RHEUMATOLOGY NURSE
PRACTICE
Accredited education for registered nurses and advanced practice providers

Inside this Issue

VOLUME **5** / ISSUE **4**

- *What are some of the primary patient and clinician barriers to the successful treatment of psoriatic arthritis (PsA)?*
- *What are the most appropriate goals of treatments for patients with PsA?*
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Doing the ***MOST*** *for Our Patients with*

PSORIATIC ARTHRITIS

RELEASE: MAR. 31, 2021 / EXPIRES: MAR. 31, 2022

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ACTIVITY DESCRIPTION

In this issue of *Rheumatology Nurse Practice*, we review the latest PsA treatment guidelines and offer insight into how these recommendations can be translated into clinical practice. We also discuss data regarding the efficacy and safety of various classes of DMARDs, including conventional synthetic, biologic, and targeted small-molecule agents, and examine how providers can optimize their patients' chances of treatment success with these options.

LEARNING OBJECTIVES

After participating in the activity, learners should be better able to:

- Identify at least two physician and patient barriers preventing optimal care of psoriatic arthritis (PsA)
- Analyze key similarities and differences in published guidelines for the treatment of PsA
- Assess the appropriate utilization of biologic and small molecule therapies approved for the treatment of PsA
- Discuss the importance of setting realistic and attainable treatment goals for patients with PsA

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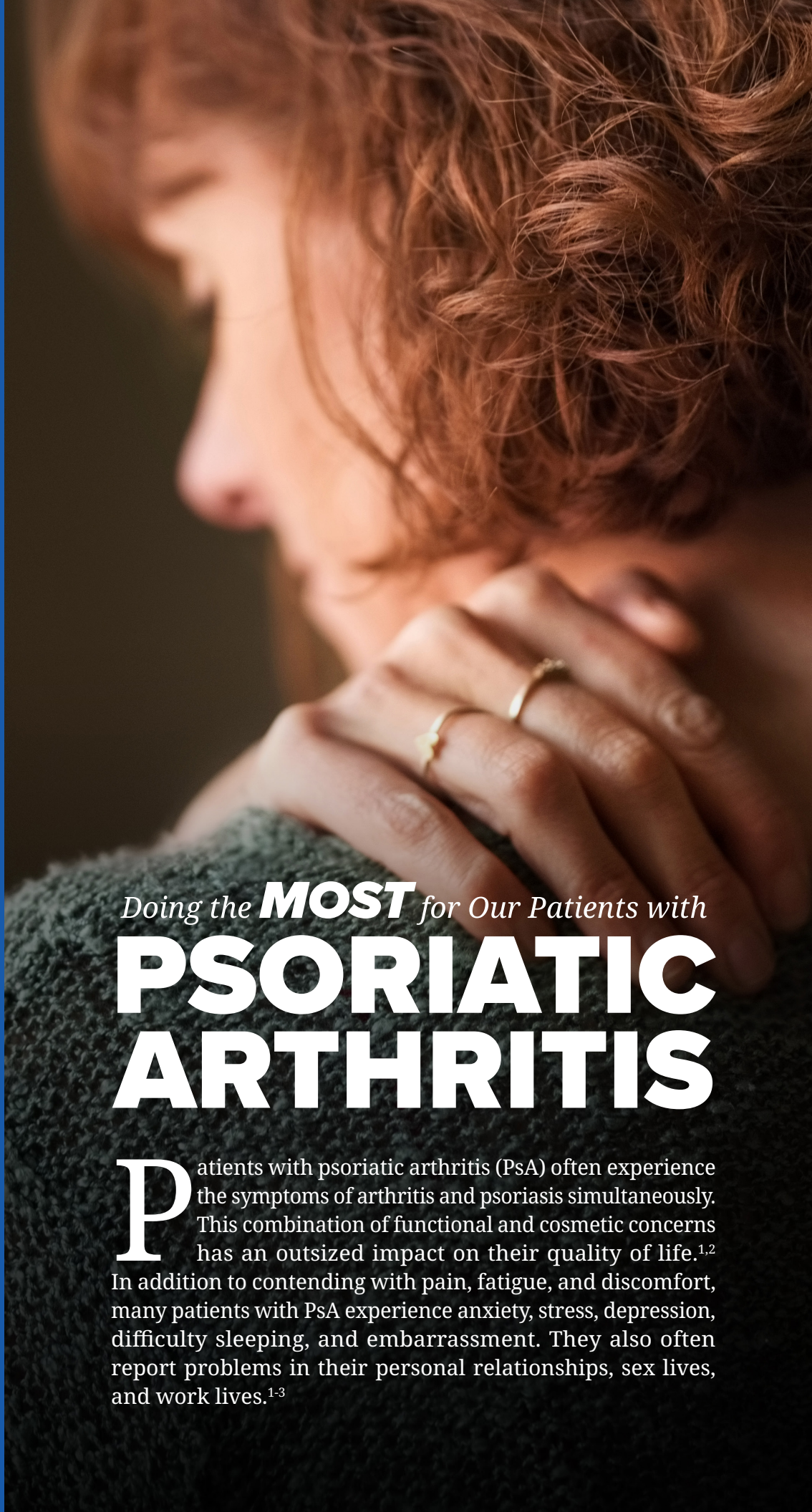

