Latest Developments and Expert Outlook On Management of Psoriatic Arthritis

Overview

Psoriatic arthritis (PsA) is a chronic, inflammatory, musculoskeletal, disabling disease, commonly associated with skin psoriasis, and estimated to affect up to 42% of the approximately 7.5 million people in the United States with psoriasis. There remains an ongoing challenge among clinicians to diagnose and treat patients, as well as to stay abreast of optimal treatment strategies. In this educational program, the latest biologic treatment recommendations are reviewed, as well as clinical trial results for novel emerging therapies. Clinician-patient communication examples are shared on how to engage patients in their management, along with best-practice, stepwise recommendations to achieve remission with minimal or low disease activity with the use of appropriate assessment and screening tools to improve overall outcomes in the PsA patient.

Content areas

- Psychosocial burden of PsA
- Classification criteria
- Clinical presentation of PsA
- Comorbidities associated with PsA
- Interdisciplinary communication
- Clinical domains of PsA
- Approved biologic treatment strategies
- Disease activity measures for PsA

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Faculty

M. Elaine Husni, MD, MPH
Vice Chair, Rheumatology
Director, Arthritis and Musculoskeletal Center
Cleveland Clinic
Assistant Professor
Cleveland Clinic Lerner College of Medicine
Case Western Reserve University
Cleveland, Ohio

Joseph F. Merola, MD, MMSc
Assistant Professor, Harvard Medical School
Director, Clinical Unit for Research Innovation and Trials (CUReIT)
Director, Center for Skin and Related Musculoskeletal Diseases
Associate Program Director, Harvard Combined Internal Medicine-Dermatology Residency Training Program
Brigham and Women's Hospital
Boston, Massachusetts

Target Audience

This activity was developed for rheumatologists, dermatologists, primary care physicians, physician assistants, nurses, advanced nurse practitioners, and other health care providers who manage patients with psoriatic arthritis.

Learning Objectives

At the conclusion of this activity, participants should be better able to:

- Describe the etiology and socioeconomic and psychosocial burden of PsA and the importance of early detection and treatment
- Incorporate classification criteria into assessment of suspected PsA cases
- Identify PsA-associated comorbidities, such as CVD, obesity, and IBD, as well as their implication on the choice of treatment options

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- Increase clinician communication to minimize differences in the assessment of PsA disease severity and to improve understanding of patient satisfaction with current treatment options
- Apply an integrated approach to therapeutic intervention, incorporating patient-centric evidence and best practice recommendations for each treatment domain of PsA
- Describe the mechanisms and latest safety and efficacy evidence for approved and emerging biologic and nonbiologic DMARDs for the treatment of patients with PsA

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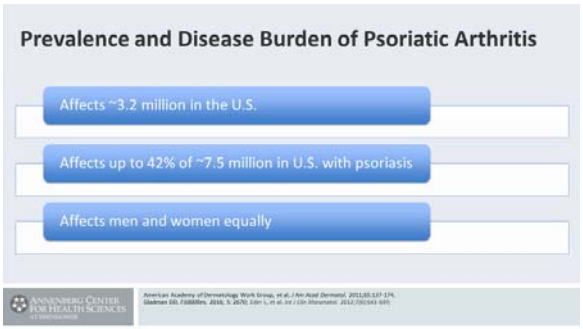
Contact Information

For help or questions about this activity please contact Continuing Education:
ce@annenberg.net
Annenberg Center for Health Sciences
39000 Bob Hope Drive
Dinah Shore Building
Rancho Mirage, CA 92270
Phone 760-773-4500
Fax 760-773-4513
8 AM – 5 PM, Pacific Time, Monday – Friday

Module 1: Prevalence and Burden of Disease; Importance of Early Screening and Classification Criteria

Joseph Merola, MD: In this module we will address the prevalence and psychosocial burden of psoriatic arthritis, as well as the ongoing clinical challenges of underdiagnosed patients suffering with psoriatic arthritis. We discuss the importance of early detection, and we'll review available screening questionnaires that can help provide an early diagnosis.

Let's talk a little bit about the prevalence and disease burden of psoriatic arthritis. There are quotes that up to 3.2 million individuals are affected with psoriatic arthritis in the United States. It affects up to 42% of around 7.5 million in the US with psoriasis, and affects men and women equally.



A few points about the prevalence and psychosocial burden, in general, we talk about how the majority of patients with psoriatic arthritis will have their skin manifestations before the psoriatic arthritis emerges, around 85% or so. The peak age of onset of the psoriatic arthritis is really during peak working years, 30 to 55 years of age. Around a third of patients—which is a good number to remember—of psoriasis patients, will go on to develop psoriatic arthritis.

In general, more men may present with axial disease with radiographic damage than women, although some of those numbers increasingly, or at least the ratio, are getting more equal in recent, prevalent studies. Women may exhibit worse functional outcomes relative to men. The psychosocial burden and quality of life seems to be worse among patients with both psoriasis and psoriatic arthritis than those with psoriasis alone. Both of these are chronic conditions that affect both the skin and joints, and can result in functional as well as cosmetic concerns, although I don't like to use the term cosmetic, for the most part, for our patients with skin psoriasis where there is really a tremendous burden of disease, even with skin disease alone.

In terms of the disease burden of psoriatic arthritis, there are a few skin features that are associated with a higher risk of developing psoriatic arthritis. Those include the presence of scalp disease, nail psoriasis, inverse or intertriginous disease, which is psoriasis that occurs in body fold areas in the axilla, in the groin folds, for example, the gluteal cleft. There have been some associations of increased risk with the extent of psoriasis, meaning having worse psoriasis or more body surface area, as associated with an increased risk of psoriatic arthritis, and a variety of genetic markers.

Most patients, around 40% to 60% of patients, will suffer progressive and/or erosive disease, with potential deforming of joints that can have an impact on quality of life, comorbidities, and can be associated with a number of extra-articular manifestations, as well.

The economic burden of underdiagnosed and undertreated psoriatic arthritis has been evaluated in several studies. At least 1 quotes up to $35.2 billion annual health care dollars of burden, and you can see that equates to about 10,000 per individual, by 2013 prices, of annual indirect costs and work disability.

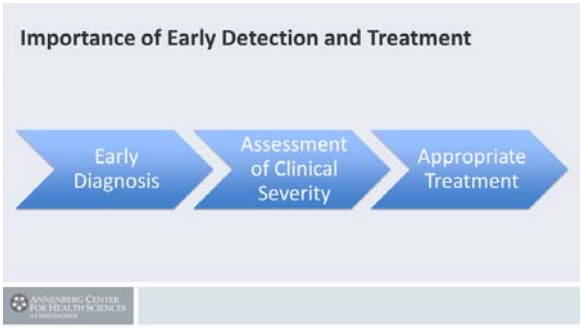
There are a few challenges with underdiagnosed psoriatic arthritis. You can see here at least 1 study, the MAPP study,

[Kavanaugh A, Helliwell P, Ritchlin CT. Psoriatic arthritis and burden of disease: Patient perspectives from the population-based multinational assessment of psoriasis and psoriatic arthritis (MAPP) Survey. *Rheumatol Ther.* 2016;3:91-102.] which reported an average delay in diagnosis of up to 5 years in subjects. That may be due to a variety of causes, including lower awareness by clinicians who may fail to connect the skin and joint symptoms that they're seeing, unfortunately. That may include some dermatologists, and hopefully, through the course of this discussion, we'll talk a little bit about how we can increase awareness and screening of psoriatic arthritis. Again, there are many reasons why this is important, including the potential for progressive joint disease, deformities, disabilities and quality of life, as we previously mentioned.

Dermatologists really play a pivotal, key role in the diagnosis of psoriatic arthritis. We are at the front line of psoriatic disease. We're seeing patients with the at-risk phenotype, which is skin psoriasis. Again, the vast majority of patients are presenting with skin disease before arthritis. We really are at the front line.

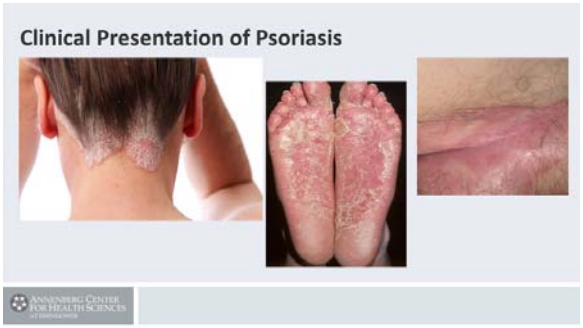
One of the studies I like to quote is from Philip Mease and colleagues [Mease P, Gladman D, Papp K, et al. Prevalence of rheumatologist-diagnosed psoriatic arthritis in patients with psoriasis in European/North American dermatology clinics. J *Am Acad Dermatol.* 2013;69(5):729–735.], who showed up to 41% of psoriasis patients with psoriatic arthritis were previously undiagnosed, in 1 study where they had a rheumatologist essentially screening dermatology patients coming out of a clinic among a psoriasis population. Even a 6-month diagnostic delay has been shown to result in long-term radiographic and functional poor outcomes, including bone erosion.

I'll just go to the point that earlier diagnosis probably does have impact on patients in terms of their functional outcomes. We'll talk a little bit about early diagnosis, assessment of clinical severity, and then getting to appropriate treatment—particularly in later modules we'll spend a little bit more time on treatment.



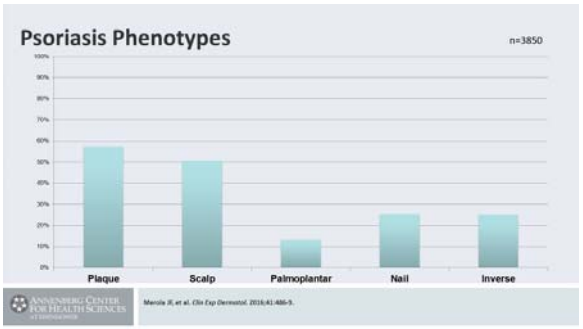
Again, the importance of early detection has to do with the fact that delayed diagnosis and misdiagnosis may have negative impact on overall health outcomes, on quality of life and on mental health of patients. Again, a little bit later we'll be talking about comorbidities in some detail with Dr. Husni. Early detection can lead to improved, appropriate, and timely treatment, and a prompt diagnosis in treatment can improve overall clinical outcomes.

