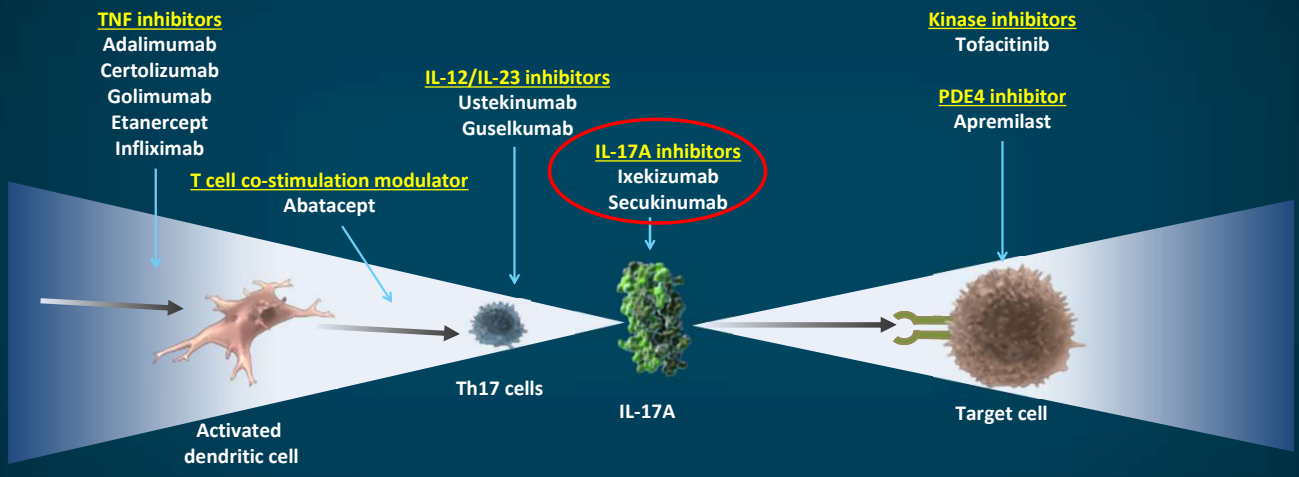
Current and Novel Treatment Options for PsA Treatment



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.

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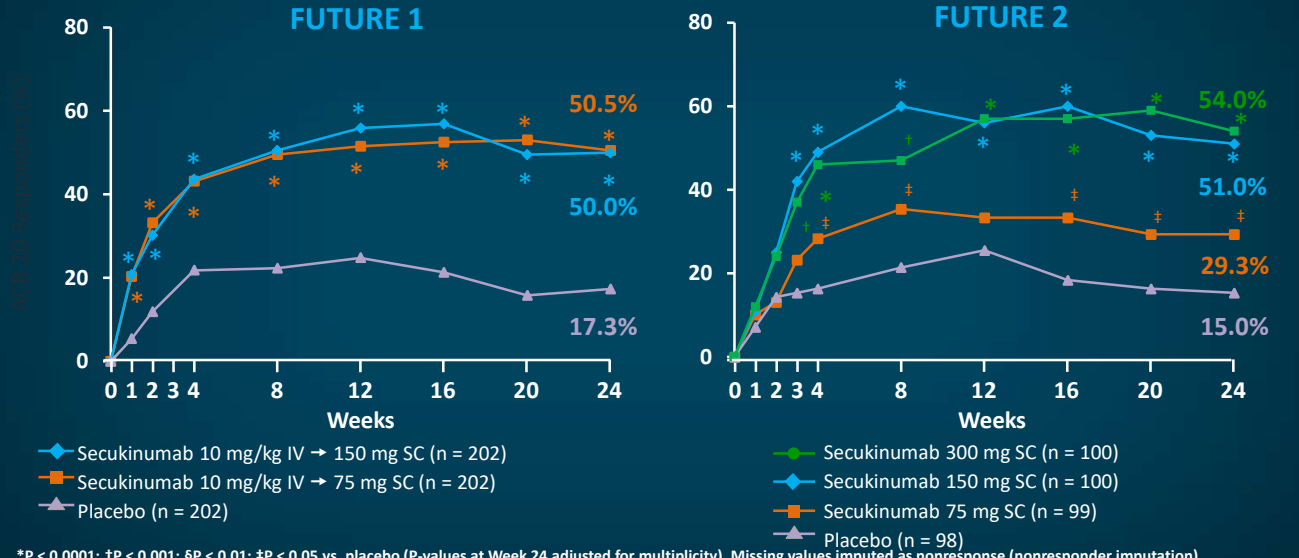
Secukinumab in PsA

ACR20: Primary Outcome Measure



*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.

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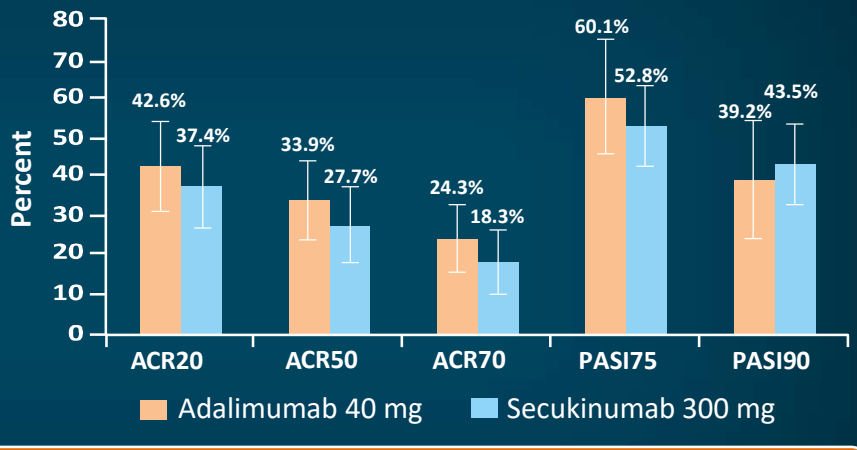
Adalimumab vs Secukinumab in PsA: Indirect Comparison

- N = 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.

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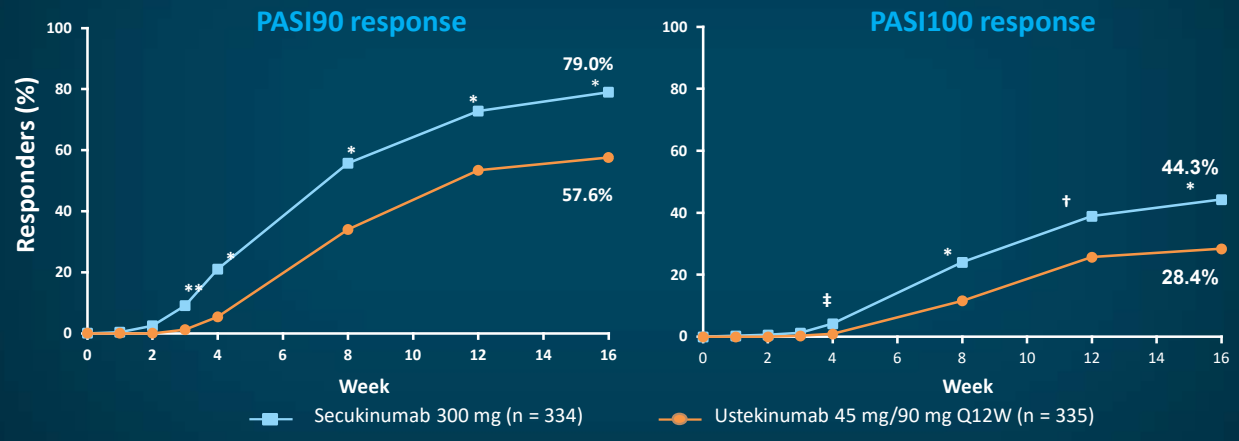
CLEAR Study: Secukinumab (aIL-17A) vs Ustekinumab (aIL-12/23) in Psoriasis



Missing data were imputed as nonresponse; only response-evaluable patients were included.

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

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

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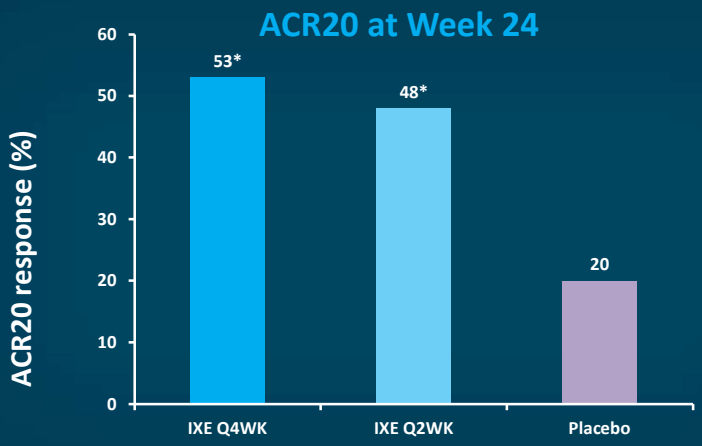
SPIRIT-P2: Ixekizumab in Patients with Active PsA and an Inadequate Response to TNFi



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.

*P<0.0001 vs placebo
IXE = ixekizumab.

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

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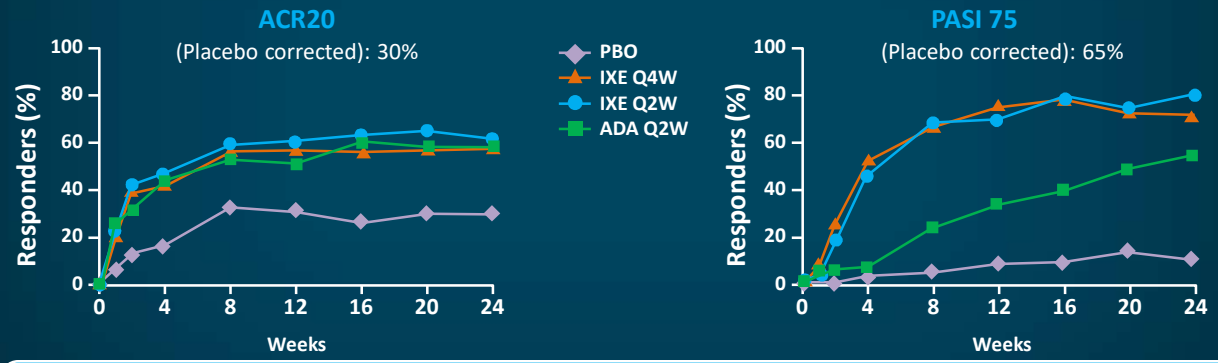
Ixekizumab vs Adalimumab for PsA

- 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< .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.

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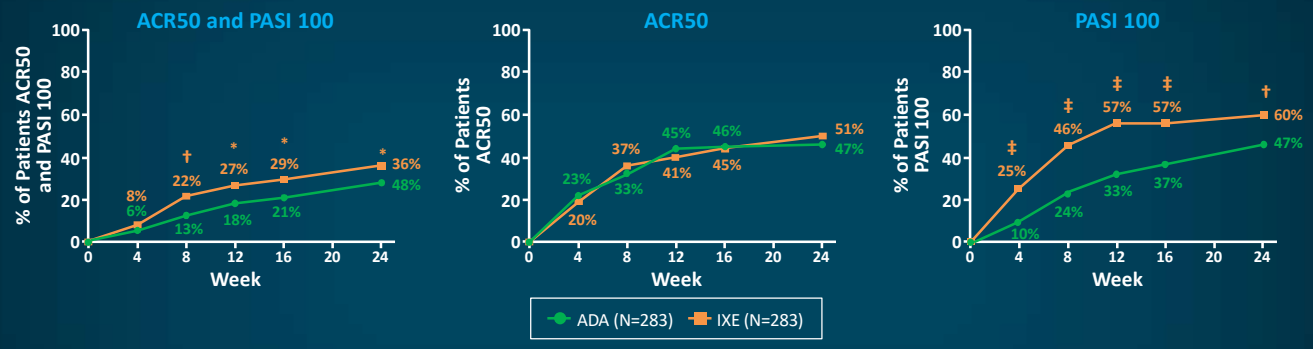
SPIRIT H2H: Head-to-Head Comparison of Ixekizumab and Adalimumab



- Ixekizumab was superior to adalimumab in achievement of simultaneous improvement in joint and skin disease (ACR50 and PASI 100) 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 PASI 100 response (IXE: 60%, ADA:47%, *P*= .001)

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

csDMARD = conventional synthetic DMARD

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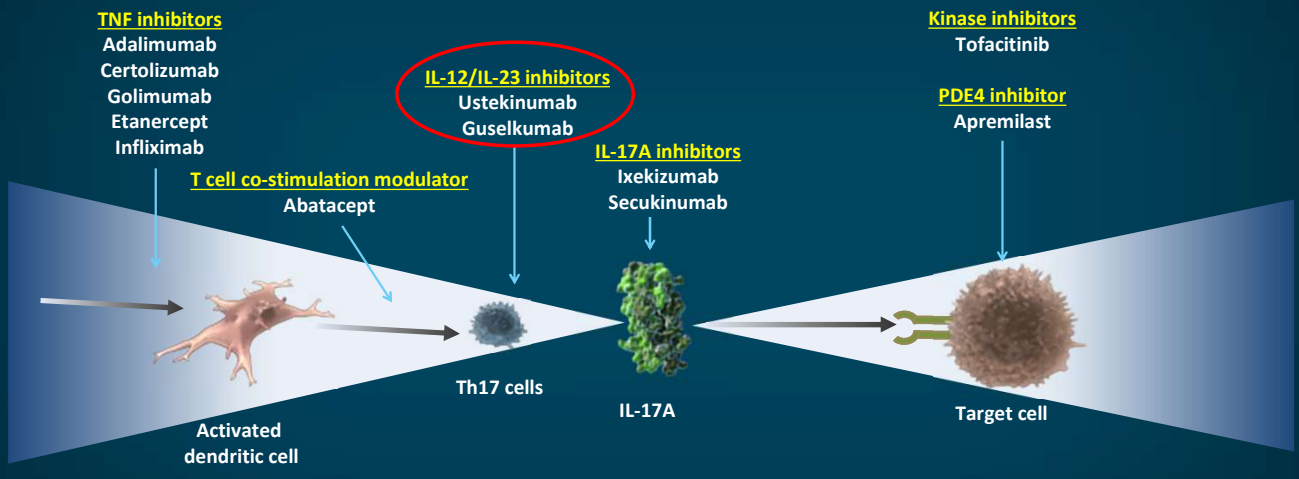
Current and Novel Treatment Options for PsA Treatment



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.

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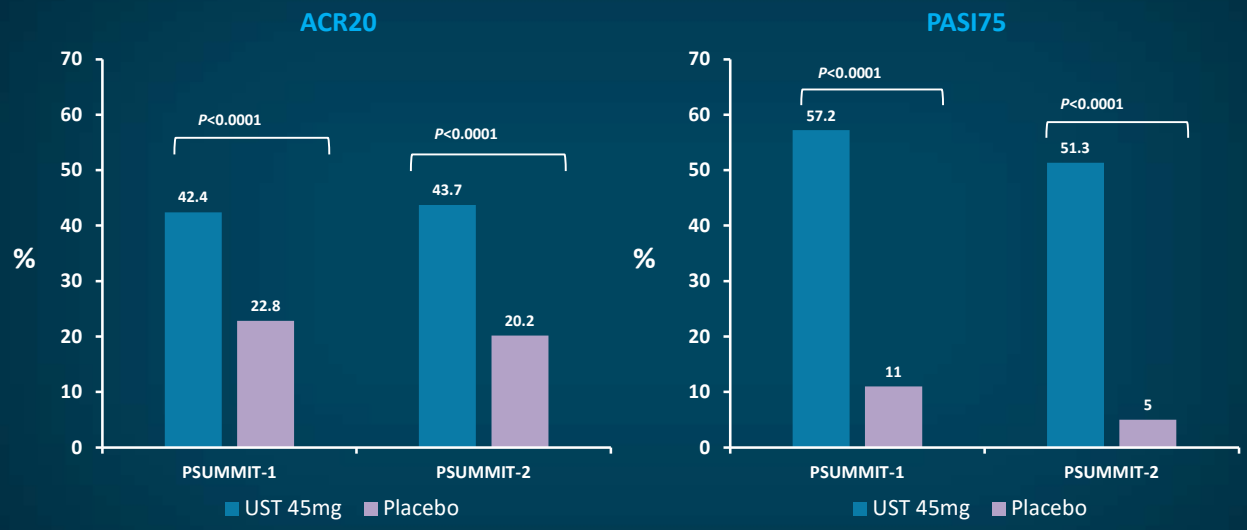
Ustekinumab: Efficacy in PsA



UST = ustekinumab.

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

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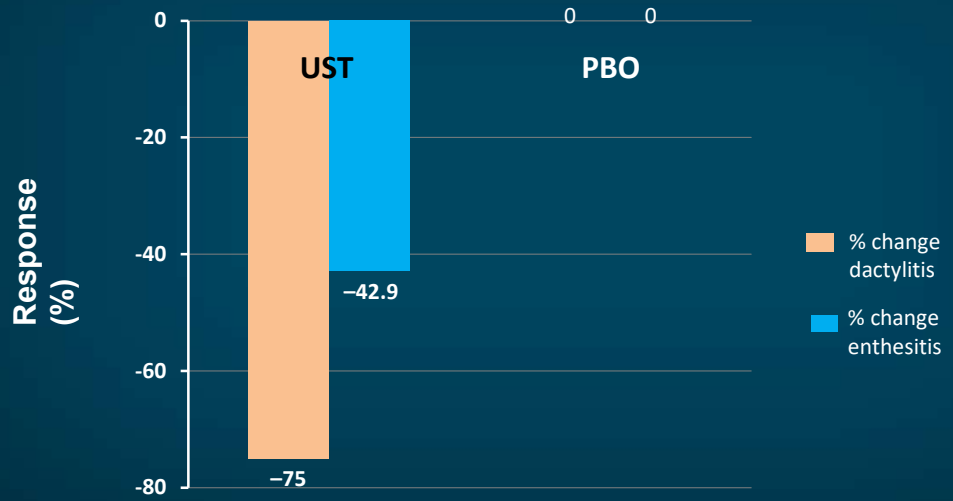
Ustekinumab Is Effective in PsA

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.

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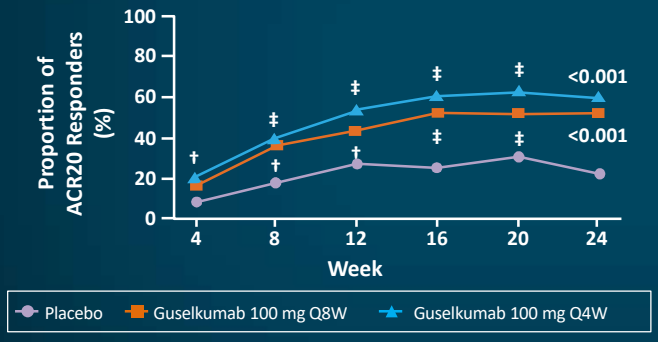
DISCOVER-1 Trial of Guselkumab

- 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 with inadequate response to prior TNFi	11/17 (64.7%)	9/15 (60.0%)	3/12 (25.0%)
% difference vs. placebo (95% CI)	42.4 (11.0, 73.9)	35.9 (0.8, 71.0)	
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.

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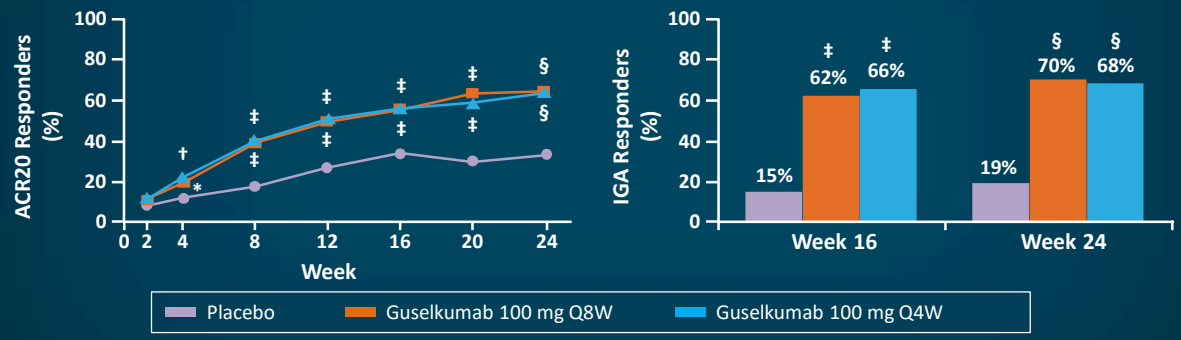
DISCOVER-2 Trial of Guselkumab

- 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.

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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.

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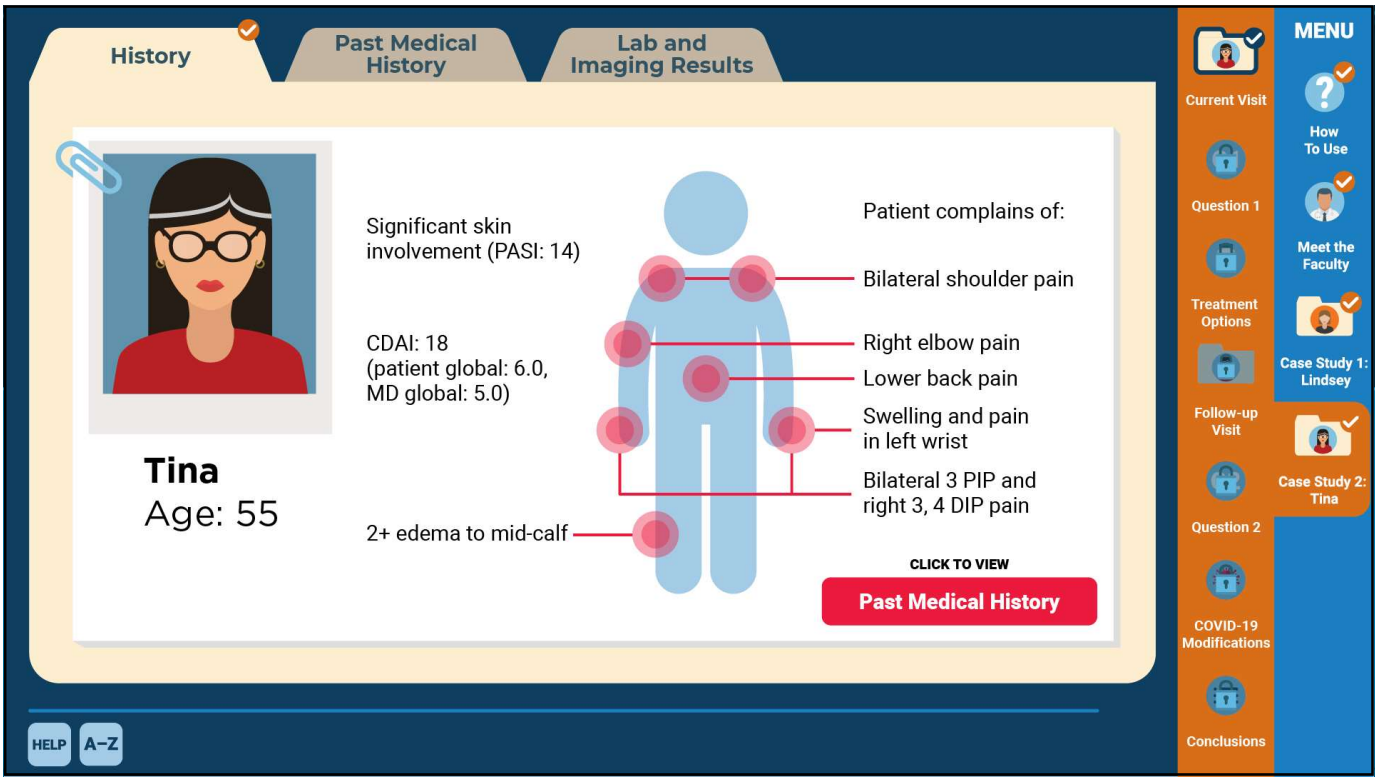
History
Past Medical History
Lab and Imaging Results
Tina
Age: 55
Significant skin involvement (PASI: 14)
CDAI: 18
(patient global: 6.0,
MD global: 5.0)
2+ edema to mid-calf
Patient complains of:
Bilateral shoulder pain
Right elbow pain
Lower back pain
Swelling and pain in left wrist
Bilateral 3 PIP and right 3, 4 DIP pain
CLICK TO VIEW
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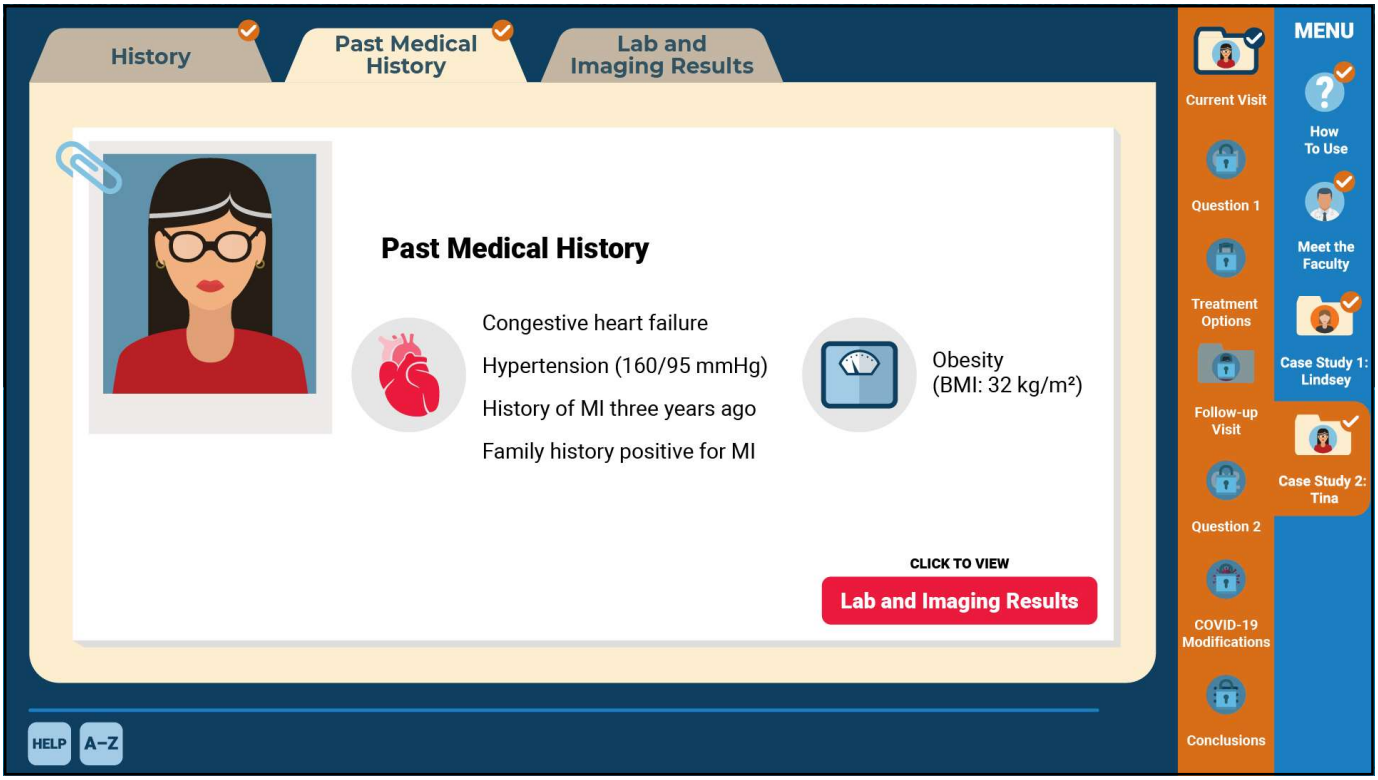
History
Past Medical History
Lab and Imaging Results
Past Medical History
Congestive heart failure
Hypertension (160/95 mmHg)
History of MI three years ago
Family history positive for MI
Obesity
(BMI: 32 kg/m²)
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History | Past Medical History | Lab and Imaging Results

Test	Result	Normal range
Hemoglobin	**10.0 g/dL**	12-16 g/dL
WBC	5.2 x 10⁹/L	4.0-11.0 x 10⁹/L
Platelets	285 x 10⁹/L	150-400 x 10⁹/L
ESR	**32 mm/hr**	0-29 mm/hr
Remainder of CBC and CMP are normal.		

Imaging results:

Radiographs of the knees show osteoarthritis on the right.

Chest film shows cardiomegaly.

CLICK TO VIEW

Question 1

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Question 1

Which of the following is the best treatment option for Tina?

Please select all appropriate choices.

A Adalimumab or infliximab

B Secukinumab or ixekizumab

C Ustekinumab

D Methotrexate or cyclosporine

Submit

ACR guideline recommendations

Treatment-naive Active PsA

- Start TNFi biologic over OSM, IL-17i biologic or IL-12/23i biologic. May consider alternative choices in some situations
- Start OSM over IL-17i biologic or IL-12/23i biologic. May consider alternative choices in some situations
- Start MTX over NSAIDs. May consider alternative choices in some situations
- Start IL-17i biologic over IL-12/23i biologic. May consider alternative choices in some situations

Discuss with the patient, since all recommendations are conditional based on low to very low quality evidence

CLICK TO VIEW

Treatment Options

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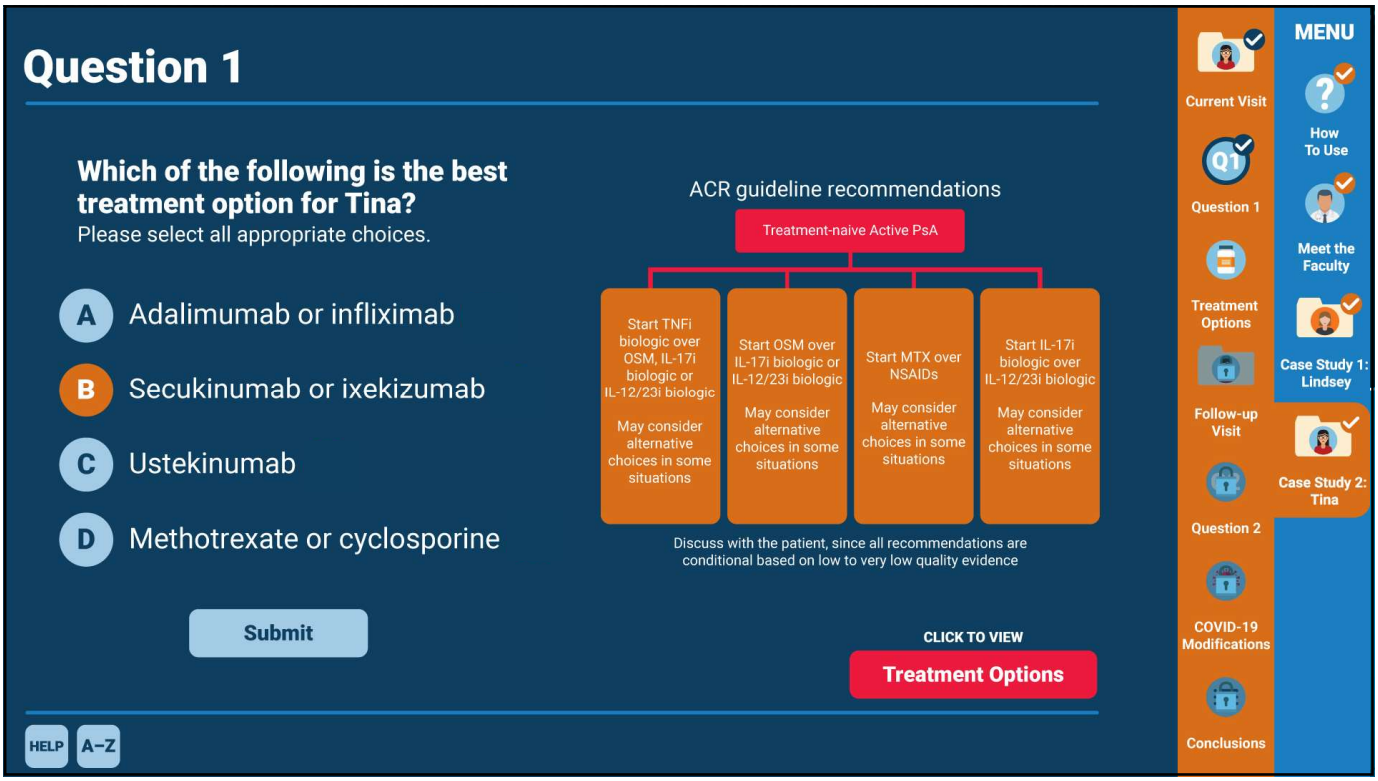
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Which of the following is the best treatment option for Tina?
Please select all appropriate choices.
A Adalimumab or infliximab
B Secukinumab or ixekizumab
C Ustekinumab
D Methotrexate or cyclosporine
Submit
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Treatment-naive Active PsA
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Start OSM over IL-17i biologic or IL-12/23i biologic
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Start IL-17i biologic over IL-12/23i biologic
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Discuss with the patient, since all recommendations are conditional based on low to very low quality evidence
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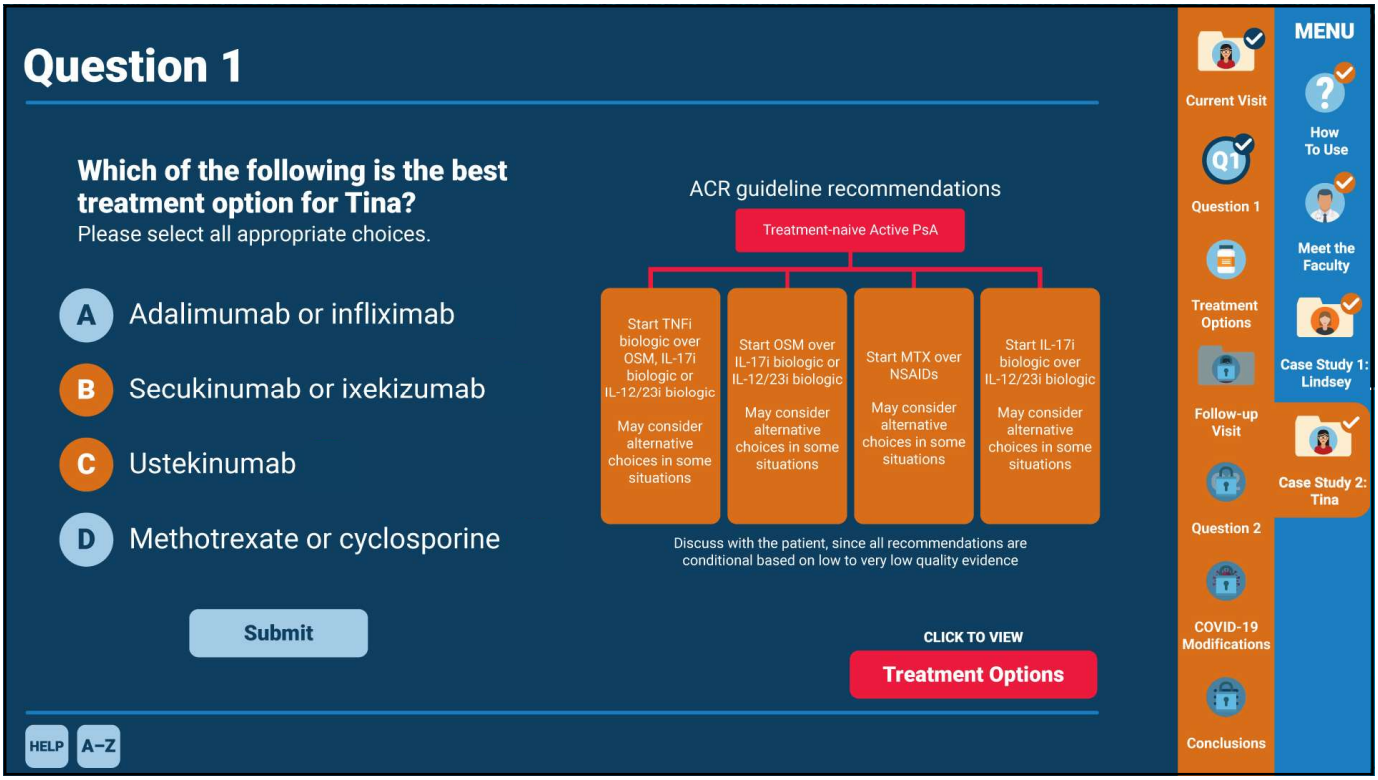
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Question 1

Which of the following is the best treatment option for Tina?
Please select all appropriate choices.