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PSORIATIC ARTHRITIS

Patients with psoriatic arthritis (PsA) often experience the symptoms of arthritis and psoriasis simultaneously. This combination of functional and cosmetic concerns has an outsized impact on their quality of life.[1,2] In addition to contending with pain, fatigue, and discomfort, many patients with PsA experience anxiety, stress, depression, difficulty sleeping, and embarrassment. They also often report problems in their personal relationships, sex lives, and work lives.[1-3]

Fortunately, patients and their healthcare providers have more treatment options than ever before. Over the past 5 years, multiple new therapies—including several first-in-class treatments—have been approved by the U.S. Food and Drug Administration (FDA), resulting in an array of options that span multiple classes. With today's therapies, many experts now consider remission a reasonable treatment goal for some patients with PsA, especially if effective treatment is provided early in the course of disease.[4] Indeed, research shows that early, effective treatment is key to improving long-term outcomes for patients with PsA.[5]

Given the complexity of the therapeutic landscape, however, selecting an effective treatment for a patient with PsA can be challenging. Although the wealth of treatment options now available is a boon for individuals who are not responding to their current medications, it forces clinicians to make complicated choices about which therapies will best serve their patients' needs. For each individual, providers must weigh the risks and benefits of available disease-modifying antirheumatic drugs (DMARDs) and decide how to sequence these therapies if a patient's current treatment is not helping them meet their goals.

Barriers to Effective Treatment

Despite the importance of adherence to treatment regimens, many individuals with PsA are not taking prescribed DMARDs to prevent their disease from progressing. In one large study of patients with PsA, nearly half (49%) reported receiving either no therapy or topical therapy only, leaving their joint disease untreated,[3] even though clinical trial data show that optimal improvement in patients' health-related quality of life requires successful treatment of both skin and joint symptoms.[6] So why aren't more patients with PsA receiving effective therapies for their disease? The answer to this question is multifaceted.

Some patients with PsA avoid medical care. In one large study, 17% of patients with PsA had not seen a provider in the past year to help manage their disease.[7] Some of these patients likely feel that therapy will not help them, especially if they have been frustrated in the past by ineffective treatment.

The cost of treatment and insurance issues are also important deterrents to seeking care in the United States. In a recent survey of more than 3,139 patients with PsA, nearly one-third reported barriers to accessing treatment, the most common of which were lack of insurance coverage for PsA treatments and high out-of-pocket expenses.[8]