What does the clinical presentation of psoriasis look like? Before you think we're out of scope from our psoriatic arthritis focus here, as previously mentioned, there are several phenotypes of skin disease that are associated with an increased risk of psoriatic arthritis, in particular—scalp, nail and inverse intertriginous disease.

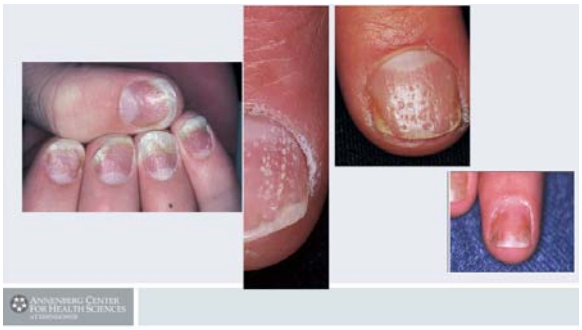


The reason those are particularly important: this is a study that we published [Merola JF, Li T, Li WQ, Cho E, Qureshi AA. Prevalence of psoriasis phenotypes among men and women in the USA. *Clin Exp Dermatol.* 2016;41(5):486-9. doi:10.1111/ced.12805.] a few years ago looking at the prevalence of some subsets of psoriasis in a cohort here in Boston, which includes both the Nurses Health Study as well as the Health Professionals Follow-up Study.

You can see that plaque disease, of course, by self-report, is quite common. Scalp disease, incredibly common. One of the things we like to point out in this study is that inverse intertriginous disease was present in up to 23% of patients, so almost a quarter of patients with this subset—which, as I mentioned earlier, is also associated with an increased risk of psoriatic arthritis. I think that's an important take-home point, both for the dermatologist but also the rheumatologist who may be seeing these patients who should be thinking about looking for psoriasis in these hidden areas.



Here we have some pictures of the nail disease that can happen in psoriasis. You can see in these pictures some pitting, some obvious pitting, what we call distal onycholysis, or the pulling away of the distal nail bed from the plate, some oil spots and other changes. Again, this being associated with an increased risk of psoriatic arthritis. In many studies, really, the nail disease is considered synonymous with enthesitis and involvement of the distal joint. We'll talk about that in a little bit more detail.



In terms of clinical presentation, the clinical presentation of psoriatic arthritis is complex and can be heterogeneous. It's also important to realize that any of these manifestations are not mutually exclusive and can happen to a patient differentially over time. The manifestations may include increased asymmetric and oligoarticular joint involvement, distal interphalangeal (or DIP) joint involvement, dactylitis—or the so-called sausage digit presentation, enthesitis or inflammation at the site of tendon insertion into bone. Again, the nail changes, the skin changes that we mentioned, and some symptoms that are typical of inflammatory arthritis, including stiffness, prolonged stiffness after a period of inactivity, pain, fatigue, and anxiety.

Many of our rheumatology colleagues who are watching this are probably familiar with these, but when we think about the potential presentations of psoriatic arthritis, there are a few clinical presentations: one being an

asymmetric oligoarthritis and a rheumatoid arthritis-like symmetric polyarthritis, involvement of the distal interphalangeal joint. Fortunately, an uncommon variant known as arthritis mutilans, which can be rapidly destructive or quite damaging to joints, and the potential for axial disease as well, including the spine.

Here we see pictures of the so-called sausage digit, or dactylitis, involving an entire digit in the intervening soft tissue. On the far right of the picture, you see an instrument called a dactylometer, which is used, particularly in clinical trials, to measure the extent of dactylitis.

Here we have a rarely seen, I think, example of enthesitis that can be seen visually. In general, I think of this as being a more palpation sort of physical-exam finding than a visual finding, but here we see swelling at the Achilles insertion into the calcaneus as a very stark example of enthesitis.

I think many of us like to think about the clinical domains of psoriatic arthritis as these 6. This is something that the GRAPPA Group has very much drilled, at least into my head, maybe in some others as well—the thought that there are really 6 clinical domains. The peripheral arthritis, axial disease, enthesitis, dactylitis, skin involvement and potential nail psoriasis. Not 1 of the expressed 6 clinical domains, but very, very important, another consideration, which is the comorbidities, which my colleague is going to go into in great detail a little bit later.

In terms of the diagnostic workup, there really is currently no standard diagnostic test. Psoriatic arthritis very much remains a clinical diagnosis. The diagnosis workup for psoriatic arthritis is based on history and physical. Blood tests, depending on the presentation, may include an evaluation, for example, for rheumatoid factor or anti-citrullinated peptide, or CCP, inflammatory markers, which can sometimes predict more erosive or aggressive disease, and imaging, just to support the diagnosis. Do we see radiographic or MRI or ultrasound changes that might suggest psoriatic arthritis?

The CASPAR Criteria, worth mentioning, are a set of classification criteria sometimes used as diagnostic criteria by some. I think we like to emphasize that these, really, are meant to be classification criteria most typically used in the setting of clinical trials. The important part of this is realizing it requires, at its stem, the

presence of inflammatory arthritis before you even apply the criteria. One has to be confident that the patient in front of them has some form of inflammatory arthritis, such as joint inflammation, spine disease, or enthesitis, for an accurate diagnosis.

These are highly specific for psoriatic arthritis in the context of a clinical trial. They include the presence of a personal history of psoriasis, either current or past, a family history of psoriasis, having psoriatic nail disease, and negative rheumatoid factor in the presence of dactylitis and/or radiographic evidence of juxta-articular new bone formation, which is a very specific radiographic finding—although I would say, not often present, or at least commented on, by our musculoskeletal radiologists.

I'd like to take advantage of my expert colleague sitting next to me to talk a little bit about some of what we just covered. Elaine, I know that we have sort of a mix of individual learners: both rheumatologists, potentially dermatologists, and others. Can you comment a little bit on how you like to use the CASPAR Criteria, if at all? How do you feel about the clinical diagnosis of psoriatic arthritis? What would be helpful both to the rheumatologist and non-rheumatologist, particularly, with regards to screening?

Elaine Husni, MD: First of all, that was an excellent overview of psoriasis, psoriatic arthritis, I think, to highlight the vast sort of presentation that can occur, and more importantly, people can present at different stages. Sometimes they can have dactylitis as their first presentation, but yet then have more of an inflammatory arthritis picture. I think that's what makes it so difficult. You talked about the delay in diagnosis, and how we're, in our research, really trying to get better at diagnosing earlier so that treatments can work.

The CASPAR Criteria, as you mentioned—I probably don't do it every day in my clinical practice—but I think in clinical trials where you're trying to get a homogeneous group, [it is] really important to have some sort of algorithm we can follow. So, I think the CASPAR Criteria is very helpful to do that.

In terms of screening, like you said, whether or not they present in front of you as a dermatologist or in front of a rheumatologist, I think are going to make differences in how early we can detect. And without a blood test and without any ensuing damage, you might not see anything on X-ray or exam right away. So, as you said, this is really tricky.

I'm excited because based on our research and what we're discovering, we're noticing that we're no longer just borrowing from RA anymore—our prototypical inflammatory arthritis. Now we have just so many more treatments that we'll talk about, as well as nuances with comorbidities regarding psoriatic arthritis. How do you use CASPAR?

Joseph Merola, MD: Yeah, it's interesting. I'm putting my dermatology hat on for a minute, and I'd like to hear your thoughts as well. I find prior to being a little more familiar with some of the rheum aspects of things, it's a challenge, I think, for the dermatologist or for the non-rheumatologist to even feel comfortable with what's inflammatory arthritis before we even get into some of the nuances that we talked about.

Sometimes I like to take a step back . . . thinking about what constitutes . . . What would make me think that the person in front of me has—beyond even asking about joint pain because that opens a can of worms with the patients—what makes us think about the patient in front of us having inflammatory arthritis or something that might constitute psoriatic

arthritis? As we said, too, I find CASPAR a challenge, because it has that requirement for the. . .

Elaine Husni, MD: Sure, the prerequisite, yeah.

Joseph Merola, MD: I know we're going to get into a little more detail, but what do you recommend for the non-rheumatologist in terms of an approach to the person sitting in front of you? Is it a screening questionnaire? Is it a certain set of questions? How do you start to . . . ?

Elaine Husni, MD: As you know in your rheumatology training, for us with rheumatology fellows, we are training them all the time to look for inflammatory arthritis. I think sometimes it might be difficult in a derm setting, where not every patient is presenting with inflammatory arthritis, and you guys are looking at all different types of skin disease. I think if you're not doing it on a daily basis, that is a lot to ask for in terms of detecting, determining, examining, X-raying for inflammatory . . .

Joseph Merola, MD: Even the primary care setting, I mean, to be fair.

Elaine Husni, MD: I agree. I agree. I think at some point that if a dermatologist is not really doing it on a regular basis, it would make sense to comanage, where they would refer early. Obviously, you wear both hats, so you're not needing . . .

Joseph Merola, MD: We have to do internal self-referrals.

Elaine Husni, MD: Internal self-referrals. You don't really need to do that, but I think the important message is not to be scared, to even pick up the phone. I think many times we're on electronic medical records, and we are just simply shooting a record over, hoping to get the answer; but as you know, we get busy. I think sometimes just picking up the phone with your dermatologist is a good way to understand, or when you're worried about a patient.

Joseph Merola, MD: One of the things we mentioned is the presence of these PsA screening tools. I know at least 1 of these you helped develop, which is the PASE and the updated PASE II. I'll just very briefly mention there are a number of PsA screening tools available to us. The PEST [Psoriasis Epidemiology Screening Tool], the ToPAS 2 [Toronto Psoriatic Arthritis Screen, Version 2], the PASE [Psoriasis Arthritis Screening and Evaluation], and a number of others. I like to say that I pick 1 tool, and use it. I think it's probably as important that we're using a screening tool, particularly for the non-rheumatologist, as we are choosing which one we like.