- A Adalimumab or infliximab ✗
- B Secukinumab or ixekizumab ✓
- C Ustekinumab ✓
- D Methotrexate or cyclosporine ✗

Submit

ACR guideline recommendations

Treatment-naive Active PsA

Start TNFi biologic over OSM, IL-17i biologic or IL-12/23i biologic	Start OSM over IL-17i biologic or IL-12/23i biologic	Start MTX over NSAIDs	Start IL-17i biologic over IL-12/23i biologic
May consider alternative choices in some situations	May consider alternative choices in some situations	May consider alternative choices in some situations	May consider alternative choices in some situations

Discuss with the patient, since all recommendations are conditional based on low to very low quality evidence

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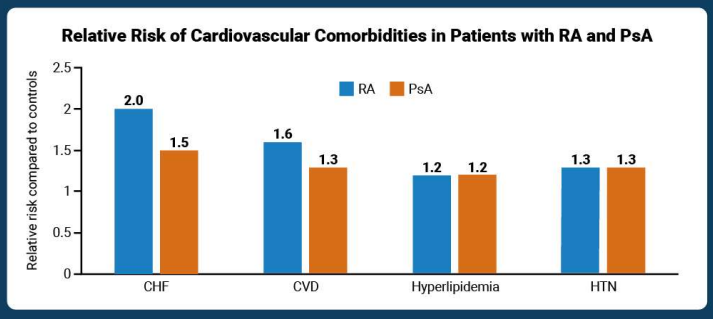
Comorbidities in Rheumatoid and Psoriatic Arthritis
Adalimumab or infliximab
Secukinumab or ixekizumab
Ustekinumab
Methotrexate or cyclosporine

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 patient had RA (1.02%) and 3,066 patients had PsA (0.11%)
Relative risk of comorbidity (all values p<0.01 compared with controls)

CLICK TO VIEW
Adalimumab or infliximab

HELP A–Z Han C, et al. *EULAR* 2005, #OP0160

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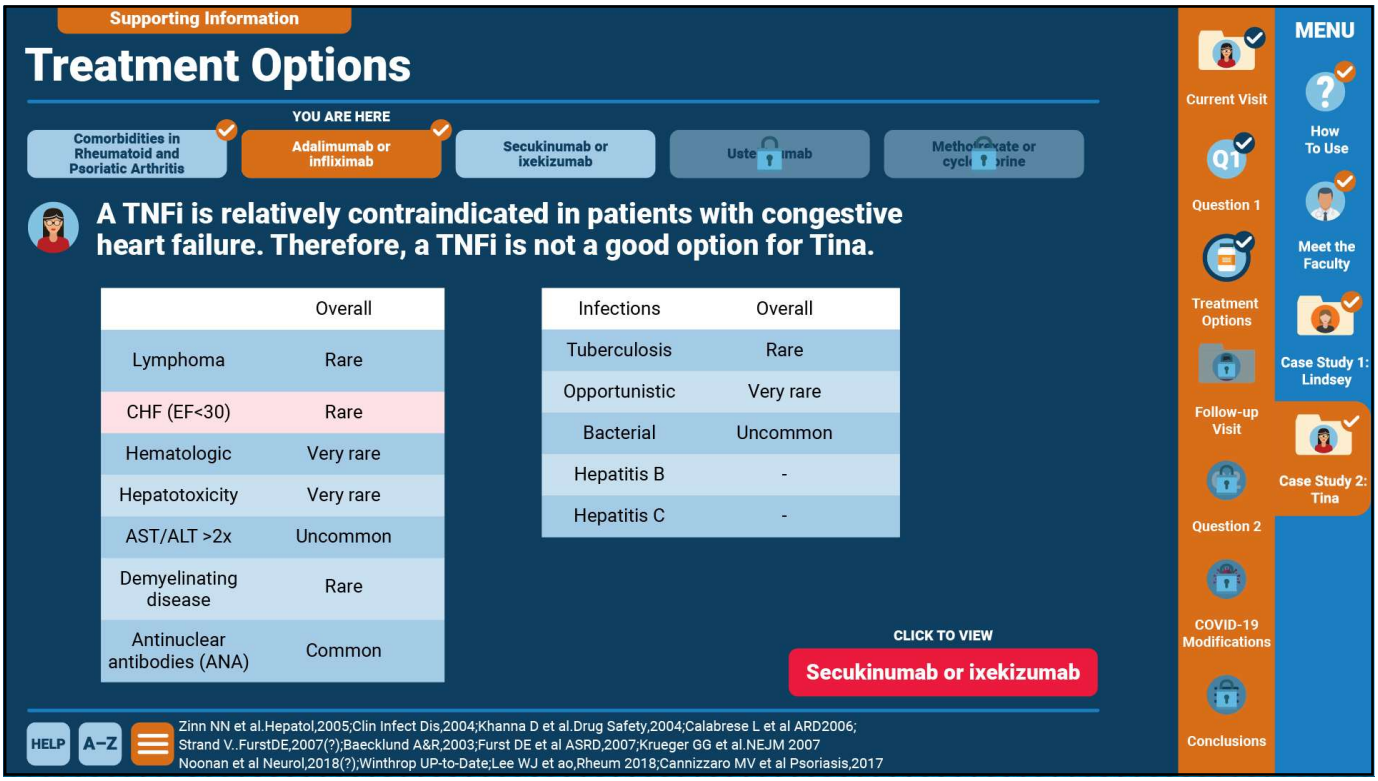
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Adalimumab or infliximab
Secukinumab or ixekizumab
Ustekinumab
Methotrexate or cyclosporine
A TNFi is relatively contraindicated in patients with congestive heart failure. Therefore, a TNFi is not a good option for Tina.
Overall
Lymphoma Rare
CHF (EF<30) Rare
Hematologic Very rare
Hepatotoxicity Very rare
AST/ALT >2x Uncommon
Demyelinating disease Rare
Antinuclear antibodies (ANA) Common
Infections Overall
Tuberculosis Rare
Opportunistic Very rare
Bacterial Uncommon
Hepatitis B -
Hepatitis C -
CLICK TO VIEW
Secukinumab or ixekizumab
HELP
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Zinn NN et al.Hepatol,2005;Clin Infect Dis,2004;Khanna D et al.Drug Safety,2004;Calabrese L et al ARD2006;
Strand V..FurstDE,2007(?);Baecklund A&R,2003;Furst DE et al ASRD,2007;Krueger GG et al.NEJM 2007
Noonan et al Neurol,2018(?);Winthrop UP-to-Date;Lee WJ et ao,Rheum 2018;Cannizzaro MV et al Psoriasis,2017
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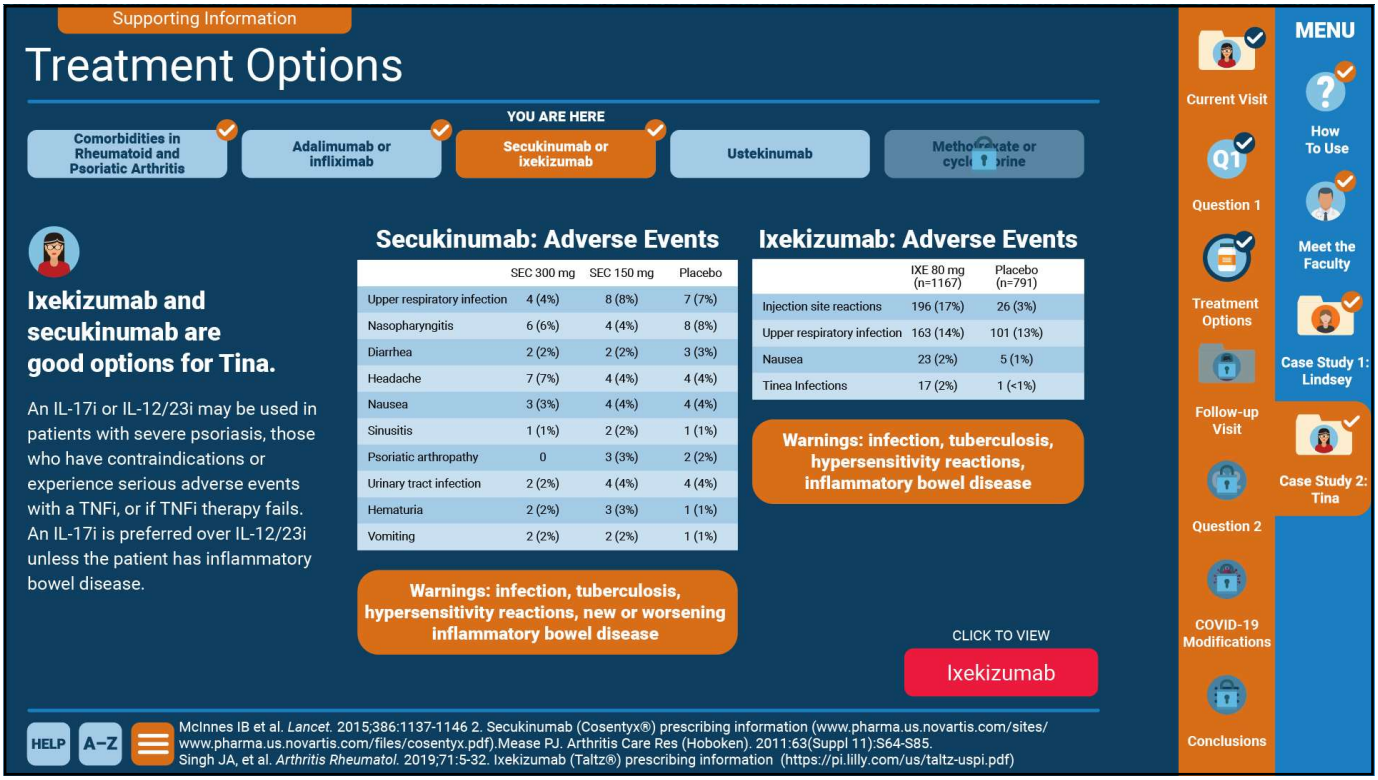
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Adalimumab or infliximab
Secukinumab or ixekizumab
Ustekinumab
Methotrexate or cyclosporine
Ixekizumab and secukinumab are good options for Tina.
An IL-17i or IL-12/23i may be used in patients with severe psoriasis, those who have contraindications 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.
Secukinumab: Adverse Events
SEC 300 mg SEC 150 mg Placebo
Upper respiratory infection 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: infection, tuberculosis, hypersensitivity reactions, new or worsening inflammatory bowel disease
Ixekizumab: Adverse Events
IXE 80 mg (n=1167) Placebo (n=791)
Injection site reactions 196 (17%) 26 (3%)
Upper respiratory infection 163 (14%) 101 (13%)
Nausea 23 (2%) 5 (1%)
Tinea Infections 17 (2%) 1 (<1%)
Warnings: infection, tuberculosis, hypersensitivity reactions, inflammatory bowel disease
CLICK TO VIEW
Ixekizumab
HELP
A–Z
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).Mease PJ. Arthritis Care Res (Hoboken). 2011:63(Suppl 11):S64-S85.
Singh JA, et al. Arthritis Rheumatol. 2019;71:5-32. Ixekizumab (Taltz®) prescribing information (https://pi.lilly.com/us/taltz-uspi.pdf)
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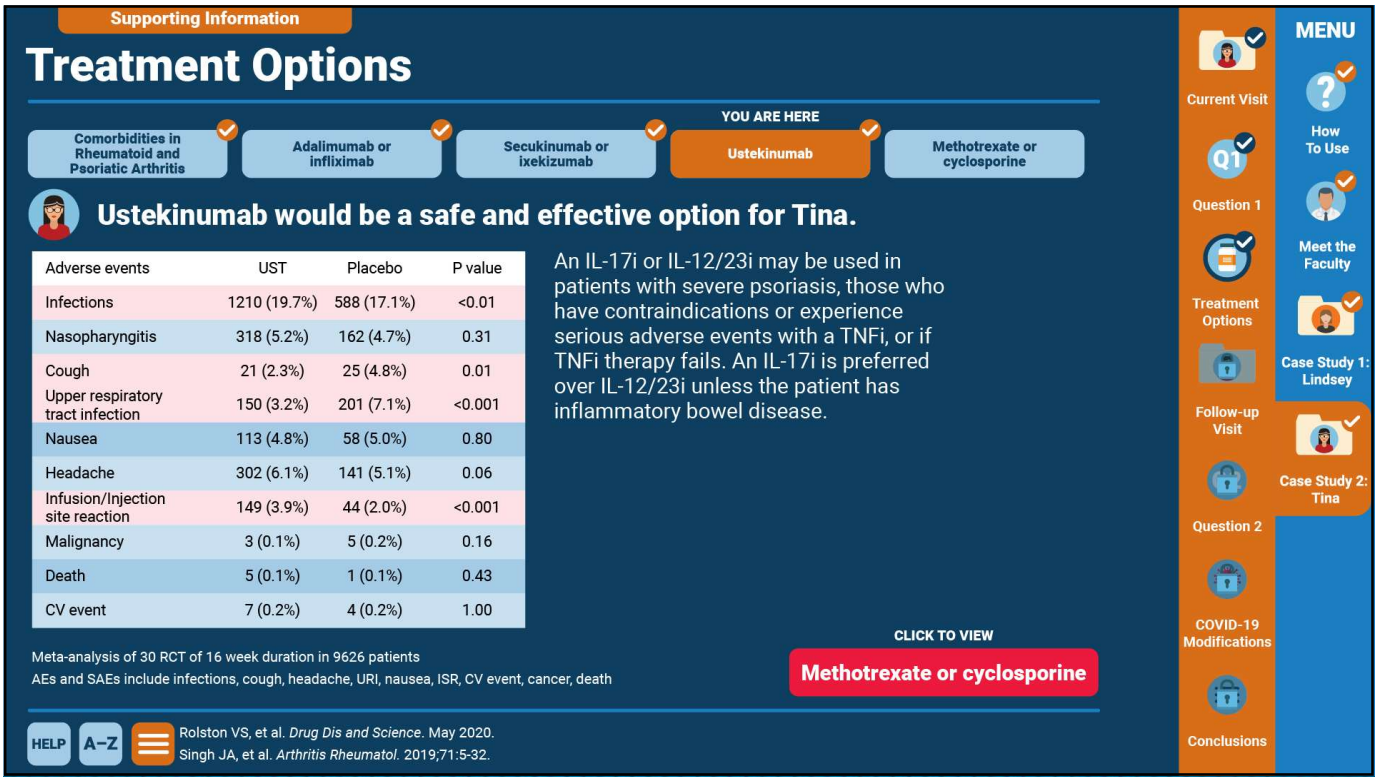
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Ustekinumab
Methotrexate or cyclosporine
Ustekinumab would be a safe and effective option for Tina.
Adverse events | UST | Placebo | P value
Infections | 1210 (19.7%) | 588 (17.1%) | <0.01
Nasopharyngitis | 318 (5.2%) | 162 (4.7%) | 0.31
Cough | 21 (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 event | 7 (0.2%) | 4 (0.2%) | 1.00
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.
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
CLICK TO VIEW
Methotrexate or cyclosporine
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Rolston VS, et al. Drug Dis and Science. May 2020.
Singh JA, et al. Arthritis Rheumatol. 2019;71:5-32.
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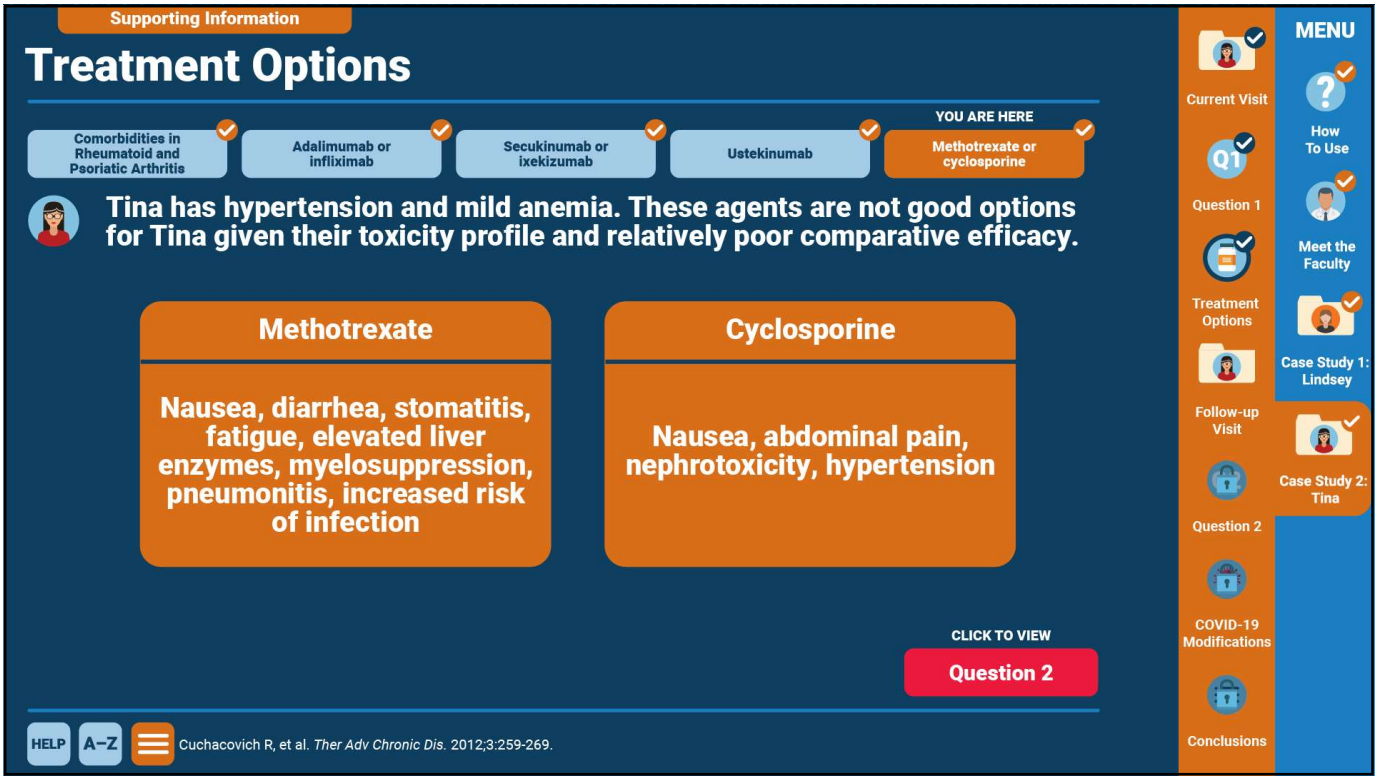
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Methotrexate or cyclosporine
Tina has hypertension and mild anemia. These agents are not good options for Tina given their toxicity profile and relatively poor comparative efficacy.
Methotrexate
Nausea, diarrhea, stomatitis, fatigue, elevated liver enzymes, myelosuppression, pneumonitis, increased risk of infection
Cyclosporine
Nausea, abdominal pain, nephrotoxicity, hypertension
CLICK TO VIEW
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Cuchacovich R, et al. Ther Adv Chronic Dis. 2012;3:259-269.
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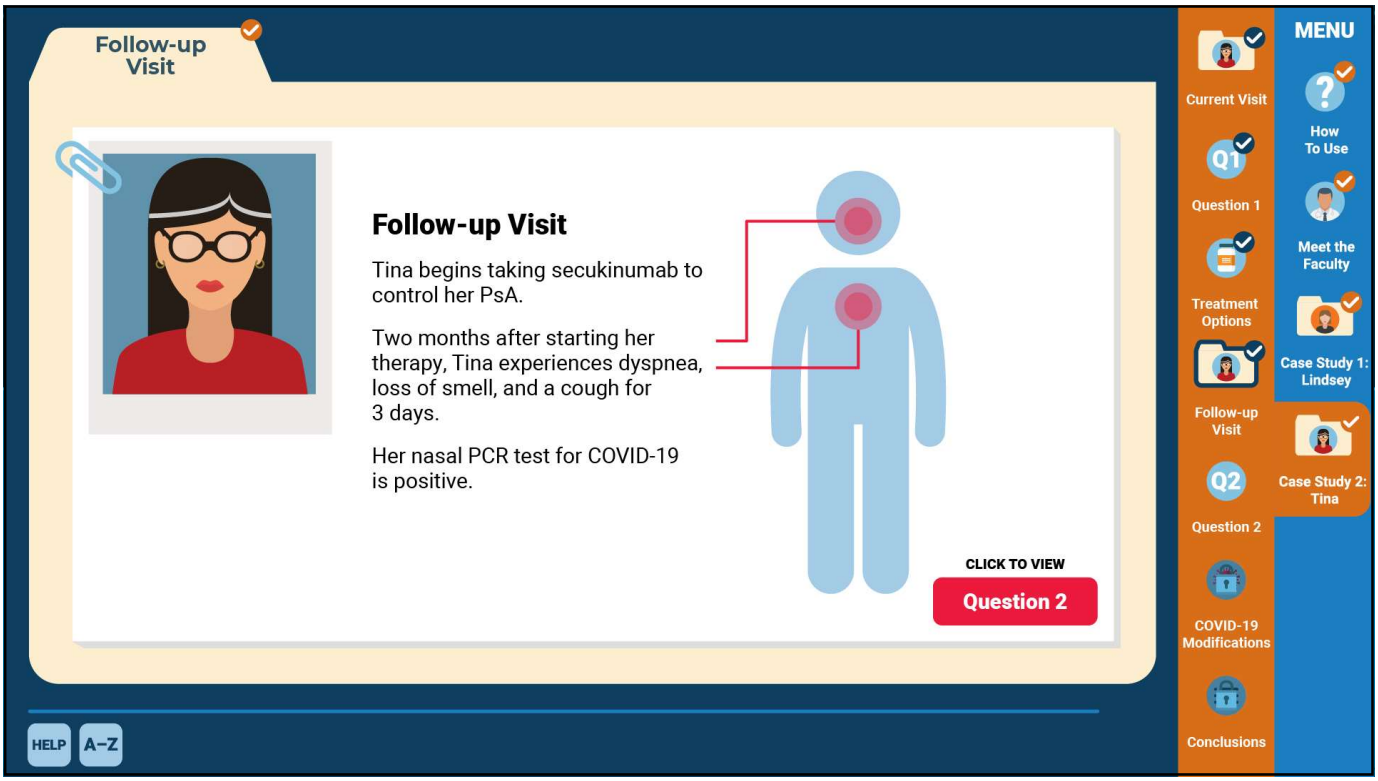
Follow-up Visit
Follow-up Visit
Tina begins taking secukinumab to control her PsA.
Two months after starting her therapy, Tina experiences dyspnea, loss of smell, and a cough for 3 days.
Her nasal PCR test for COVID-19 is positive.
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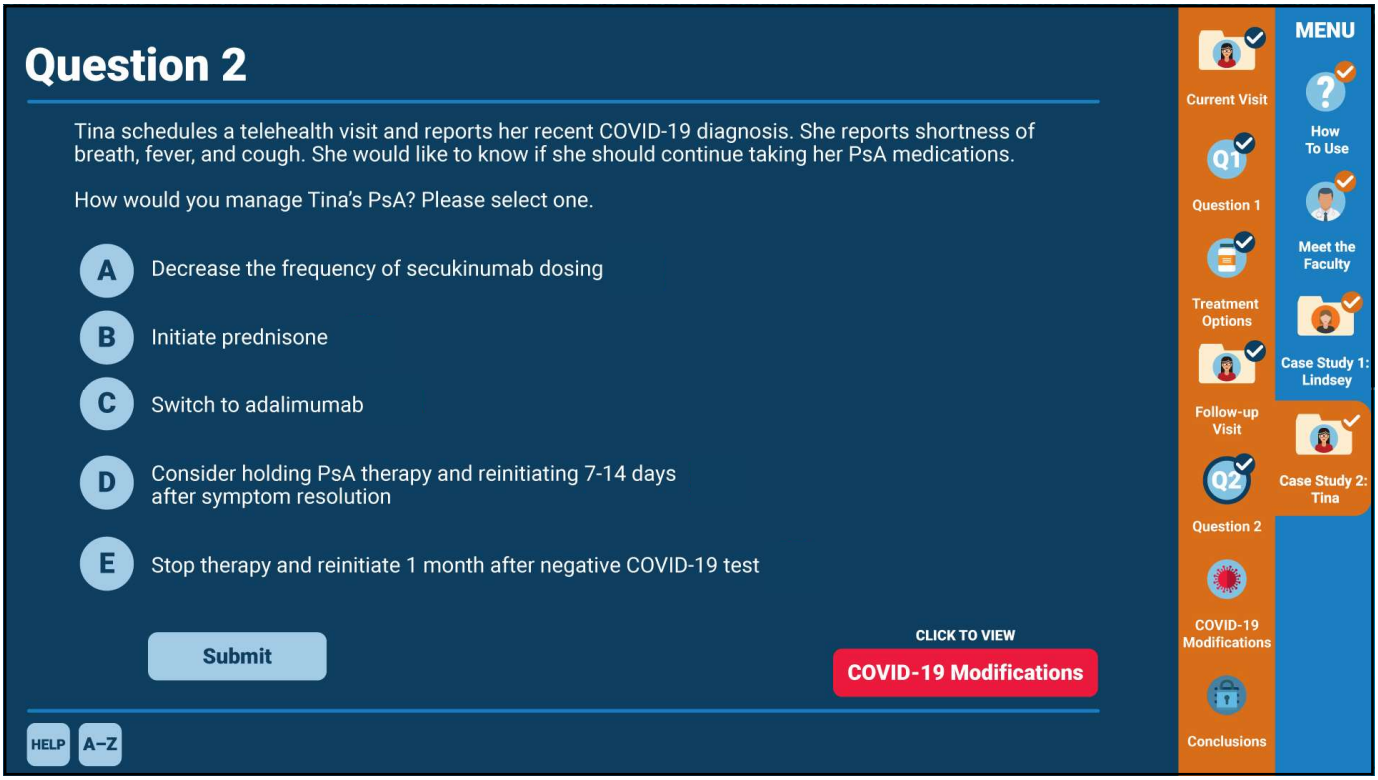
Question 2
Tina schedules a telehealth visit and reports her recent COVID-19 diagnosis. She reports shortness of breath, fever, and cough. She would like to know if she should continue taking her PsA medications.
How would you manage Tina's PsA? Please select one.
A Decrease the frequency of secukinumab 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
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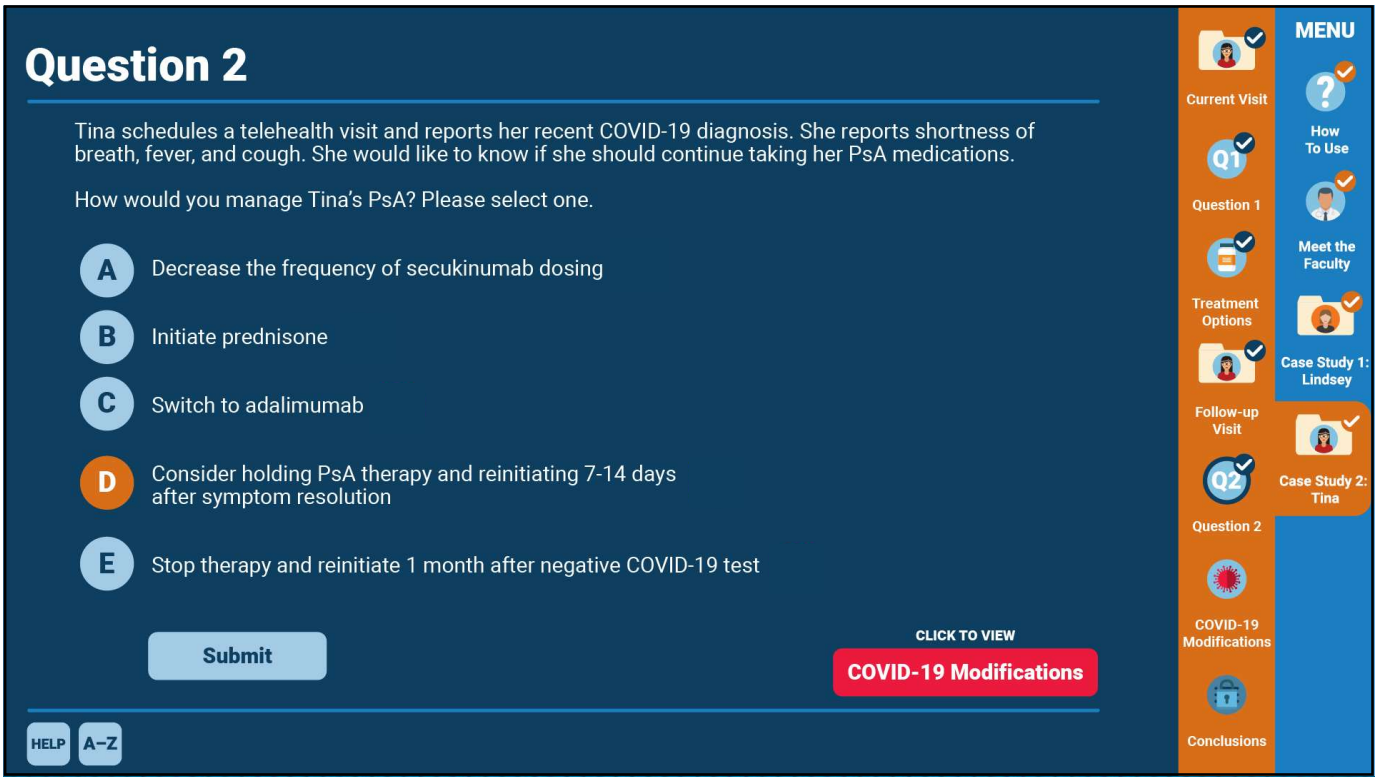
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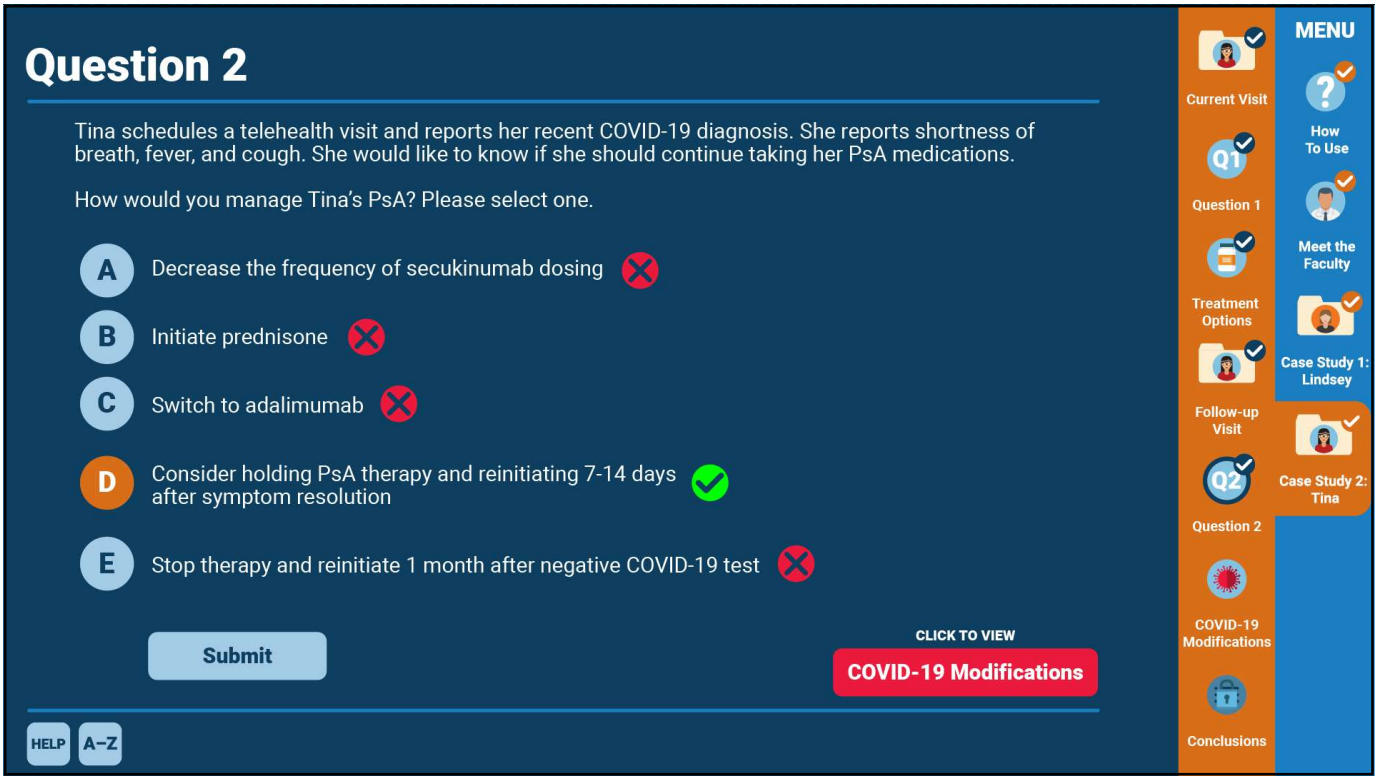
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COVID-19 Modifications

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

Treatment of Rheumatic Disease During the COVID-19 Pandemic

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
Immunosupressants (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 inihibitors	Withhold or stop therapy
NSAIDs	Should be stopped in patients with respiratory symptoms

Recommendation appropriate for Tina

CLICK TO VIEW

Conclusions

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

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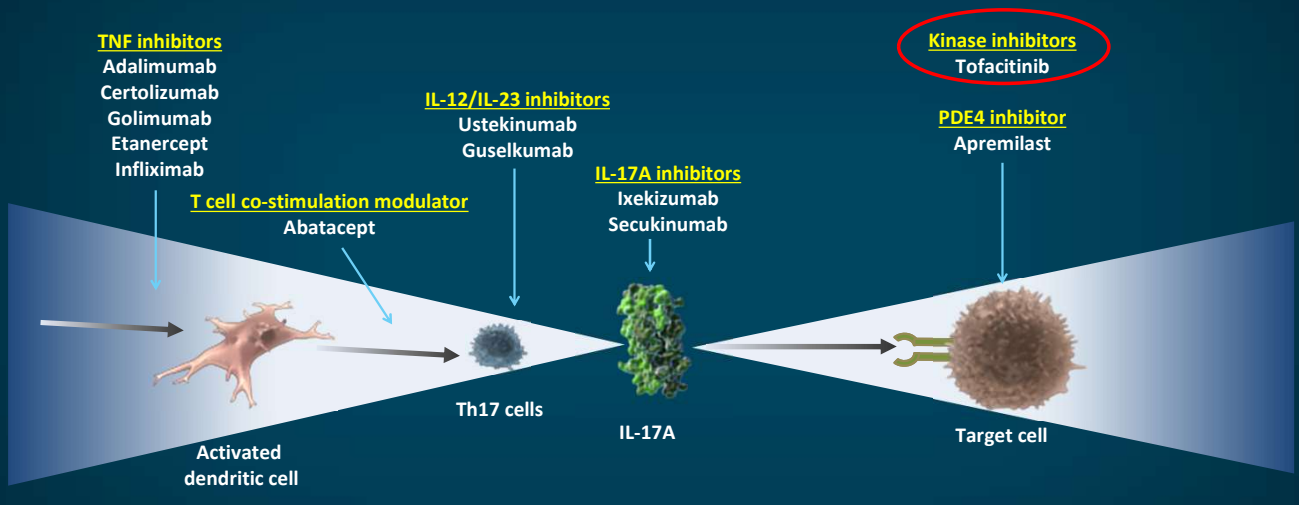
Current and Novel Treatment Options for PsA Treatment



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.

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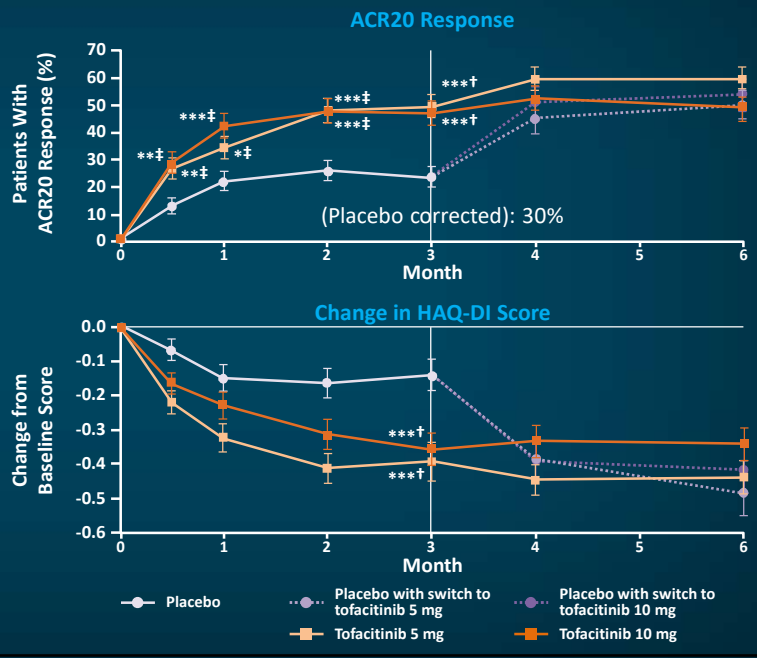
Efficacy of Tofacitinib in PSA

- 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.

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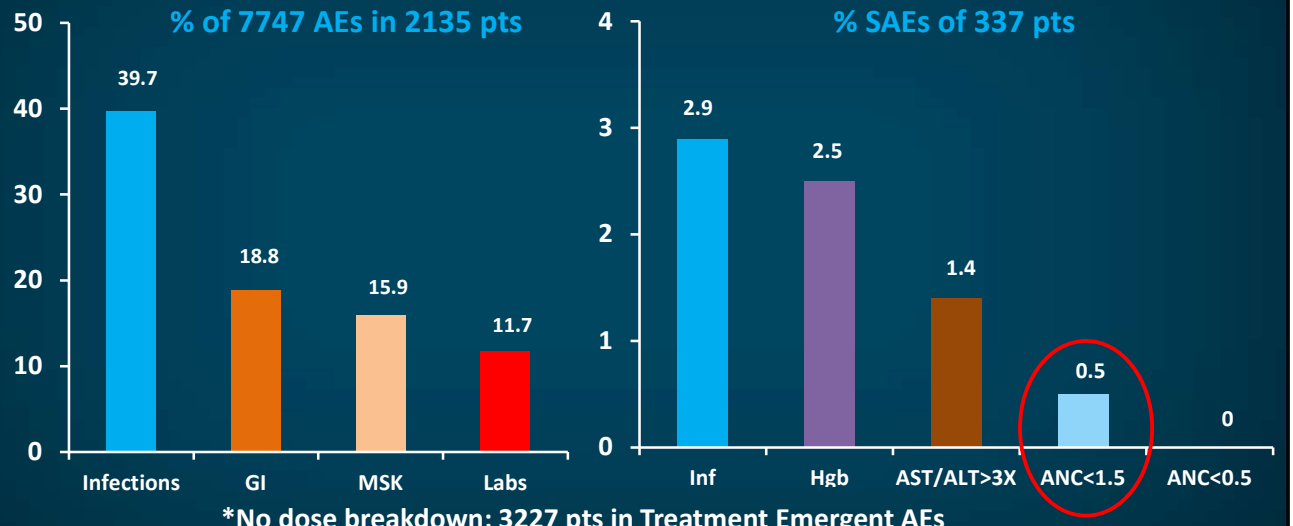
Adverse Events in 3118 Patient-Years in Tofacitinib Open-Label, Long-Term Extension Study of Therapy for RA*



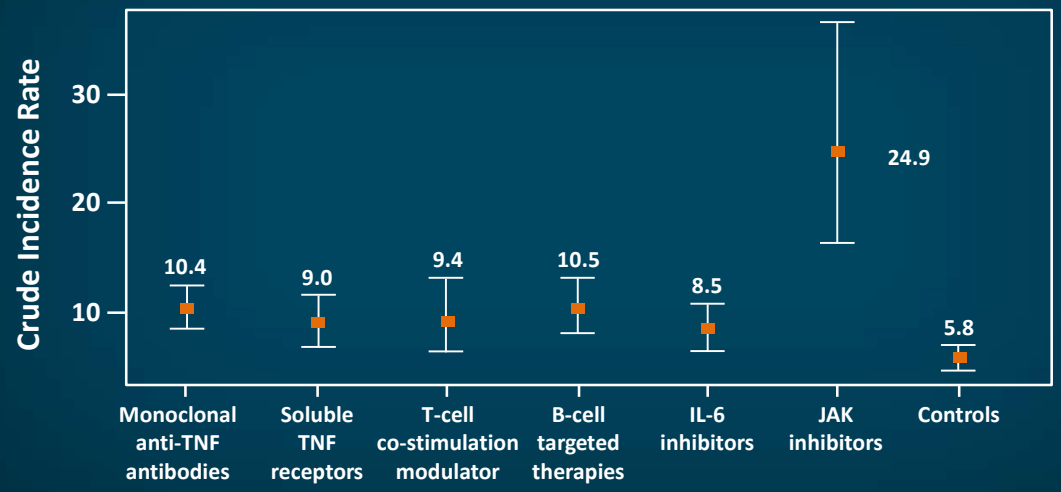
*No dose breakdown; 3227 pts in Treatment Emergent AEs

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.

75

Incident Rates of Herpes Zoster in RA Patients



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

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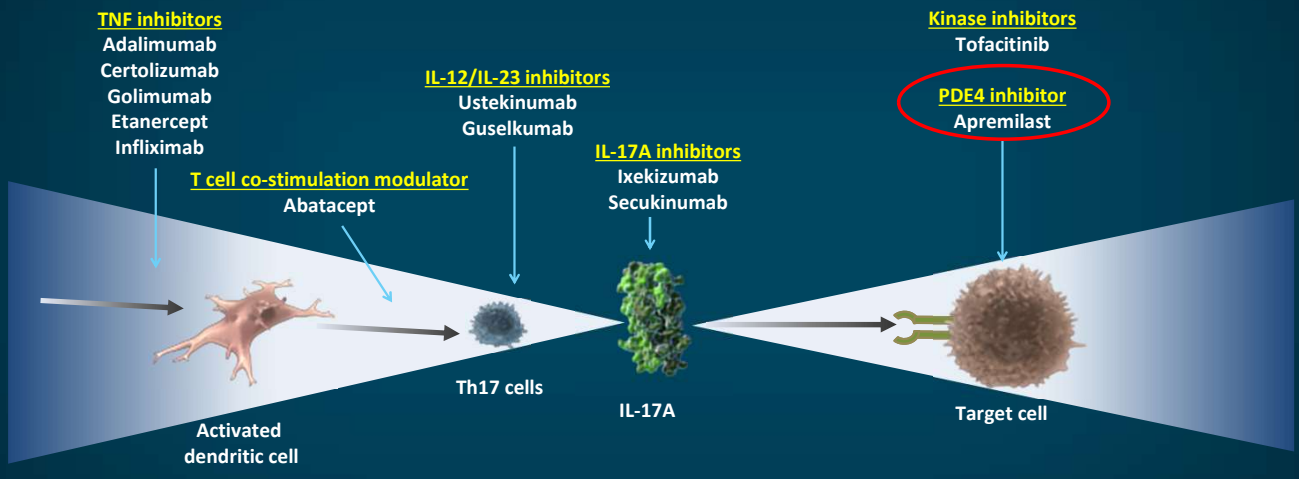
Current and Novel Treatment Options for PsA Treatment



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.

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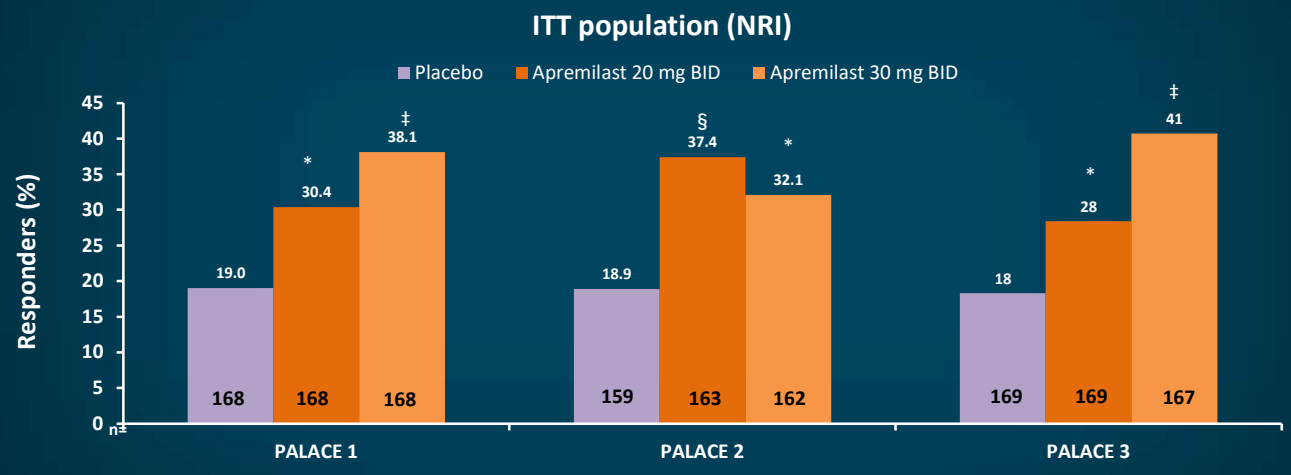
Apremilast in PsA: PALACE 1, 2, and 3

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.

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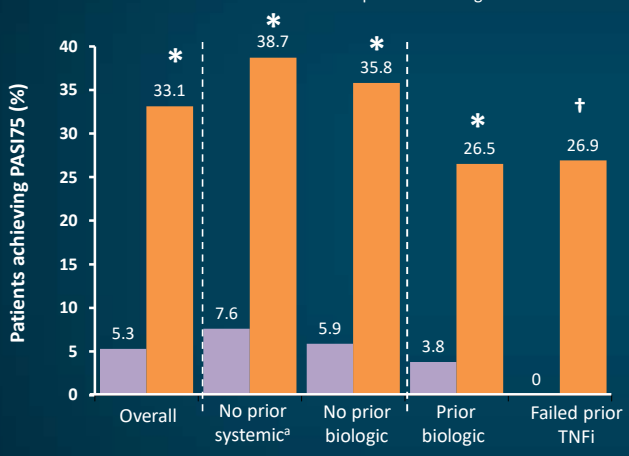
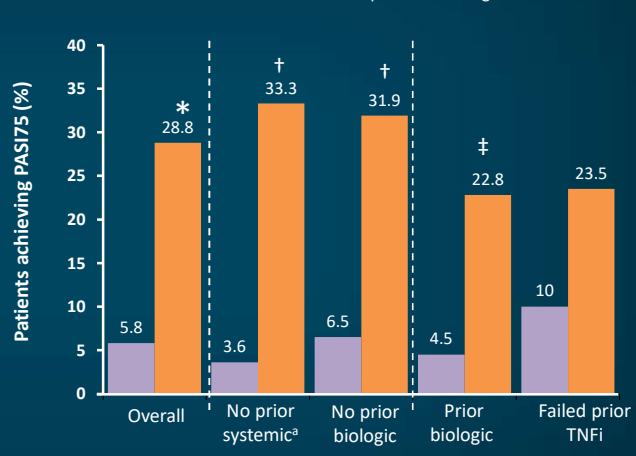
Apremilast in Moderate-to-Severe Psoriasis

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.

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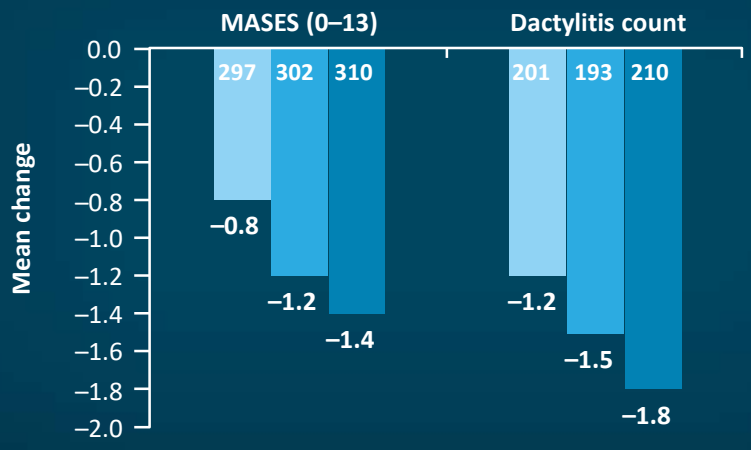
Apremilast Effects on Enthesitis and Dactylitis

Data pooled from PALACE 1–3, week 24



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

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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)
URTI	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).