Many patients with PsA do not receive effective treatment even when they are under the care of a healthcare provider. In a recent study of 3,714 patients with PsA from 18 different countries who were being treated primarily by rheumatologists and dermatologists, 41% had never received DMARD therapy.[9] Why such a high number? Although some patients may be reluctant to start DMARD therapy, decisions made by their clinicians are also an important factor. Clinical recommendations for the treatment of PsA state that rheumatologists are the specialists who should primarily care for the musculoskeletal manifestations of patients with PsA.[10] However, in reality, many patients with PsA receive care from other specialists, often dermatologists or primary care providers. Many of these providers mistakenly believe that PsA has a mild course and thus does not warrant aggressive treatment.[2] They may also be unaware of the benefits of promptly referring patients with PsA to a rheumatologist. In some cases, patients with PsA who present with less familiar manifestations, such as axial symptoms or enthesitic pain, may even be referred to an orthopedist or physical therapist rather than a rheumatologist, further delaying effective treatment.[11]

Although patient choices and delayed referrals certainly contribute to the lack of early and effective treatment of PsA, one of the most important barriers to quality care is the complexity of the decisions that a rheumatology specialist must make when selecting the most appropriate regimen for a given patient. This problem is magnified by the limited information available to guide PsA treatment decisions, especially relative to the evidence base available for other rheumatic diseases such as rheumatoid arthritis (RA). This lack of evidence has led to shifting and sometimes conflicting expert consensus on treatment approaches.

There are currently three different sets of clinical practice guidelines for managing PsA, one released by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) in 2015,[12] another from the American College of Rheumatology (ACR)/National Psoriasis Foundation (NPF) in 2018,[5] and the last from the European League Against Rheumatism (EULAR) in 2019 (Table 1).[10] In this issue, we will attempt to synthesize the key recommendations that providers should be aware of when treating patients with PsA.

In general, when choosing which set of guidelines to prioritize in a given scenario, clinicians should keep in mind that because the GRAPPA guidelines were released in 2015, they predate approval of some of the newer PsA therapies such as the JAK inhibitor tofacitinib, the CTLA4-Ig fusion protein abatacept, and newer members of other biologics classes. However, the GRAPPA guidelines are unique in their emphasis on tailoring treatment recommendations to the domain of a patient's body that is most affected (e.g., peripheral joints, axial joints, dactylitis, enthesitis, skin, nails).[12] The ACR/NPF guidelines present treatment recommendations in ranked order whenever possible, providing a degree of specificity that the other guidelines do not.[5] The EULAR guidelines are the most recently updated.[10]

Table 1 *DMARDs Approved to Treat PsA*

Type of Treatment		Agent	Administration Mode
Conventional synthetic DMARD		Methotrexate	Oral or SC
		Sulfasalazine	Oral
		Cyclosporine	Oral
		Leflunomide	Oral
Biologic	TNF inhibitor	Etanercept	SC
		Infliximab	IV
		Adalimumab	SC
		Golimumab	SC
		Certolizumab pegol	SC
	IL-12/23 inhibitor	Ustekinumab	SC
	IL-23 inhibitor	Guselkumab	SC
	IL-17 inhibitor	Secukinumab	SC
		Ixekizumab	SC
		Brodalumab	SC
	CTLA4-Ig fusion protein targeting CD80 and CD86	Abatacept	SC or IV
Targeted synthetic	JAK inhibitor	Tofacitinib	Oral
	PDE-4 inhibitor	Apremilast	Oral

Abbreviations: IV, intravenous infusion; SC, subcutaneous injection

Setting Treatment Goals for PsA

All three sets of PsA clinical practice guidelines now recommend that clinicians use a treat to target (T2T) approach to assess patient response to therapy. This recommendation is based on the results of a clinical trial that compared outcomes for patients with newly diagnosed PsA who received either T2T care (an assessment every 4 weeks, with escalation of therapy if sufficient progress was not achieved) or standard care (an assessment every 12 weeks, with no specific criteria for escalating treatment).[13] At 48 weeks, joint and skin outcomes were significantly better in the T2T group: almost 40% of patients who received T2T care had achieved minimal disease activity (MDA) vs. only 25% in the standard care arm.[14]