One of the slightly shorter screening tools is the PEST. It is available in a variety of different forms, including one of our organizations, GRAPPA, has an app that's freely available for download, and it includes the PEST in multiple languages. I and my clinic, particularly with our dermatology residents and rheumatology fellows coming through, we use the PASE within our combined clinic setting. But I think, again, find 1 of these that you like, and use it. The nice thing about a lot of these is that they are very much patient-facing. It doesn't really have to take a lot of the physician's time. They can be given by office staff or some allied professional.

PsA Screening Tools	Number of Questions	Sensitivity % or Range	Specificity % or Range
PEST Psoriasis Epidemiology Screening Tool	5 + joint diagram	0.28 to 0.77 97% sensitivity	0.37 to 0.98 79% specificity
ToPAS 2 Toronto Psoriatic Arthritis Screen, Version 2	11 + pictures/diagram	86.8% sensitivity	93.1% specificity
PASE Psoriasis Arthritis Screening and Evaluation	15	0.24 to 0.75 82% sensitivity	0.39 to 0.94 73% specificity
PASQ Psoriasis and Arthritis Screening Questionnaire	10 + joint diagram self-report		
CONTEST, developed from combinations of questions from PASE, PEST, and TO PAS		38% to 86%	35% to 89%

Elaine Husni, MD: Yeah, I think it's wonderful to see all these different screening tools because in practice, you are always going to gravitate to the 1 you're comfortable with. I do think it's important to understand that there are some differences between these screening tools.

PASE, for example, is a patient-facing questionnaire that's used for patients who are seen in the dermatology department. While some of the other screening questionnaires are using internal medicine or as all-comers. I think that these screening tools—it's great for me to see that there are so many that are out there so that people have choice, which is important, but secondly, what's more important is what practice you are in, and then using an appropriate screening tool for that practice to increase sensitivity and specificity.

Joseph Merola, MD: Fantastic. Moving on a little bit in terms of depth of thinking about our psoriatic arthritis patients, there are a number of activity measures that have been put forth for the measurement of psoriatic disease, psoriatic-arthritis-disease activity. It's worth mentioning, at least, a few here. Some of these have been validated for us in the psoriatic arthritis population. Some are extrapolated a bit from rheumatoid arthritis, and others inflammatory arthritis. We'll mention these very briefly.

In terms of some of the more readily used composite measures for psoriatic arthritis, you see here the MDA or minimal disease activity measure. This one, I think, has moved to the forefront for a variety of reasons, including its use as part of the TICOPA trial, the tight control of psoriatic arthritis trial, which we'll mention a little bit later. It's a very easy-to-use composite of a number of measures that we'll come back to in just a little bit.

Minimal disease activity includes 7 items. To meet minimal disease activity, we have to have 5 of the 7 criteria met, and again, we'll mention that a little bit later. There's the CPDAI or Composite Psoriatic Disease Activity Index, the DAPSA, again, Disease Activity and Psoriatic Arthritis Score. There are some cutoffs for what's considered DAPSA remission, which we'll talk about a little bit later. There's the PASDAS, another composite measure that looks at psoriatic arthritis disease activity.

The RAPID-3 is often used, particularly in North America. This is increasingly being validated for psoriatic arthritis, and a number of practices have—again, particularly in North America—have used this because of its feasibility in the clinical setting.

Here, we go into a little bit more depth about minimal disease activity. The criteria listed here . . . it includes a tender joint count (TJC), swollen joint count (SJC) less than or equal to 1. It includes skin criteria, importantly, with a Psoriasis Area and Severity Index (PASI) of less than or equal to 1, or BSA of less than or equal to 3%.

There's a patient pain VAS [visual analog scale], a patient global activity VAS, a HAQ [Health Assessment Questionnaire] with a score of less than or equal to 0.5 and tender entheseal points of less than or equal to 1. Again, minimal disease activity is met when 5 out of 7 of the criteria are listed. And, what's considered very low disease activity is met when all 7 of the

criteria are met. This is something that we collect in the course of our clinic visits.

Elaine Husni, MD: I think it's great to reach that target of low disease activity and to be able to have some measure where we can reach that low disease activity, so, from serial visits, we have a way to measure. And, it's a luxury that we have many different ones to use, and I agree with you that the RAPID-3 and the MDA are gaining popularity in use.

Joseph Merola, MD: This ends our first module, which is a quick glance at psoriatic arthritis as a disease state, a little bit about how to screen for psoriatic arthritis, particular for the non-rheumatologist, and a quick look at disease assessment, particularly using some slightly newer composite measures, such as the MDA and the RAPID-3.

Module 2: Comorbidities

Elaine Husni, MD: In this module we're going to discuss common comorbidities and risk factors associated with psoriatic arthritis, and implications to disease management.

So, we're going to address some important comorbidities. We know that there's increased prevalence and incidence of cardiovascular disease, diabetes, obesity, depression, and anxiety in patients with active PsA. These could occur in 50% of patients with psoriatic arthritis, hav[ing] at least 1 comorbidity, and this results in decreased quality of life. It does have implications in disease management, and we want to review patient satisfactions with current treatment options.

So, comorbidities that are associated with PsA. We know that PsA has more than the general population. There's been a lot of talk about IBD and psoriasis and psoriatic arthritis. Are you screening for IBD?

Joseph Merola, MD: That's an interesting question. You know, I think we're a little bit hypersensitive because we have a referral clinic bias, including a comanagement relationship with our GI docs, so we do tend to. I wouldn't say we're doing it as frequently as say our PsA screening among our psoriasis patients who have cardiovascular screening. I think it's moved to second tier, but we try to remember to ask our patients about a personal and family history of known IBD, for sure, because it affects our treatment choices. Then our comfort with screening is another challenge. Certainly, I don't feel [like] a qualified IBD or GI specialists, but we try to incorporate it into our comorbidities list.

Elaine Husni, MD: Sure. So, I think education around this is important. We know that there is a greater risk [for IBD], so it's important to ask and educate. There's also, as you had mentioned, a higher risk of cardiovascular disease. So, this has been much more well studied—both in RA and PsA. It is the leading cause of death in patients with psoriatic arthritis. Identifying those high-risk cardiovascular patients will then warrant more aggressive intervention.

There's also a higher risk of depression and mental health issues in patients with both psoriasis and psoriatic arthritis. And, the presence of this comorbidity of depression may also affect adherence to treatment. Do you have any tricks in terms of looking at depression? Are you asking on a more visit basis, every visit basis?

Joseph Merola, MD: Yeah, we try to remember, as part of our comorbidities list of items, to hit anxiety and depression. I think, again, one of

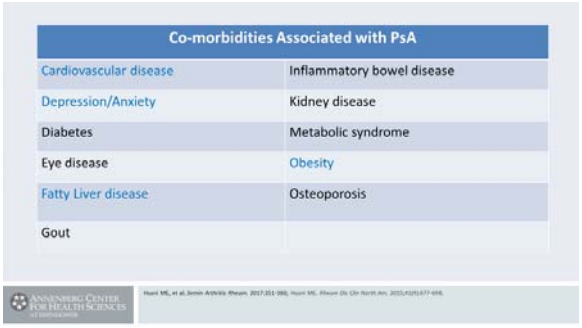
the reminders for us that come up in our discussion about choice of agents. One of the things I use to jog my memory about comorbidities is when we get to—particularly with a new patient or a patient changing therapies—when we get to the discussion of potential treatment options, I like to think about asking about these as relevant to both the underlying disease, but to our treatment choice, as well. So, if I get to a drug that I know potentially has some increased risk, say of depression and/or suicide, depending on the drug we're talking about, I remember to try to screen and ask at that point.

In general, we try to teach our residents and fellows to—with some frequency—go down the list. One of the tricks we've been trying to use is to include it in our EMR templates, in our electronic medical record templates, a few items about comorbidities, just to jog our visit in terms of asking.

Elaine Husni, MD: Right, so more patient-directed questionnaires that we have available now, which is great. I always find it a bit challenging, because you are also starting to talk to them about a chronic disease, a lifelong disease, of having psoriasis and psoriatic arthritis. So, I think sometimes there's a mood change knowing this, and then looking at long-term depression symptoms, which is always challenging.

So, I love the use of questionnaires. We do the same thing, and then as we're getting to know the patient, we also have an opportunity, in this lifelong management, to make adjustments and to have them comanaged by psychologists and psychiatrists, as well.

So, here's a list of the common comorbidities that are associated with psoriatic arthritis. The ones in blue are the ones that are probably better studied. So, that's the cardiovascular, depression, fatty liver disease, and obesity, which we'll go into in a little more detail. But then it's also important to look at some of the other comorbidities that are on the rise. We do see diabetes, gout, IBD that we talked about; kidney disease, metabolic syndrome, and osteoporosis, as well, and then of course eye disease or inflammatory eye diseases we've known have a long-term association with the spondyloarthropathies.



So, why are comorbidities important to recognize? This allows a more comprehensive evaluation and management of the patient, so not just solely looking at the skin and the joints, but also the other associated conditions. It may also affect the choice of therapy, which we touched upon. Cardiovascular disease, for example, we use a lot of NSAIDs, and as you know, NSAIDs have a risk-benefit ratio. In our patients and [the] need to balance cardiovascular risks, especially with hypertension and lipid abnormalities.

The use of NSAIDs is also associated with reduced cardiovascular mortality. This has been looked at in rather large studies. I was involved with the PRECISION trial, as well, which was just published in the *New England Journal* [Nissen SE, Yeomans ND, Solomon DH, et al. Cardiovascular safety of celecoxib, naproxen, or ibuprofen for arthritis. *N Engl J Med.* 2016:2519-2529. doi:10.1056/NEJMoa1611593] that's looking at differences between COX-2 selective and nonselective NSAIDs, and their

risk of cardiovascular disease. It has been shown in this noninferiority trial that things like a COX-2 selective NSAID is equal to, in terms of cardiovascular risk, a nonselective NSAID.