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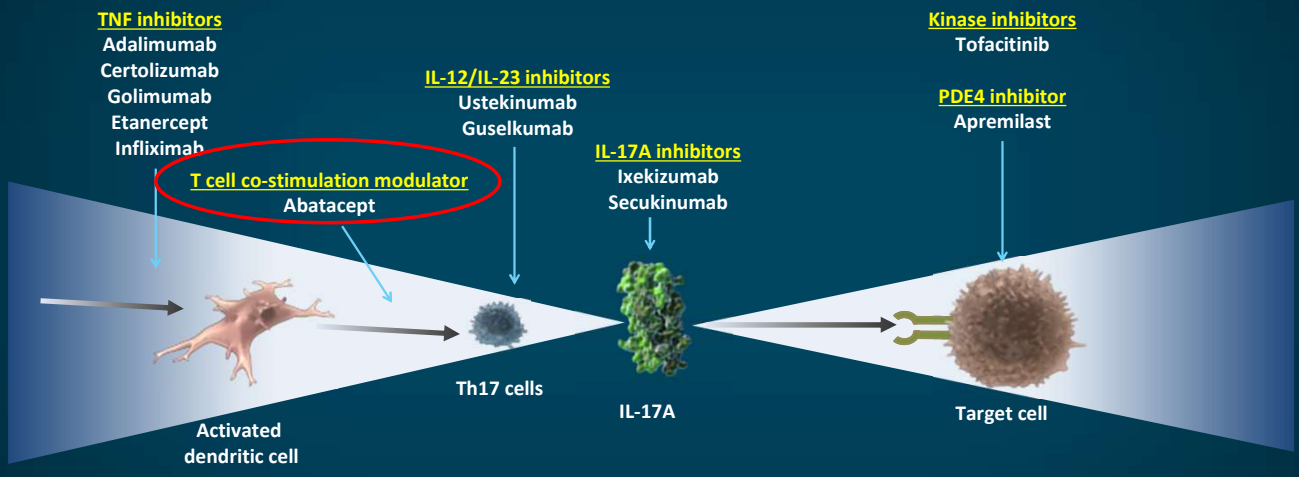
Current and Novel Treatment Options for PsA Treatment



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.

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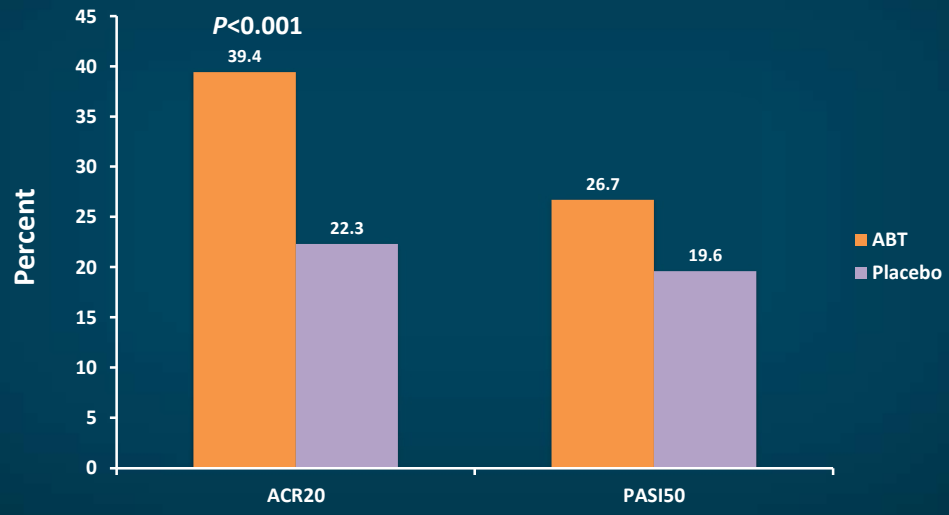
Abatacept: Phase III Trial



ABT = abatacept.

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

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Decision Aid

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Initial Presentation

- Carol is a 55-year old woman who reports worsening pain and stiffness in her fingers, ankle pain, and swelling of her finger and elbow
- Physical exam:
  - **Tenderness in right 3 DIPs, bilateral 4 PIPs**
  - Left elbow swollen and tender
  - Right ankle swollen with **enthesitis** present
  - CDAI: 20
- Plaque psoriasis present on elbows, forearms, trunk and scalp
  - Scaling with minor fissures. PASI: 12

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History of Present Illness

- PMH: **hypertension, type 2 diabetes, obesity**
- Diagnosed with psoriasis 8 years ago and PsA 1 year ago
- Initially managed with methotrexate (15 mg/week)
  - Elevated AST and ALT 2 months after starting methotrexate
  - Methotrexate discontinued
- Carol is currently taking **etanercept** 50 mg/week

86

Lab Results

Lab	Results	Normal Range
Hemoglobin	13 g/dL	12.0-15.5 g/dL
WBC	6800 cells/µL	4500-11,000 cells/µL
ESR	**27 mm/hr**	0-22 mm/hr
RF	9 IU/mL	0-20 IU/mL
CCP	12 u/mL	0-20 u/mL
CRP	**70 mg/L**	<10 mg/L
HbA1c	7.1%	<5.7%

- Carol reports that her husband was diagnosed with COVID-19 last week
  - Carol does not have any symptoms of COVID-19

How would you manage this patient?

87

Decision Tree for the Management of Psoriatic Arthritis

This activity is best viewed on Google Chrome or Mozilla Firefox. Free downloads are available here:

Download Chrome | Download Firefox

Progress will be lost if this activity is closed, please do not close the activity until it is completed.

Begin Activity

88

Decision Tree: Question 1 of 4

Does your patient find any of the following symptoms to be unacceptably bothersome?
Click all that apply.

- Swollen/tender joints (peripheral arthritis)
- Dactylitis
- Enthesitis
- Axial disease
- Active skin involvement
- Active nail involvement
- Uveitis
- Inflammatory bowel disease

OR

- Patient has no symptoms

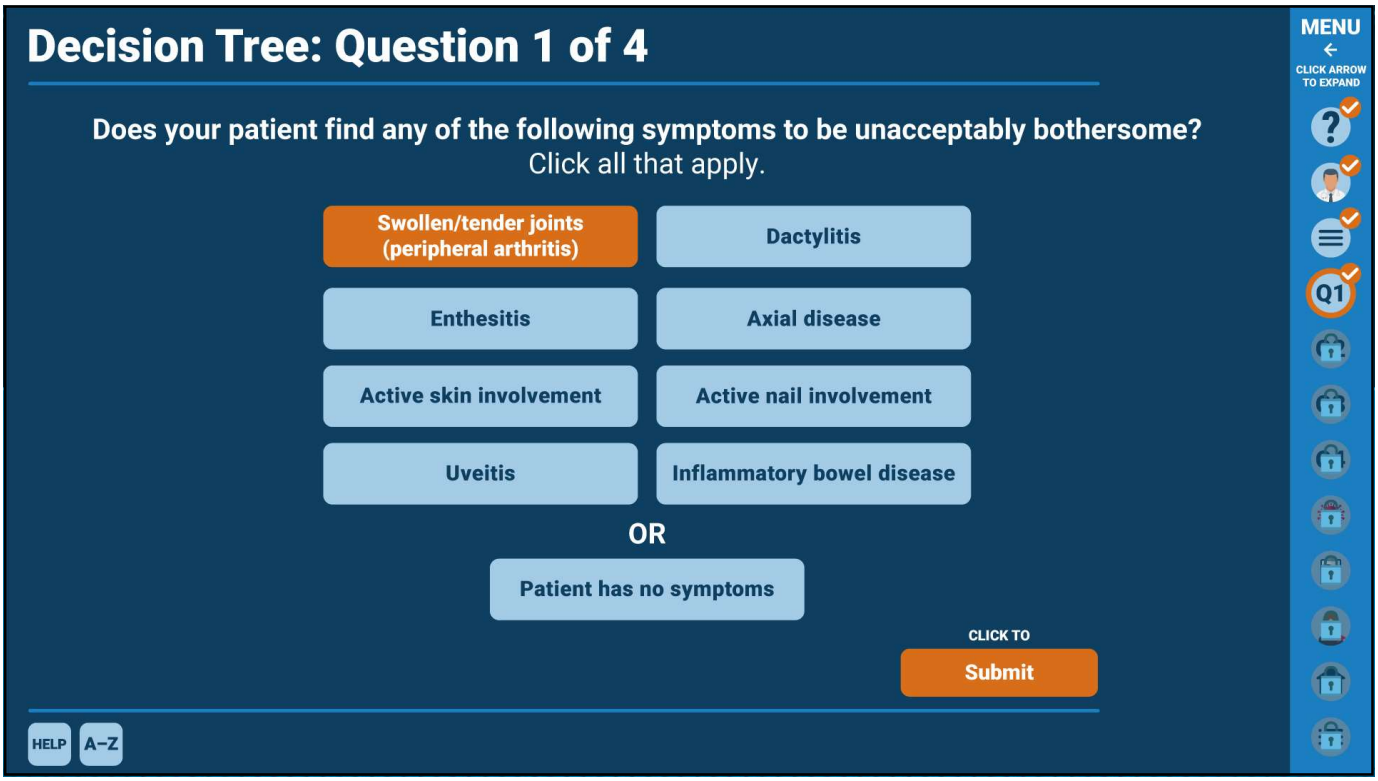
CLICK TO Submit

HELP | A–Z

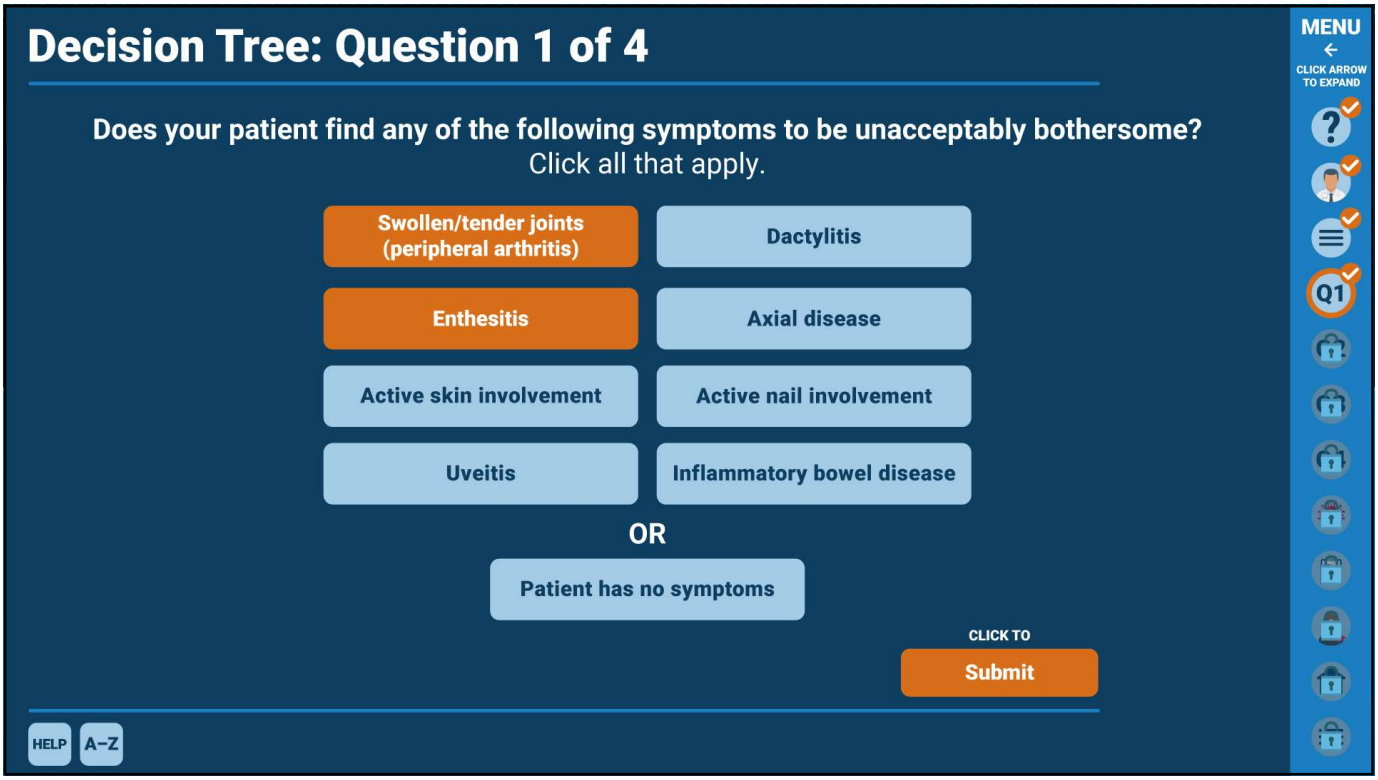
MENU
CLICK ARROW TO EXPAND

Q1

89


Decision Tree: Question 1 of 4
MENU
CLICK ARROW TO EXPAND
Does your patient find any of the following symptoms to be unacceptably bothersome?
Click all that apply.
Swollen/tender joints (peripheral arthritis)
Dactylitis
Enthesitis
Axial disease
Active skin involvement
Active nail involvement
Uveitis
Inflammatory bowel disease
OR
Patient has no symptoms
CLICK TO
Submit
HELP
A–Z
Q1

90


Decision Tree: Question 1 of 4
MENU
CLICK ARROW TO EXPAND
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Click all that apply.
Swollen/tender joints (peripheral arthritis)
Dactylitis
Enthesitis
Axial disease
Active skin involvement
Active nail involvement
Uveitis
Inflammatory bowel disease
OR
Patient has no symptoms
CLICK TO
Submit
HELP
A–Z
Q1

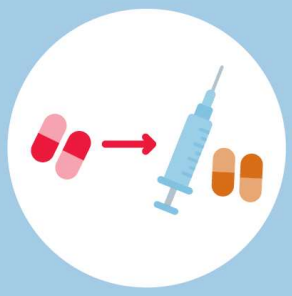
91

Question 1: Patient has symptoms

Patients with active psoriatic arthritis may require a change to their medication regimen.

Active PsA is defined as disease with symptoms that are unacceptably bothersome to a patient, and at least 1 of the following symptoms is present and due to PsA:

- Swollen/tender joints
- Dactylitis
- Enthesitis
- Axial disease
- Active skin and/or nail involvement
- Extraarticular inflammatory manifestations, such as uveitis or inflammatory bowel disease.



CLICK TO: Reset

CLICK TO VIEW: Question 2

HELP A–Z

MENU
CLICK ARROW TO EXPAND

92

Decision Tree: Question 2 of 4

Which of the following therapies is your patient currently taking?
Click all that apply.

- **Oral small molecules (OSM):** methotrexate, sulfasalazine, cyclosporine A, leflunomide, apremilast
- **Tumor necrosis factor inhibitors (TNFi):** etanercept, infliximab, adalimumab, golimumab, certolizumab pegol
- **IL-12/23i:** ustekinumab
- **Interleukin-17 inhibitor (IL-17i):** ixekizumab, secukinumab
- **TNFi + MTX**
- **NSAIDs**

OR

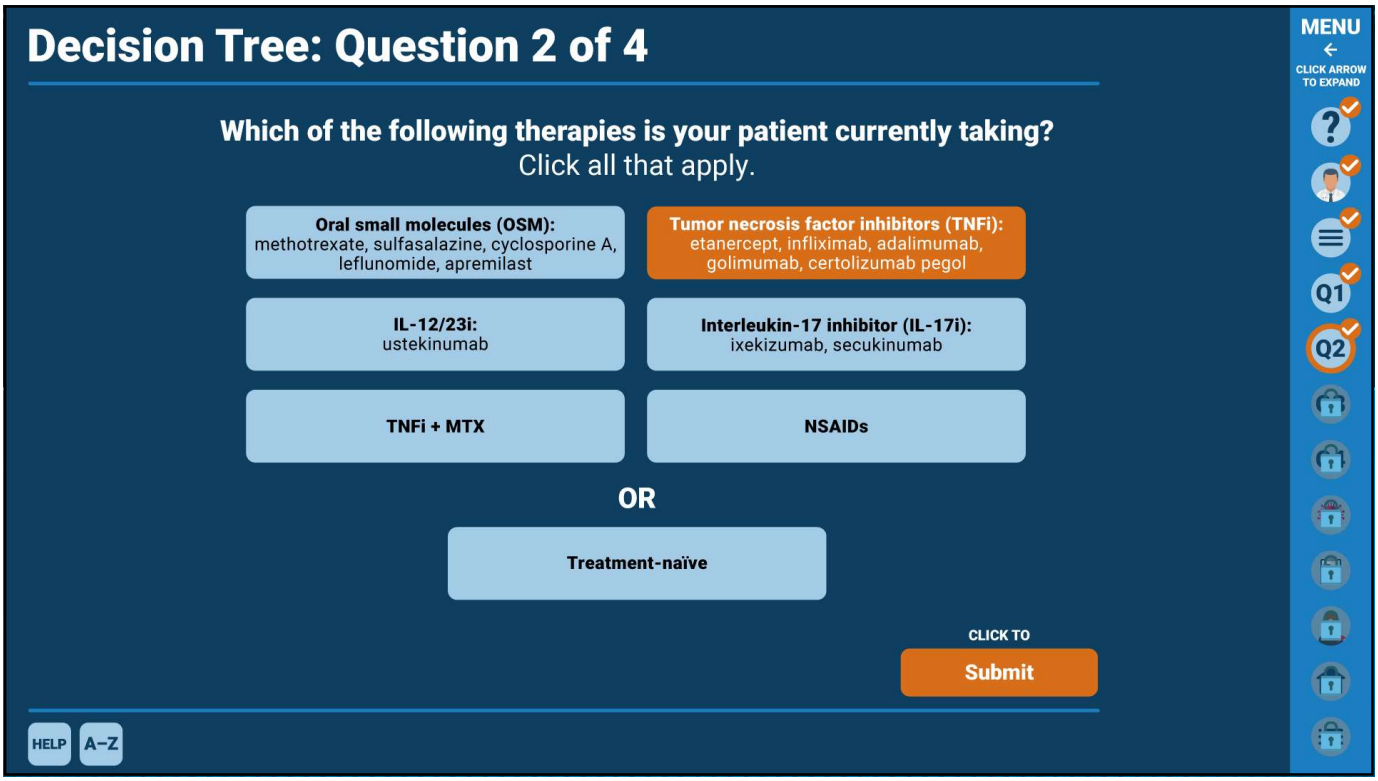
- **Treatment-naïve**

CLICK TO: Submit

HELP A–Z

MENU
CLICK ARROW TO EXPAND

93


Decision Tree: Question 2 of 4
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Tumor necrosis factor inhibitors (TNFi): etanercept, infliximab, adalimumab, golimumab, certolizumab pegol
IL-12/23i: ustekinumab
Interleukin-17 inhibitor (IL-17i): ixekizumab, secukinumab
TNFi + MTX
NSAIDs
OR
Treatment-naïve
CLICK TO
Submit
HELP
A–Z
MENU
CLICK ARROW TO EXPAND
Q1
Q2

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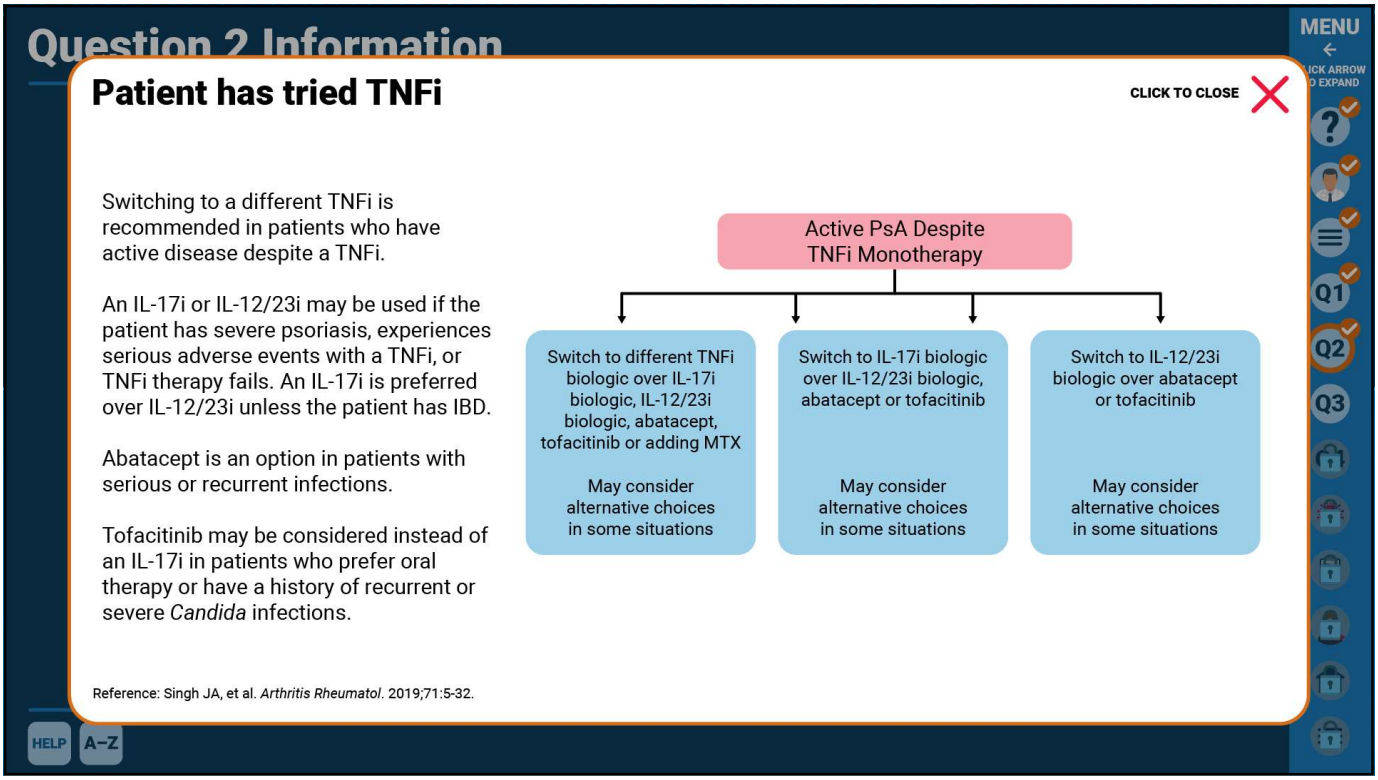
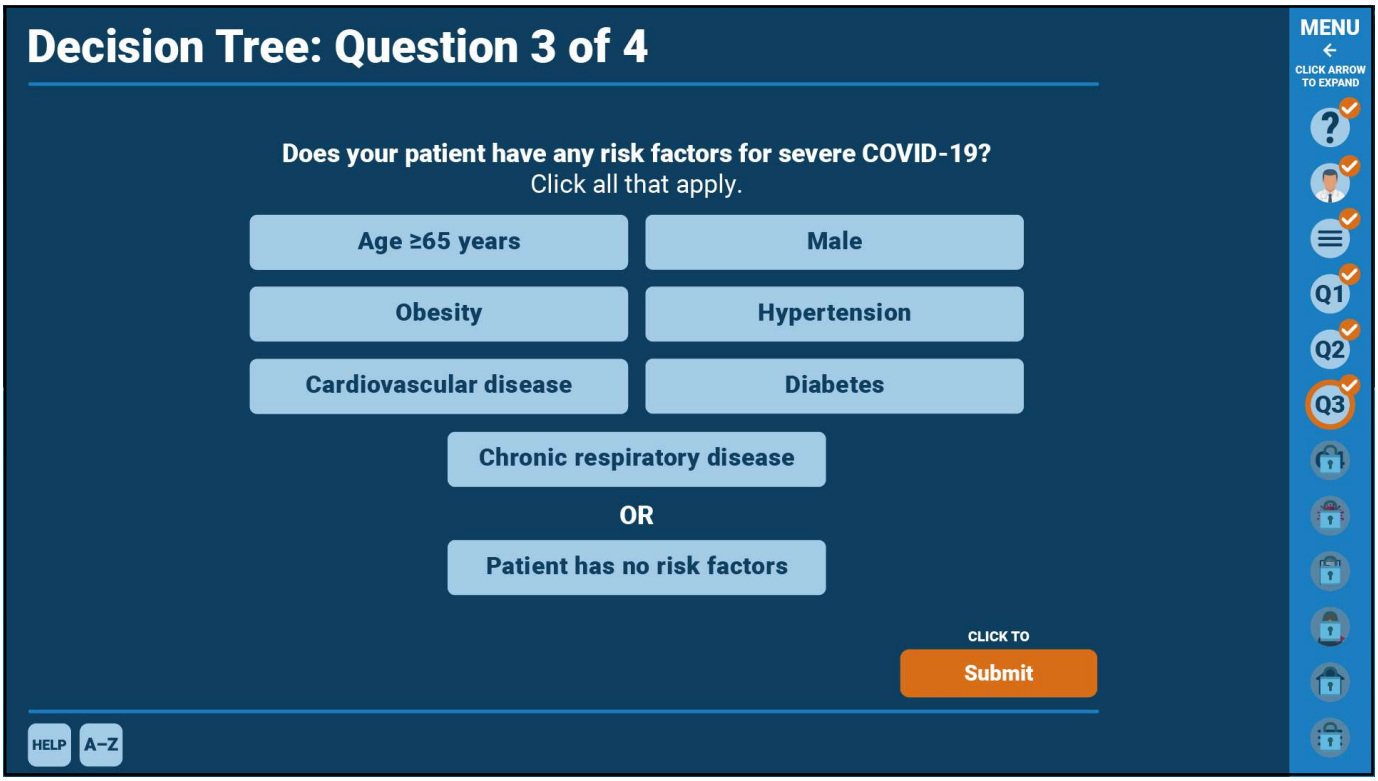

Question 2 Information
Patient has tried TNFi
CLICK TO CLOSE
Switching to a different TNFi is recommended in patients who have active disease despite a TNFi.
An IL-17i or IL-12/23i may be used if the patient has severe psoriasis, experiences serious adverse events with a TNFi, or TNFi therapy fails. An IL-17i is preferred over IL-12/23i unless the patient has IBD.
Abatacept is an option in patients with serious or recurrent infections.
Tofacitinib may be considered instead of an IL-17i in patients who prefer oral therapy or have a history of recurrent or severe Candida infections.
Active PsA Despite TNFi Monotherapy
Switch to different TNFi biologic over IL-17i biologic, IL-12/23i biologic, abatacept, tofacitinib or adding MTX
May consider alternative choices in some situations
Switch to IL-17i biologic over IL-12/23i biologic, abatacept or tofacitinib
May consider alternative choices in some situations
Switch to IL-12/23i biologic over abatacept or tofacitinib
May consider alternative choices in some situations
Reference: Singh JA, et al. Arthritis Rheumatol. 2019;71:5-32.
HELP
A–Z
MENU
Q1
Q2
Q3

95


Decision Tree: Question 3 of 4
Does your patient have any risk factors for severe COVID-19?
Click all that apply.
Age ≥65 years
Male
Obesity
Hypertension
Cardiovascular disease
Diabetes
Chronic respiratory disease
OR
Patient has no risk factors
CLICK TO
Submit
HELP
A–Z
MENU
CLICK ARROW TO EXPAND
Q1
Q2
Q3

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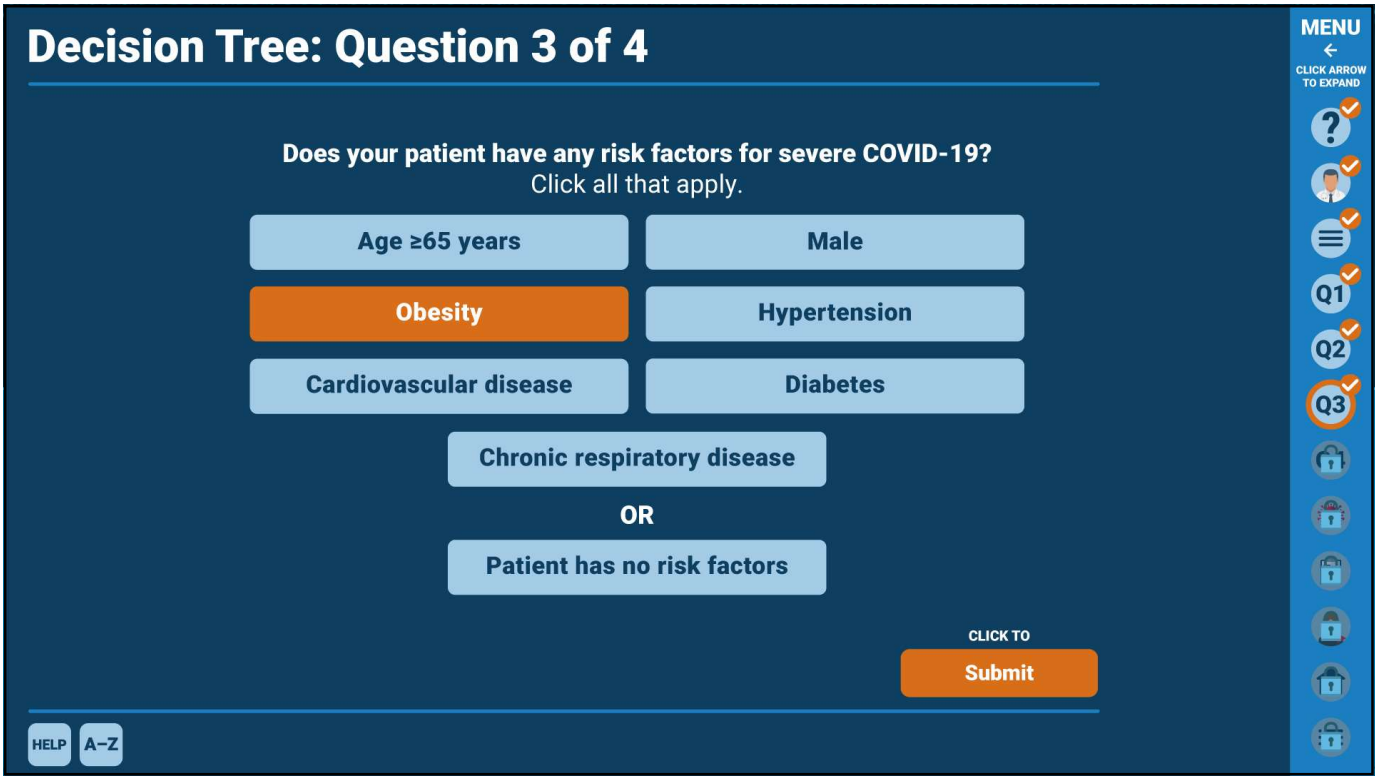
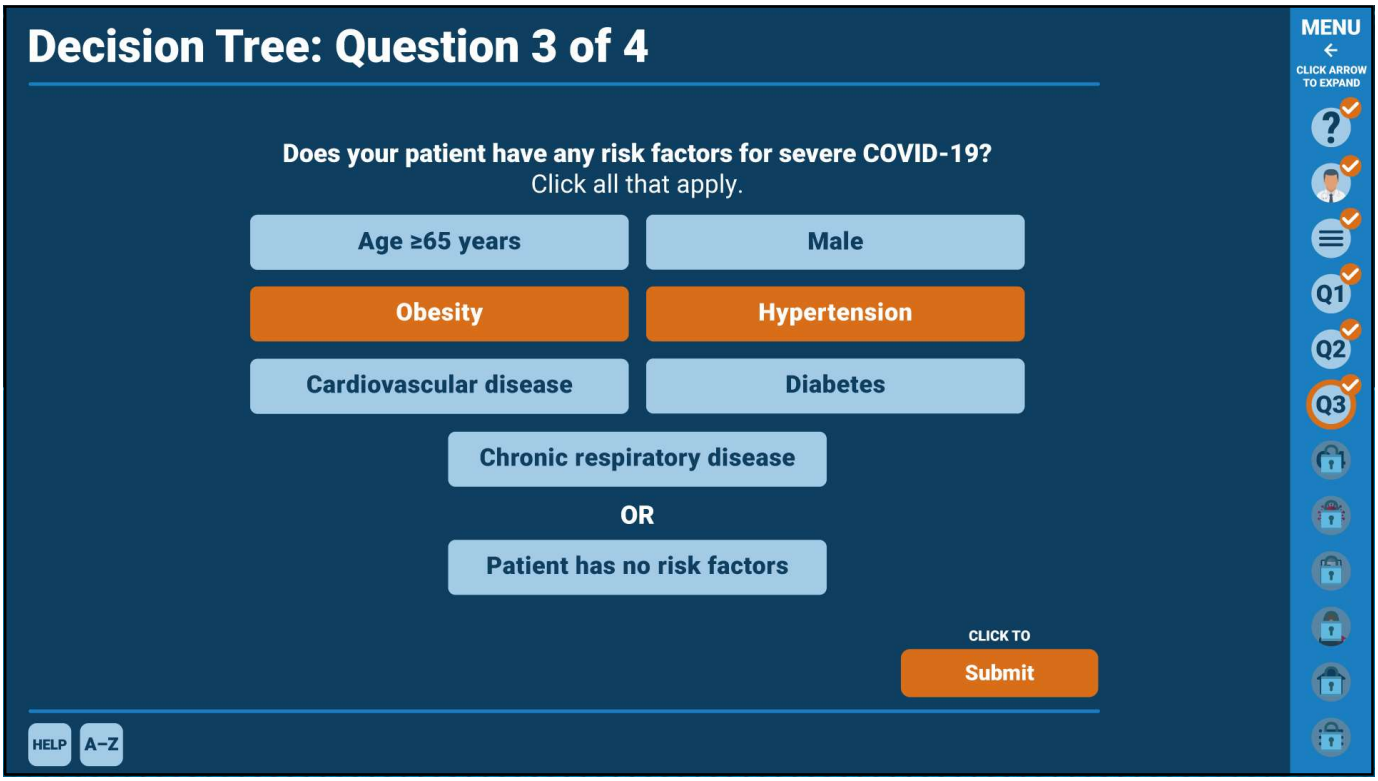

Decision Tree: Question 3 of 4
Does your patient have any risk factors for severe COVID-19?
Click all that apply.
Age ≥65 years
Male
Obesity
Hypertension
Cardiovascular disease
Diabetes
Chronic respiratory disease
OR
Patient has no risk factors
CLICK TO
Submit
HELP
A–Z
MENU
CLICK ARROW TO EXPAND
Q1
Q2
Q3

97


Decision Tree: Question 3 of 4
Does your patient have any risk factors for severe COVID-19?
Click all that apply.
Age ≥65 years
Male
Obesity
Hypertension
Cardiovascular disease
Diabetes
Chronic respiratory disease
OR
Patient has no risk factors
CLICK TO
Submit
HELP
A–Z
MENU
CLICK ARROW TO EXPAND
Q1
Q2
Q3

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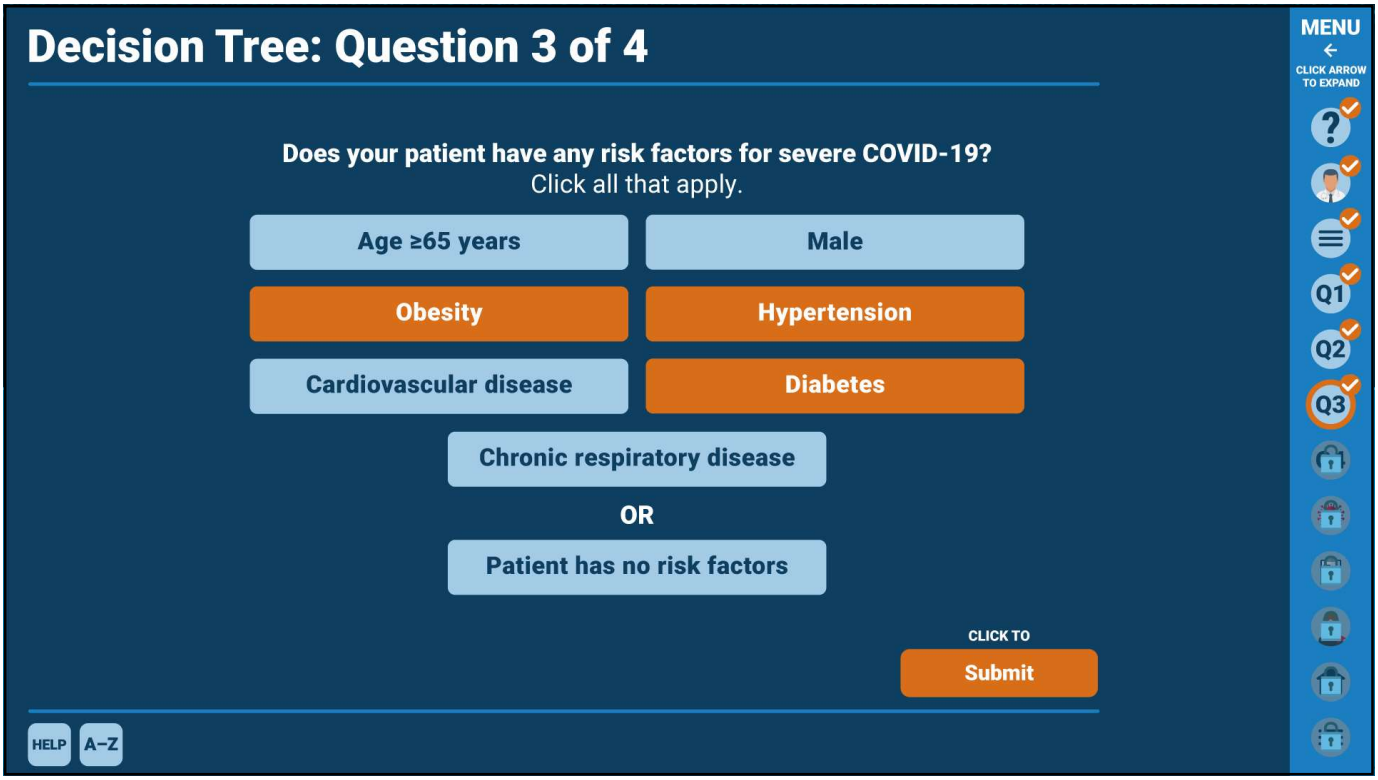
Decision Tree: Question 3 of 4
Does your patient have any risk factors for severe COVID-19?
Click all that apply.
Age ≥65 years
Male
Obesity
Hypertension
Cardiovascular disease
Diabetes
Chronic respiratory disease
OR
Patient has no risk factors
CLICK TO
Submit
HELP
A–Z
MENU
CLICK ARROW TO EXPAND
Q1
Q2
Q3

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Question 3: Guidance for patient with risk factors

MENU

CLICK ARROW TO EXPAND

Patient with risk factors

Patients with PsA are not at increased risk of death or serious complications from COVID-19 due to their disease.

However, PsA is associated with a higher incidence of CV disease, metabolic syndrome, obesity, diabetes, dyslipidemia, and IBD.

Risk of poor outcomes from COVID-19 appears to be related to general risk factors such as older age, male sex, and comorbidities (obesity, diabetes, hypertension, CV or lung disease) .

Variable	Relative risk from COVID-19 (95%CI) (Non-rheumatic cohort / Rheumatic cohort)	P value
Age over 60 years	1.99 3.70 6.93 / 2.30 4.04 7.08	0.841
Male sex	1.39 2.16 3.35 / 1.09 1.58 2.29	0.286
Obesity	0.72 1.22 2.06 / 1.10 1.62 2.36	0.393
Diabetes	0.53 0.95 1.70 / 1.34 1.93 2.79	0.038
Hypertension	1.07 1.64 2.53 / 1.49 2.27 3.46	0.290
CV disease	0.90 1.44 2.33 / 2.04 2.92 4.17	0.020
Lung disease	1.00 1.57 2.46 / 1.19 1.74 2.55	0.723

0 2 4 6 8

CLICK TO: Reset

CLICK TO VIEW: Question 4

HELP A–Z

Mikuls TR, et al. *Arthritis Rheumatol.* 2020;72:e1-e12.
Pablos JL, et al. *Ann Rheum Dis.* 2020:218296.
Wu Z, et al. *JAMA.* 2020;323:1239-1242.
Wollina U, et al. *Dermatol Ther.* 2020;33:e13743.
Pablos JL, et al. *Ann Rheum Dis.* 2020;Epub ahead of print.

100

Decision Tree: Question 4 of 4

MENU

CLICK ARROW TO EXPAND

Should your patient's medication regimen be modified due to the COVID-19 pandemic?

What is your patient's COVID-19 status? Click one answer below.