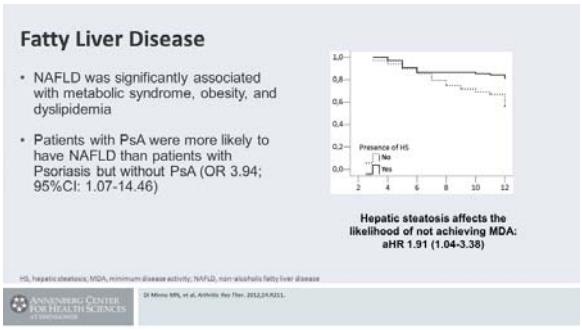
IBD, we talked a lot about, and then uveitis, the inflammatory eye disease. As you know, monoclonal antibodies in TNFs are a better treatment option than receptor antagonists. Sulfasalazine may also play a role in helping patients with more mild symptoms, as well.

So, focusing on cardiovascular comorbidities. As we know, that's the more common one that we see. There are 3 large studies [Han C, Robinson DW Jr, Hackett MV, Paramore LC, Fraeman KH, Bala MV. Cardiovascular disease and risk factors in patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. *J Rheumatol.* 2006;33(11):2167-72, Gladman DD, Ang M, Su L, Tom BD, Schentag CT, Farewell VT. Cardiovascular morbidity in psoriatic arthritis. *Ann Rheum Dis.* 2009;68(7):1131-5. doi:10.1136/ard.2008.094839, and Ahlehoff O, Gislason GH, Charlot M, et al. Psoriasis is associated with clinically significant cardiovascular risk: a Danish nationwide cohort study. *J Intern Med.* 2011;270(2):147-57. doi:10.1111/j.1365-2796.2010.02310.x] that have confirmed an increased cardiovascular morbidity in psoriatic arthritis, and that includes ischemic heart disease, congestive heart failure, as well as peripheral vascular disease.

These have varying study designs and different cardiovascular endpoints. So, it's been very difficult to really understand exactly which type of cardiovascular disease everyone's at more risk of, but broadly—compared to other chronic diseases, such as diabetes and RA—we know that there's definitely increased risk, and we need to be screening for cardiovascular risk factors. Psoriatic arthritis also has an increase in mortality rates of 1.3 due to cardiovascular compared to the general population.

So, we have a lot of data on this. We also know that perhaps treating patients with psoriatic arthritis and psoriasis might lower that risk, but unfortunately the studies, perspective wise, have not borne fruit yet, but we do know that treating them would lower the inflammatory burden.

Fatty liver disease—we know that there is significantly association with both metabolic syndrome, obesity, as well as dyslipidemia. Patients with psoriatic arthritis are more likely to have fatty liver than patients with psoriasis that don't have psoriatic arthritis. You can see the odds ratio there. So, fatty liver is a big issue. Are you screening at all in your practice or only in patients who have abnormal liver function tests?



Joseph Merola, MD: Yeah, it's interesting. We, obviously, are heavily reliant on abnormal LFTs, persistently elevated LFTs, and certainly by some further testing. It's interesting, we think very much about the . . for example, the chronic RA patient on methotrexate, obviously, very differently than we think about our obese psoriatic patients, in terms of their fatty liver disease risk.

We are increasingly using—in our patients with either very chronic long-term methotrexate and/or persistently elevated LFTs—ultrasound elastography and/or MR elastography to ease our minds, if not in collaboration with our GI liver colleagues.

Elaine Husni, MD: Right, so the higher risk goes on to other additional screening.

Joseph Merola, MD: Yeah, but we do worry, and it's interesting. I think some of my dermatology colleagues have a little bit more of a fear of the liver disease from the methotrexate-psoriasis experience, even than some of my rheumatology colleagues, who are used to the RA methotrexate.

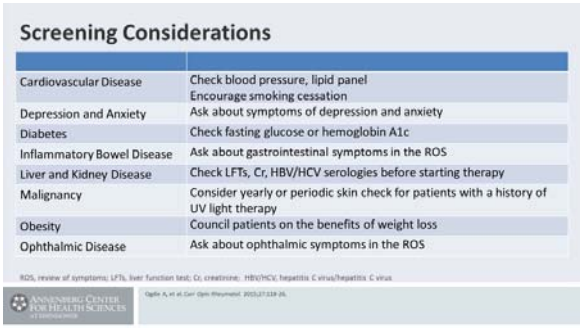
Elaine Husni, MD: Right, and it's interesting that our guidelines, rheumatology guidelines (in terms of methotrexate monitoring), and the dermatology guidelines (in terms of methotrexate monitoring), are getting a little bit closer. I think that derms were sort of biopsying too much.

Joseph Merola, MD: Less liver biopsies.

Elaine Husni, MD: Yes, less liver biopsy overall. I think that kind of helps in terms of talking about how we're changing looking at a liver disease. But fatty liver disease is definitely on the rise, and it's interesting how we're doing different things to help screen, and I agree with you on that.

Other screening considerations. So, we talked a little bit about cardiovascular disease already, mental health issues, and fatty liver, but also looking at diabetes. We have seen an increased association, so looking at fasting glucose, hemoglobin A1C. IBD we talked about in terms of GI symptoms, liver and kidney disease.

Malignancy. So, that's an interesting one . . considering whether or not, how often we should be doing periodic skin checks for these patients, especially when they're not what you think in terms of past PUVA light treatment. Do you treat those patients a little differently than those who have never had PUVA light treatment?



Joseph Merola, MD: Yeah, that's interesting. I think it's a bit of a nuanced discussion, and we have some data, but not perfect data, about how we treat those patients. For our patients who have had PUVA with recurrent nonmelanoma skin cancers, we certainly have a discussion about what the risk might look like, in terms of therapies that would otherwise further increase their risk of nonmelanoma skin cancer.

We sometimes use, to our benefit, medications like acitretin and others to try to mitigate that risk a little bit in combination therapy; but, it certainly is a consideration in terms of what we're talking to our patients about.

Elaine Husni, MD: Right, and then in terms of eye disease, I think from a rheumatology standpoint, we're very comfortable about asking about uveitis and episcleritis in RA. I think in dermatology you might [have] a little bit less comfort level, in terms of what these eye symptoms might mean.

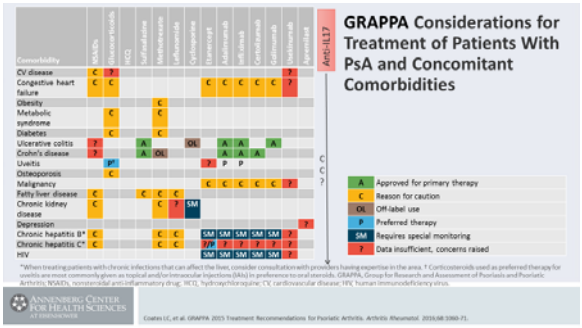
Joseph Merola, MD: Absolutely. There's a nice mnemonic, and some awareness from a physician who's a rheumatologist/ophthalmologist in the northwest, Dr. Rosenbaum, who reminds us that eye pain is an important sign. I try to remind my derm colleagues, at least, to ask a little bit about some of the photophobia eye pain and such that comes with uveitis. But it can

be challenging, for sure, from a screening standpoint.

Elaine Husni, MD: Sure. So, this list isn't meant to be . . . something that you may have to ask at every visit, [which] may seem overwhelming, but I think it's important to sort of educate, be comfortable with some of these comorbidities. And then many of these patients come back on multiple visits, and to have some sort of algorithm to check on these, or at least educate our patients, so they can alert us if any of these symptoms play a bigger role in their life.

So, GRAPPA treatment guidelines, which I know we both were involved with. I really like this slide because it does highlight all of the concomitant comorbidities, and then more importantly, it looks at each of the drug considerations, and tells us whether or not—in these color-coded boxes—whether or not we should have special reason for caution, if they have a certain comorbidity.

So, in an ideal world, you treat psoriasis and psoriatic arthritis with algorithms. But as you know, patients have different associated conditions and comorbidities, and, therefore, I love this treatment guideline that includes comorbidities to help us drill down on the different treatments that are available.



Joseph Merola, MD: Yeah, I like to use this as a teaching slide, also. I think it's quite a busy slide, but it emphasizes just some of the complexities that we deal with when thinking about these patients and trying to layer the comorbidities with new treatment decisions as we transition into some of the treatment discussions.

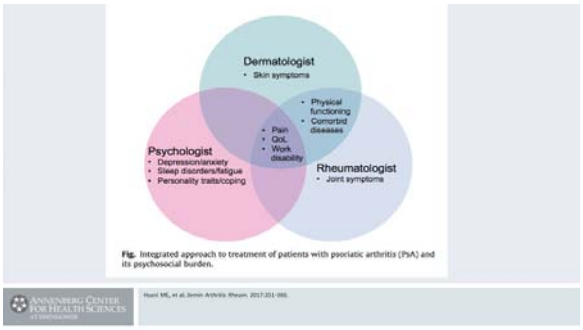
Elaine Husni, MD: Right, exactly. So, in terms of implications for disease management, I think we went over some of the things that we should be screening for and educating our patients about. Then we also highlighted perhaps some of the comorbidities that might affect treatment decisions.

So, for example, if somebody is more prone or has a diagnosis of depression, for example, there are certain medications that we may shy away from. Or perhaps IBD, sometimes the IL-17 may not be our first line treatment, since we have other options. So, these are some examples, and I think the GRAPPA treatment guidelines did a nice job of trying to filter through that, as well.

Module 3: Provider Interdisciplinary and Clinician-Patient Communication

Joseph Merola, MD: In this module we emphasize the importance of interdisciplinary communication. We will discuss how to develop care models through clinician communication. A patient-centered approach to treatment strategy, as well as the significance of clinician-patient communication, addressing adherence.

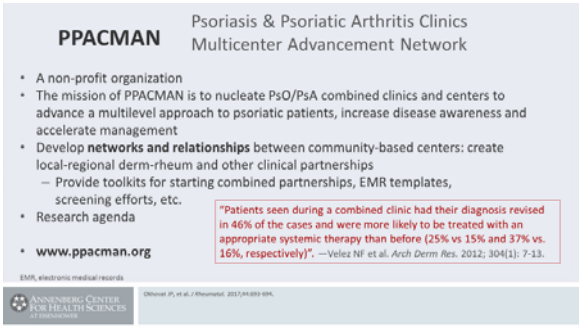
We've learned, at least in the last module, if you were with us for comorbidities, that there's a lot to the treatment of psoriatic disease beyond even the skin and the joints, and it takes a little bit of a clinician village to take care of these patients. This slide emphasizes a little bit about the various players that should be involved in the care of the patient with psoriasis, psoriatic arthritis, and it goes well beyond this, as well. So, there's a lot of complication in their treatment.