- Not infected
- Known exposure to COVID-19
- Asymptomatic COVID-19
- Mild COVID-19
- Severe COVID-19

CLICK TO: Reset

CLICK TO VIEW: COVID-19 Treatment Modifications

HELP A–Z

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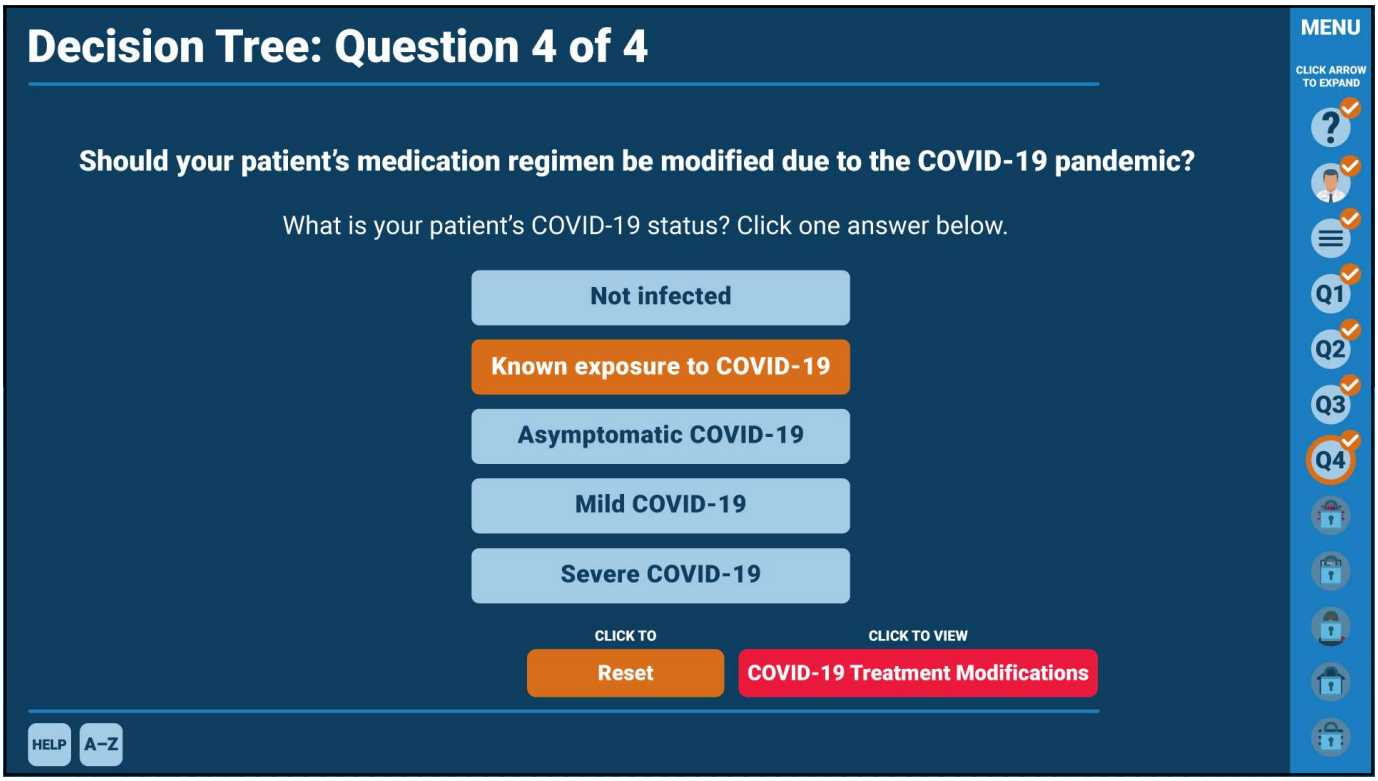
Decision Tree: Question 4 of 4
MENU
CLICK ARROW TO EXPAND
Should your patient's medication regimen be modified due to the COVID-19 pandemic?
What is your patient's COVID-19 status? Click one answer below.
Not infected
Known exposure to COVID-19
Asymptomatic COVID-19
Mild COVID-19
Severe COVID-19
CLICK TO
Reset
CLICK TO VIEW
COVID-19 Treatment Modifications
HELP
A–Z
Q1
Q2
Q3
Q4

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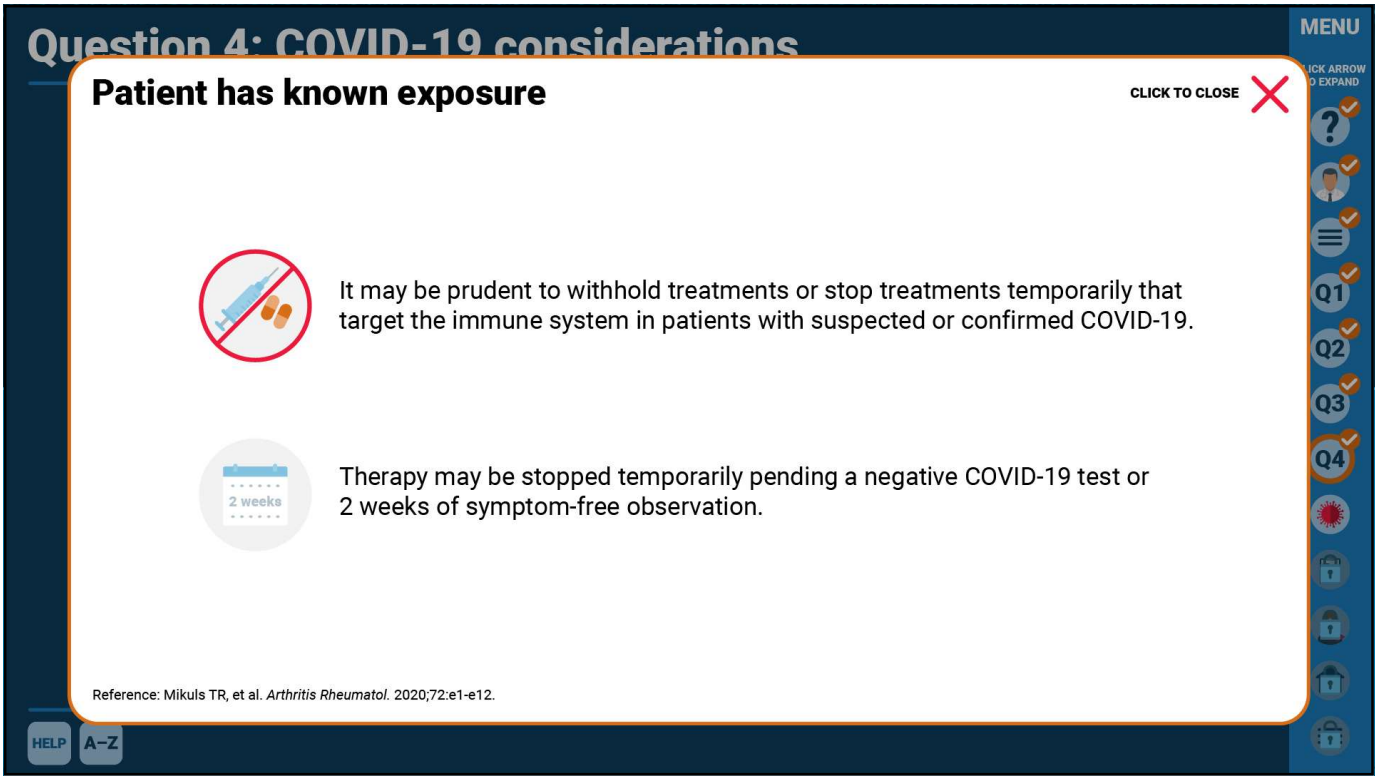
Question 4: COVID-19 considerations
MENU
Patient has known exposure
CLICK TO CLOSE
It may be prudent to withhold treatments or stop treatments temporarily that target the immune system in patients with suspected or confirmed COVID-19.
2 weeks
Therapy may be stopped temporarily pending a negative COVID-19 test or 2 weeks of symptom-free observation.
Reference: Mikuls TR, et al. Arthritis Rheumatol. 2020;72:e1-e12.
HELP
A–Z
Q1
Q2
Q3
Q4

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Summary

- Patient goals are important:
  - Improve QoL, function, and social participation
  - Control symptoms and inflammation (enthesitis, dactylitis, joints)
  - Prevent joint damage
- Start treatment early.
- Multidisciplinary care: communication is key! Work together to minimize comorbidities.
- Therapy should be monitored and adjusted—sometimes every 8-to-12 weeks.
- Use telemedicine to reduce the risk of COVID-19.
- It may be prudent to withhold treatments that target the immune system in patients with suspected or confirmed COVID-19.

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

104

Post-test Questions

105

Pre-test Question 1

Tim has used etanercept for 1 year to control his psoriatic arthritis. However, he was diagnosed with COVID-19 three days ago. Which of the following changes would you make to Tim's treatment regimen?

a) Continue taking etanercept.
b) Add prednisone to reduce the risk of COVID-19 complications.
c) Switch from etanercept to a JAK inhibitor.
d) Stop etanercept and reinitiate 7-14 days after COVID-19 symptoms resolve.

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Pre-test Question 2

Linda reports worsening psoriatic arthritis symptoms and a recent flare-up of psoriasis. She is prescribed adalimumab and diclofenac. After 12 weeks of therapy, her CDAI increased from 16 to 20 and her PASI increased from 8 to 10. Which of the following is the best treatment option for Linda?

a) Continue adalimumab and diclofenac for 1 more month and reassess.
b) Switch to ixekizumab.
c) Switch to ustekinumab.
d) Switch to tofacitinib.

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Pre-test Question 3

Which of the following statements regarding telemedicine in the management of psoriatic arthritis is TRUE?

a) Regular blood monitoring should not be postponed due to the COVID-19 pandemic.
a) Patient-reported outcomes scales may be used to identify patients who require in-person visits.
b) Telemedicine appointments generally take less time than traditional in-office visits.
c) Telemedicine is useful for the triage of patients but should not replace routine in-person evaluations.

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Psoriatic Arthritis

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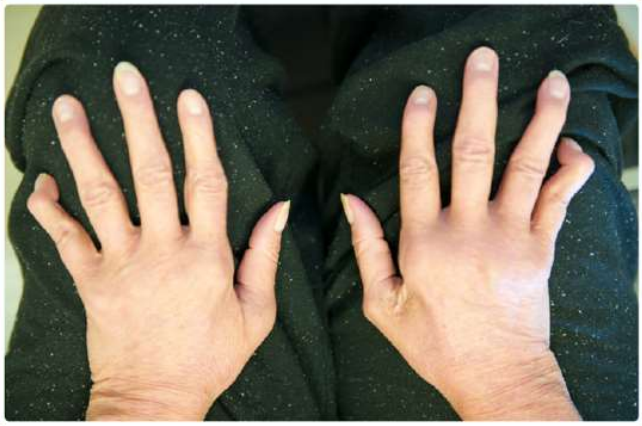
Psoriatic Arthritis Manifestations

PsA is a chronic, inflammatory musculoskeletal disease associated with psoriasis.

Symptoms include fatigue and joint pain, swelling, and stiffness.

Other disease manifestations include:

Spondylitis	Urethritis
Enthesitis	Nail disease
Dactylitis	Other extra-articular features (such as inflammatory bowel disease)
Iritis	
Conjunctivitis	



Lloyd P, et al. *Arthritis.* 2012;2012:176298. Boyd T, et al. *Rheum Dis Clin North Am.* 2015;41:739-754.

110

CASPAR Classification Criteria for PsA

- To meet CASPAR criteria, a patient must have inflammatory articular disease (joint, spine, entheseal) with ≥3 total points from any of the following 5 categories.

Criterion	Points
1. Psoriasis (psoriatic skin or scalp disease)	2
• Current psoriasis on examination OR	
• Personal history OR	
• Family history in first- or second-degree relative	
2. Psoriatic nail dystrophy (eg, onycholysis, pitting, hyperkeratosis) on examination	1
3. Negative test for rheumatoid factor	1
4. Dactylitis (inflammatory swelling of an entire finger or toe)	
• Current dactylitis on examination OR	1
• Personal history in first- or second-degree relative	1
5. Juxta-articular new bone formation on plain radiographs of hands or feet	1

98.7% specificity, 91.4% sensitivity

Taylor W, et al. *Arthritis Rheum.* 2006;54:2665-2673.

111

Differentiating PsA from Other Forms of Inflammatory Arthritis

Variable	PsA	RA	Gout	Osteoarthritis
Joint distribution at onset	Asymmetric	Symmetric	Asymmetric	Asymmetric
No. of affected joints	Oligoarticular	Polyarticular	Monoarticular or oligoarticular	Monoarticular or oligoarticular
Sites of hands or feet involved	Distal	Proximal	Distal	Distal
Areas involved	All joints of a digit	Same joint across digits	Usually monoarticular	Same joint across digits
Tenderness (kg on dolorimeter)	7	4	NA	NA
Purplish discoloration	Yes	No	Yes	No
Spinal involvement	Possible	Uncommon	Absent	Non-inflammatory
Sacroiliitis	Possible	Absent	Absent	Absent

Ritchlin CT, et al. *N Engl J Med.* 2017;376:957-970.

112

Does Your Patient Have Severe Disease?

- No widely agreed-upon definitions of disease severity in PsA or psoriasis
- Severity should be judged on case-by-case basis
- ACR/NPF suggest the presence of ≥1 of the following qualifies as severe disease:

Severe Psoriatic Arthritis	Severe Psoriasis
• Erosive disease • Elevated markers of inflammation (ESR, CRP) attributable to PsA • Long-term damage that interferes with function (i.e. joint deformities) • Highly active disease that causes a major impairment in quality of life • Active PsA at many sites including dactylitis, enthesitis • Function-limiting PsA at a few sites • Rapidly progressive disease	• PASI of 12 or more • BSA of 5-10% or more • Significant involvement in specific areas (e.g., face, hands or feet, nails, intertriginous areas, scalp) where the burden of the disease causes significant disability • Impairment of physical or mental functioning can warrant a designation of moderate-to-severe disease despite the lower amount of surface area of skin involved

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

113

New Treatment Paradigm

Patients with PsA are at increased risk of a host of comorbidities, including CV disease, metabolic syndrome, obesity, diabetes, dyslipidemia, IBD, and others.

The management of patients with PsA should be holistic and include:

BMI, vitals	Examination of dentition
Assessment of alcohol intake	Fasting lipids and CMP
Sleep problems	Fasting sugars and HbA1c
Skin involvement, with patient input	Diet/exercise and weight-loss program
Monitoring for inflammatory arthritis	Smoking cessation

Wollina U, et al. *Dermatol Ther.* 2020;33:e13743.

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Psoriatic Arthritis and COVID-19

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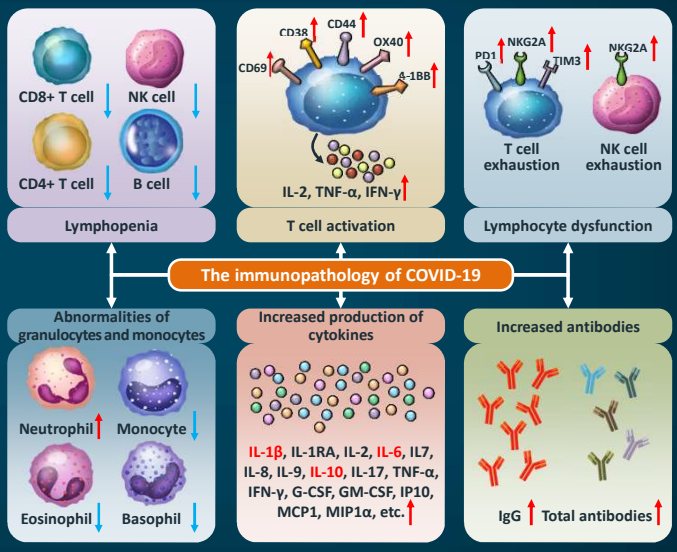
COVID-19-associated Hyperinflammation

- Clinical deterioration in COVID-19 often occurs 7-10 days after symptom onset when viral titres decline
  - Pathology likely driven by inflammation rather than direct viral injury
- 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.

116

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.

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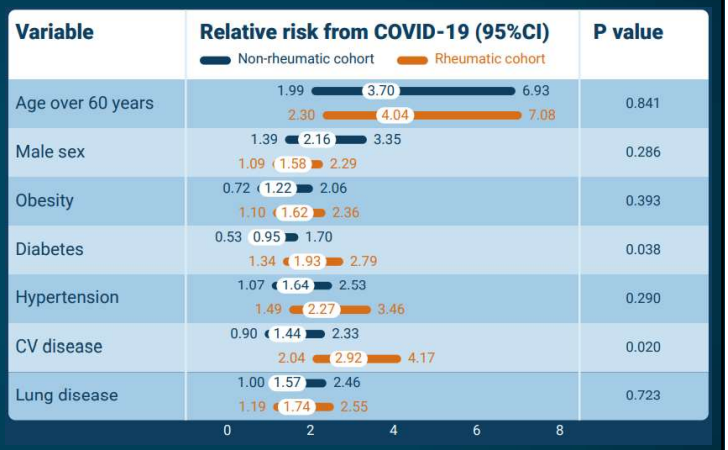
Impact of PsA Comorbidities on COVID-19 Outcomes

- PsA is associated with a higher incidence of CV disease, metabolic syndrome, obesity, diabetes, dyslipidemia, and inflammatory bowel disease
- Risk of poor outcomes for COVID-19 appears to be related to general risk factors such as older age, male sex, and comorbidities (obesity, diabetes, hypertension, CV or lung disease)



CV = cardiovascular; IBD = inflammatory bowel disease

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

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COVID-19 Treatment Modifications

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

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.

119

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.

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ACR COVID-19 Vaccination Guidance for Rheumatic Patients

Medication	Timing Considerations for Immunomodulatory Therapy and Vaccination
Hydroxychloroquine; IVIG; glucocorticoids, prednisone-equivalent dose <20mg/day	No modifications to either immunomodulatory therapy or vaccination timing
SSZ; LEF; MMF; AZA; Cyclophosphamide (oral); TNFi; IL-6R; IL-1; IL-17; IL-12/23; IL-23; Belimumab; oral calcineurin inhibitors; Glucocorticoids, prednisone-equivalent dose ≥20mg/day	No modifications to either immunomodulatory therapy or vaccination timing
Methotrexate	Hold MTX 1 week after each vaccine dose, for those with well-controlled disease; no modifications to vaccination timing
JAKi	Hold JAKi for 1 week after each vaccine dose; no modification to vaccination timing
Abatacept SQ	Hold SQ abatacept both one week prior to and one week after the first COVID-19 vaccine dose (only); no interruption around the second vaccine dose
Abatacept IV	Time vaccine administration so that the first vaccination will occur four weeks after abatacept infusion (i.e., the entire dosing interval), and postpone the subsequent abatacept infusion by one week (i.e., a 5-week gap in total); no medication adjustment for the second vaccine dose
Cyclophosphamide IV	Time CYC administration so that it will occur ~1 week after each vaccine dose, when feasible
Rituximab	Assuming that patient's COVID-19 risk is low or is able to be mitigated by preventive health measures (e.g., self-isolation), schedule vaccination so that the vaccine series is initiated approximately 4 weeks prior to next scheduled rituximab cycle; after vaccination, delay RTX 2-4 weeks after 2nd vaccine dose, if disease activity allows

ACR COVID-19 Vaccine Clinical Guidance Summary. Available at: https://www.rheumatology.org/Portals/0/Files/COVID-19-Vaccine-Clinical-Guidance-Rheumatic-Diseases-Summary.pdf.

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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, 78.7% of these interruptions were NOT recommended by a physician.

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%)

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.

122

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.

123

Strategies to Increase Telehealth Uptake

- **Use technology** that allows you to send and receive patient-reported outcomes scales.

- **Prescreen patients with disease activity scales** and request in-person visit if scores are high.

- **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.

124

Treatment Options for Psoriatic Arthritis

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Initiating Therapy

Treatment-naïve Active PsA

Discuss with the patient, since all recommendations are conditional based on low to very low quality evidence

- Start TNFi biologic over OSM, IL-17i biologic or IL-12/23i biologic
  - May consider alternative choices in some situations
- Start OSM over IL-17i biologic or IL-12/23i biologic
  - May consider alternative choices in some situations
- Start MTX over NSAIDs
  - May consider alternative choices in some situations
- Start IL-17i biologic over IL-12/23i biologic
  - May consider alternative choices in some situations

- 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

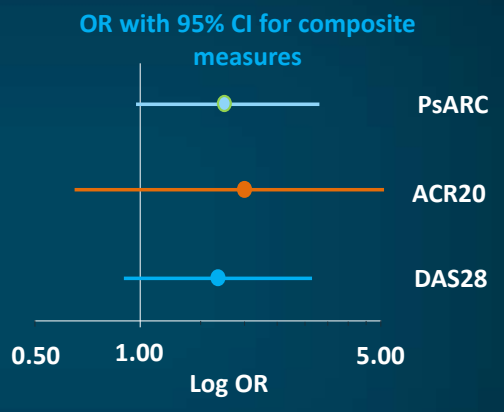
APR = apremilast; CSA = cyclosporine; IL = interleukin; LEF = leflunomide; MTX = methotrexate; NSAID = nonsteroidal anti-inflammatory drug; OSM = oral small molecule; SSZ = sulfasalazine; TNFi = tumor necrosis factor-alpha inhibitor.

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

126

Methotrexate Is Not a DMARD in PsA

- 6-month DBRCT of MTX 15 mg/week vs PBO
- Primary outcome: PsARC
  Secondary outcomes: ACR20, DAS28, global and skin scores
- 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)



Despite issues with study design, MTX does not have disease-remitting properties.

CRP = C-reactive protein; DBRCT = double-blind, randomized controlled trial; ESR = erythrocyte sedimentation rate; MTX = methotrexate; PBO = placebo; PsARC = PsA response criteria; DAS = Disease Activity Score; SJC = swollen joint count; TJC = tender joint count.

Kingsley GH, et al. *Rheumatology (Oxford).* 2012;51:1368-1377.

127

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 Cyclosporin 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	+

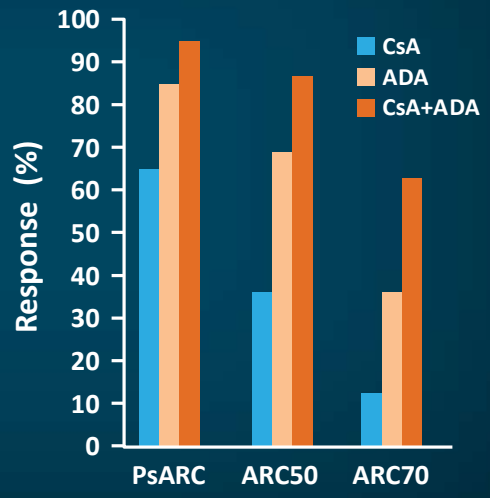
*NSAID +/- prednisone 5 mg daily +/- analgesics

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

128

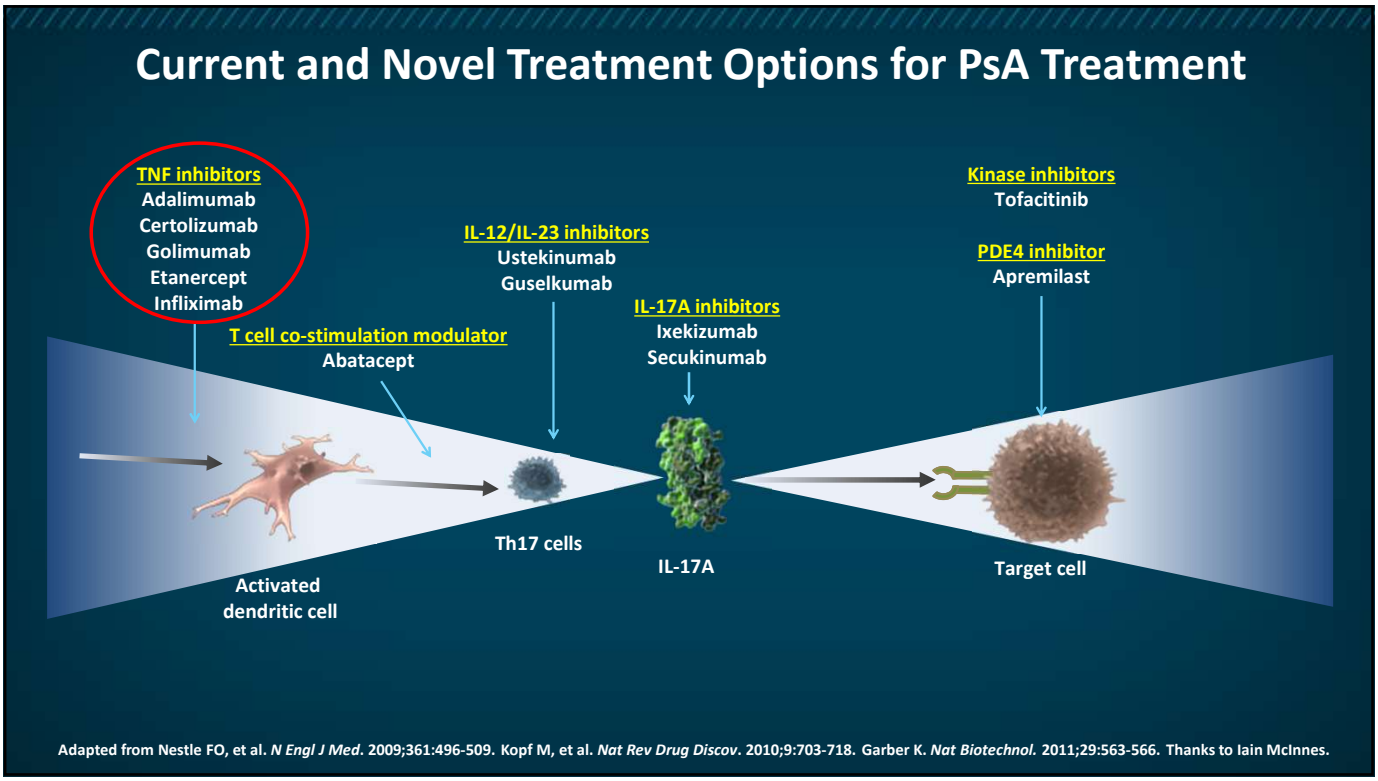
Adalimumab Or Cyclosporine as Monotherapy or Combination For Severe PsA: A Prospective, 12-month, Observational Study

- A 12-month, observational study of 170 TNFi- and cyclosporine-naïve patients
- Patients who received adalimumab (40mg Q2W) (n=57), cyclosporine (2.5-3.75 mg/kg/day) (n=58), or their combination (n=55)
- MTX-IR (25 mg weekly or less, for a minimum of 6 months)
- Assessments: 0.5, 1, 2, 3, 4, 5, 6, 8, 10, and 12 months
- Combination therapy improved PASI50 response rates but NOT beyond the effect of cyclosporine monotherapy (not shown)

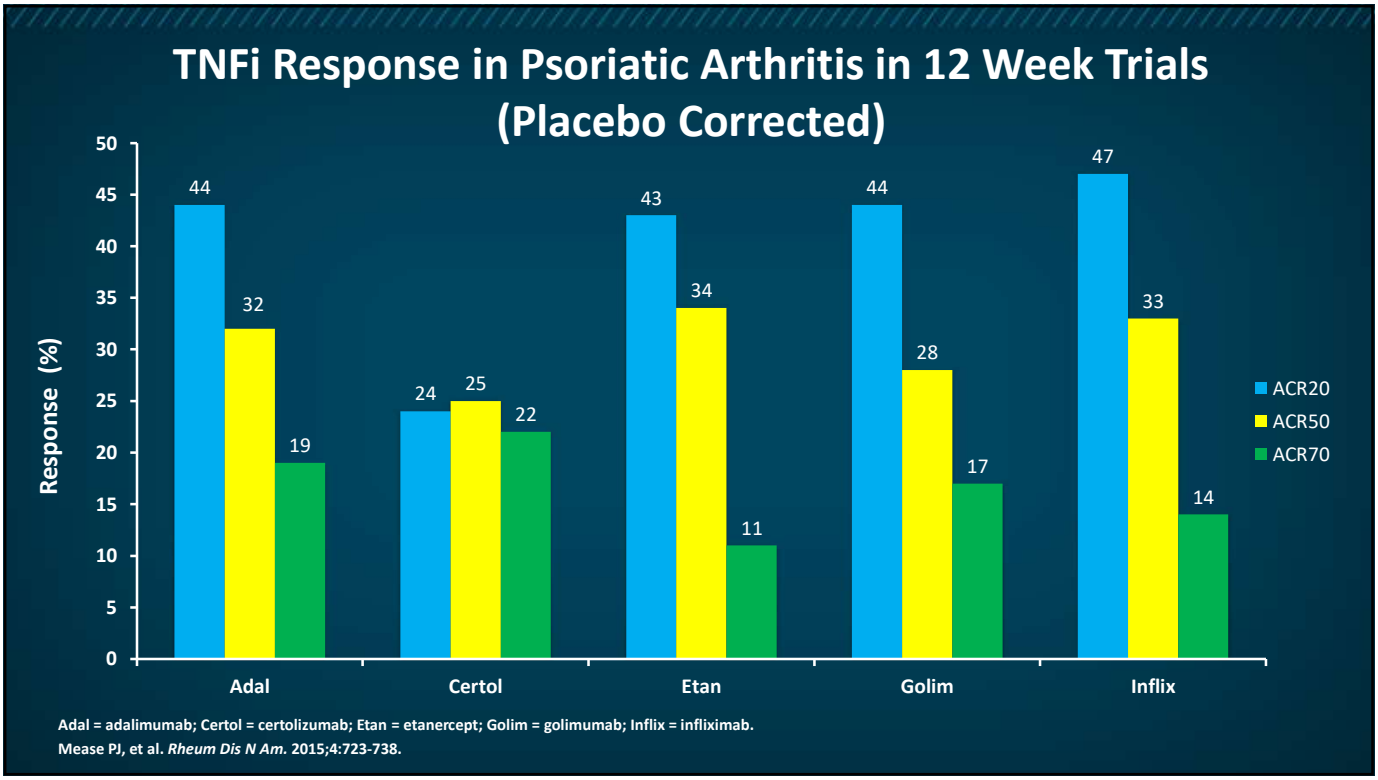


MTX-IR = methotrexate inadequate response
Karanikolas GN, et al. *J Rheumatol*. 2011;38:2466-2474.

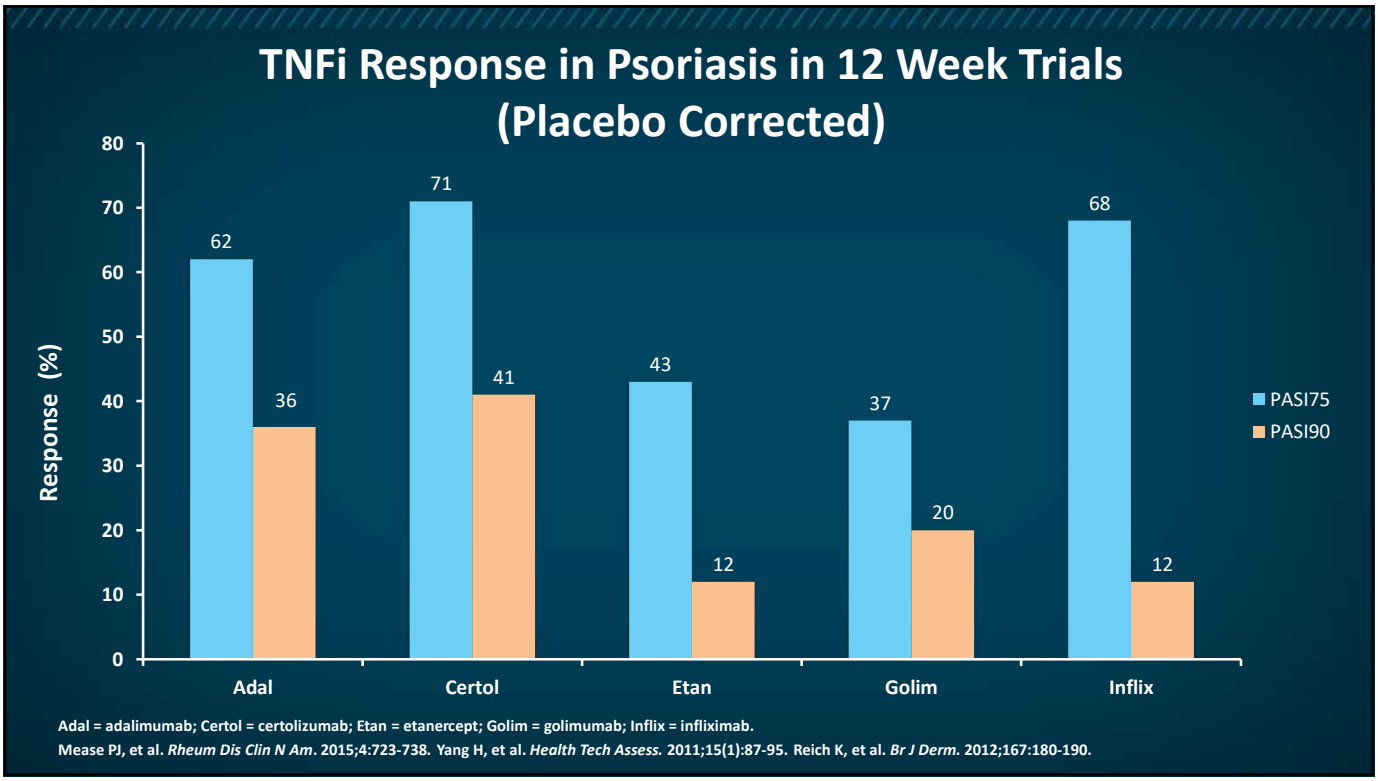
129


Current and Novel Treatment Options for PsA Treatment
TNF inhibitors
Adalimumab
Certolizumab
Golimumab
Etanercept
Infliximab
T cell co-stimulation modulator
Abatacept
IL-12/IL-23 inhibitors
Ustekinumab
Guselkumab
IL-17A inhibitors
Ixekizumab
Secukinumab
Kinase inhibitors
Tofacitinib
PDE4 inhibitor
Apremilast
Activated dendritic cell
Th17 cells
IL-17A
Target cell
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.

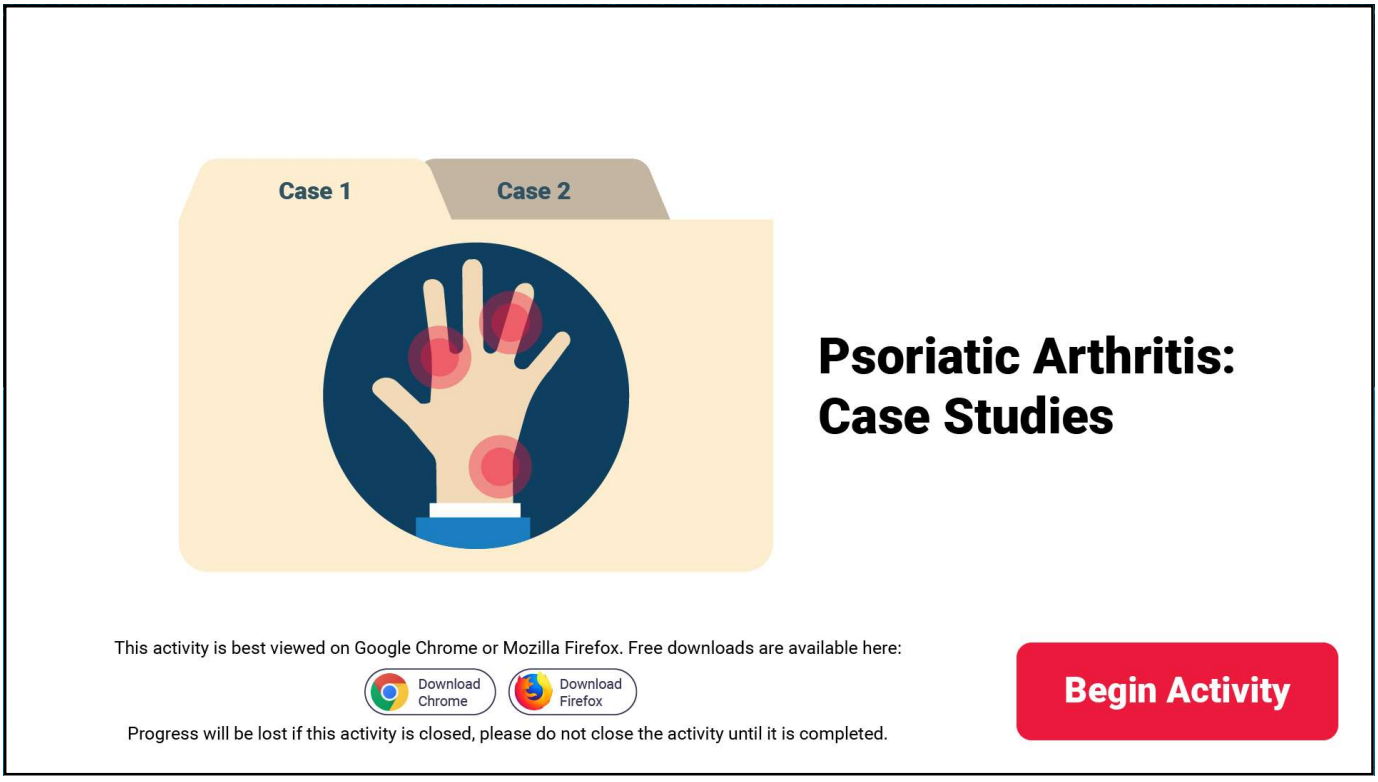
130


TNFi Response in Psoriatic Arthritis in 12 Week Trials (Placebo Corrected)
Response (%)
50
45
40
35
30
25
20
15
10
5
0
44
32
19
24
25
22
43
34
11
44
28
17
47
33
14
Adal
Certol
Etan
Golim
Inflix
ACR20
ACR50
ACR70
Adal = adalimumab; Certol = certolizumab; Etan = etanercept; Golim = golimumab; Inflix = infliximab.
Mease PJ, et al. Rheum Dis N Am. 2015;4:723-738.

131


TNFi Response in Psoriasis in 12 Week Trials
(Placebo Corrected)
Response (%)
80
70
60
50
40
30
20
10
0
62
36
71
41
43
12
37
20
68
12
Adal
Certol
Etan
Golim
Inflix
PASI75
PASI90
Adal = adalimumab; Certol = certolizumab; Etan = etanercept; Golim = golimumab; Inflix = infliximab.
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.

132


Case 1
Case 2
Psoriatic Arthritis:
Case Studies
This activity is best viewed on Google Chrome or Mozilla Firefox. Free downloads are available here:
Download Chrome
Download Firefox
Progress will be lost if this activity is closed, please do not close the activity until it is completed.
Begin Activity

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MENU
How To Use
Meet the Faculty
Case Study 1: Lindsey
Case Study 2: Tina
Case Study 1: Lindsay
Continue
HELP
A–Z
All definitions are defined in the glossary.