Elaine Husni, MD: And I think what's important, sorry to interrupt, but not only do the patients have to understand this communication, but physicians also, need to become more comfortable talking with each other, as well.

Joseph Merola, MD: Elaine and I are a bit biased in this regard. I think we've both bought into this concept of, at least in an academic setting, of a combined-clinics approach, where we have dermatologists and rheumatologists, physically in the same place, at the same time, seeing these patients. And I think our patients very much appreciate it, and the trainees certainly appreciate it. It's [a] very rich training and learning environment, educationally. What I hope to share over the next few slides, and Elaine will share her experiences, as well, but this concept that it isn't just about having 2 people in the same place, at the same time. I think we both very much believe that there is the opportunity for local-regional partnerships, and just picking up the phone and increasing communication—and all of the things that will ultimately help get the patient to the right care.

So, to that end I will just mention this organization quickly, and then we can spend a little bit more time on communication. But, the PPACMAN Group, PPACMAN stands for Psoriasis & Psoriatic Arthritis Clinics Multicenter Advancement Network. This is a nonprofit organization that was started a few years ago. Elaine and I are both part of the leadership of this group. The mission of this group is to try to nucleate combined clinics and centers to advance a multilevel approach to psoriatic patients, increase disease awareness, and accelerate management. That includes everything from increasing psoriatic arthritis screening to increasing communication among providers.



We very much are interested in developing networks and relationships between community-based centers, local/regional derm-rheum, and other clinical partnerships. There are a few tools to help do this, to provide what

we call tool kits, to how to start a combined clinic. Providing some EMR templates that can be used by derm-rheums and primary care docs, and other folks who are taking care of psoriatic-disease patients. We also have a number of research items that we work on. There's a website [www.ppacman.org] there.

Elaine Husni, MD: You know, it's very energizing to be at these meetings and not just to think about your own combined clinic, but really share best practices, because everyone practices in a very different environment. So, this has been a really great way to improve on what I'm doing, locally, as well as sharing best practices.

Joseph Merola, MD: Right, right. And I think it's interesting for me to see that there are a number of folks who are dedicated to the derm-rheum collaborative, but we have some colleagues around the country, I know in Rochester, Chris Ritchlin has an embedded psychologist, I believe. It is, as well, for some of the psychiatric comorbidities. I know that at the Brigham, we've started a few other . . . There's a cardiovascular person embedded in rheumatology. I think there's a lot of crosstalk that could be happening.

Again, we're preaching to the choir here, but there's a lot of benefits to comanagement and increased communication. So, how to communicate with other providers? I think it's important to think about establishing roles. Who's taking the primary lead on the patient. I'm curious to hear, Elaine, how you think that is established. Is it by the disease manifestation? By what's more active? How do you think of who's sort of taking charge of the patient?

Elaine Husni, MD: I actually let my patients run that. So, I feel that certain patients have developed a relationship with one or another physician, and usually that creates one of the better roles in terms of adherence and communication between the patient and the physician. And depending on where the patient kind of goes, if they've been having a long-term relationship with the dermatologist, then I'm there to help consult. I don't run in there and say, "Okay, now I have to take over," or vice versa. Maybe I've developed a long-term relationship with the patient, and all of sudden needed more derm or psych or GI input. So, I find that letting the patient lead sometimes has been very helpful.

Joseph Merola, MD: Great. And then I see, we mentioned communication with the primary care physician, as well. I have tried to go out of my way to at least cc [copy], it's a minimal step, but cc their primary care doctor, at least know who it is so they're understanding why we're making decisions that we're making. And hopefully embedding something about the comorbid conditions and screening for things that we may . . . and to put the dermatology hat on for a minute. I think sometimes the visits are quite brief with some of our patients, and we have to think about collaborating from a feasibility standpoint, but remembering to put in my note, "Please be sure to screen for diabetes, hypertension, and other cardiovascular comorbidities at your next visit," for example.

Elaine Husni, MD: Yeah, I think that's a great point to utilize the team to help, and that screening becomes important, because as you know, we're seeing more patients with less time, and we want to improve patient outcomes, and one of the ways is to work as a village, as you mentioned before.

Joseph Merola, MD: I think "not enough time" should resonate with just about everyone who's taken the time to watch this, right. Think about referral to rheumatology, to a psychologist as appropriate. And then, thinking about sharing

notes and picking up the phone. I think you made that point earlier and that it's a simple one but it really is tremendously impactful.

So, in any case. Shared decision-making is sort of a buzzword, but it is truly very important in the care of our patients. We have an ever-increasing list of treatment options, and it's important to include the patient in what they want to see as their treatment and treatment goals. And we're going to talk about some of the treat-to-target stuff in a little bit. But, it is as important to try to think about bringing colleagues on board with that, as well. It's often important for me to explain why I'm making the change that I want to make to the other half of the team, in trying to choose the right treatment for a patient.

In terms of, again, communicating, it's clear that it improves patient adherence to treatment, that's another important aspect. And again, to avoid rebound risk and nonadherence to therapy for example. Increasingly, all of us are either utilizing or interacting with ancillary providers, physician assistants, allied health professionals.

And I'm curious, Elaine, whether it's in your practice or with community interactions, do you find any particular challenges and/or ways to communicate with the non-rheumatologist, the non-dermatologists, or physician extender when you're dealing with comorbidities or otherwise?

Elaine Husni, MD: I think that's a really great point. We use physician . . . both physician assistants, as well as nurse practitioners in our practice, in most of rheumatology. And patients love it. Because, I think they are, sometimes, more accessible than we are. And it creates . . .

Joseph Merola, MD: They spend a little more time, potentially.

Elaine Husni, MD: Completely. And they create that extra dialogue that I think is very helpful. Like you said, this sort of open communication has not been as emphasized as [when] we were in med school, because I think we were so self-selected into our specialty, and what you say is what goes. But now I think it is much more commonplace for physicians to have team-based care. I don't think that was so much emphasized when I was in med school, so I think it's a relearning of team-based care, sharing best practices, open communication. Even though that sounds easy to do, I don't really feel like it was emphasized during the time I was in med school, but now [it's] becoming much more of the way we practice.

Joseph Merola, MD: I think it's interesting too, I was thinking some of our therapies, when they were first introduced, they tended to be introduced variably to a different group first. And one of the things that I've found helpful in the communication, is to learn from the other half, how they're using the drug. Where it fits into their practice, so I understand—where I can almost imagine—where a change might happen, or how to . . . this even occurs with the IBD coprevalence. Now, I have to think a few steps ahead. It used to be that the GI doctor was just using it, maybe a TNF, and now they've moved on, as well. I have to think, how will their decision fit into my change. If I make this change, will it cover their Crohn's or ulcerative colitis, or how do we think about that so . . .

Elaine Husni, MD: And then comanagement with methotrexate, which you know is always a challenge for all of us, right? The GI folks might use it one way, the dermatologist, and the rheumatologist . . . and I don't think there's one right answer, but I think it's very interesting that certain patients respond with a combination, and some patients do very well with monotherapy.

Module 4: Therapeutic Management Patient-Centered Approach to Treatment

Elaine Husni, MD: In this module we're going to focus on mechanism of action of approved biologic treatment options, as well as the latest safety and efficacy data. We'll provide insights into improving patient adherence, as well.

We have updated guideline recommendations. We have the 2016 EULAR Guideline updates, and based on these new pharmacologic agents since 2009, we actually have a lot to talk about. We have the IL-17 class, we have the IL-12/23 family, the PDE-4 inhibitors, and also some new TNF inhibitors that came on the market with approval for psoriasis and psoriatic arthritis. We have a focus on musculoskeletal manifestations, so looking at the EULAR algorithms, what we're talking about is there's some new outcome measures. So, in addition to skin and joints, we also can talk about dactylitis, enthesitis, and different treatment outcomes that we are looking for to improve our patients.

We also have the GRAPPA-recommendation guidelines. These are a little bit different than the traditional guidelines, I think, that we're used to reading. These select therapy based on the most severe element or domain of the patient's disease. So, a focus on achieving low disease activity for disease domains of psoriatic arthritis helps to optimize function, minimize complications, and improve quality of life. It takes a more active role in educating primary care providers, as well. We also talk about comorbidities, as we did in Module 2, including obesity, anxiety, depression, as well as skin cancer issues. And we monitor and adjust treatments regularly. So, [we are] basing this on different domains that might be heavily affected.

We also want to share a little bit about the 2018 ACR guidelines, and my fellow colleague, Joe Merola, has also been involved with the ACR guidelines, which have not been published, but will be soon. We were both involved in our guideline updates with the American College of Rheumatology, which has been done in association with the National Psoriasis Foundation, for the first time, this year. So, with all these guidelines out there . . . We have EULAR, we have GRAPPA, now we'll have the ACR-NPF guidelines. What advice do you have to [give] people? Because there's obviously nuances and differences between these guidelines, and how do you think people should think about it?

Joseph Merola, MD: I'm completely lost, frankly. [laughter] No. So, it's a good question, and I'd like to hear from you. I think these are only guidelines.

I think it's helpful for us to be familiar with them, and then, of course, like everything else, all of these are tailored to the patient. As we go on a little bit more to some of the treat-to-target, I think it helps us think about and frame how we want to apply guidelines to get the patient to where they want to be ultimately. In addition, to layer on some complexity to all of these PsA guidelines, we even have some guidance in terms of treat-to-target on what the skin target is, what the joint targets are. There's a lot to talk about today. So, I think we'll get there. It's probably worth mentioning briefly, these ACR guidelines, that we were both part of . . . They have not been published, although there was some top line presented at the ACR meeting back in October in San Diego.

That started to push . . . [there] was a little bit of a paradigm shift in terms of how we think about first-line therapies, and such, and we can certainly discuss that a little bit more. But I think that the top line was maybe thinking a

little bit more about biologics up front. And that's a big shift, in many respects.