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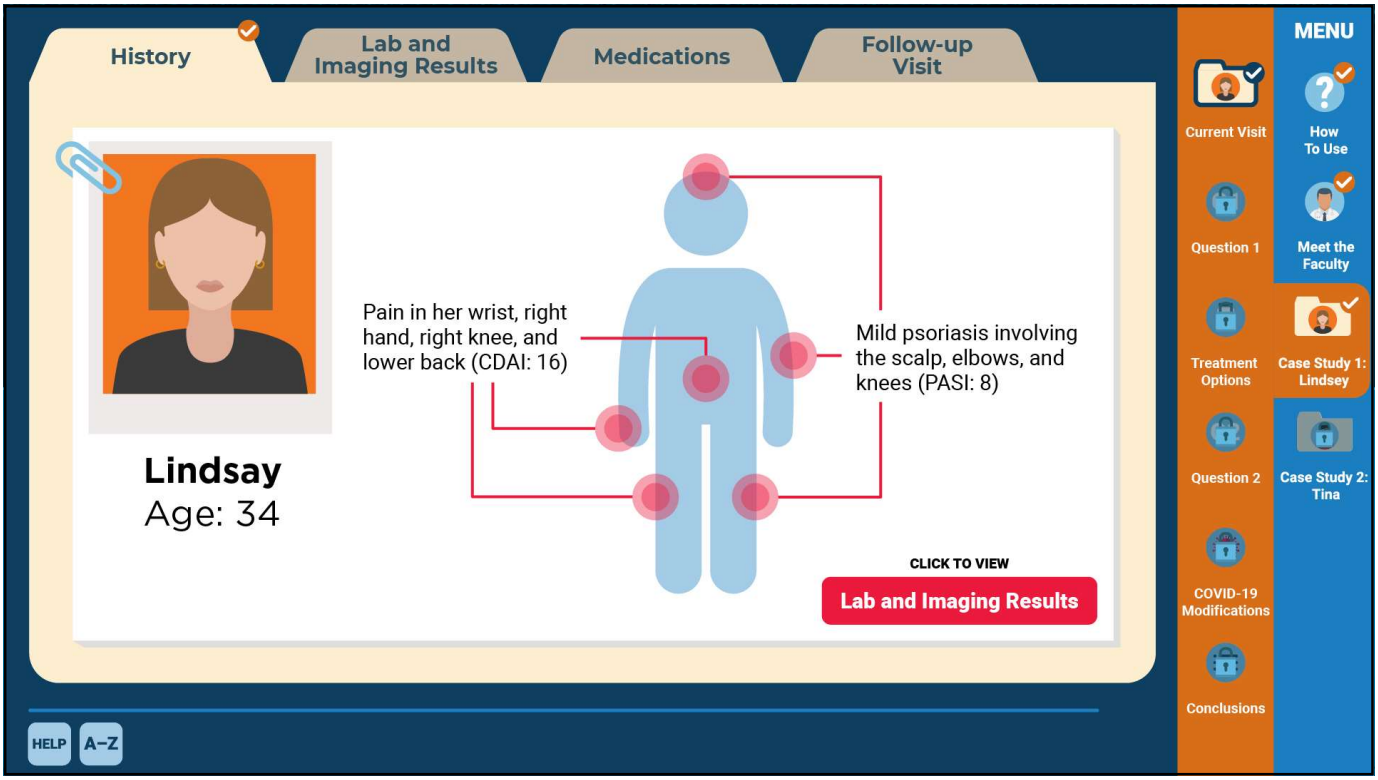
History
Lab and Imaging Results
Medications
Follow-up Visit
Lindsay
Age: 34
Pain in her wrist, right hand, right knee, and lower back (CDAI: 16)
Mild psoriasis involving the scalp, elbows, and knees (PASI: 8)
CLICK TO VIEW
Lab and Imaging Results
Current Visit
Question 1
Treatment Options
Question 2
COVID-19 Modifications
Conclusions
MENU
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Meet the Faculty
Case Study 1: Lindsey
Case Study 2: Tina
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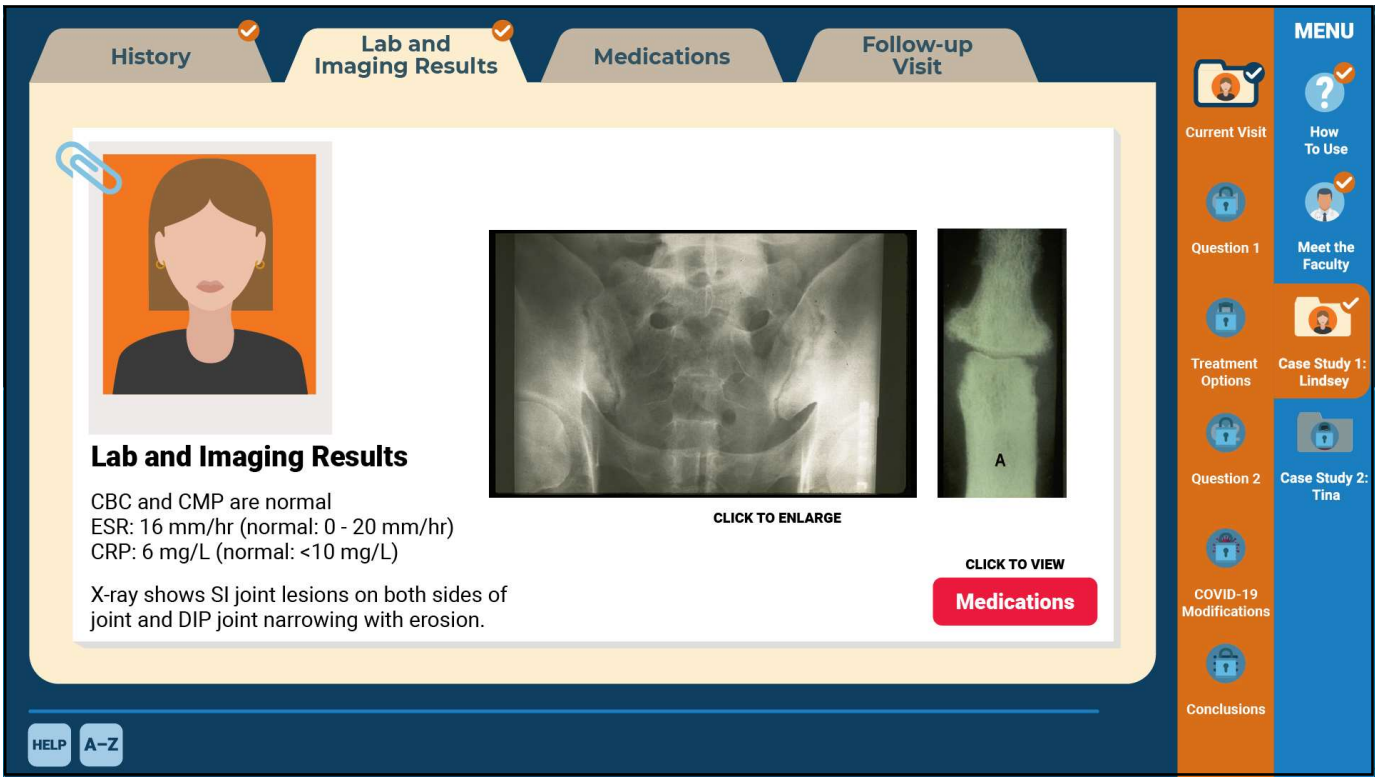
History
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Case Study 2: Tina
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Lab and Imaging Results
CBC and CMP are normal
ESR: 16 mm/hr (normal: 0 - 20 mm/hr)
CRP: 6 mg/L (normal: <10 mg/L)
X-ray shows SI joint lesions on both sides of joint and DIP joint narrowing with erosion.
A
CLICK TO ENLARGE
CLICK TO VIEW
Medications
HELP
A–Z

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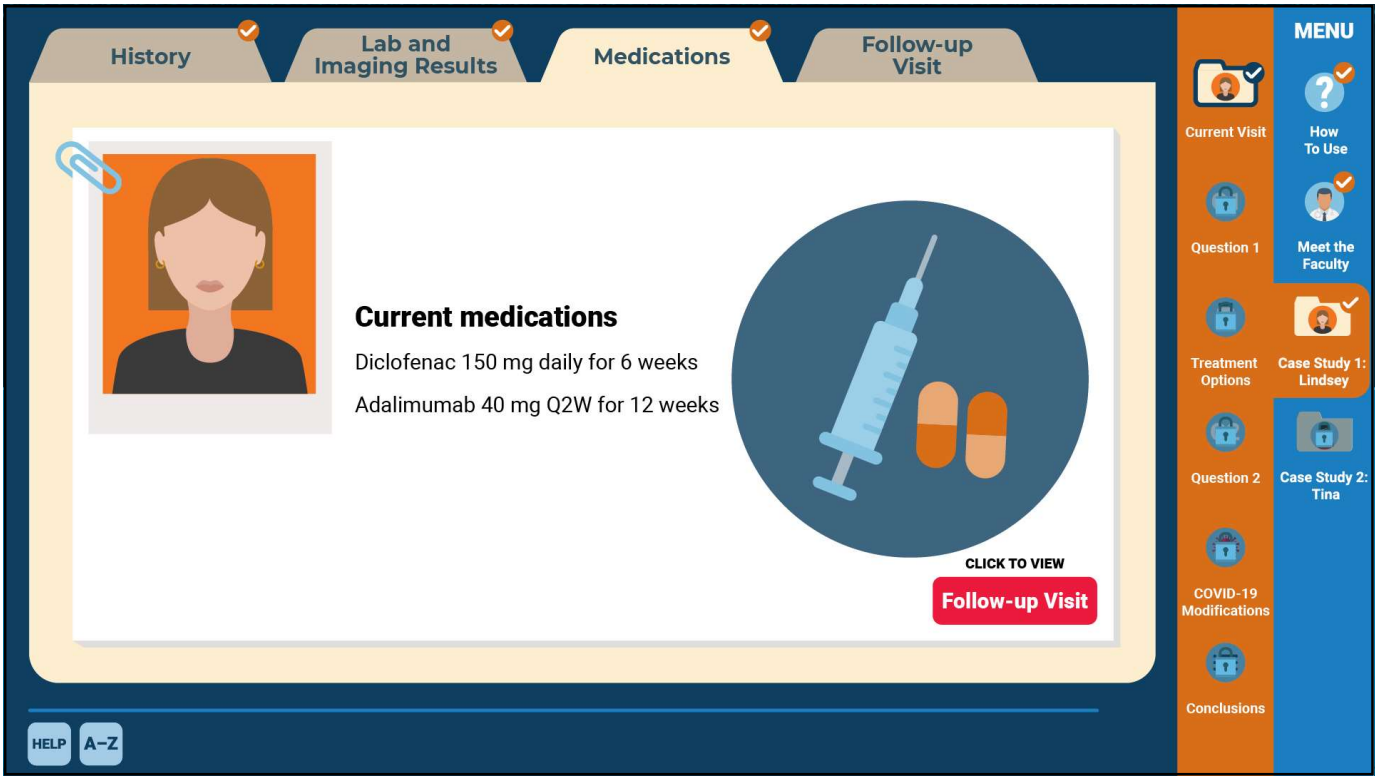
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Case Study 2: Tina
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Current medications
Diclofenac 150 mg daily for 6 weeks
Adalimumab 40 mg Q2W for 12 weeks
CLICK TO VIEW
Follow-up Visit
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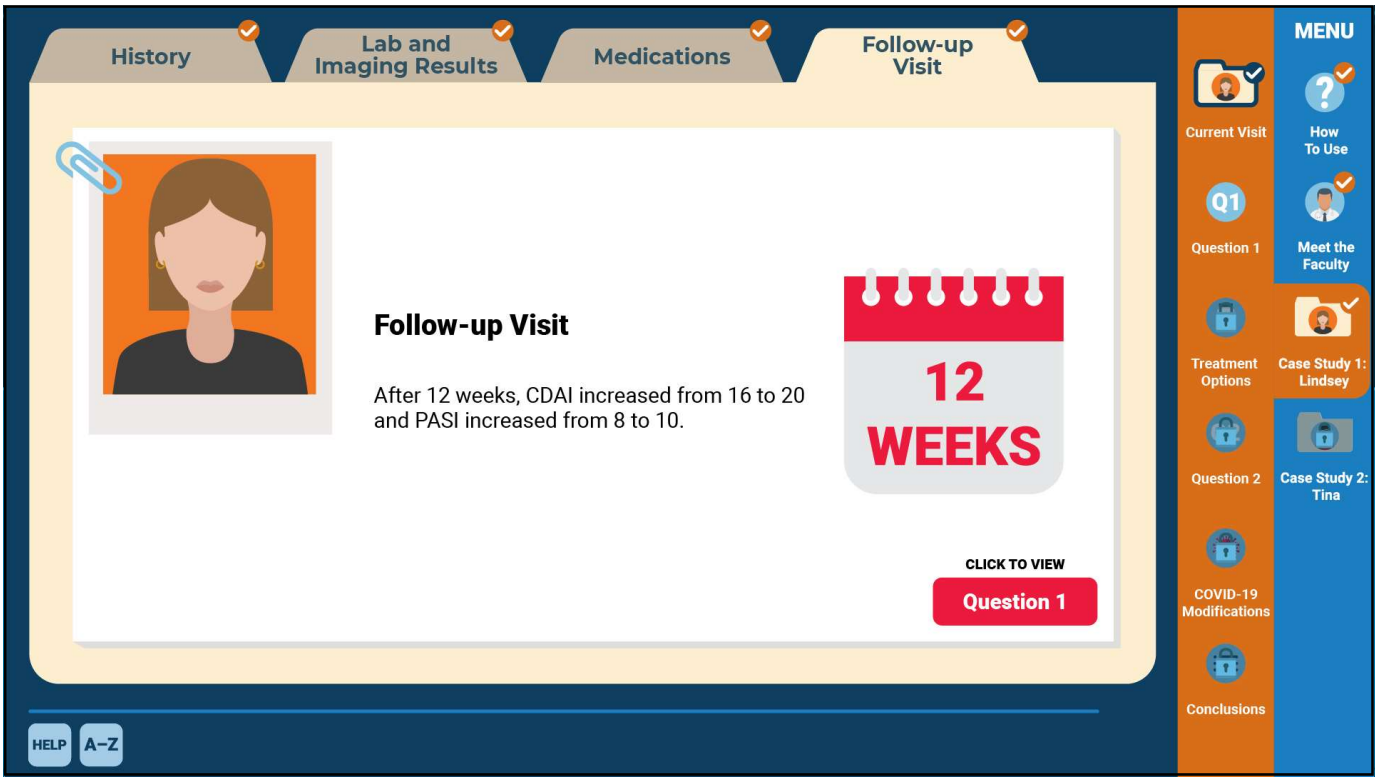
History
Lab and Imaging Results
Medications
Follow-up Visit
Follow-up Visit
After 12 weeks, CDAI increased from 16 to 20 and PASI increased from 8 to 10.
12 WEEKS
CLICK TO VIEW
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Question 2
Case Study 2: Tina
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Conclusions

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Question 1
Which of the following is the best treatment option for Lindsay?
Please select all appropriate choices.
A Ixekizumab
B Infliximab
C Guselkumab
D Ustekinumab
Submit
ACR guideline recommendations
Active PsA despite TNFi monotherapy
Switch to different TNFi biologic over IL-17i biologic, IL-12/23i biologic, abatacept, tofacitinib or adding MTX.
May consider alternative choices in some situations.
Switch to IL-17i biologic over IL-12/23i biologic, abatacept, or tofacitinib.
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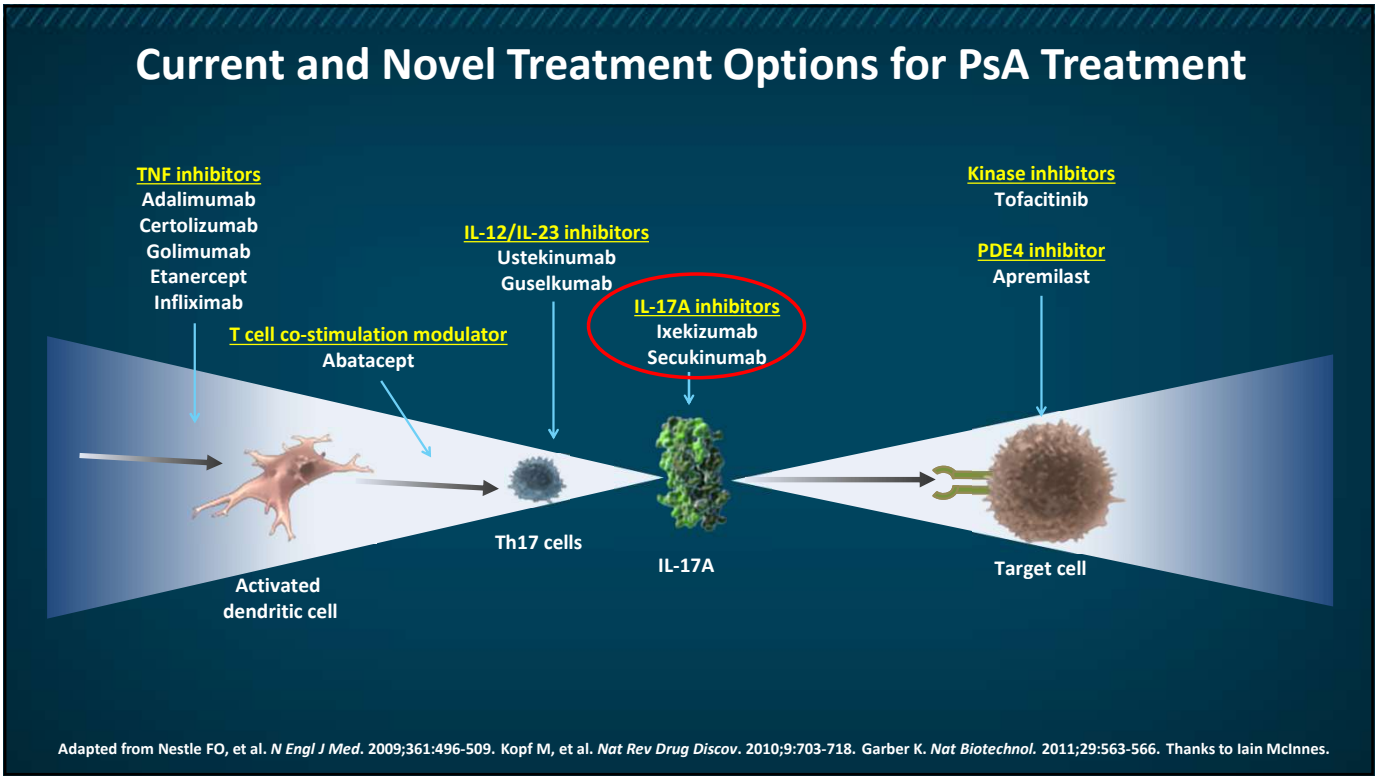
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Ustekinumab
Guselkumab
IL-17A inhibitors
Ixekizumab
Secukinumab
Kinase inhibitors
Tofacitinib
PDE4 inhibitor
Apremilast
Activated dendritic cell
Th17 cells
IL-17A
Target cell
Adapted from Nestle FO, et al. N Engl J Med. 2009;361:496-509. Kopf M, et al. Nat Rev Drug Discov. 2010;9:703-718. Garber K. Nat Biotechnol. 2011;29:563-566. Thanks to Iain McInnes.

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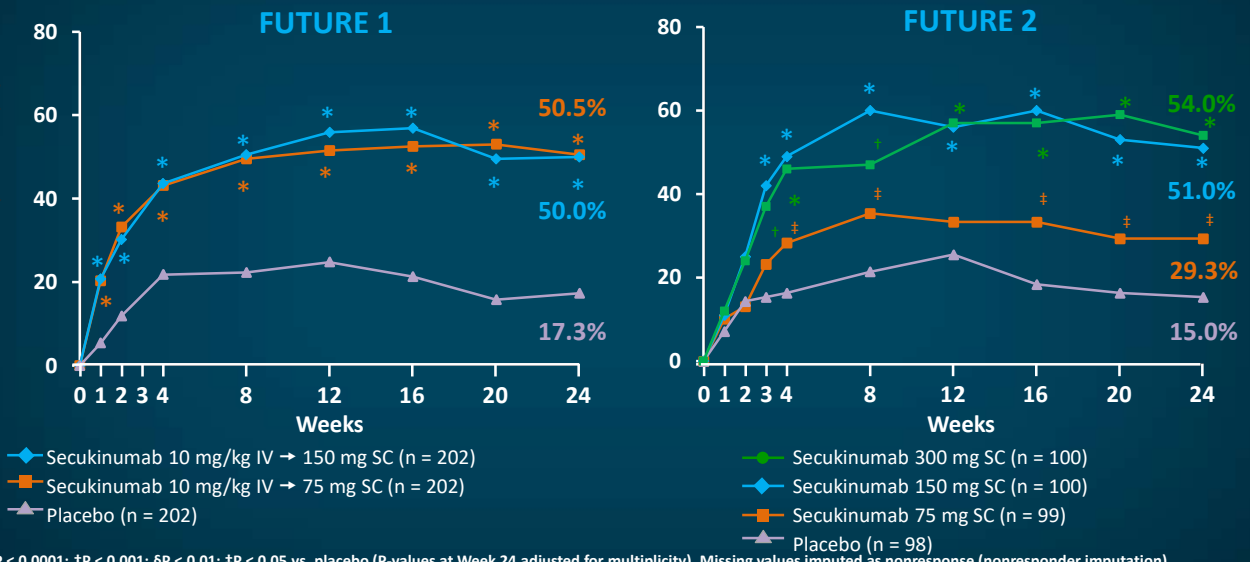
Secukinumab in PsA

ACR20: Primary Outcome Measure

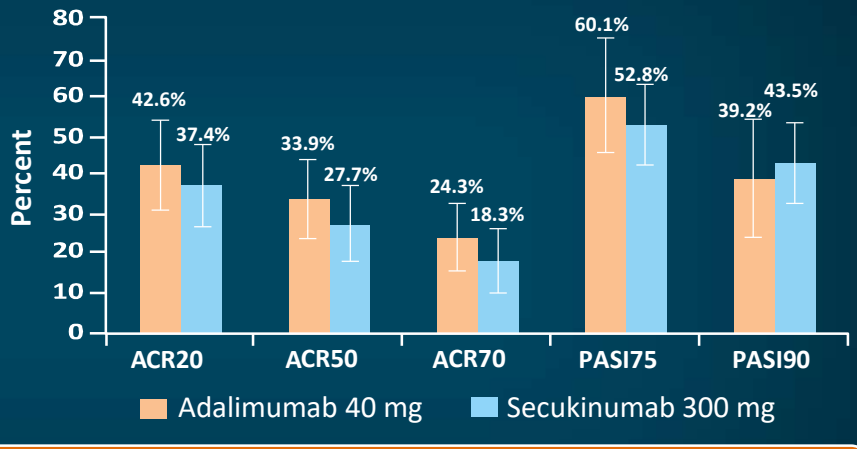


*P < 0.0001; †P < 0.001; §P < 0.01; ‡P < 0.05 vs. placebo (P-values at Week 24 adjusted for multiplicity). Missing values imputed as nonresponse (nonresponder imputation).
IV =intravenous; SC = subcutaneous.
Mease PJ, et al. *N Engl J Med.* 2015;373:1329-1339. McInnes IB, et al. *Lancet.* 2015;386:1137-1146.

144

Adalimumab vs Secukinumab in PsA: Indirect Comparison

- N = 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

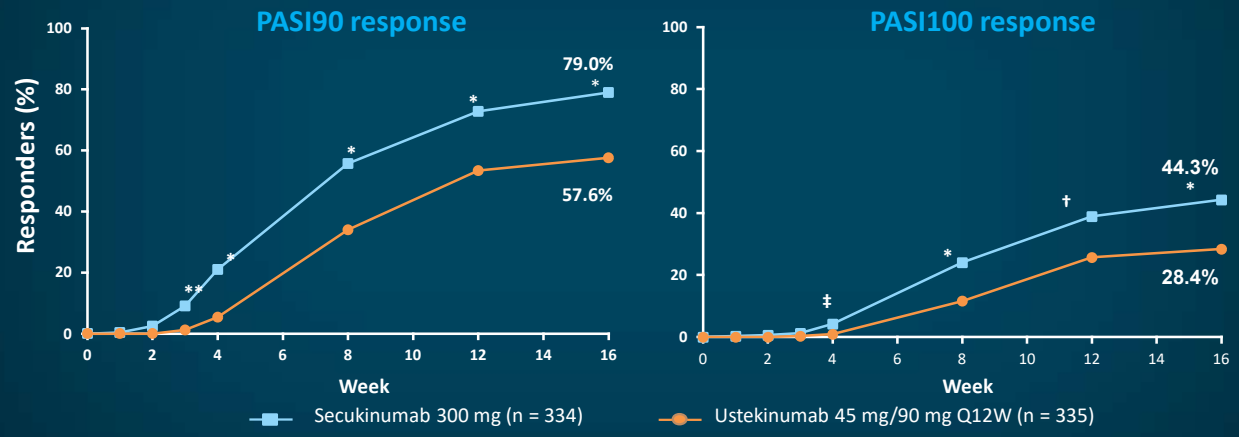


Conclusion: Secukinumab (anti-IL-17) was shown to be as effective or slightly less effective than adalimumab for PsA (numerical only).

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

145

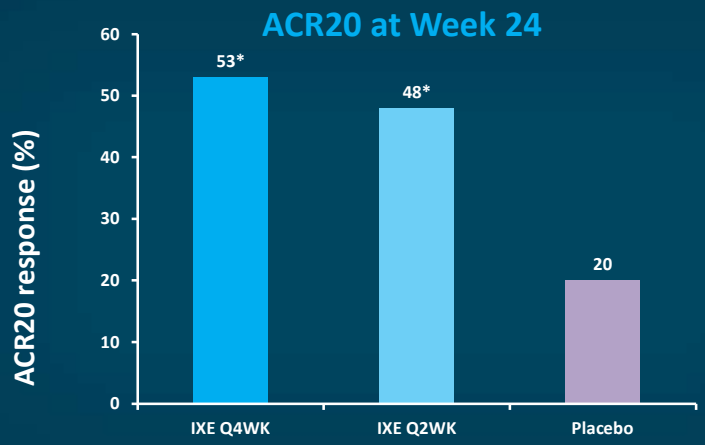
CLEAR Study: Secukinumab (aIL-17A) vs Ustekinumab (aIL-12/23) in Psoriasis



Missing data were imputed as nonresponse; only response-evaluable patients were included.
***P*<0.0001; ****P*=0.0001; †*P*<0.001; ‡P<0.05**
Thaci D, et al. *JAAD*. 2015;73(3):400-409.

146

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



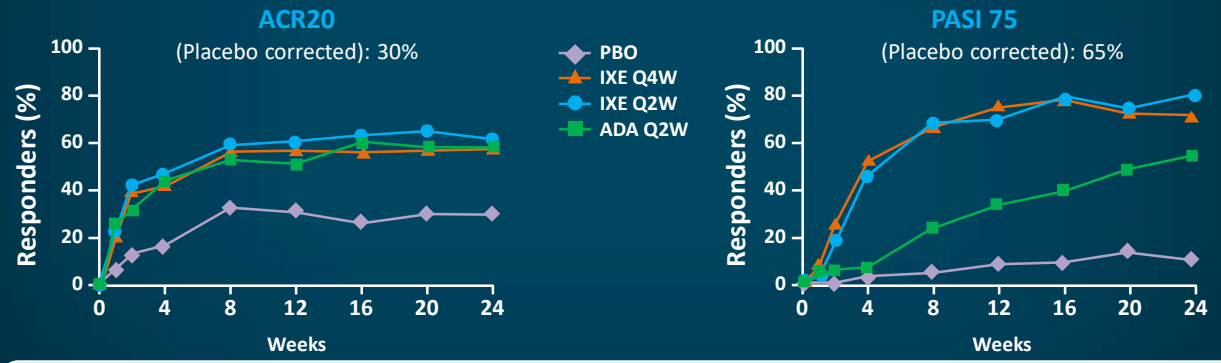
Both the 2-week and 4-week ixekizumab dosing regimens improved the signs and symptoms of patients with active PsA who had an inadequate response to TNFi therapy.

***P*<0.0001 vs placebo**
IXE = ixekizumab.
Nash P, et al. *Lancet*. 2017;389:2317-2327.

147

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*< .01)

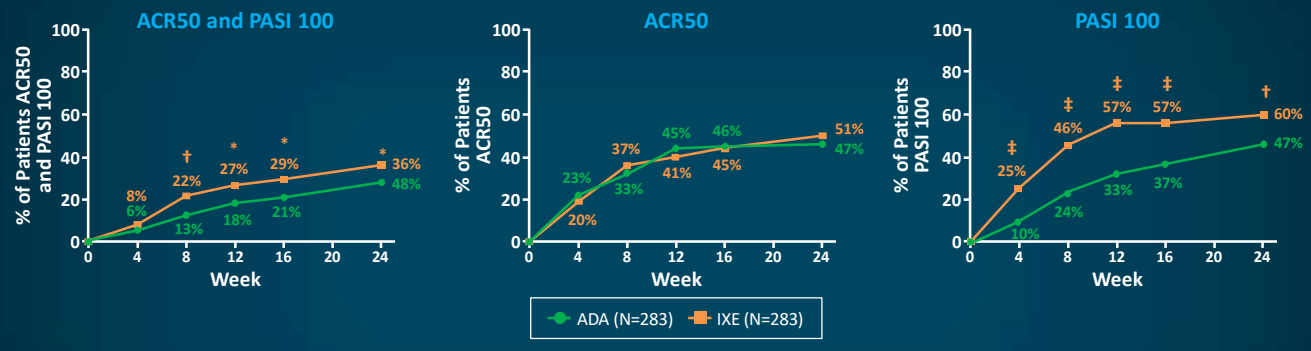


Conclusion: Ixekizumab and adalimumab were both equally better than placebo in PsA. Ixekizumab was better than adalimumab for psoriasis.

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

148

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 PASI 100) 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 PASI 100 response (IXE: 60%, ADA:47%, *P*= .001)

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

csDMARD = conventional synthetic DMARD

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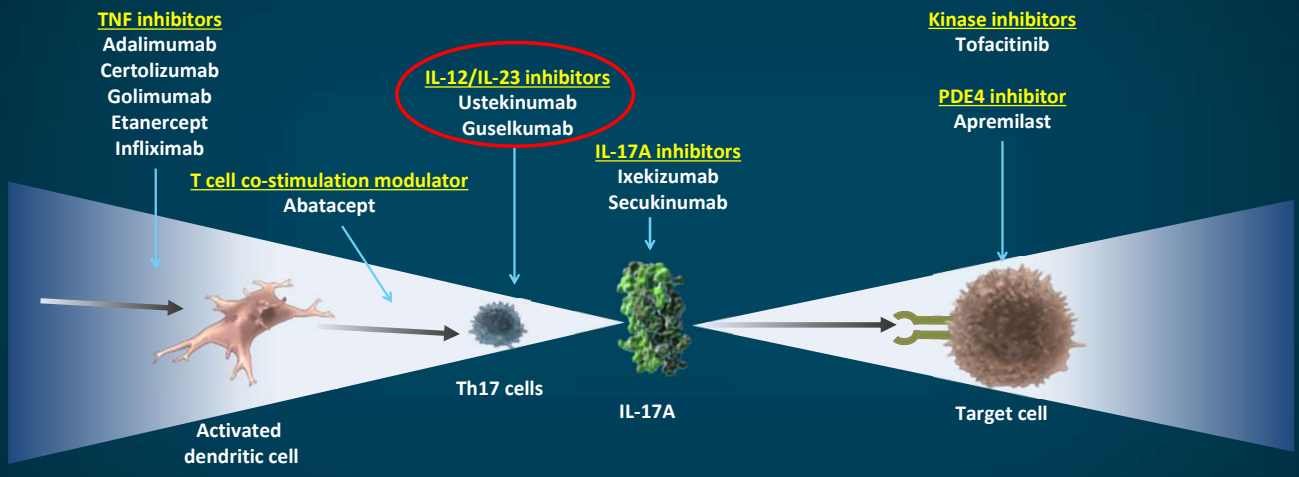
Current and Novel Treatment Options for PsA Treatment



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.

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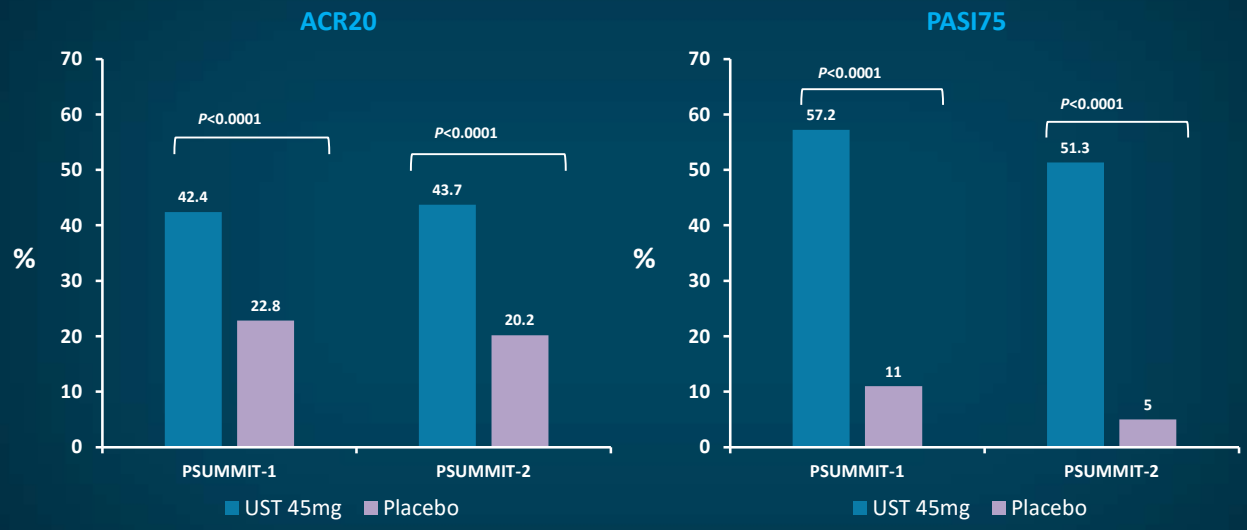
Ustekinumab: Efficacy in PsA



UST = ustekinumab.

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

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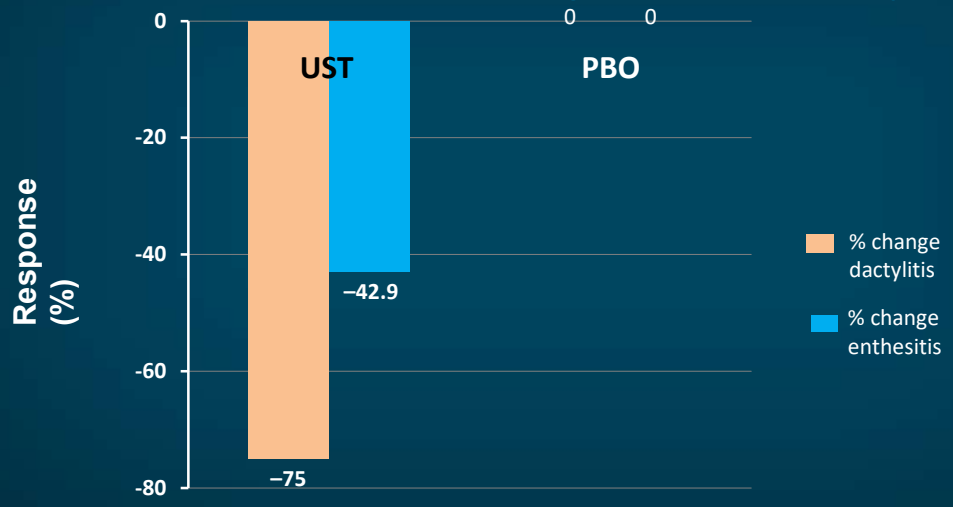
Ustekinumab Is Effective in PsA

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.

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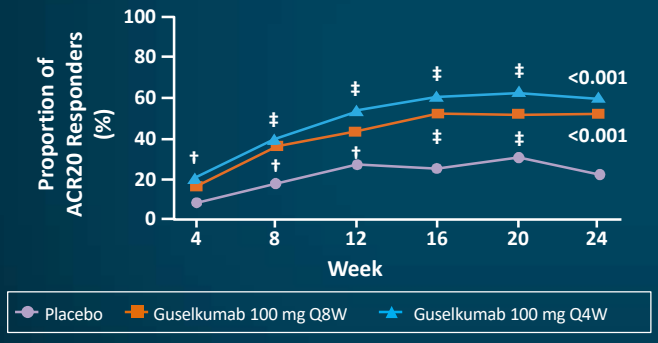
DISCOVER-1 Trial of Guselkumab

- 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 with inadequate response to prior TNFi	11/17 (64.7%)	9/15 (60.0%)	3/12 (25.0%)
% difference vs. placebo (95% CI)	42.4 (11.0, 73.9)	35.9 (0.8, 71.0)	
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.

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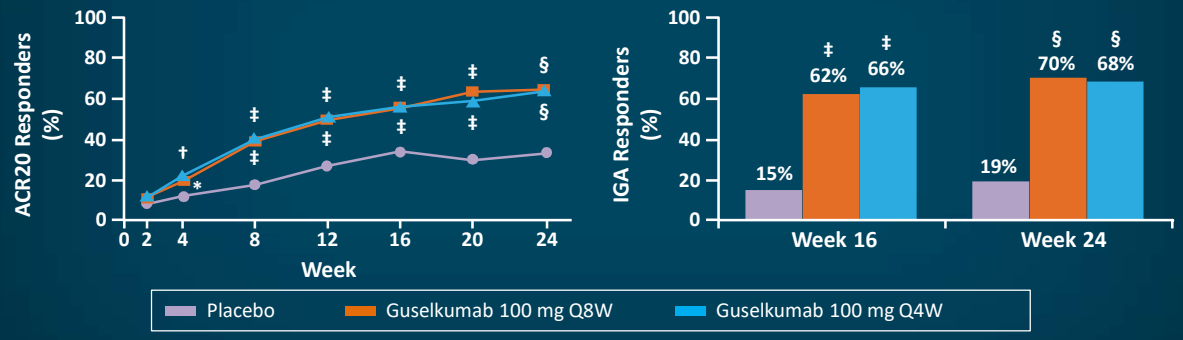
DISCOVER-2 Trial of Guselkumab

- 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.

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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.

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All definitions are defined in the glossary.