Elaine Husni, MD: I think as you said, guidelines are really used as a framework, but not so much as a recipe, right? So, I think many of us are a bit overwhelmed by the amount of approvals for psoriasis and psoriatic arthritis, but I think that is also a good thing. Because each of our patients need choices, and now we've got them, and now we are learning together, as a group. I do probably have a little more affinity for the domains treatment. I really like that because, I think, patients present with certain domains that are more important to them, are more aggressive or severe. And I do like having that option of making domains.

Joseph Merola, MD: I do, too, and just to add to that, I like to think of our therapies in some way as which face a domain may be a little bit more than others. Many of them cross multiple domains, but I think when we're pulling apart the literature, looking at some data, I like to think about how will this particular therapy match up with a given domain, and try to piece things together, as well. So, I think for many reasons, the domain approach is a nice one.

Elaine Husni, MD: I think it's a good problem to have. More treatments options, so that's good.

We also want to be mindful of the patient-centered approach to treatment strategy. So, what do we mean by that? What does it mean by considering the whole patient? Not only are we considering skin and joints, but also the known comorbidities that are associated. It's important for patient involvement. We talked a little bit about shared decision-making and treat-to-target. Clinicians should really convey details of the treatment options and side effects, because these are the patients who are taking these drugs, and they need to, perhaps, have a say in some of the options and side effects.

That includes mode of administration, that includes what their family history [is], what side effects they're most worried about. Providing clinician-to-patient education on looking at the trigger factors, the ideology, the treatment options, and side effects, I think become very important in a shared decision-making process.

We want to also establish treatment options. There are people in the early stages who are often treated with established agents. Some of the early stages, we think of nonsteroidals, corticosteroids, and also oral DEMARDs, or disease-modifying agents, [for example] leflunomide and the role of sulfasalazine. And then, depending on the following patient-related factors which we talked about, which disease? Is it mostly skin affected, much more than joints? Is it joints affected much more, or is it more the entheseal component that is predominant in a patient?

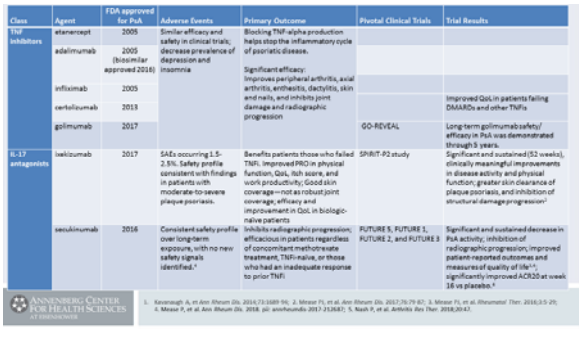
And then looking at poor prognostic factors, looking at associated comorbidities, which we talked about in Module 2, looking at severity of disease, and how they present, as well as patient-treatment preference based on mode of administration, frequency . . . I know I have many patients who travel, and sometimes it's difficult to keep things refrigerated, and maybe one of the newer pill forms are going to be a better option for them, for example.

Current evidence-based treatment strategies, so we want to have a continuing understanding of the immunopathogenesis of psoriatic arthritis, that leads to the development of new novel agents. So, this is the new alphabet soup, right? We're learning about each of these cytokines that are being blocked, and how do we know . . . in which patient, blocking which

cytokine might be more important for their disease?

Biologics do block actions of certain cells and proteins that play a major role in developing psoriasis and psoriatic arthritis, but [it's not the same in] every patient. We also know that some people may or may not be able to do subcutaneous injections. Some may or may not want to have appointments for their infusion when they have to come in, drive, park, and get an appointment. And then there's always oral options, as well. So, this is a slide to make us sit back and think about a patient's lifestyle in addition to their treatment options.

The next 2 slides may look a bit overwhelming. What it's meant to do is to highlight all the different classes that are out there. We do have TNF agents, which by far are what Joe and I are the most comfortable with. We have started with TNF in rheumatoid arthritis as far back as 2005, and now in 2017, just last year, we are getting approvals. So, IV golimumab, for example, had some great data looking at psoriatic arthritis. And then an exciting class is IL-17, which has been approved earlier on for derm, before it was approved for the arthritis part. And in derm, as you can probably teach us, we have seen clearing PASI 100, which is something we haven't seen before.



Class	Agent	FDA approved for PsA	Adverse Events	Primary Outcome	Pivotal Clinical Trials	Trial Results
TNF inhibitors	etanercept	2005	Similar efficacy and safety in clinical trials; decrease prevalence of depression and insomnia	Blocking TNF-alpha production helps stop the inflammatory cycle of psoriatic disease. Significant efficacy: Improves peripheral arthritis, axial arthritis, enthesitis, dactylitis, skin and nails, and inhibits joint damage and radiographic progression		
	adalimumab	2005 (biosimilar approved 2016)				
	infliximab	2005				
	certolizumab	2013				Improved QoL in patients failing DMARDs and other TNFis
	golimumab	2017			GO-REVEAL	Long-term golimumab safety/efficacy in PsA was demonstrated through 5 years.
IL-17 antagonists	ixekizumab	2017	SAEs occurring 1.5-2.5%. Safety profile consistent with findings in patients with moderate-to-severe plaque psoriasis.	Benefits patients those who failed TNFi. Improved PRO in physical function, QoL, fish score, and work productivity; Good skin coverage—not as robust joint coverage; efficacy and improvement in QoL in biologic-naïve patients	SPIRIT-P2 study	Significant and sustained (52 weeks), clinically meaningful improvements in disease activity and physical function; greater skin clearance of plaque psoriasis, and inhibition of structural damage progression[1]
	secukinumab	2016	Consistent safety profile over long-term exposure, with no new safety signals identified.[4]	Inhibits radiographic progression; efficacious in patients regardless of concomitant methotrexate treatment, TNFi-naïve, or those who had an inadequate response to prior TNFi	FUTURE 5, FUTURE 1, FUTURE 2, and FUTURE 3	Significant and sustained decrease in PsA activity; inhibition of radiographic progression; improved patient-reported outcomes and measures of quality of life[4,5]; significantly improved ACR20 at week 16 vs placebo.[4]

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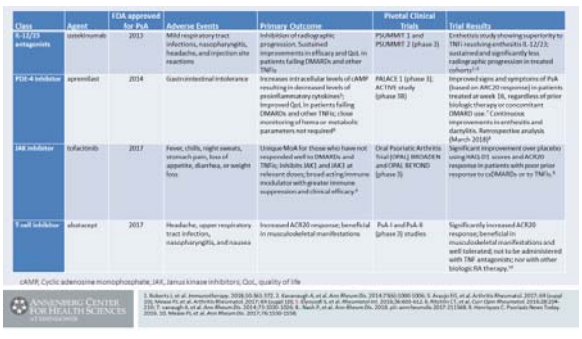
1. Kavanaugh A, et al. Ann Rheum Dis. 2014;73:1689-96. 2. Mease PJ, et al. Ann Rheum Dis. 2017;76:79-87. 3. Mease PJ, et al. Rheumatol Ther. 2016;3:5-29; 4. Mease P, et al. Ann Rheum Dis. 2018. pii: annrheumdis-2017-212687. 5. Nash P, et al. Arthritis Res Ther. 2018;20:47.

And what are your thoughts on longevity of this PASI 100 in patients?

Joseph Merola, MD: It's interesting. I think the newer agents are really starting to push the envelope in terms of what we're telling patients. And our expectations for PASI 90 and 100, and some of the newer primary endpoints are moving towards and shifting from PASI 75 to PASI 90. It's as good a time as any to have psoriasis, I think, with some of the newer agents. We do have to again think about it. This is where we come back to that domain discussion. Where do these fit relative to comorbidities? Where do they fit relative to joints? But we're definitely making good progress from a skin efficacy standpoint.

Elaine Husni, MD: So, have you seen these great PASI 90–100s? Have you seen them last? These studies are out to . . . Definitely, the 1-year data looks good, but in terms of the longer term . . .

Joseph Merola, MD: Yeah. Good question. We've seen long-term efficacy data from a number of these agents, and they do look quite good over time. Granted, any trial setting is not necessarily real-world practice, in terms of adherence to drug, in terms of some of the other factors that might affect efficacy in the real world. But there seems to be good persistence data among these agents, and I think they're increasingly being used in our hands or skin, no question.



Class	Agent	FDA approved for PsA	Adverse Events	Primary Outcome	Pivotal Clinical Trials	Trial Results
IL-12/23 antagonists	ustekinumab	2013	Mild respiratory tract infections, nasopharyngitis, headache, and injection site reactions	Inhibition of radiographic progression. Sustained improvements in efficacy and QoL in patients failing DMARDs and other TNFis	PSUMMIT 1 and PSUMMIT 2 (phase 3)	Enthesitis study showing superiority to TNFi resolving enthesitis IL-12/23; sustained and significantly less radiographic progression in treated cohorts[1-3]
PDE-4 inhibitor	apremilast	2014	Gastrointestinal intolerance	Increases intracellular levels of cAMP resulting in decreased levels of proinflammatory cytokines[1]; Improved QoL in patients failing DMARDs and other TNFis; close monitoring of homeo or metabolic parameters not required[2]	PALACE 1 (phase 3); ACTIVE study (phase 3B)	Improved signs and symptoms of PsA (based on ARC 20 response) in patients treated at week 16, regardless of prior biologic therapy or concomitant DMARD use.[1] Continuous improvements in enthesitis and dactylitis. Retrospective analysis (March 2018)[3]
JAK inhibitor	tofacitinib	2017	Fever, chills, night sweats, stomach pain, loss of appetite, diarrhea, or weight loss	Unique MoA for those who have not responded well to DMARDs and TNFis; inhibits JAK1 and JAK3 at relevant doses; broad acting immune modulator with greater immune suppression and clinical efficacy.[2]	Oral Psoriatic Arthritis Trial (OPAL) BROADEN and OPAL BEYOND (phase 3)	Significant improvement over placebo using HAQ-DI scores and ACR20 response in patients with poor prior response to csDMARDs or to TNFis.[4]
T-cell inhibitor	abatacept	2017	Headache, upper respiratory tract infection, nasopharyngitis, and nausea	Increased ACR20 response; beneficial in musculoskeletal manifestations	PsA I and PsA II (phase 3) studies	Significantly increased ACR20 response; beneficial in musculoskeletal manifestations and well tolerated; not to be administered with TNF antagonists; nor with other biologic RA therapy.[5]

cAMP, Cyclic adenosine monophosphate; JAK, Janus kinase inhibitors; QoL, quality of life

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Elaine Husni, MD: Yeah, of course, I'm jealous because we don't really have the ACR20/50/70 or ACR100 equivalent. We are not, but still very exciting to hear in terms of skin improvement. And then of course, we have many other agents that we can highlight, including the IL-12/23s, the PDE-4 inhibitors, the JAK, which has just been approved. Oral Janus kinase inhibitors have been seen in RA but now [are] approved for psoriatic arthritis, as well as T-cell inhibitors, like abatacept, which are newer to the market. And we're getting more experience with them in psoriatic arthritis, as well.

In addition to the efficacious part of treatments, we also look at safety of approved biologics. There are some of the common adverse events that we are very familiar with in biologic agents, meaning the URI [upper respiratory infection] symptoms, the slight increased rate of serious infections that do require hospitalization. We also know that patients with higher BMIs may have a harder time reaching that target. So, if you are overweight, it does look like it can be harder for some of these biologic agents to maintain minimal disease activity.

IL-17s also do not seem to predict against flares of IBD, so these nuances of comorbidities that were out there . . . some of the safety signals we need to be aware of. We know that some of the oral JAK inhibitors, for example, do look like they have maybe a little bit more incidence of zoster compared to the biologic agents. There's a lot out there that we have to learn about side effects, as well.

We also want to think about optimal treatment selection. In a particular patient, how do we look at long-term safety data? What are the contraindications, as we talked about with the comorbidities? The tolerability, the cost to these, as well as assessing clinical severity. So, skin vs joints: which ones are more severe in how we think about these biologic agents, vs all the other treatment aspects?

Strategies of treatment order—so this treat-to-target, which we'll talk a little bit more in detail in the next module, but looking at that tight control of psoriatic arthritis. And, also sort of having that initiating systemic therapy, and then vs maintaining systemic therapy.

I wanted to ask you, Joe. In my combined clinics, I'm always struck by the dermatologists that sometimes do intermittent therapy based on how the skin's doing. Well, [those of] us in rheumatology, I don't really have that concept. Once I initiate treatment, I tell my patients they're on lifelong DEMARDs. And I was just wondering, in your skin patients only . . .?

Joseph Merola, MD: I think maybe I was influenced by rheumatology, as well. I think we're of the mindset of getting our patients clear, that this is, at present—in 2018—a chronic disease with a chronic therapy, and we are also of the initiate-and-maintain mindset. Outside of . . .Also, we'll introduce and take away combination therapies, of course, as needed. A topical here and there, excimer laser, other things to top off their skin, coming and going with minor flares.

In terms of biologics, we are also about sticking on therapy for sure.

Elaine Husni, MD: So I think you know we are obviously looking at all the comorbidities in keeping the inflammatory burden down. I do think it's interesting that in RA they are starting some of those withdrawal trials, and I think [there is] more to come in terms of psoriasis and psoriatic arthritis.

Joseph Merola, MD: Aside from the skin world, as we've seen the p19 inhibitors, now that R23 inhibitors are coming, where the frequency of

dosing is—for some of them—every 2 or 3 months, where many of our skin patients will clear and have prolonged clearance well beyond that frequency, where you're given a few doses and are clear for many months. I think our patients are going to teach us about what tapering off looks like. I think the natural history will be to skip a bit and see. I think we're going to learn a little bit more about dosing intervals as a natural [course].

Elaine Husni, MD: There's not a week that goes by where a patient says, "Well, you know, I didn't refill my prescription, and it's been X amount of weeks," and they are clear. And, so, I think, like you said, we're going to learn from each other.

But in terms of patient adherence, here are some . . . the MAPP survey results of patients with psoriatic arthritis. So, 45% discontinued oral or biologic therapy due to issues of safety or tolerability or lack of efficacy. And over 60% were concerned about health risks with long-term therapy, and 90% . . . 90%, expressed a need for better therapies. So, there is still room to wiggle here, where we're trying to develop treatment plans that are not just initiating but maintaining, and what to do when somebody is in what I consider deep remission. They've been good for greater than 2, 3 years without an ounce of activity. Are those the patients who we start thinking about [for] these withdrawal therapies or not?

Joseph Merola, MD: De-escalation of some sort.

Elaine Husni, MD: Correct, correct. It's also important to take this to the next level. We talked a little bit about treatment algorithms. We talked a little bit about looking at patient adherence. And now looking at patient-reported outcomes, right? Many of these questionnaires that we talked about earlier, the RAPID3 and the PsAID. The RAPID3 is a routine assessment of patient index data. This has been validated very strongly for rheumatoid arthritis patients and, as you said, increasingly validated in psoriatic arthritis patients. And these are a core set of patient self-reported measures, looking at physical function, pain, and patient global estimates. And then PsAID, which is more specific to the psoriatic arthritis impact of disease questionnaire, they have several types of PsAID. One is mostly for clinical trials and one is used in clinical practice, which have different types of domains. The ones in clinical practice have 12 domains, while the one in clinical trials have 9 domains. Looking at patient reported outcomes, and then the DLQI which is specific for dermatology, looking at a dermatology life quality index.

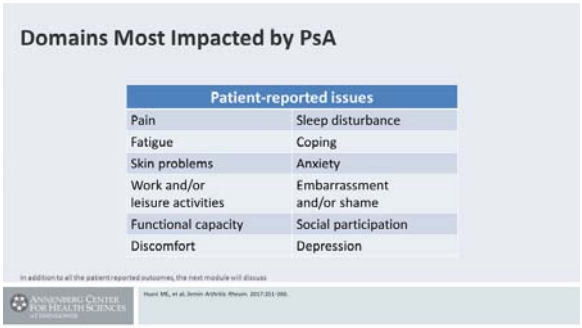
So, in terms of patient reported outcomes, I think this is a hot, growing area. I think we are getting better at facilitating patient outcome reported back to us as a physician. And then the question to you is, how do you use that?

Joseph Merola, MD: Right. I think one of the important things in the clinical practice setting . . I think a lot of these PROs are of great interest in the clinical-trial setting, particularly in great detail like a PsAID, for example. Particularly in dermatology practice, thinking about the derm aspect, I think feasibility is incredibly important. So, choosing something that you can interpret with your patient, together, is important. Things like a simple patient goal sometimes makes sense, at least to give you a baseline starting point for discussion. If they're thinking about what their goals might be, and what the components are that are driving their answer. Similarly, a DLQI, thinking about what domain is driving their dissatisfaction and trying to figure that out. I think it's important. I'm not sure that we have, yet, come to the perfect (nor do I think there's necessarily a perfect) PRO in this setting. We measure in the rheumatology clinic

. . . We try to measure pain increasingly in our combined clinic, thinking about measuring RAPID3 from a PsA standpoint, as well. What are you doing in your clinic?

Elaine Husni, MD: I think what I find the most helpful . . . I think right now we're very good at measuring patient-reported outcomes. There's just a lot of questionnaires that are out there. We now have a tablet where the patients can . . I'm sure you do, as well. I think the big role for us is having that conversation back to the patient, where we're actually taking that information and doing something with it. I think nobody really wants to answer a bunch of questionnaires without feedback. So, I think we are dealing . . .I think the first aspect was trying to understand which PROs are important to measure, like you said, without causing questionnaire fatigue, right? I think what we are really interested in is how do we give back that information and create an open dialogue so we can move forward?

The domains that are most impacted by psoriatic arthritis, as you see listed here. We're looking at things that are important to the patient is pain, fatigue, their skin problems, how it's related to their work, their functional capacity, their level of comfort, sleep, coping, anxiety, embarrassment or shame. Social participation, I think, is a big issue component, as well as depression. So, here's a list of domains that are important to patients. And many of them match what is important, that we see in clinical trials, as well, that we're measuring.



Joseph Merola, MD: Can I ask you a little bit about that? I think particularly in psoriatic arthritis patients, but our psoriasis patients, as well, fatigue always seems to come to the top. The physicians seem to downplay the fatigue, or the impact of fatigue, and don't tend to ask about it as much, at least in my experience. But [to] the patients, it's a big deal. What do you do about assessment? How do you start to approach fatigue in your practice?

Elaine Husni, MD: I'm actually honest with my patients. I think the reason that I don't deal with fatigue is because I don't have a treatment for it. Does that make sense? So, I've noticed that I tend to want to . . . oh, see a skin plaque, I have treatment for that. I see a joint inflammatory, I have treatment for that. Enthesitis . . . and I think when I started going down symptoms like fatigue, where I feel that I'm hoping that these drugs affect fatigue, but sometimes when they don't I'm a little bit less comfortable. And, so, I try to be honest. I'm like, "You know, fatigue is something that is very bothersome." But I also have to be honest with them, that the data coming back . . . that I might not be able to know which treatment would be better for fatigue. Does that make sense? As I'm much more comfortable with which treatments are better for skin or joints.

Joseph Merola, MD: Agreed. To that end, we do our best to assess quality. We have an increasing research interest in assessing sleep quality and thinking about that.

Elaine Husni, MD: Right, which would be a big component of fatigue, right?

Joseph Merola, MD: Could be. It's harder to tell. And as you said, in terms of therapeutics, I think the biologics tend to face fatigue maybe a little bit more than certain other things. One of the tolerability side effects, I think of methotrexate, sometimes, can be the fatigue, at least from the patient perspective. So, we'll sometimes have that discussion, as well, as much as we can.

Elaine Husni, MD: But I'm always very reassured that we are now . . . I feel much more comfortable measuring fatigue than I did even a couple years ago. So, I think that's really pushing the field forward.