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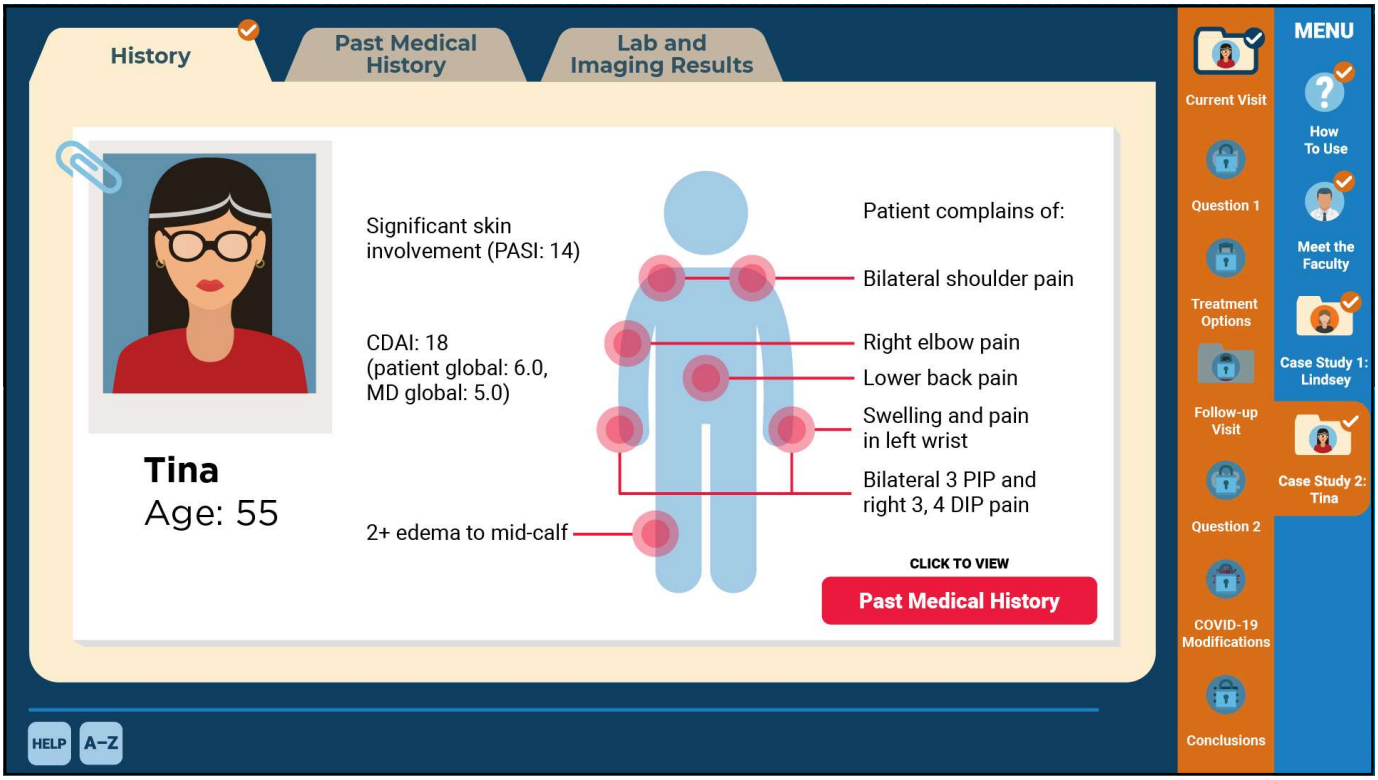
History
Past Medical History
Lab and Imaging Results
Tina
Age: 55
Significant skin involvement (PASI: 14)
CDAI: 18
(patient global: 6.0,
MD global: 5.0)
2+ edema to mid-calf
Patient complains of:
Bilateral shoulder pain
Right elbow pain
Lower back pain
Swelling and pain in left wrist
Bilateral 3 PIP and right 3, 4 DIP pain
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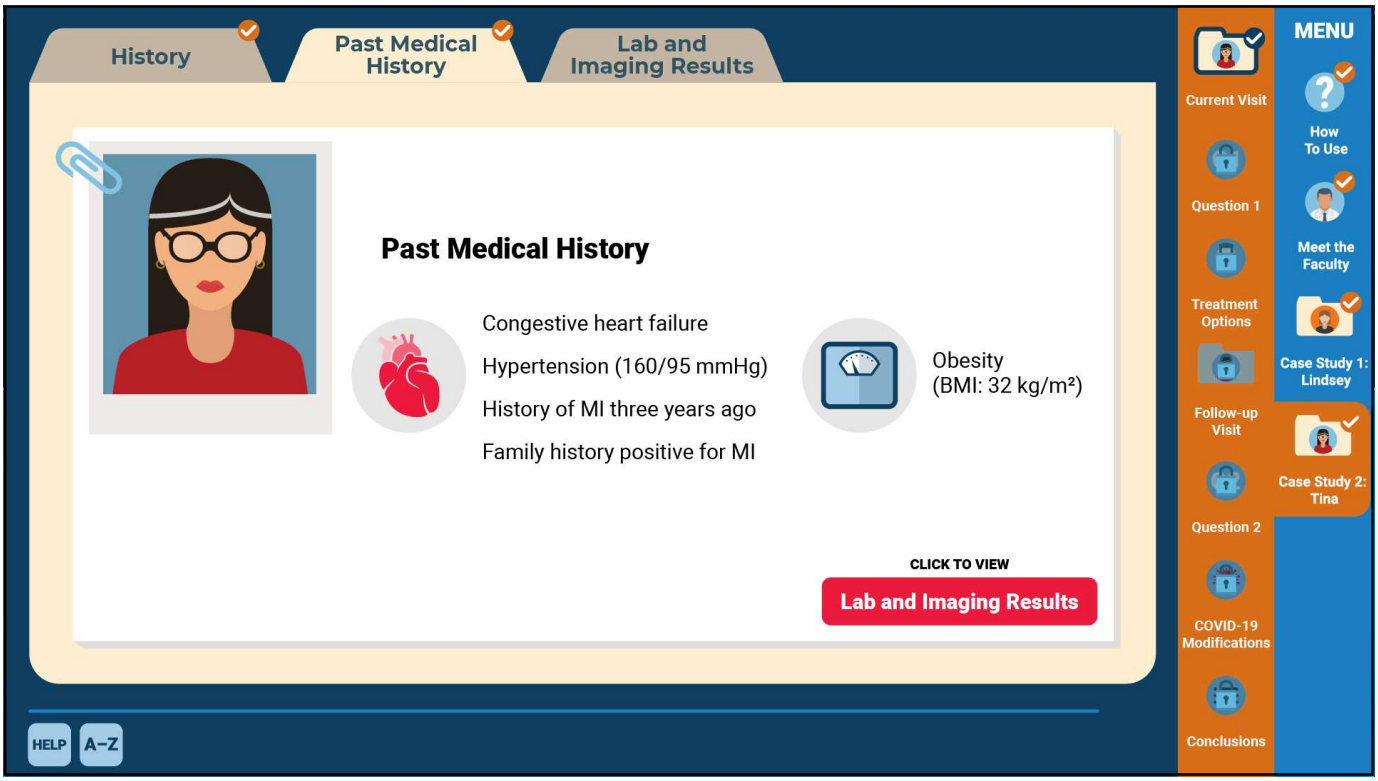
History
Past Medical History
Lab and Imaging Results
Past Medical History
Congestive heart failure
Hypertension (160/95 mmHg)
History of MI three years ago
Family history positive for MI
Obesity (BMI: 32 kg/m²)
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Lab and Imaging Results
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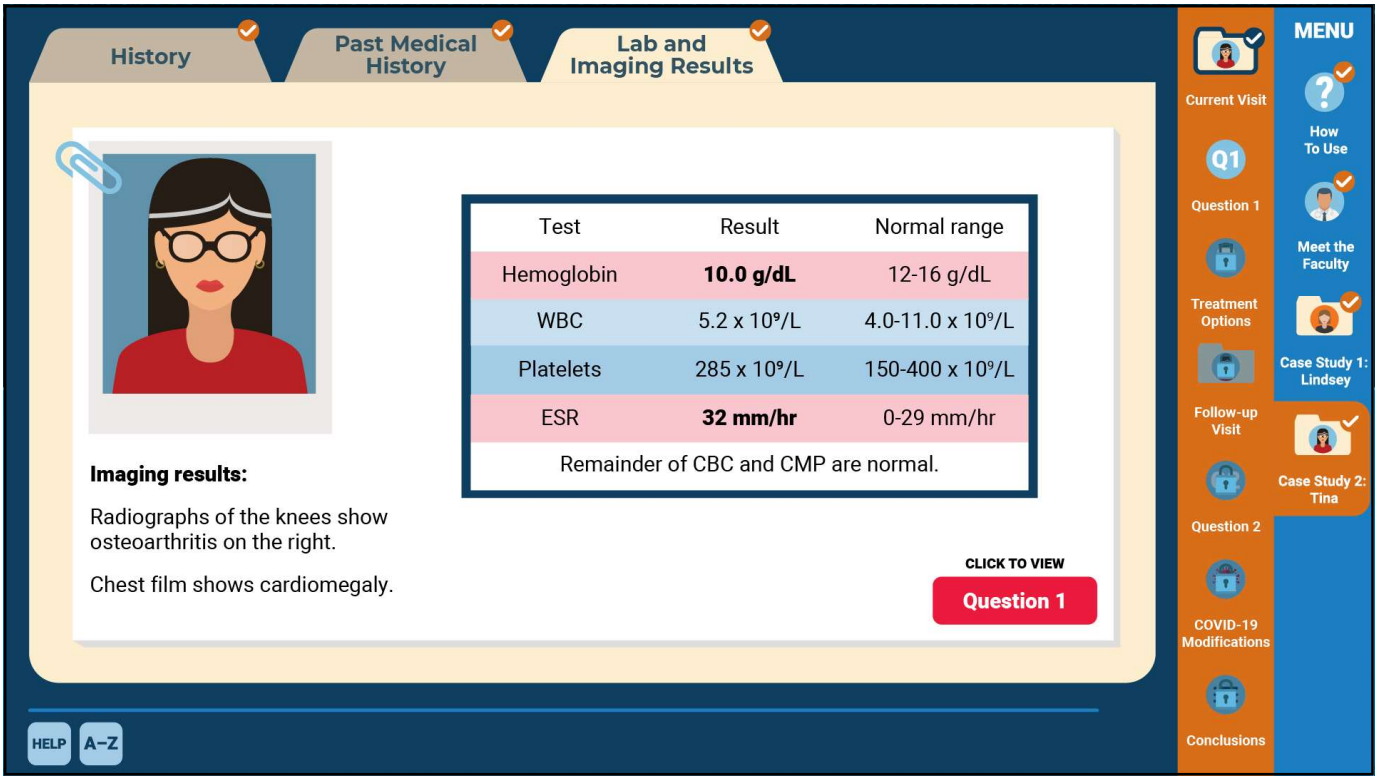
History
Past Medical History
Lab and Imaging Results
Test | Result | Normal range
Hemoglobin | 10.0 g/dL | 12-16 g/dL
WBC | 5.2 x 10⁹/L | 4.0-11.0 x 10⁹/L
Platelets | 285 x 10⁹/L | 150-400 x 10⁹/L
ESR | 32 mm/hr | 0-29 mm/hr
Remainder of CBC and CMP are normal.
Imaging results:
Radiographs of the knees show osteoarthritis on the right.
Chest film shows cardiomegaly.
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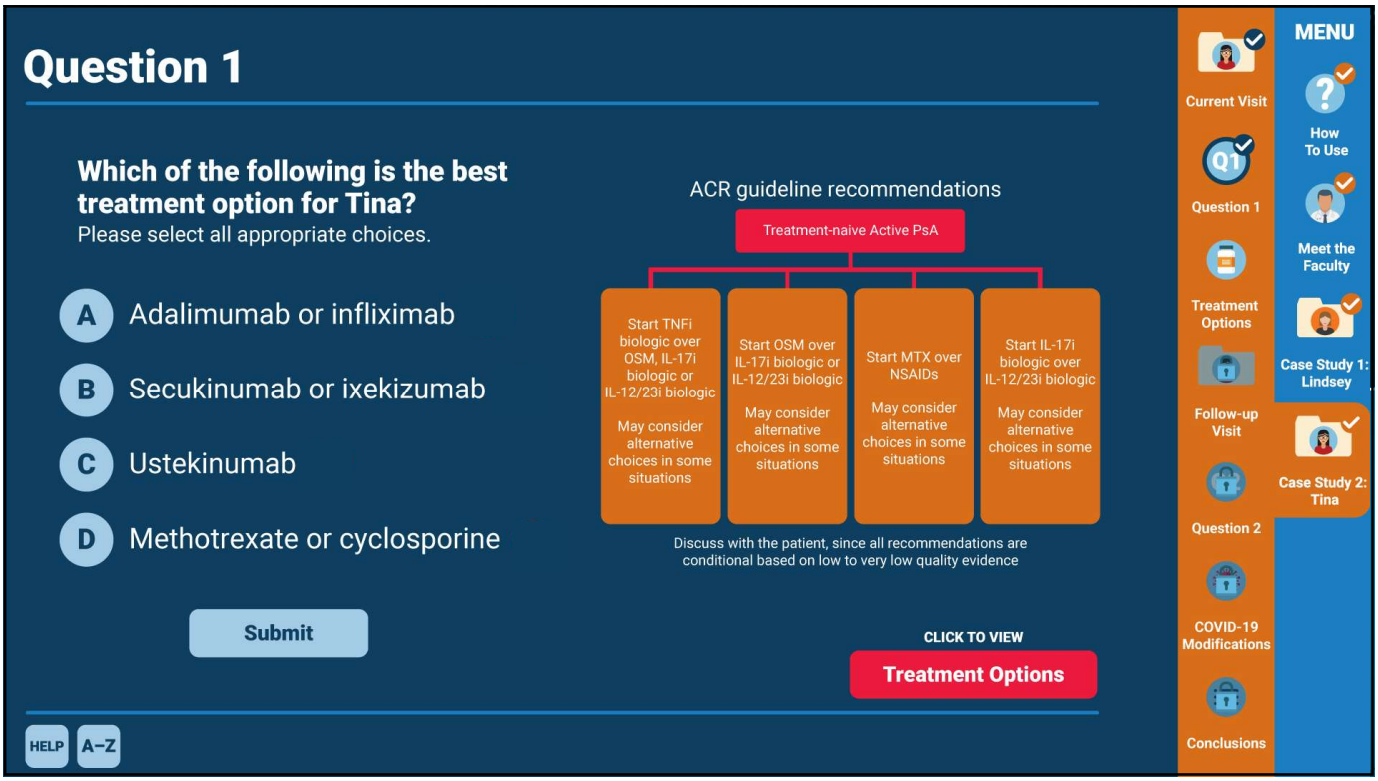
Question 1
Which of the following is the best treatment option for Tina?
Please select all appropriate choices.
A Adalimumab or infliximab
B Secukinumab or ixekizumab
C Ustekinumab
D Methotrexate or cyclosporine
Submit
ACR guideline recommendations
Treatment-naive Active PsA
Start TNFi biologic over OSM, IL-17i biologic or IL-12/23i biologic
May consider alternative choices in some situations
Start OSM over IL-17i biologic or IL-12/23i biologic
May consider alternative choices in some situations
Start MTX over NSAIDs
May consider alternative choices in some situations
Start IL-17i biologic over IL-12/23i biologic
May consider alternative choices in some situations
Discuss with the patient, since all recommendations are conditional based on low to very low quality evidence
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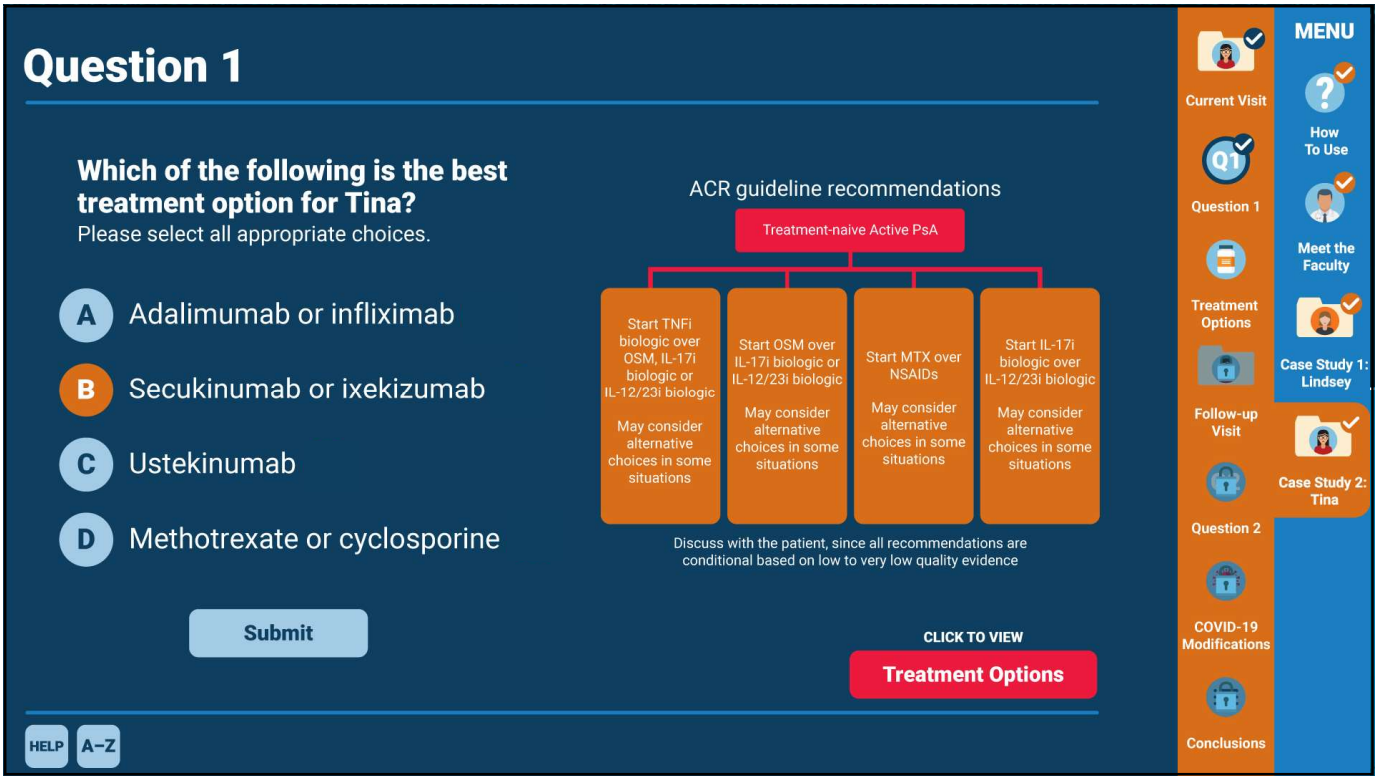
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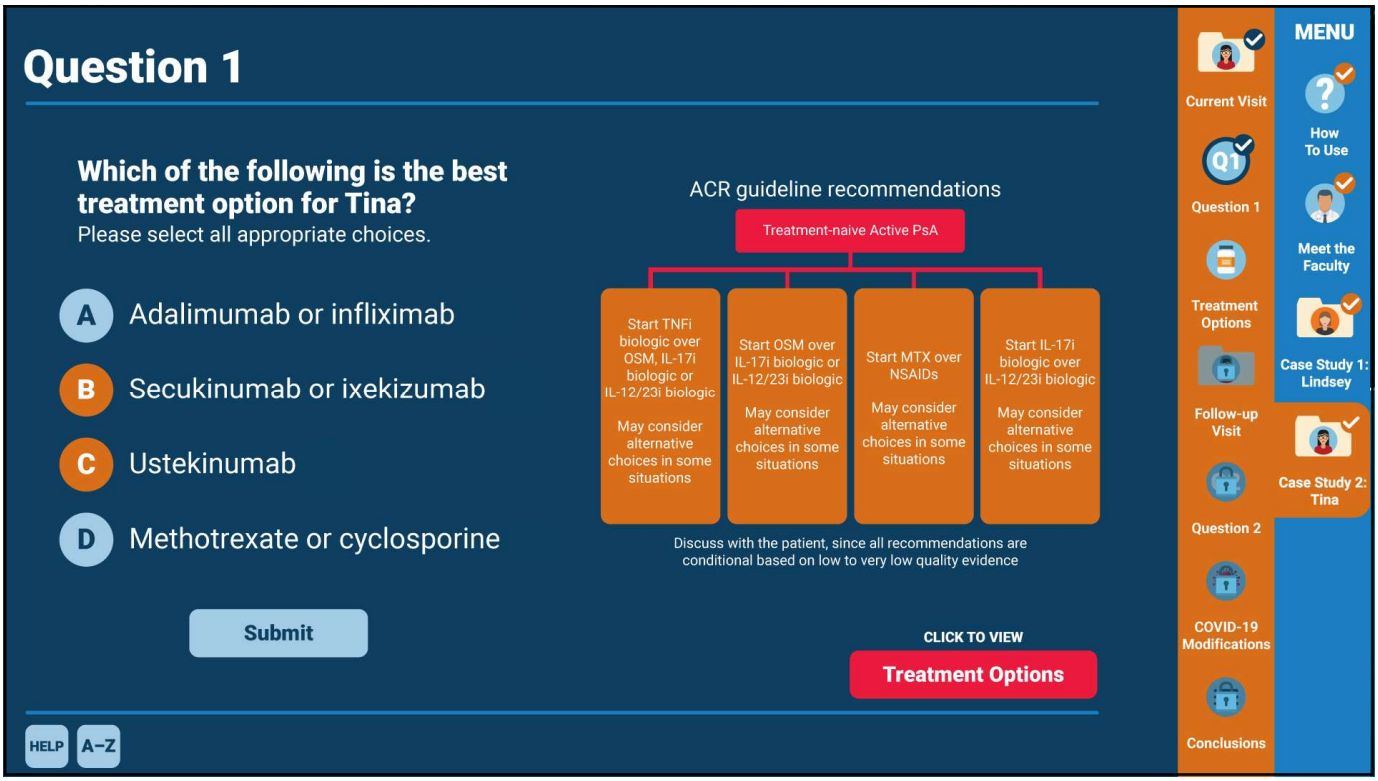
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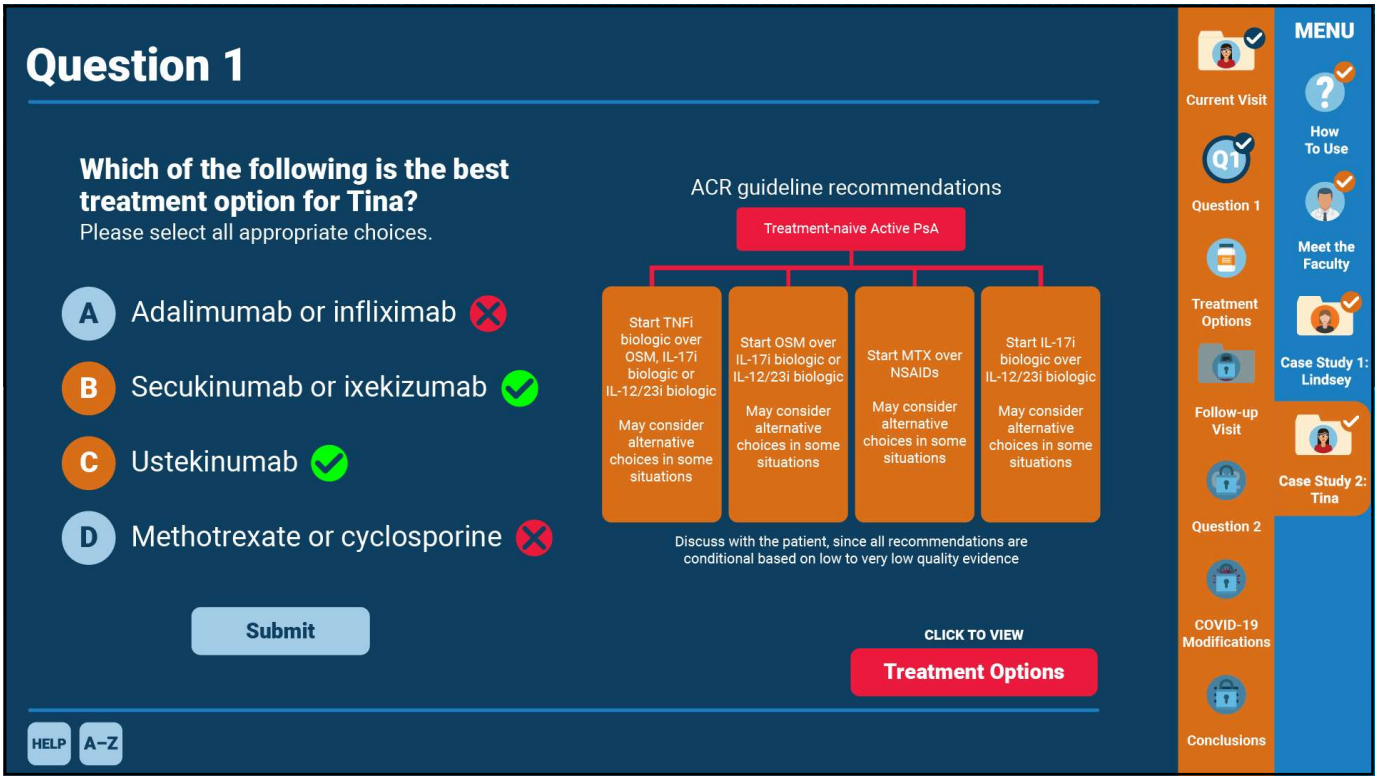
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Treatment-naive Active PsA
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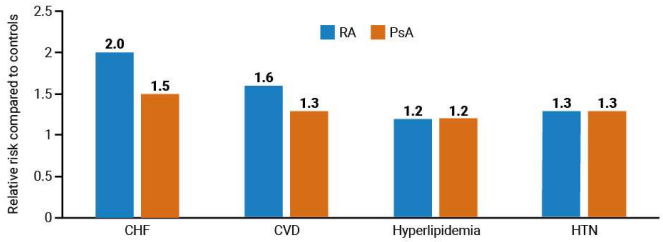
Comorbidities in Rheumatoid and Psoriatic Arthritis | Adalimumab or infliximab | Secukinumab or ixekizumab | Ustekinumab | Methotrexate or cyclosporine

Patients with PsA have an increased risk of cardiovascular complications.

Tina has CHF, hypertension, a history of MI, and obesity.

Relative Risk of Cardiovascular Comorbidities in Patients with RA and PsA



Managed care claims database of >2.7 million patients
28,200 patient had RA (1.02%) and 3,066 patients had PsA (0.11%)
Relative risk of comorbidity (all values p<0.01 compared with controls)

CLICK TO VIEW

Adalimumab or infliximab

HELP | A–Z | Han C, et al. *EULAR* 2005, #OP0160

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Comorbidities in Rheumatoid and Psoriatic Arthritis | Adalimumab or infliximab | Secukinumab or ixekizumab | Ustekinumab | Methotrexate or cyclosporine

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

	Overall
Lymphoma	Rare
CHF (EF<30)	Rare
Hematologic	Very rare
Hepatotoxicity	Very rare
AST/ALT >2x	Uncommon
Demyelinating disease	Rare
Antinuclear antibodies (ANA)	Common

Infections	Overall
Tuberculosis	Rare
Opportunistic	Very rare
Bacterial	Uncommon
Hepatitis B	-
Hepatitis C	-

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Secukinumab or ixekizumab

HELP | A–Z | Zinn NN et al.Hepatol,2005;Clin Infect Dis,2004;Khanna D et al.Drug Safety,2004;Calabrese L et al ARD2006; Strand V..FurstDE,2007(?);Baecklund A&R,2003;Furst DE et al ASRD,2007;Krueger GG et al.NEJM 2007 Noonan et al Neurol,2018(?);Winthrop UP-to-Date;Lee WJ et ao,Rheum 2018;Cannizzaro MV et al Psoriasis,2017

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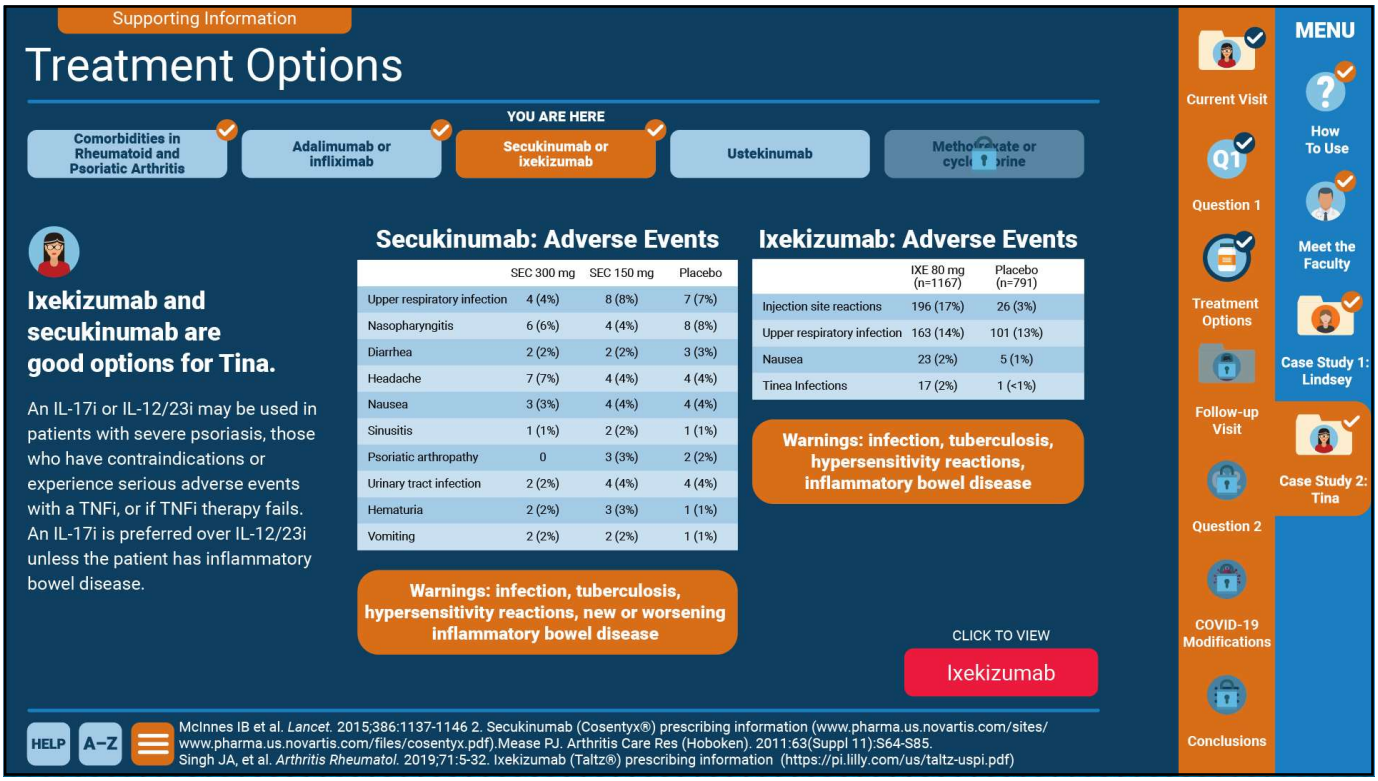
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Comorbidities in Rheumatoid and Psoriatic Arthritis
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Secukinumab or ixekizumab
Ustekinumab
Methotrexate or cyclosporine
Ixekizumab and secukinumab are good options for Tina.
An IL-17i or IL-12/23i 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.
Secukinumab: Adverse Events
SEC 300 mg | SEC 150 mg | Placebo
Upper respiratory infection 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: infection, tuberculosis, hypersensitivity reactions, new or worsening inflammatory bowel disease
Ixekizumab: Adverse Events
IXE 80 mg (n=1167) | Placebo (n=791)
Injection site reactions 196 (17%) 26 (3%)
Upper respiratory infection 163 (14%) 101 (13%)
Nausea 23 (2%) 5 (1%)
Tinea Infections 17 (2%) 1 (<1%)
Warnings: infection, tuberculosis, hypersensitivity reactions, inflammatory bowel disease
CLICK TO VIEW
Ixekizumab
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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).Mease PJ. Arthritis Care Res (Hoboken). 2011:63(Suppl 11):S64-S85.
Singh JA, et al. Arthritis Rheumatol. 2019;71:5-32. Ixekizumab (Taltz®) prescribing information (https://pi.lilly.com/us/taltz-uspi.pdf)
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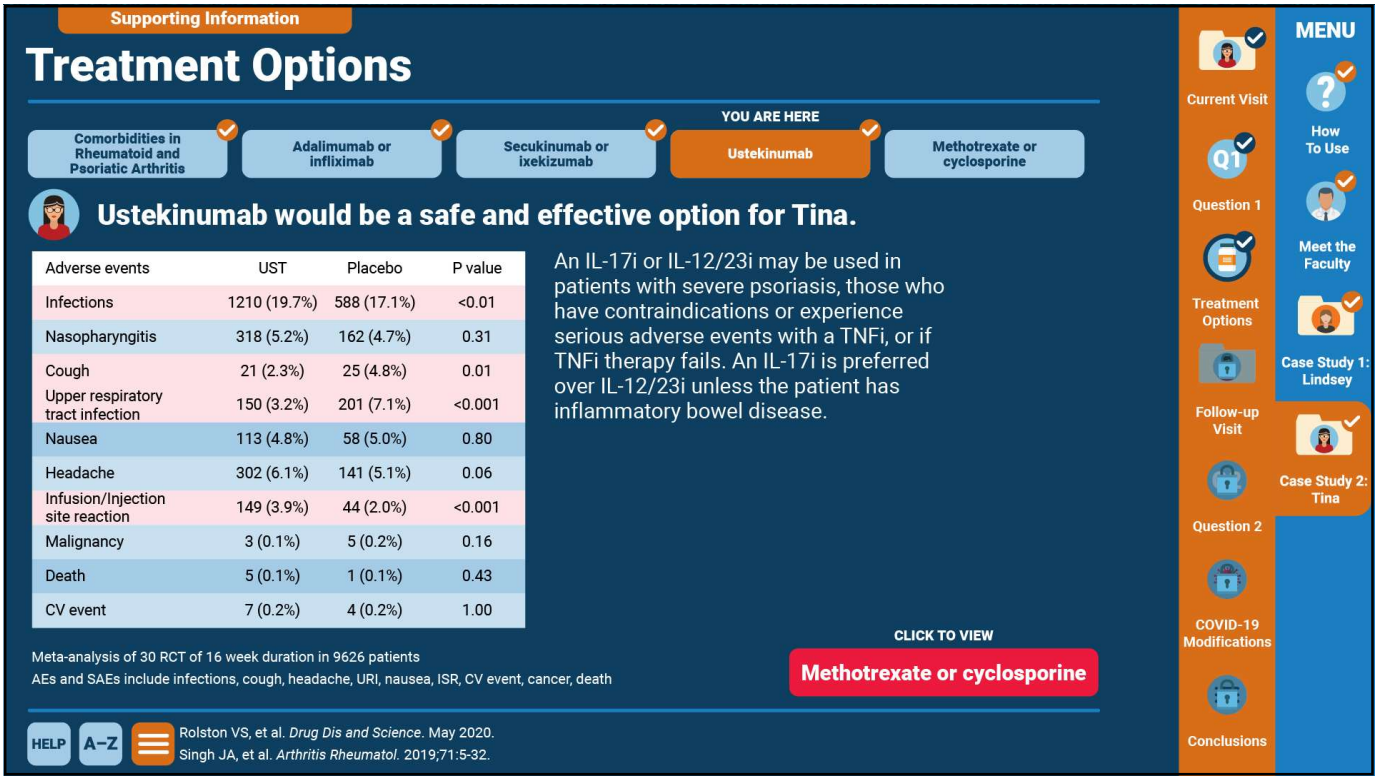
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Comorbidities in Rheumatoid and Psoriatic Arthritis
Adalimumab or infliximab
Secukinumab or ixekizumab
Ustekinumab
Methotrexate or cyclosporine
Ustekinumab would be a safe and effective option for Tina.
Adverse events | UST | Placebo | P value
Infections 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 event 7 (0.2%) 4 (0.2%) 1.00
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
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.
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Methotrexate or cyclosporine
HELP
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Rolston VS, et al. Drug Dis and Science. May 2020.
Singh JA, et al. Arthritis Rheumatol. 2019;71:5-32.
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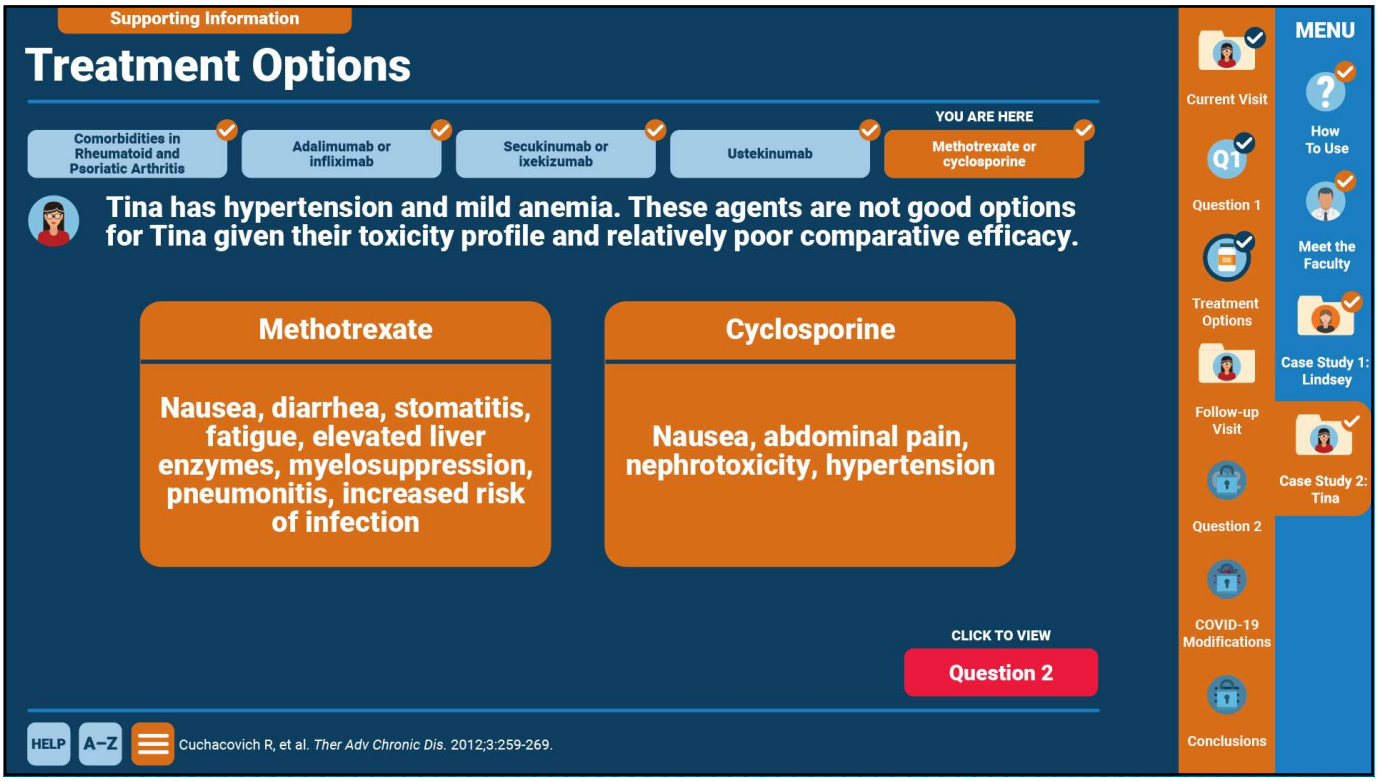
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Methotrexate or cyclosporine
Tina has hypertension and mild anemia. These agents are not good options for Tina given their toxicity profile and relatively poor comparative efficacy.
Methotrexate
Nausea, diarrhea, stomatitis, fatigue, elevated liver enzymes, myelosuppression, pneumonitis, increased risk of infection
Cyclosporine
Nausea, abdominal pain, nephrotoxicity, hypertension
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Cuchacovich R, et al. Ther Adv Chronic Dis. 2012;3:259-269.
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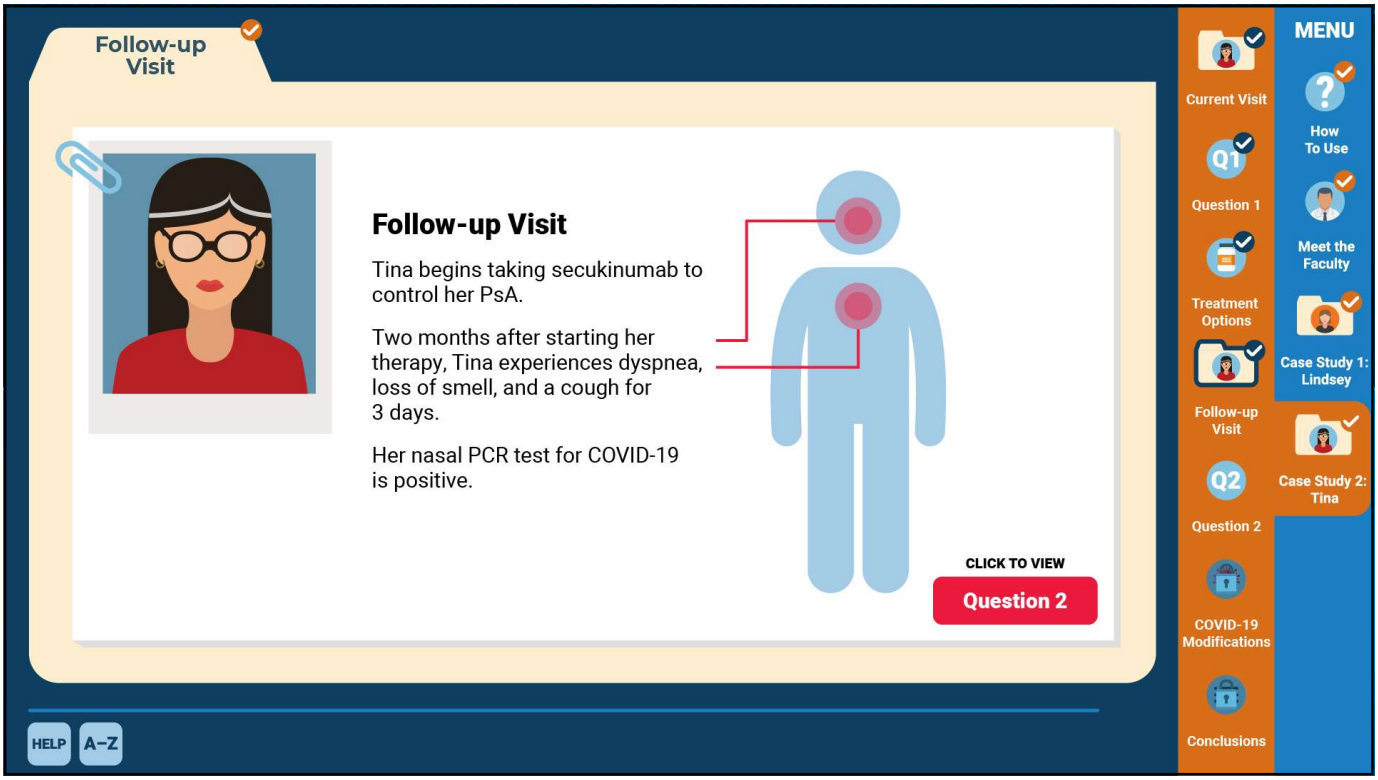
Follow-up Visit
Follow-up Visit
Tina begins taking secukinumab to control her PsA.
Two months after starting her therapy, Tina experiences dyspnea, loss of smell, and a cough for 3 days.
Her nasal PCR test for COVID-19 is positive.
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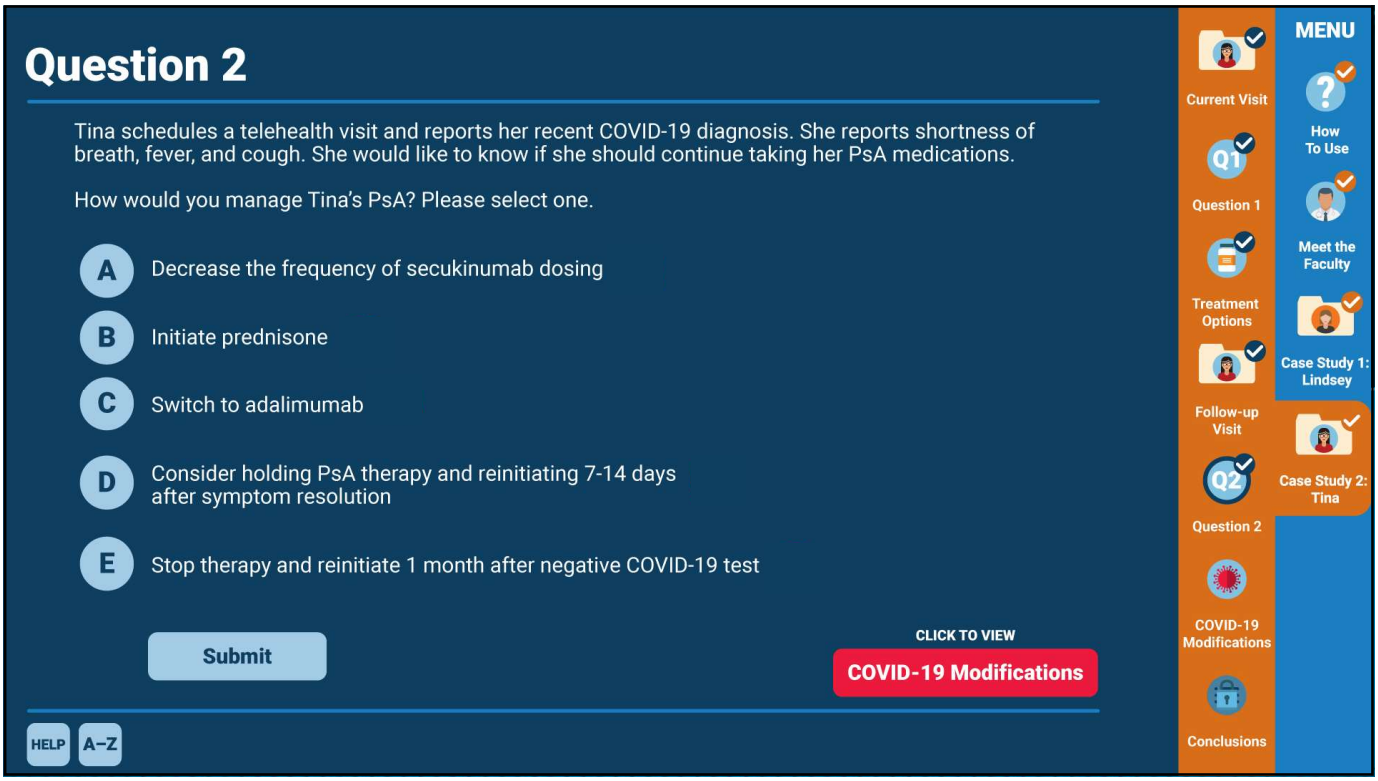
Question 2
Tina schedules a telehealth visit and reports her recent COVID-19 diagnosis. She reports shortness of breath, fever, and cough. She would like to know if she should continue taking her PsA medications.
How would you manage Tina's PsA? Please select one.
A Decrease the frequency of secukinumab 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
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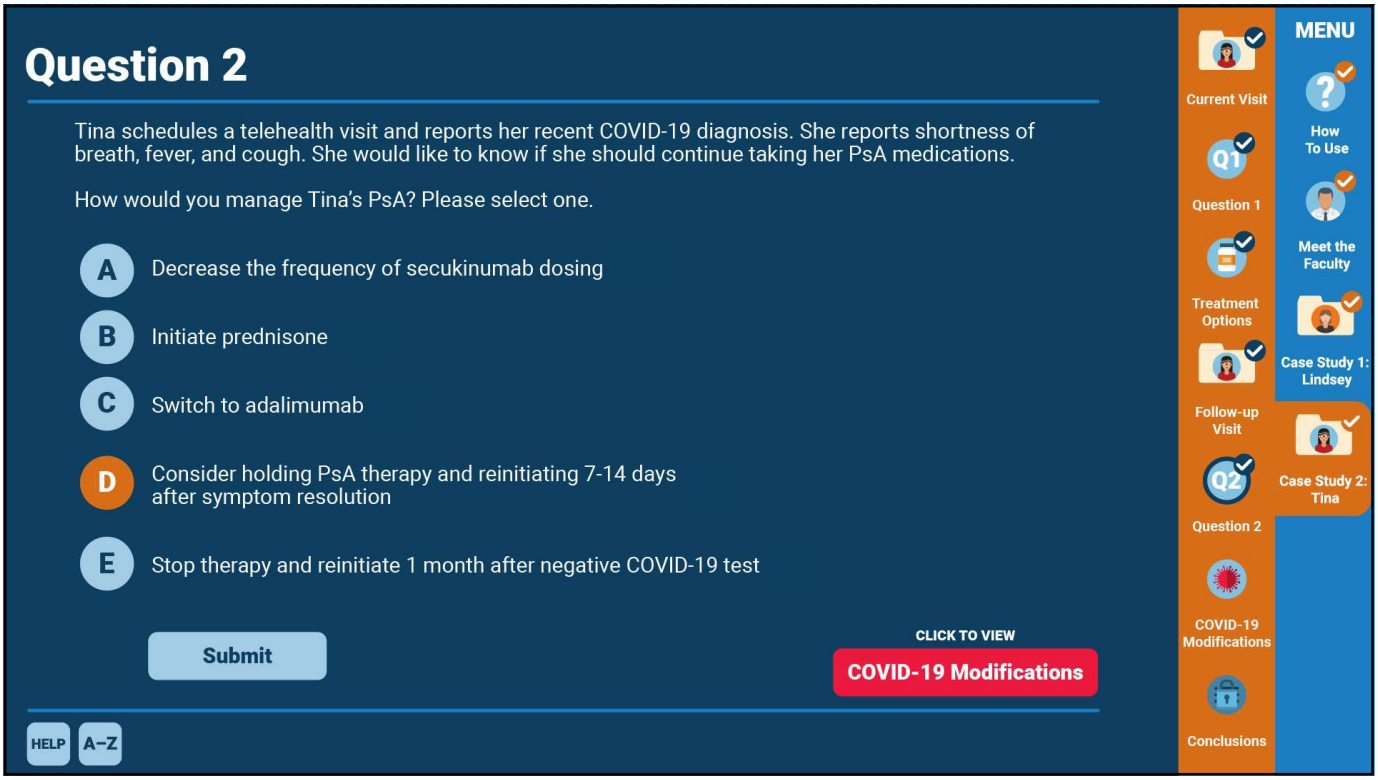
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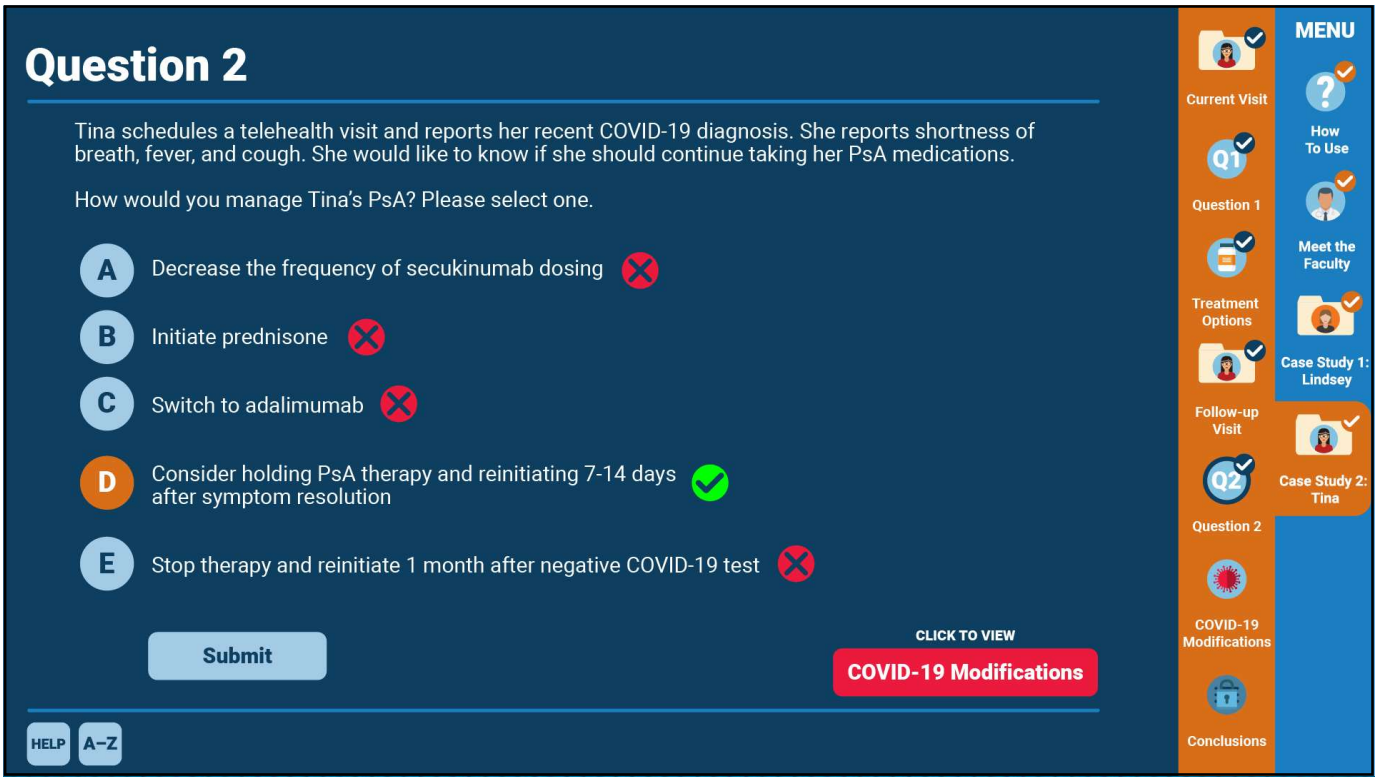
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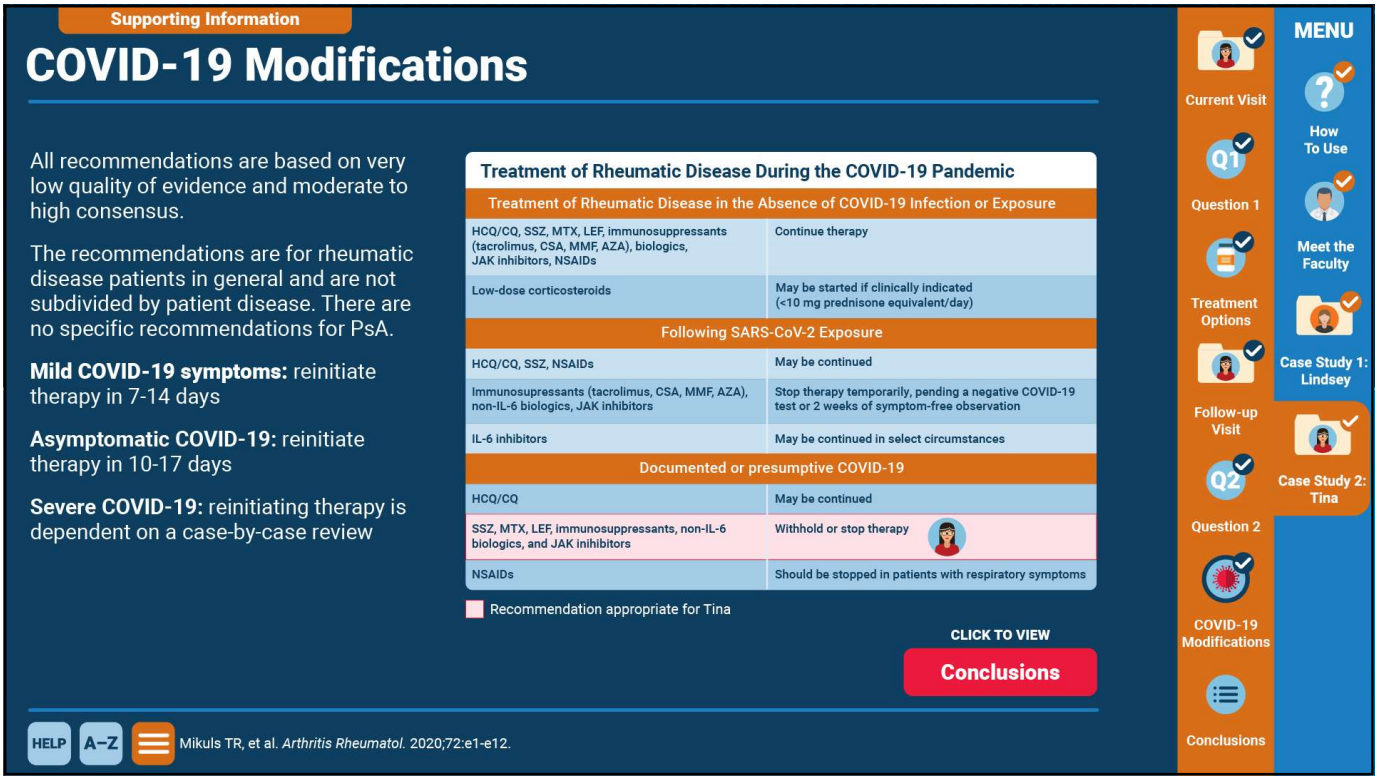
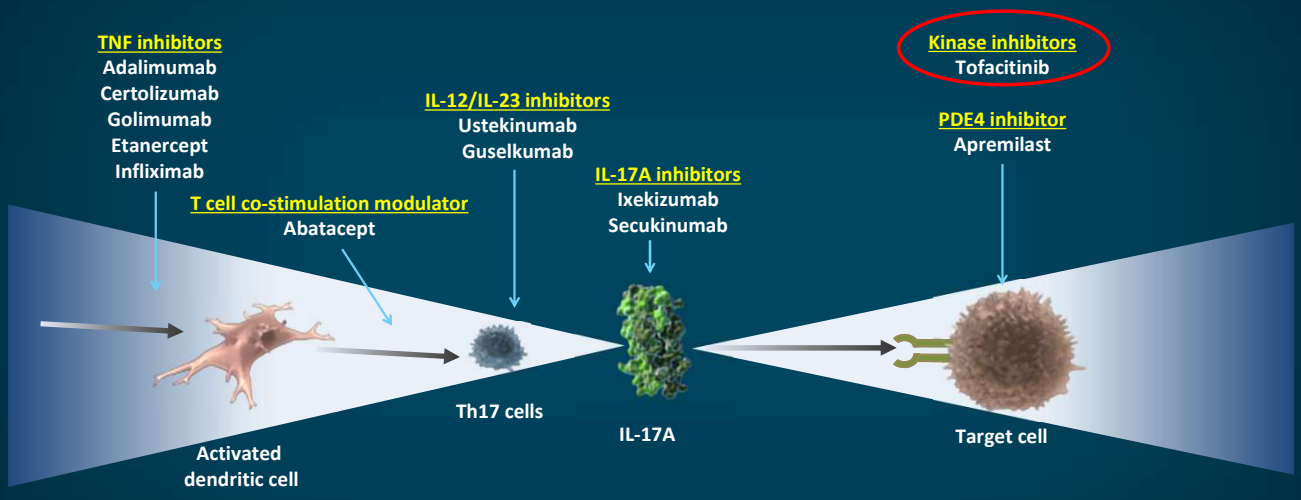