Module 5: Therapeutic Management (Treat to Target)

Joseph Merola, MD: In this module, we review treatment objectives, including treat-to-target strategy and treatment management, which includes continued assessment of musculoskeletal disease, skin disease, and health-related quality of life.

I think there are a few treat-to-target concepts that are worth mentioning. The more recent involves a treat-to-target guideline set forth by the National Psoriasis Foundation. This is specifically a skin target that looks at a target response being a body surface area of less than or equal to 1%. For those who may be less familiar, we typically talk about a body surface area of 1% being about the size of a patient's palm print. So, it's quite an aspirational target, an aggressive target.

That's at 3 months, as well as at the 6-month assessment. They also set out a potentially acceptable alternative response of a body surface area of less than or equal to 3% at 3 months, or 75% improvement from baseline. That [body surface area] BSA of 3%, you'll notice may be familiar from the minimal disease activity criteria that we saw for psoriatic arthritis.

So, here again we have those minimal disease activity criteria for psoriatic arthritis. This is a composite of 7 items. If you may remember from an earlier module we reviewed that the minimal disease activity includes 7 items: a tender joint count of less than or equal to 1; a swollen joint count of less than or equal to 1; those skin criteria, again, of a PASI of less than or equal to 1.

I think not a lot of rheumatologists, in particular, are doing PASI scores, but alternatively a body surface area of less than or equal to 3%. A patient pain VAS, a patient global activity score as a VAS HAQ; and a tender entheseal point count. Meeting 7 out of 7 of these is considered very low disease activity. I think these are both fairly stringent treat-to-target criteria.

I'm curious to ask Elaine, we're going to talk about a few other potential treat-to-targets, but which do you use, and do you follow these at what sort of interval in your clinic?

Elaine Husni, MD: Yeah, I mean I usually see my patients every 3 months or so, interval-wise. That's what we do unless they have more symptomatic, then they'll come back sooner. I do like MDA, and I do look at other ones, as well, trying to get more familiar with each one, and seeing which one I like.

I think the trouble I have many times is even though the skin might be less than 3% or 1%, but what happens if it's in an area that's really affected by them? I had a construction worker

the other day where it was on the soles of their feet, and they couldn't get into their boots to do their job. So yes, everything else was minimal disease activity, but of the area that was minimal, it was very problematic.

Joseph Merola, MD: I would say one of the shortcomings of these minimal disease criteria, it's 5 out of 7 still leaves the possibility that you could have quite bad skin disease, even with minimal disease activity, which I think is facing psoriatic arthritis in some ways. It's a great point, I think; that's an important point.

Maybe I'll share a few others, and we'll come back to the concept of treat-to-target, how we deal with it. We didn't get a lot of chance in these modules to talk about the type of control of psoriatic arthritis.

In the [COPA] study, that was very much hinging upon these minimal disease activity as the endpoint for considerations of therapeutic management. Probably worth noting that those who met this minimal disease activity seemed to fare better in that study. However, it was, on balance, with slightly increased adverse events, and they didn't look at this—but I'm sure that cost is also in the balance there, for sure.

Elaine Husni, MD: Yeah. I think these are very helpful, but I think in certain situations, we just need to be mindful that there are particular instances where it might not all apply.

Joseph Merola, MD: Some other treat-to-target targets that are worth mentioning, [disease activity in psoriatic arthritis] DAPSA remission, another validated target to consider in terms of where we want our patients to be. Very much facing psoriatic arthritis, the DAPSA remission criteria, less than or equal to 4, considered a remission cutoff. If anyone is doing a PASDAS, there are also established cutoffs for remission with a PASDAS of, I believe, less than or equal to 1.9.

So, how do we use these treat-to-target strategies? I think we certainly, increasingly, are encouraged to use some quantitative measure to be measuring disease activity in our patients over the course of visits, and using some of these cutoffs as a target. I will say I think, in a practical sense, a lot of this is about a discussion with the patient on where they want to be. I'm going to bring Elaine back into the conversation again. I think what's interesting . . . I'll speak to the skin aspect for a moment.

The NPF target we just talked about, for example, is quite stringent. Some therapies may get a patient to that endpoint; we certainly . . . I think most patients want to be clear. But I have some patients . . . I don't want to single any out . . . but I have some older gentlemen, for example, who frankly aren't as bothered by the extent of their psoriasis. Maybe they don't want to be pushed into a systemic biologic or have their therapy changed, if their joints are happy. How do you think about treat-to-target strategies, how do you use them? Well, we've heard about a few of them here.

Elaine Husni, MD: I think that's a really great point. And I think that also highlights how do you use the patient-reported outcomes, right? So, there's the physician measures, which these do a good job. And then there's also the patient measures, and how do you balance when they believe they're in low disease remission, but yeah, they don't meet all the criteria for our low disease remission.

So, I think that shared decision-making comes into play. I think it's also important to screen for some of these high-risk comorbidities, so they know whether or not they're at risk for some of these things. Because if they are, for cardiovascular disease or metabolic syndrome,

for example, then it becomes important that they understand the reason why we want to get them in lower disease activity, lower disease treat-to-target.

So, I think it becomes more of an educational phase, as well. Not just meeting checkboxes.

Joseph Merola, MD: Right. I think just to go back to some of the collaborative-care stuff that we talked about—communication: I found it increasingly interesting to see whether—I'm not sure—whether we have data on this, but whether or not some of these composite treat-to-target endpoints encourage communication and referral.

If you're say, going down the checkbox, and you see that the joints are met, the joint endpoints are met, but maybe the skin isn't, does that encourage you to say, "Hey, maybe we should have you pop into your dermatologist to talk to you about the skin," or vice versa. If I'm a dermatologist, and I'm looking at one of these composite endpoints, would I get to the point of saying, "Your skin looks good, but I see you're not meeting X endpoint." And then sort of pull out.

There may be more food for thought as we think about collaborating and sharing . . . You know, we talked about sharing note templates. Maybe our notes or templates include some cutoffs for each other to think about shared management.

Elaine Husni, MD: I think, overall, it's just great that we're at a stage where we're looking at low disease activity. And I actually have some checkboxes to review. So, I think from that approach, I think this is really great. But I think these special cases are a good way to maybe increase our comanagement and research it.

Joseph Merola, MD: One of the other concepts where we mentioned remission and the joints, some folks have thrown around the concept of remission in the skin, and what does remission really mean. This sort of absence of clinical and lab evidence, I think of inflammation and/or minimal disease activity, or no disease activity.

I think the definition is still a bit in flux. It may mean something different to us as clinicians—than what it means to patients. A lot of our patients would consider themselves in remission when they're no longer on a therapy or needing a therapy, for example. And what does that look like over time?

It's a good segue to some of the newer therapeutics, at least in skin, where we have these large points of time in between injections, for example, in between therapies . . .

Elaine Husni, MD: Twelve weeks.

Joseph Merola, MD: . . . At what point are we considering remission there, or at what point do we de-escalate therapy? And that's been a theme that we've brought up a few times, as well.

I think another point that might be worth bringing up—we can have a little discussion about—is how do we think about treat-to-target, or think about endpoints in a patient with unbalanced activity? Where the joints don't meet the skin, or don't meet entheseal activity is active where you've corrected, say, peripheral joint issue. Or how do you think about that?

Elaine Husni, MD: I definitely have patients who have a lot more active skin, let's say, than joints. And, so, I do think that these treat-to-target, sometimes, is a one-size-fits-all. Sometimes when I do get those patients who have recalcitrant skin disease, I usually would pick up

the phone or try to talk to the dermatologist again and say, "Hey, listen, they look like they're doing well. They're meeting sort of treat-to-target, but listen, their skin is still active, and we need to look at topicals or other adjunctive therapy."

So, I like your point about still communicating that, when needed, even if they might be close to reaching treatment target.

Joseph Merola, MD: And do you consider . . . Do you actually say, "Write a topical?" Do you feel comfortable maybe topping the patient off who's got a little disease activity, or do you always defer? Or how do you sort of manage?

Elaine Husni, MD: Yeah, I think that's a really great point. I think maybe asking me might be a little bit different because I've been working with a dermatologist closely. But when I think back when I didn't have access to a dermatologist, I would refer. But now I'm a little comfortable with topicals.

But like you said, depending on where it is, because topicals in a sun-exposed area in the face can lead to other issues, if you're not prescribing it correctly. So, it depends also on where those plaques are, and where you're doing it. And cycling, where the skin might be thinner and things like that.

Joseph Merola, MD: So, in terms of treatment algorithms and switching, I think one of the themes is tailoring treatment for individual patients, taking into account a variety of factors: how active is their disease, how severe is their disease? Certainly, prognostic factors; I think this may be a little bit more of a concern, for example, with psoriatic arthritis, when we think about an erosive phenotype; elevated inflammatory markers on things that might portend the worse outcome; comorbidities, as we heard in one of our other modules in great detail; cardiometabolic risk factors; their treatment history, their treatment preferences, of course, in terms of motive therapy, for example.

Access is always a question. Sometimes it's not us or our patients deciding, but it's instead the payer, for example, deciding which way we head in therapy. I'm sure you're subject to that, as well.

And so ultimately incorporating the assessment and management of all factors, including psychological and the physical concerns of the patients into our decision making.

So, I think we've had a number of important takeaways from this entire session, including that early diagnosis and early aggressive treatment should aim to halt or minimize joint damage, and think about clearing skin psoriasis. We mentioned that we're getting to a point where treat-to-target strategies and some of the newer therapies are really getting patients, particularly skin, to ever-more new levels of clear. And that's making our patients very happy.

We talked about treating key clinical domains, whether that be peripheral arthritis, axial disease, enthesitis, dactylitis, skin and nail disease. Being aware of comorbidities, thinking about some comanagement when it comes to comorbidities, and appropriate communication with other providers.

Again, collaboration and an interdisciplinary approach to care, both in terms of screening, but also management of patients. We mentioned treat-to-target strategies in this module to improve patient outcomes. We didn't spend as much time on direct patient education, but certainly bringing patients into treatment decisions is crucial. Shared decision-making, being, I think the buzzword around;

really thinking about how to incorporate patients in their own care. And their well-being, ultimately around their disease.

And then helping patients gain a better understanding of their condition, and how to manage it.