Supporting Information
COVID-19 Modifications
All recommendations are based on very low quality of evidence and moderate to high consensus.
The recommendations are for rheumatic disease patients in general and are not subdivided by patient disease. There are no specific recommendations for PsA.
Mild 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
Treatment of Rheumatic Disease During the COVID-19 Pandemic
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
Immunosupressants (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 respiratory symptoms
Recommendation appropriate for Tina
CLICK TO VIEW
Conclusions
HELP
A–Z
Mikuls TR, et al. Arthritis Rheumatol. 2020;72:e1-e12.
MENU
Current Visit
How To Use
Question 1
Meet the Faculty
Treatment Options
Case Study 1: Lindsey
Follow-up Visit
Case Study 2: Tina
Question 2
COVID-19 Modifications
Conclusions

173

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.

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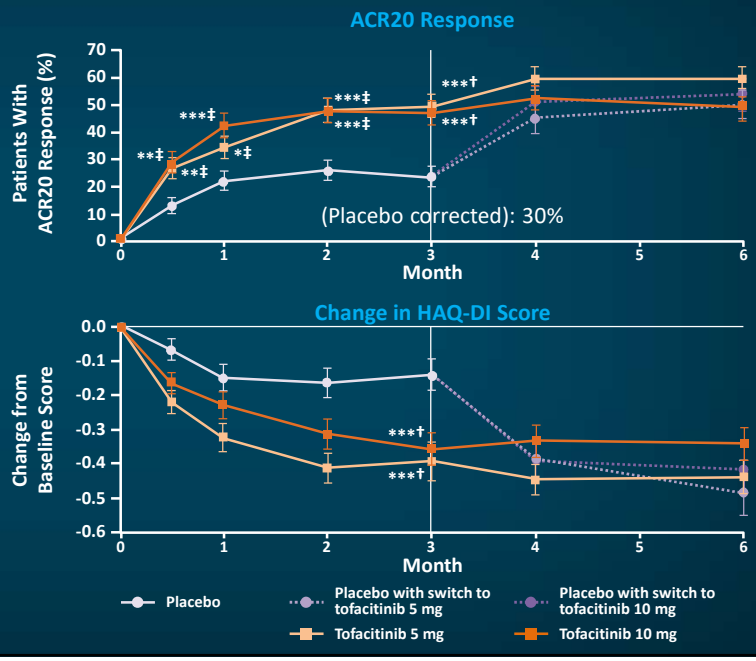
Efficacy of Tofacitinib in PSA

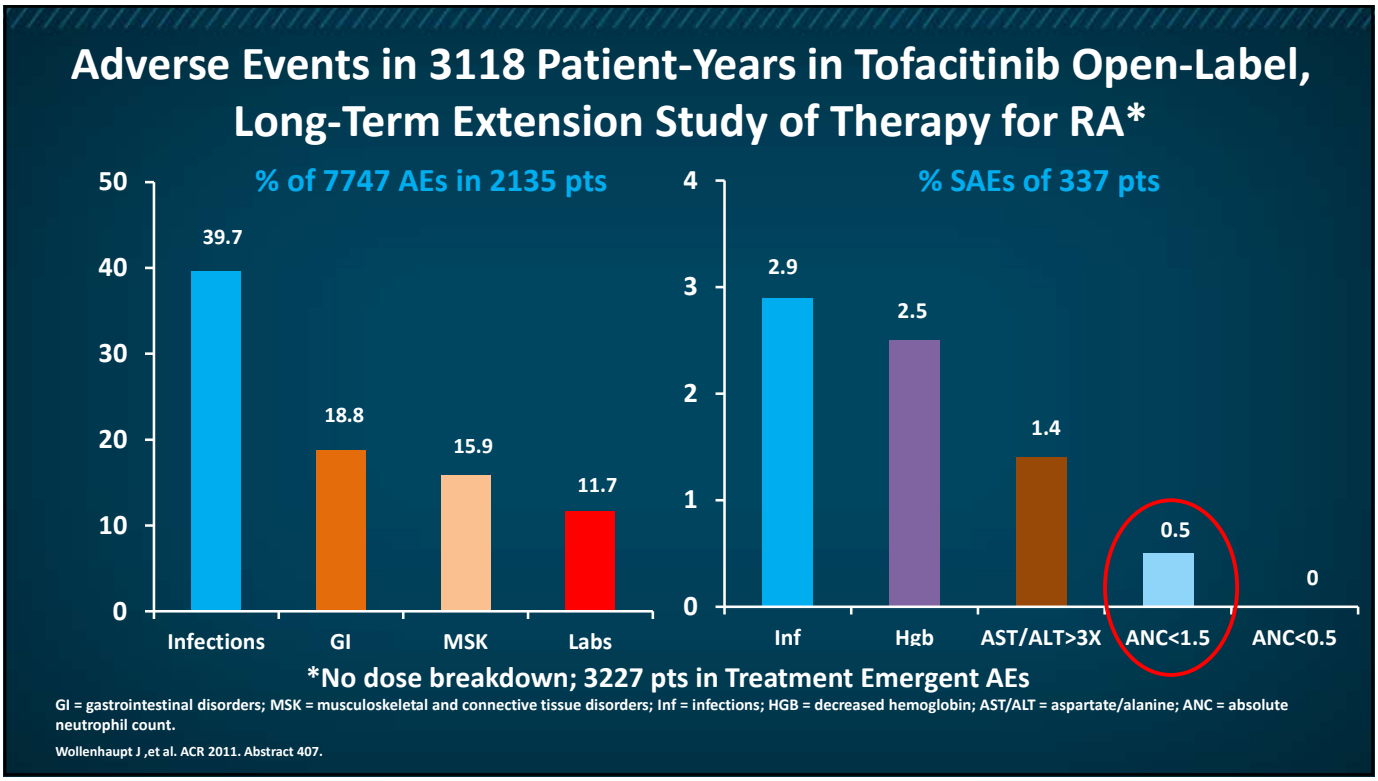
- 395 patients with active PsA and an inadequate response to TNFi were randomized to:
  - Tofacitinib 5 mg BID
  - Tofacitinib 10 mg BID
  - Placebo, with a switch to 5 mg or 10 mg tofacitinib BID at 3 months
- No efficacy noted on Leeds Enthesitis Index, Dactylitis Severity Score, FACIT-F total score,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

175


Adverse Events in 3118 Patient-Years in Tofacitinib Open-Label, Long-Term Extension Study of Therapy for RA*
% of 7747 AEs in 2135 pts
50
40
30
20
10
0
39.7
18.8
15.9
11.7
Infections
GI
MSK
Labs
% SAEs of 337 pts
4
3
2
1
0
2.9
2.5
1.4
0.5
0
Inf
Hgb
AST/ALT>3X
ANC<1.5
ANC<0.5
*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.

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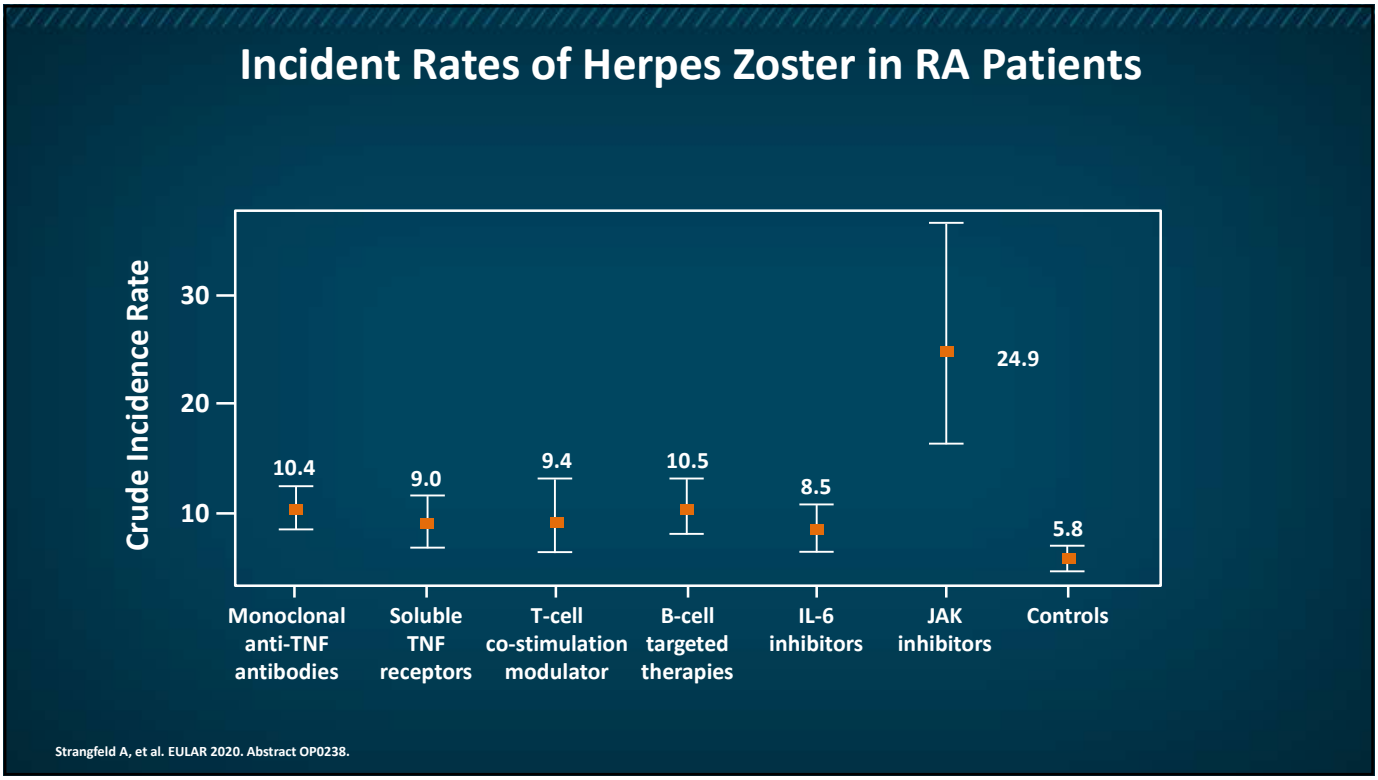
Incident Rates of Herpes Zoster in RA Patients
Crude Incidence Rate
30
20
10
10.4
9.0
9.4
10.5
8.5
24.9
5.8
Monoclonal anti-TNF antibodies
Soluble TNF receptors
T-cell co-stimulation modulator
B-cell targeted therapies
IL-6 inhibitors
JAK inhibitors
Controls
Strangfeld A, et al. EULAR 2020. Abstract OP0238.

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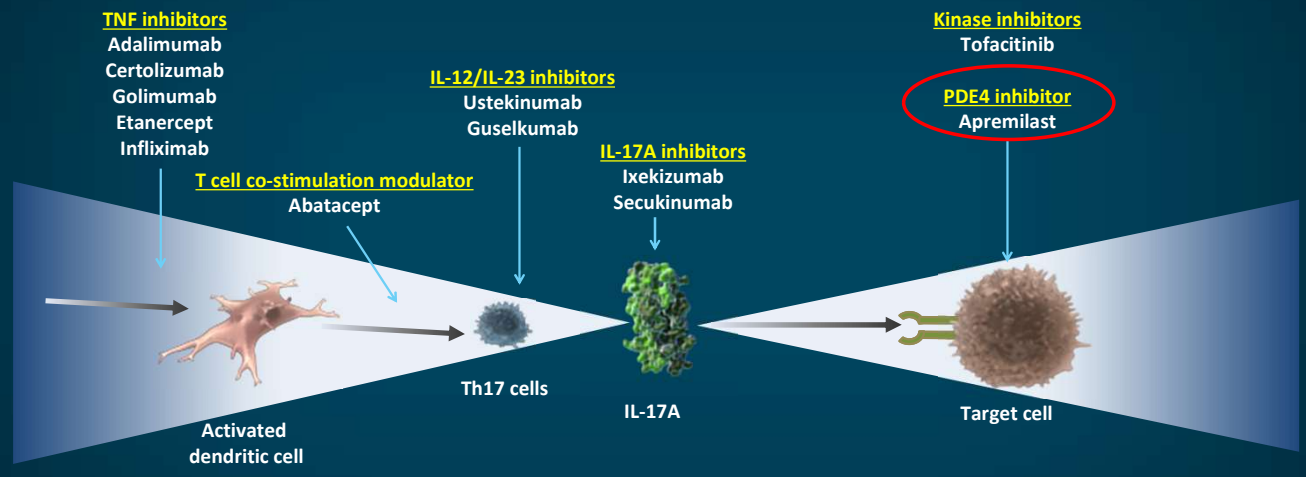
Current and Novel Treatment Options for PsA Treatment



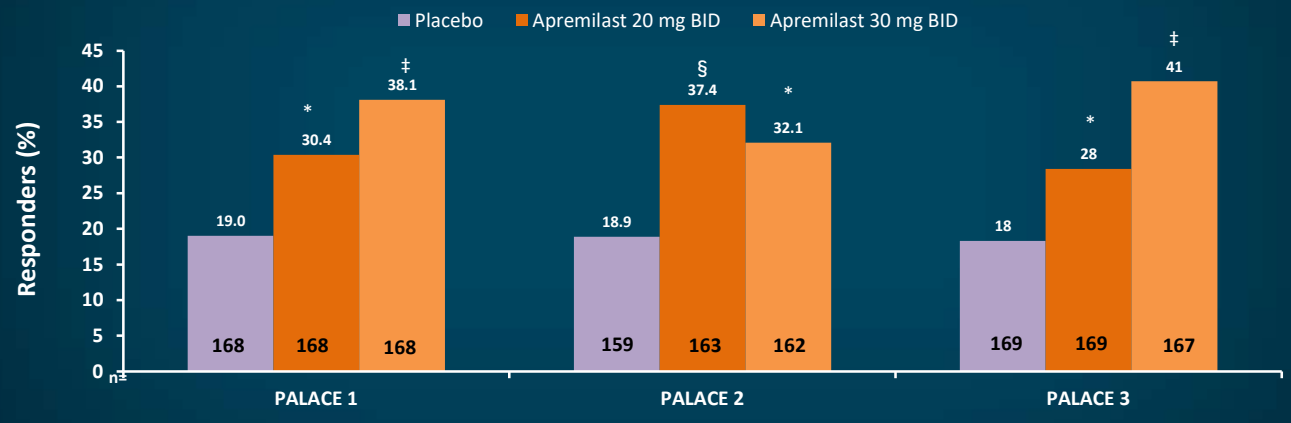
Adapted from Nestle FO et al. *N Engl J Med*. 2009;361:496-509. Kopf M et al. *Nat Rev Drug Discov*. 2010;9:703-718. Garber K. *Nat Biotechnol.* 2011;29:563-566. Thanks to Iain McInnes.

178

Apremilast in PsA: PALACE 1, 2, and 3

Primary endpoint across studies: ACR20 response at week 16

ITT population (NRI)



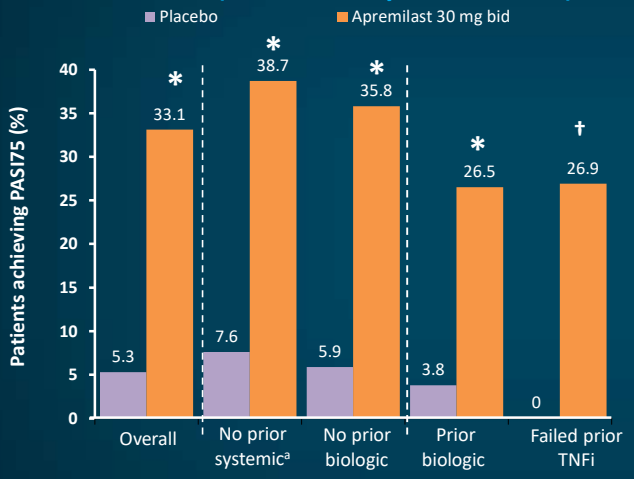
*P<0.05; §P<0.005; ‡P≤0.0001 vs placebo.
NRI = non-responder imputation

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.

179

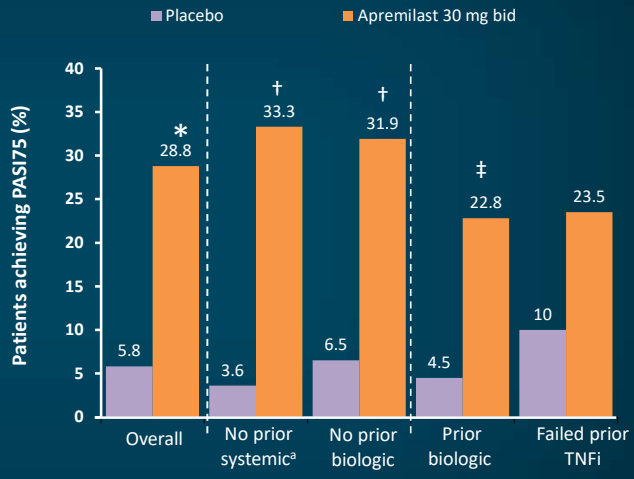
Apremilast in Moderate-to-Severe Psoriasis

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

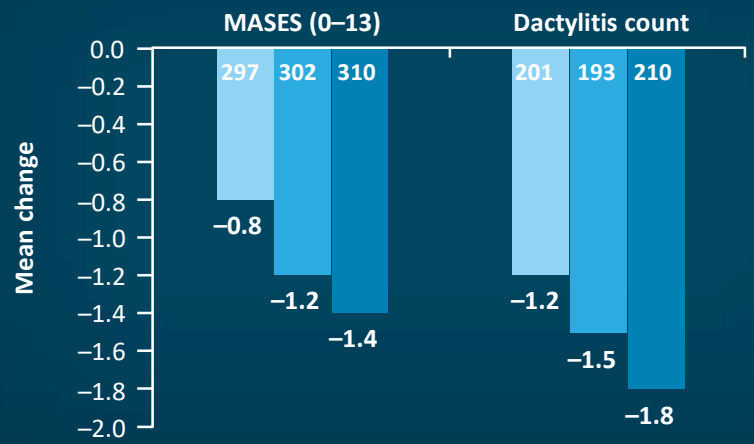
LOCF = last observation carried forward.

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.

180

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).

181

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)
URTI	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]:

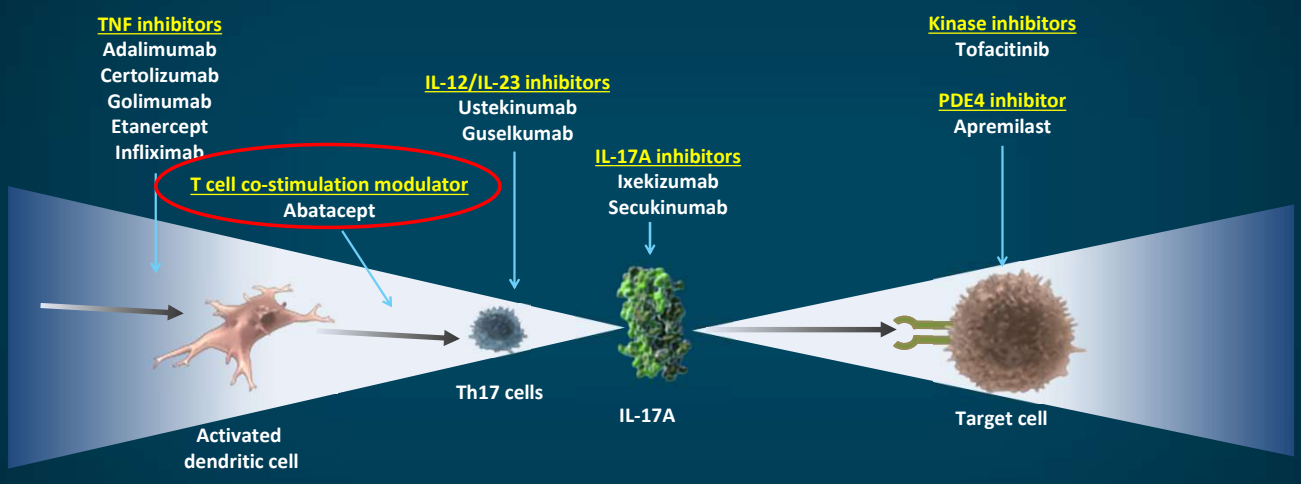
1. Depression and suicidal behavior
2. Weight loss

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).

182

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.

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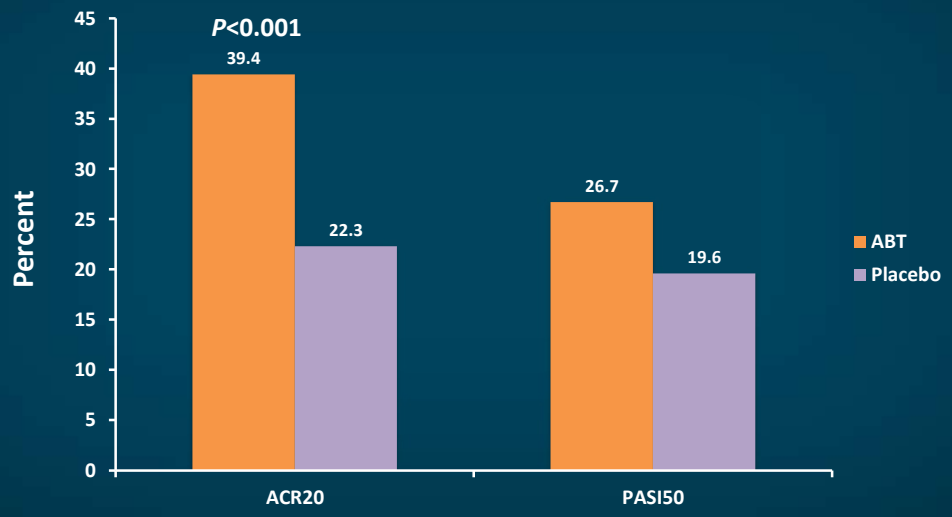
Abatacept: Phase III Trial



ABT = abatacept.

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

184

Decision Aid

185

Initial Presentation

- Carol is a 55-year old woman who reports worsening pain and stiffness in her fingers, ankle pain, and swelling of her finger and elbow
- Physical exam:
  - **Tenderness in right 3 DIPs, bilateral 4 PIPs**
  - Left elbow swollen and tender
  - Right ankle swollen with **enthesitis** present
  - CDAI: 20
- Plaque psoriasis present on elbows, forearms, trunk and scalp
  - Scaling with minor fissures. PASI: 12

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History of Present Illness

- PMH: **hypertension, type 2 diabetes, obesity**
- Diagnosed with psoriasis 8 years ago and PsA 1 year ago
- Initially managed with methotrexate (15 mg/week)
  - Elevated AST and ALT 2 months after starting methotrexate
  - Methotrexate discontinued
- Carol is currently taking **etanercept** 50 mg/week

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Lab Results

Lab	Results	Normal Range
Hemoglobin	13 g/dL	12.0-15.5 g/dL
WBC	6800 cells/µL	4500-11,000 cells/µL
ESR	**27 mm/hr**	0-22 mm/hr
RF	9 IU/mL	0-20 IU/mL
CCP	12 u/mL	0-20 u/mL
CRP	**70 mg/L**	<10 mg/L
HbA1c	7.1%	<5.7%

- Carol reports that her husband was diagnosed with COVID-19 last week
  - Carol does not have any symptoms of COVID-19

How would you manage this patient?

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Decision Tree for the Management of Psoriatic Arthritis

This activity is best viewed on Google Chrome or Mozilla Firefox. Free downloads are available here:

Download Chrome | Download Firefox

Progress will be lost if this activity is closed, please do not close the activity until it is completed.

Begin Activity

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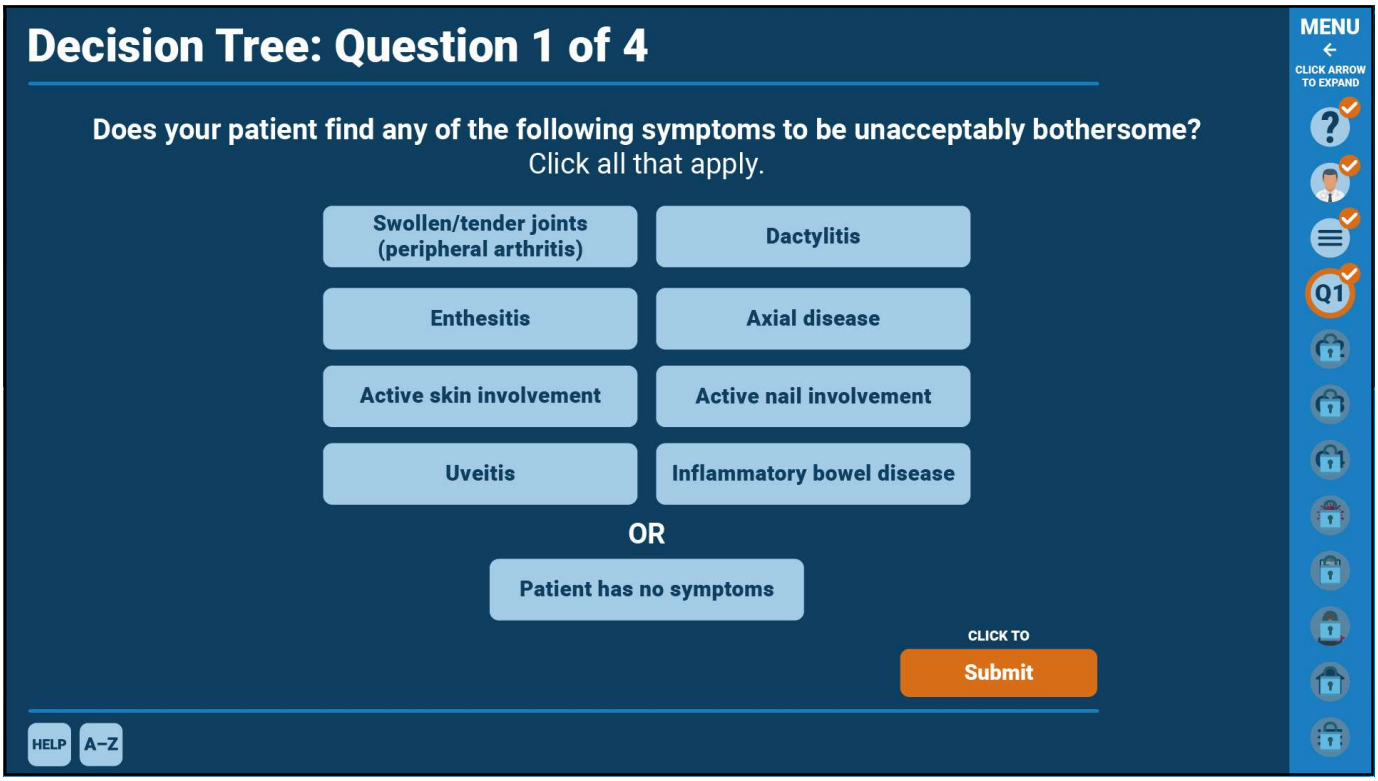
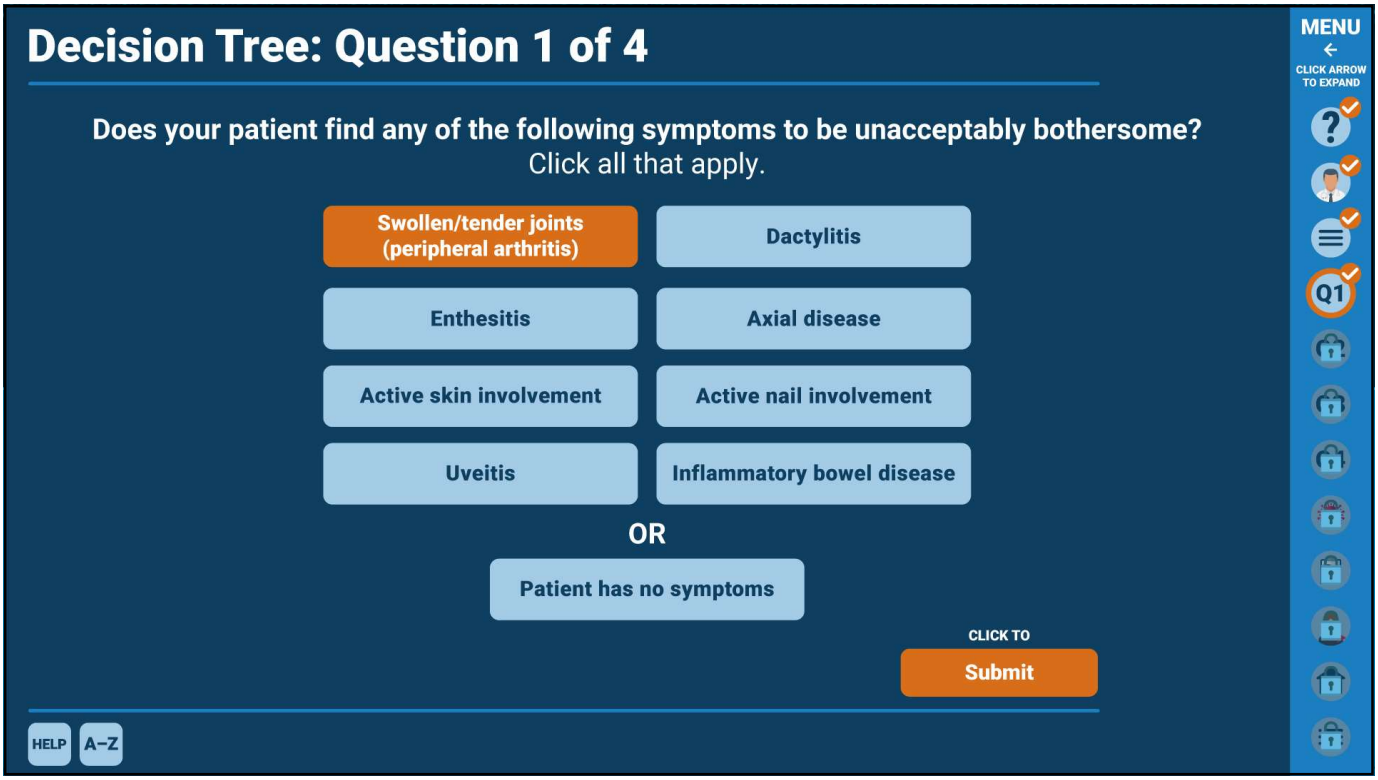

Decision Tree: Question 1 of 4
MENU
CLICK ARROW TO EXPAND
Does your patient find any of the following symptoms to be unacceptably bothersome?
Click all that apply.
Swollen/tender joints (peripheral arthritis)
Dactylitis
Enthesitis
Axial disease
Active skin involvement
Active nail involvement
Uveitis
Inflammatory bowel disease
OR
Patient has no symptoms
CLICK TO
Submit
HELP
A–Z
Q1

190


Decision Tree: Question 1 of 4
MENU
CLICK ARROW TO EXPAND
Does your patient find any of the following symptoms to be unacceptably bothersome?
Click all that apply.
Swollen/tender joints (peripheral arthritis)
Dactylitis
Enthesitis
Axial disease
Active skin involvement
Active nail involvement
Uveitis
Inflammatory bowel disease
OR
Patient has no symptoms
CLICK TO
Submit
HELP
A–Z
Q1

191

Decision Tree: Question 1 of 4

MENU
CLICK ARROW TO EXPAND

Does your patient find any of the following symptoms to be unacceptably bothersome?
Click all that apply.

- Swollen/tender joints (peripheral arthritis)
- Dactylitis
- Enthesitis
- Axial disease
- Active skin involvement
- Active nail involvement
- Uveitis
- Inflammatory bowel disease

OR

- Patient has no symptoms

CLICK TO
Submit

HELP A–Z

192

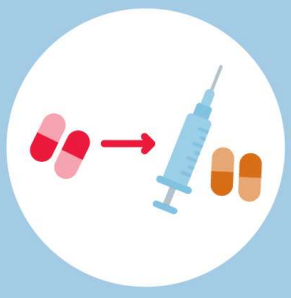
Question 1: Patient has symptoms

MENU
CLICK ARROW TO EXPAND

Patients with active psoriatic arthritis may require a change to their medication regimen.

Active PsA is defined as disease with symptoms that are unacceptably bothersome to a patient, and at least 1 of the following symptoms is present and due to PsA:

- Swollen/tender joints
- Dactylitis
- Enthesitis
- Axial disease
- Active skin and/or nail involvement
- Extraarticular inflammatory manifestations, such as uveitis or inflammatory bowel disease.



CLICK TO
Reset

CLICK TO VIEW
Question 2

HELP A–Z

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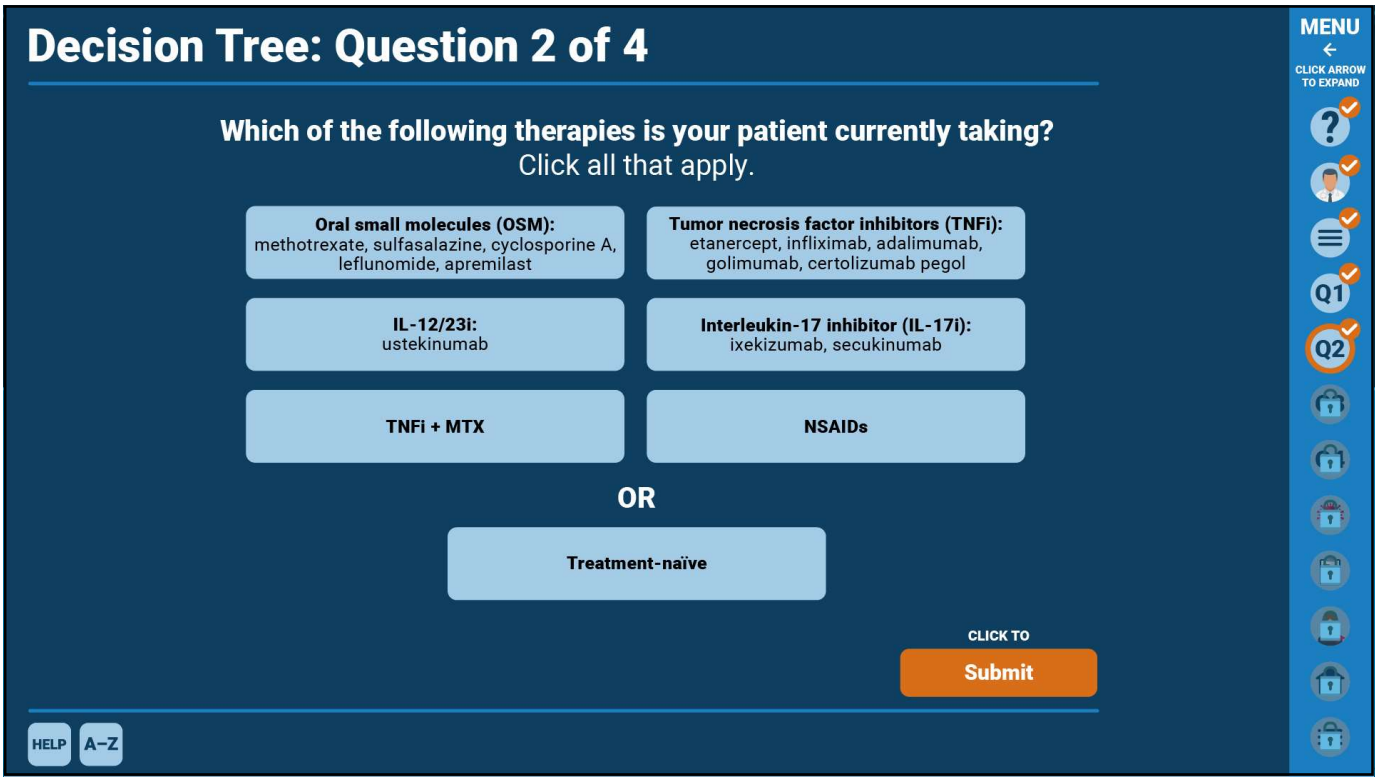
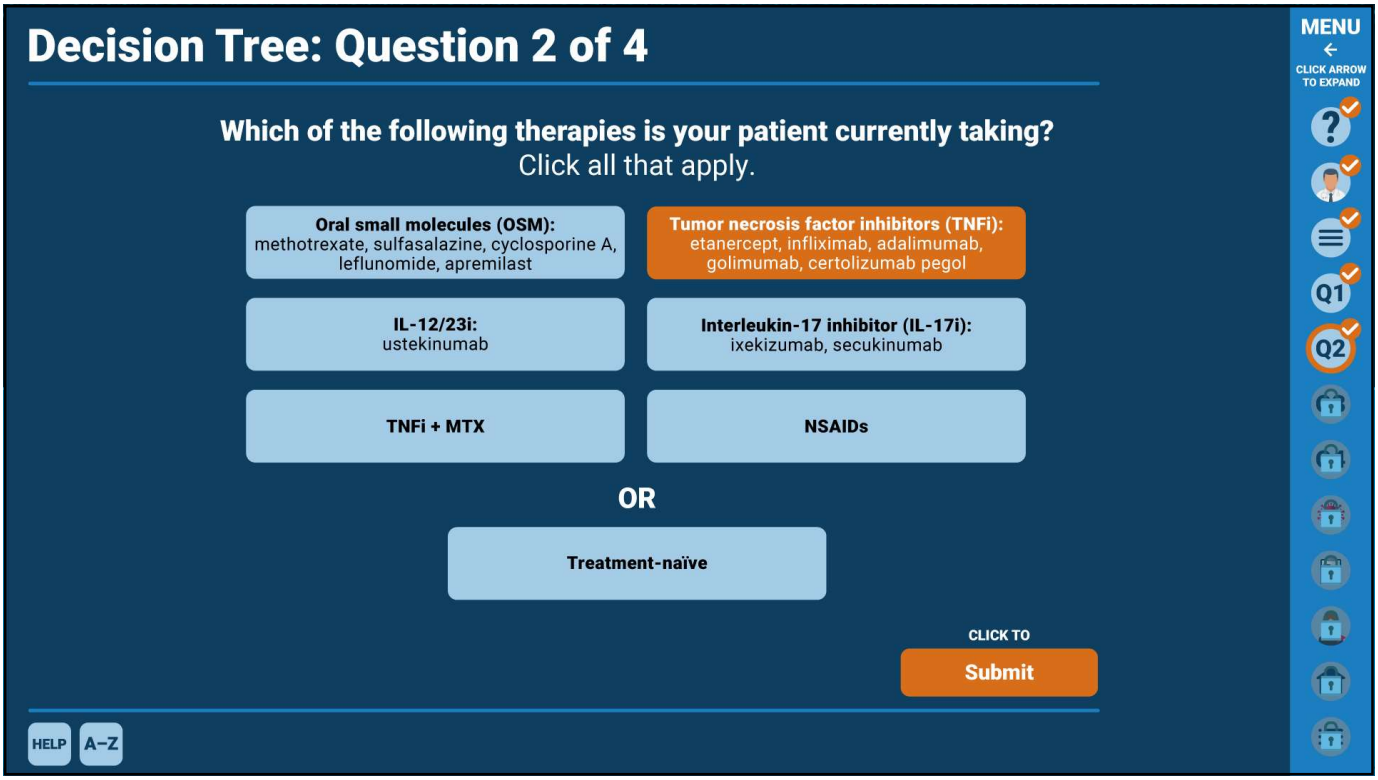
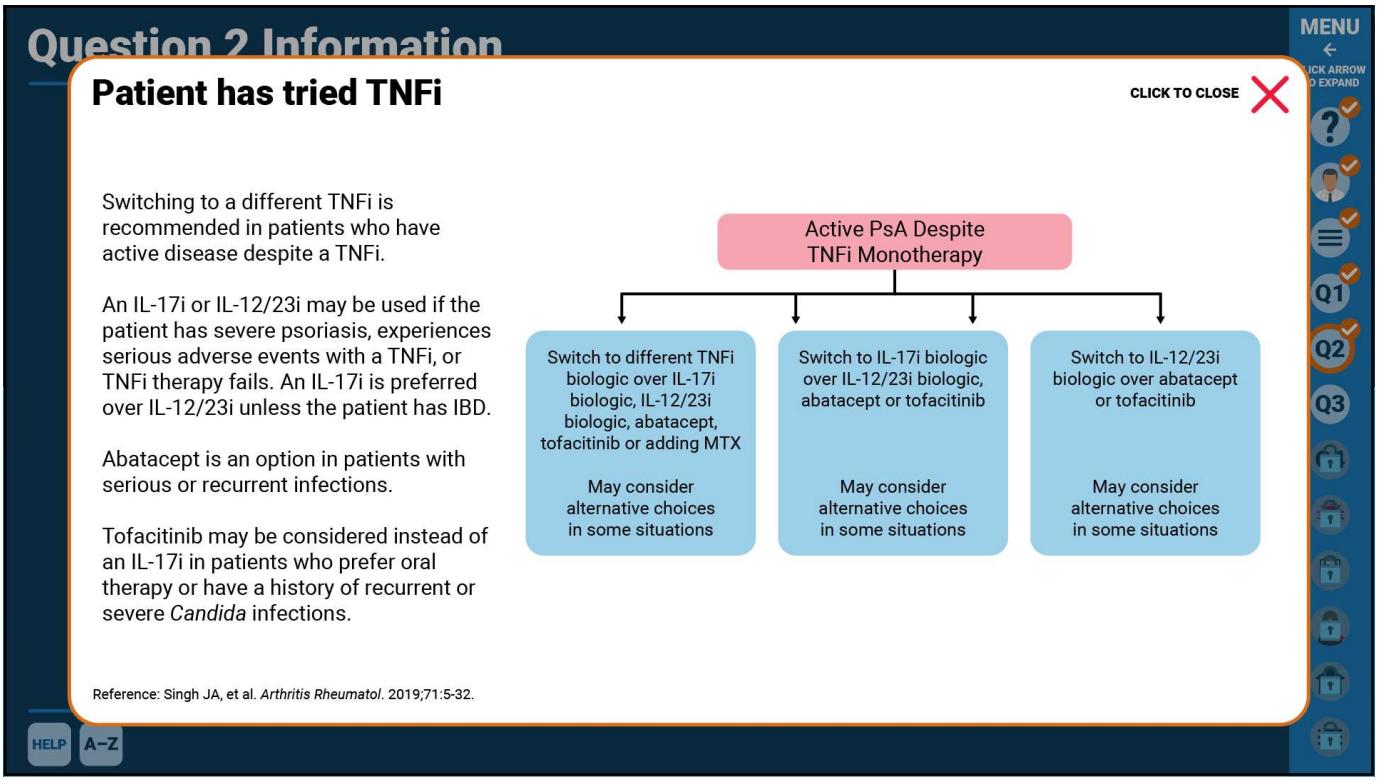

Decision Tree: Question 2 of 4
Which of the following therapies is your patient currently taking?
Click all that apply.
Oral small molecules (OSM): methotrexate, sulfasalazine, cyclosporine A, leflunomide, apremilast
Tumor necrosis factor inhibitors (TNFi): etanercept, infliximab, adalimumab, golimumab, certolizumab pegol
IL-12/23i: ustekinumab
Interleukin-17 inhibitor (IL-17i): ixekizumab, secukinumab
TNFi + MTX
NSAIDs
OR
Treatment-naïve
CLICK TO
Submit
HELP
A–Z
MENU
CLICK ARROW TO EXPAND
Q1
Q2

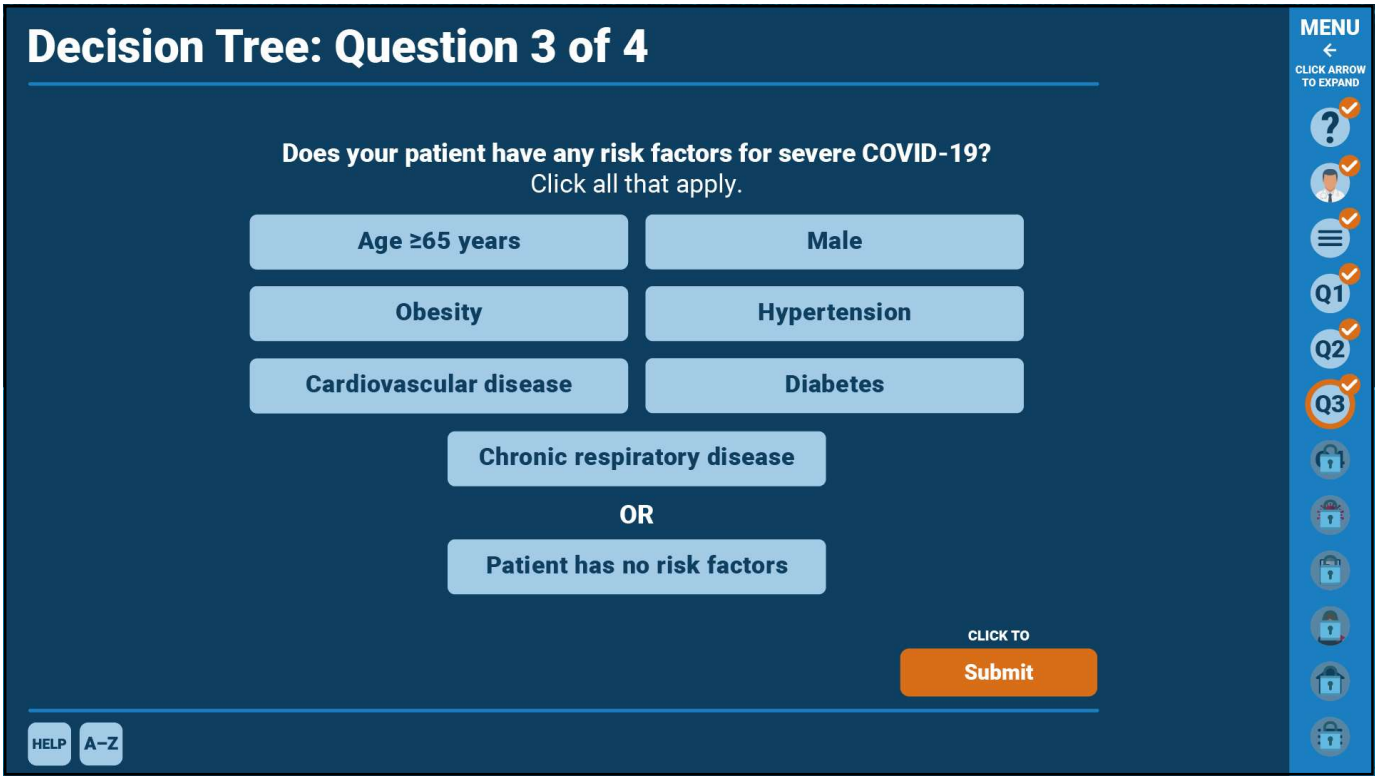
194


Decision Tree: Question 2 of 4
Which of the following therapies is your patient currently taking?
Click all that apply.
Oral small molecules (OSM): methotrexate, sulfasalazine, cyclosporine A, leflunomide, apremilast
Tumor necrosis factor inhibitors (TNFi): etanercept, infliximab, adalimumab, golimumab, certolizumab pegol
IL-12/23i: ustekinumab
Interleukin-17 inhibitor (IL-17i): ixekizumab, secukinumab
TNFi + MTX
NSAIDs
OR
Treatment-naïve
CLICK TO
Submit
HELP
A–Z
MENU
CLICK ARROW TO EXPAND
Q1
Q2

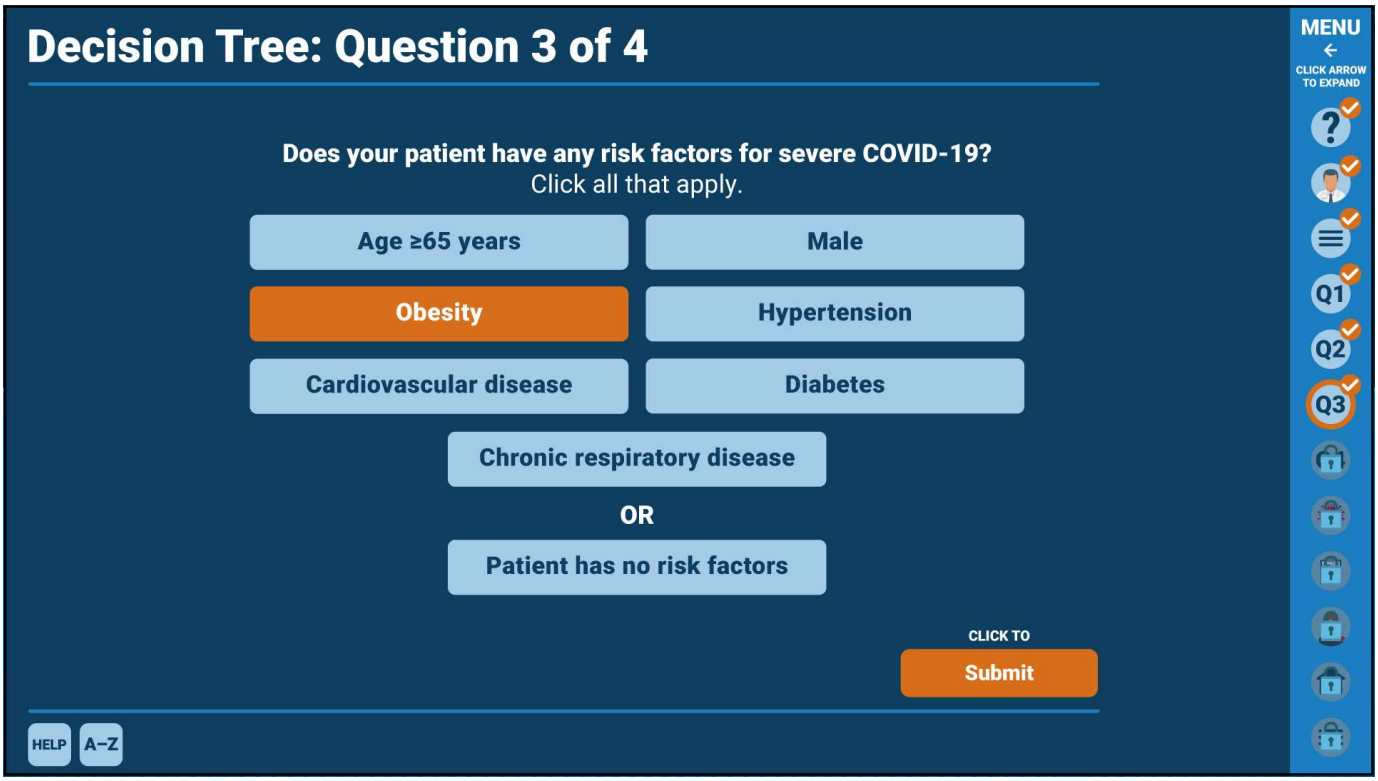
195


Question 2 Information
MENU
CLICK ARROW TO EXPAND
Patient has tried TNFi
CLICK TO CLOSE
Switching to a different TNFi is recommended in patients who have active disease despite a TNFi.
An IL-17i or IL-12/23i may be used if the patient has severe psoriasis, experiences serious adverse events with a TNFi, or TNFi therapy fails. An IL-17i is preferred over IL-12/23i unless the patient has IBD.
Abatacept is an option in patients with serious or recurrent infections.
Tofacitinib may be considered instead of an IL-17i in patients who prefer oral therapy or have a history of recurrent or severe Candida infections.
Active PsA Despite TNFi Monotherapy
Switch to different TNFi biologic over IL-17i biologic, IL-12/23i biologic, abatacept, tofacitinib or adding MTX
May consider alternative choices in some situations
Switch to IL-17i biologic over IL-12/23i biologic, abatacept or tofacitinib
May consider alternative choices in some situations
Switch to IL-12/23i biologic over abatacept or tofacitinib
May consider alternative choices in some situations
Reference: Singh JA, et al. Arthritis Rheumatol. 2019;71:5-32.
HELP
A–Z

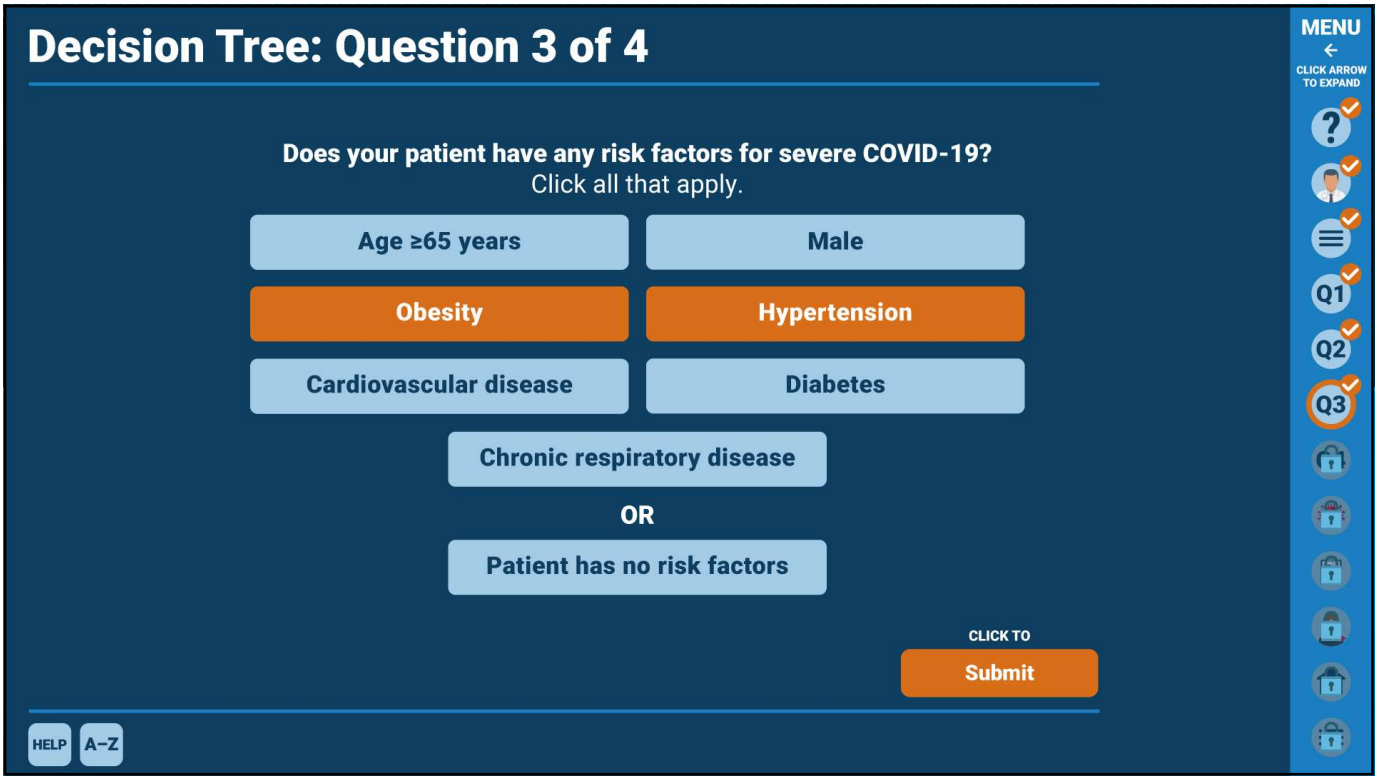
196


Decision Tree: Question 3 of 4
MENU
CLICK ARROW TO EXPAND
Does your patient have any risk factors for severe COVID-19?
Click all that apply.
Age ≥65 years
Male
Obesity
Hypertension
Cardiovascular disease
Diabetes
Chronic respiratory disease
OR
Patient has no risk factors
CLICK TO
Submit
HELP
A–Z

197


Decision Tree: Question 3 of 4
Does your patient have any risk factors for severe COVID-19?
Click all that apply.
Age ≥65 years
Male
Obesity
Hypertension
Cardiovascular disease
Diabetes
Chronic respiratory disease
OR
Patient has no risk factors
CLICK TO
Submit
HELP
A–Z
MENU
CLICK ARROW TO EXPAND
Q1
Q2
Q3

198


Decision Tree: Question 3 of 4
Does your patient have any risk factors for severe COVID-19?
Click all that apply.
Age ≥65 years
Male
Obesity
Hypertension
Cardiovascular disease
Diabetes
Chronic respiratory disease
OR
Patient has no risk factors
CLICK TO
Submit
HELP
A–Z
MENU
CLICK ARROW TO EXPAND
Q1
Q2
Q3

199

Decision Tree: Question 3 of 4

Does your patient have any risk factors for severe COVID-19?
Click all that apply.

- Age ≥65 years
- Male
- Obesity
- Hypertension
- Cardiovascular disease
- Diabetes
- Chronic respiratory disease

OR

- Patient has no risk factors

CLICK TO
Submit

HELP A–Z

MENU
CLICK ARROW TO EXPAND
Q1 Q2 Q3

200

Question 3: Guidance for patient with risk factors

Patient with risk factors

Patients with PsA are not at increased risk of death or serious complications from COVID-19 due to their disease.

However, PsA is associated with a higher incidence of CV disease, metabolic syndrome, obesity, diabetes, dyslipidemia, and IBD.

Risk of poor outcomes from COVID-19 appears to be related to general risk factors such as older age, male sex, and comorbidities (obesity, diabetes, hypertension, CV or lung disease) .

Variable	Relative risk from COVID-19 (95%CI) (Non-rheumatic cohort / Rheumatic cohort)	P value
Age over 60 years	1.99 3.70 6.93 / 2.30 4.04 7.08	0.841
Male sex	1.39 2.16 3.35 / 1.09 1.58 2.29	0.286
Obesity	0.72 1.22 2.06 / 1.10 1.62 2.36	0.393
Diabetes	0.53 0.95 1.70 / 1.34 1.93 2.79	0.038
Hypertension	1.07 1.64 2.53 / 1.49 2.27 3.46	0.290
CV disease	0.90 1.44 2.33 / 2.04 2.92 4.17	0.020
Lung disease	1.00 1.57 2.46 / 1.19 1.74 2.55	0.723

0 2 4 6 8

CLICK TO
Reset

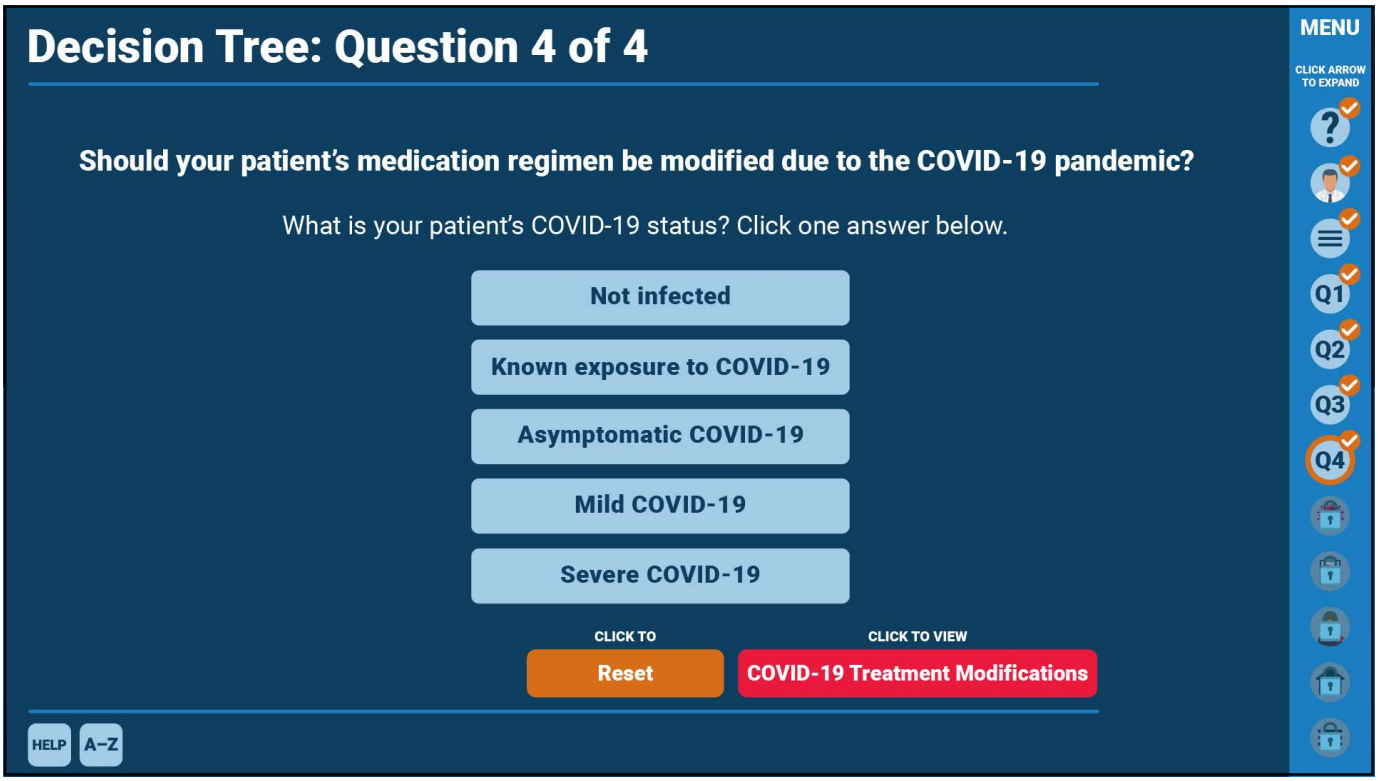
CLICK TO VIEW
Question 4

HELP A–Z

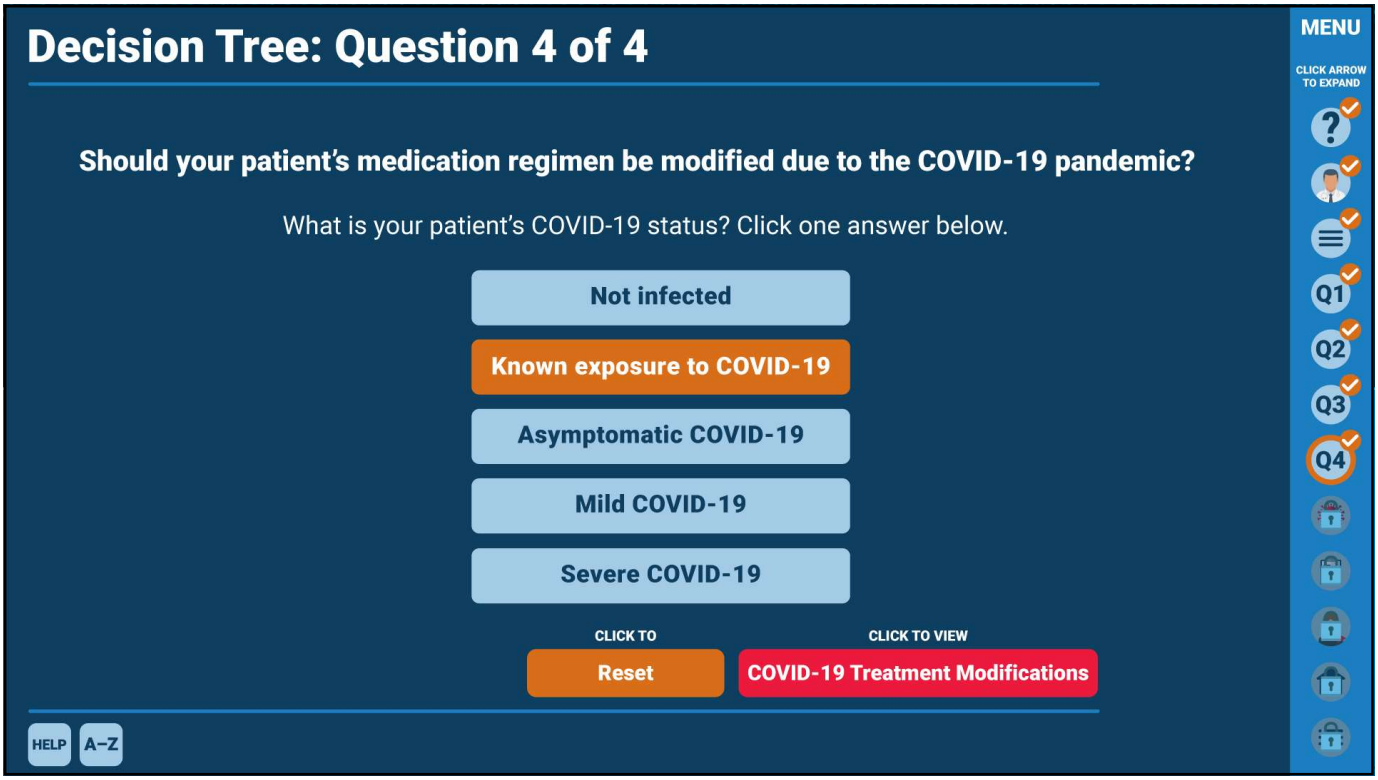
Mikuls TR, et al. *Arthritis Rheumatol.* 2020;72:e1-e12.
Pablos JL, et al. *Ann Rheum Dis.* 2020:218296.
Wu Z, et al. *JAMA.* 2020;323:1239-1242.
Wollina U, et al. *Dermatol Ther.* 2020;33:e13743.
Pablos JL, et al. *Ann Rheum Dis.* 2020;Epub ahead of print.

MENU
CLICK ARROW TO EXPAND
Q1 Q2 Q3 Q4

201


Decision Tree: Question 4 of 4
Should your patient's medication regimen be modified due to the COVID-19 pandemic?
What is your patient's COVID-19 status? Click one answer below.
Not infected
Known exposure to COVID-19
Asymptomatic COVID-19
Mild COVID-19
Severe COVID-19
CLICK TO
Reset
CLICK TO VIEW
COVID-19 Treatment Modifications
HELP
A–Z
MENU
CLICK ARROW TO EXPAND
Q1
Q2
Q3
Q4

202


Decision Tree: Question 4 of 4
Should your patient's medication regimen be modified due to the COVID-19 pandemic?
What is your patient's COVID-19 status? Click one answer below.
Not infected
Known exposure to COVID-19
Asymptomatic COVID-19
Mild COVID-19
Severe COVID-19
CLICK TO
Reset
CLICK TO VIEW
COVID-19 Treatment Modifications
HELP
A–Z
MENU
CLICK ARROW TO EXPAND
Q1
Q2
Q3
Q4

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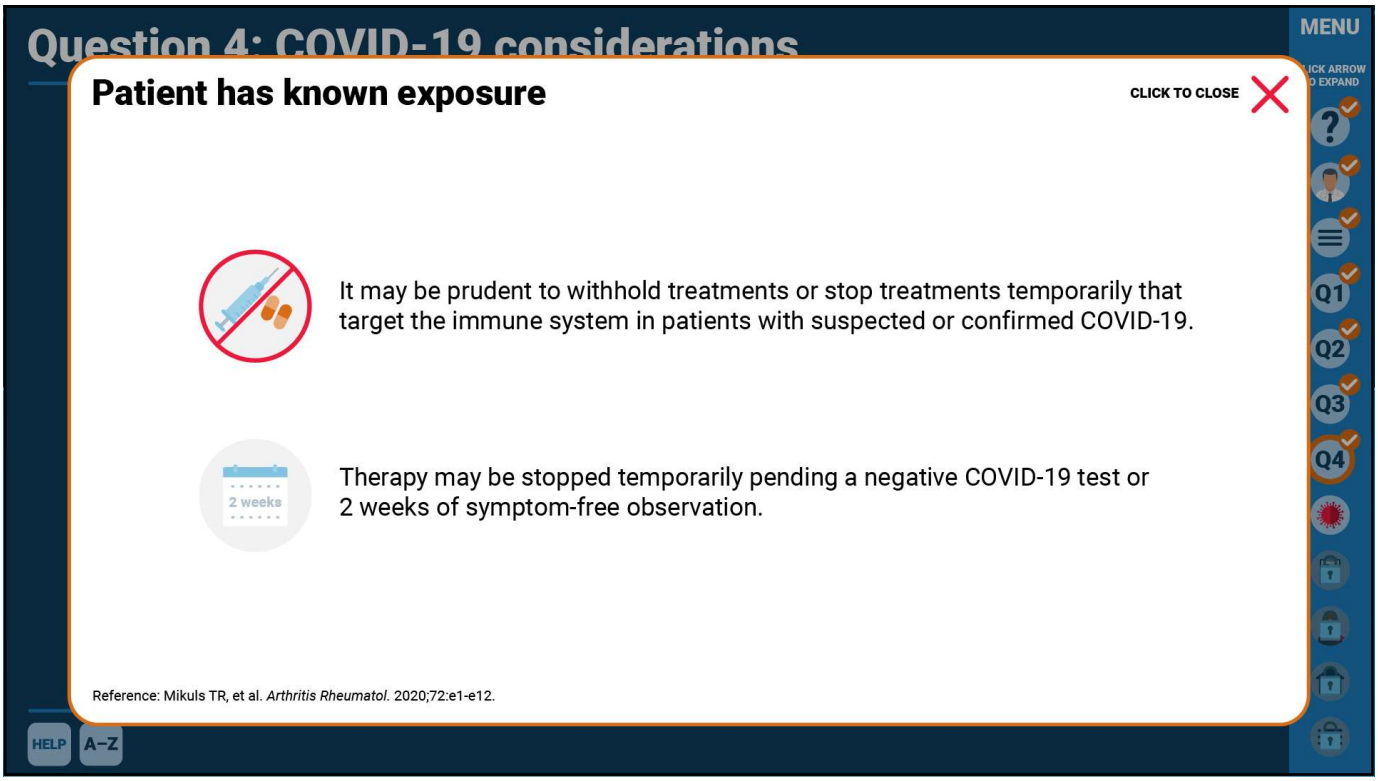
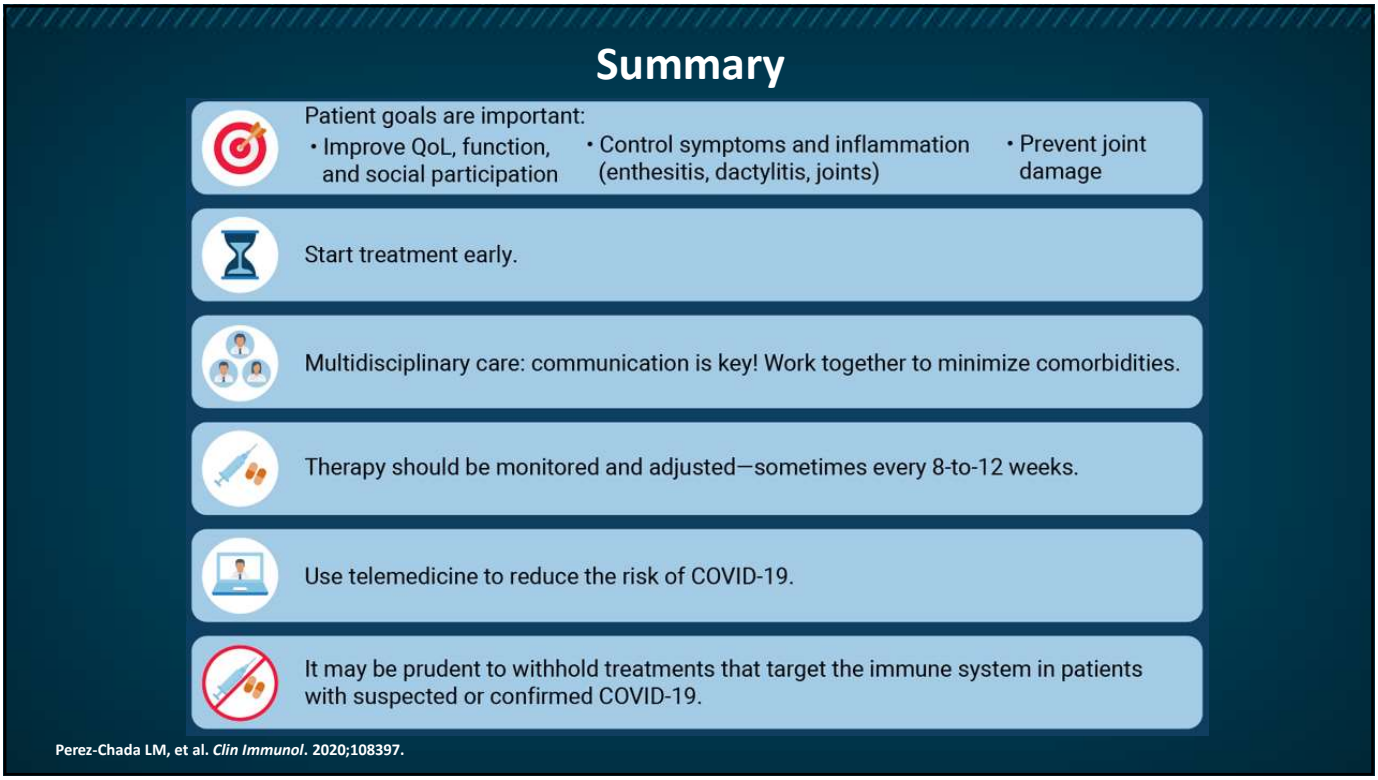

Question 4: COVID-19 considerations
MENU
Patient has known exposure
CLICK TO CLOSE
It may be prudent to withhold treatments or stop treatments temporarily that target the immune system in patients with suspected or confirmed COVID-19.
2 weeks
Therapy may be stopped temporarily pending a negative COVID-19 test or 2 weeks of symptom-free observation.
Reference: Mikuls TR, et al. Arthritis Rheumatol. 2020;72:e1-e12.
HELP
A–Z
Q1
Q2
Q3
Q4

204


Summary
Patient goals are important:
• Improve QoL, function, and social participation
• Control symptoms and inflammation (enthesitis, dactylitis, joints)
• Prevent joint damage
Start treatment early.
Multidisciplinary care: communication is key! Work together to minimize comorbidities.
Therapy should be monitored and adjusted—sometimes every 8-to-12 weeks.
Use telemedicine to reduce the risk of COVID-19.
It may be prudent to withhold treatments that target the immune system in patients with suspected or confirmed COVID-19.
Perez-Chada LM, et al. Clin Immunol. 2020;108397.

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Thank You
Question and Answers

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Please visit our two interactive PsA learning activities.

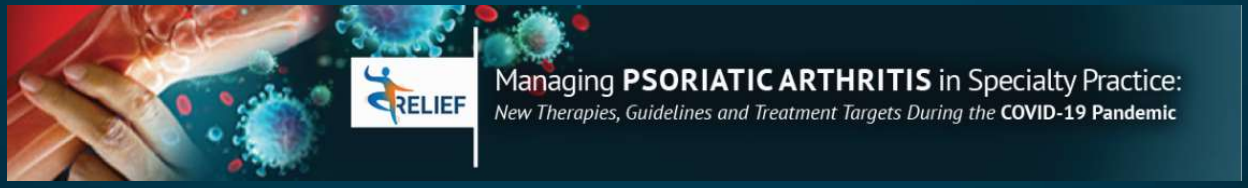
Decision Aid

Receive patient-specific treatment recommendations from the latest guidance on PsA and COVID-19.

Interactive Case Studies

Test your knowledge and review clinical trial data with these interactive patient cases.

Click on MLG Decision Trees at relief-as.com to use these interactive tools!



This activity is supported by an educational grant from Lilly.

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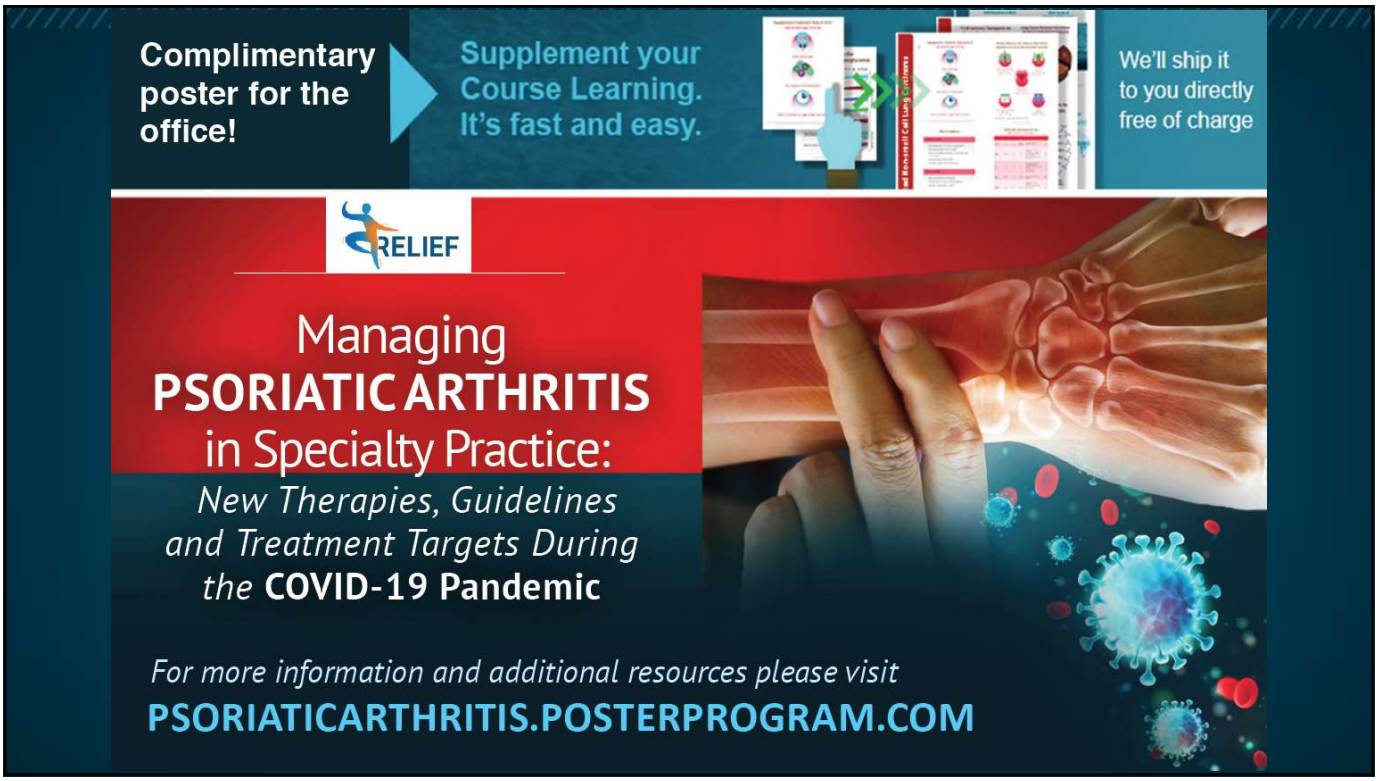
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