However, translating T2T into clinical practice for patients with PsA has proven challenging. In RA, a condition for which T2T care is well established, selecting a target and measuring progress toward that target is relatively straightforward. In PsA, by contrast, there is not yet consensus over what the typical treatment target should be or how improvement should be measured. Not surprisingly, a recent survey found that only 56% of providers currently use T2T to manage their patients with PsA.[15]

Defining a quantifiable treatment target for PsA is difficult since the disease can manifest in so many ways. When analyzing the severity of a patient's PsA, a clinician must consider disease activity levels for the musculoskeletal system (including involvement of peripheral and axial

joints, dactylitis, enthesitis, and spine inflammation) and skin and nails, as well as extra-articular manifestations such as uveitis and inflammatory bowel disease.[1,16] The challenge, then, is to select a meaningful target toward which a patient's progress can be assessed using a composite measure. This composite measure must capture the complexity of PsA, but must also be able to performed during the a typical 15-20 minute office visit. A difficult task indeed.

Currently, the EULAR PsA guidelines are the only ones that specify a T2T target, suggesting remission in most cases and low disease activity in others.[10] A previous international task force dedicated to using T2T for spondyloarthritis (including PsA) emphasized that any treatment target should be chosen using a shared decision making approach.[17] This, they claimed, is because the best goal for a given patient will depend on their unique circumstances and goals.[18,19] For example, in a patient with newly diagnosed PsA who does not have comorbid medical conditions, remission might be an appropriate target. However, for a patient who has already tried multiple PsA therapies and still has high disease activity, or for a patient with comorbid conditions or a medical history that impacts the risk/benefit consideration for aggressive PsA treatment, a goal of low disease activity might be more appropriate.

This leaves open the question of how to measure a patient's progress toward the target. Currently, no clear criteria for measuring progress toward remission exist, limiting the use of this target.[20] However, a number of criteria have been proposed for measuring progress toward low disease activity.[21,22] The guidelines for using T2T to treat spondyloarthritis recommend clinicians use the minimal disease activity (MDA) or disease activity in psoriatic arthritis (DAPSA) criteria, which are among the easiest, fastest composite measures to carry out in the clinic.[15,17]

To date, the MDA criteria represent the only composite measure that has been used in a clinical trial of T2T for PsA,[13] and a recent survey of physicians found that MDA is currently the most popular T2T target for this disease.[15] The MDA criteria consist of seven components that measure psoriasis activity, joint pain, and the patient's ability to function, incorporating assessments from both the provider and patient (Figure 1) . Although no uniform definition for low disease activity using the MDA criteria has yet been established, an MDA score of 7/7 has been proposed in the literature.[21]

Hopefully, ongoing research will provide insight into how best to carry out T2T for PsA in the real world, answering questions such as how often patients should be assessed, which types of targets and composite measures are most helpful, and whether risk factors for joint damage can be used to identify patients who might benefit most from early and intensive T2T care.[15,19]

Figure 1

Criteria for Minimal Disease Activity:[36]

- Tender joint count ≤1
- Swollen joint count ≤1
- Psoriasis Area and Severity Index ≤1 or body surface area ≤3
- Patient Pain Visual Analogue Score ≤15
- Patient Global Activity Visual Analogue Score ≤20
- Health Assessment Questionnaire ≤0.5
- Tender entheseal points ≤1

When to Start Treatment in Patients with PsA

Clinical practice guidelines emphasize that all individuals with active PsA should have access to the treatments they need to optimize their quality of life.[10] Thus, providers should ensure that patients are given access to effective treatment as early as possible during the course of their disease, as available evidence indicates that it is best for patients with active PsA to start treatment as soon as possible. In particular, clinical trial data suggest that although all patients with PsA benefit from treatment, patients who initiate therapy within 2 years of their diagnosis experience greater improvements than those who initiate therapy later.[23]

DMARDs are the only medications that can actually prevent joint damage in patients with PsA. Therefore, the ACR/NPF guidelines recommend DMARD-based treatment for all patients with PsA.[5] Non-DMARD therapies such as nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended only if a patient does not have severe PsA or psoriasis AND their risk from taking a DMARD appears to outweigh the benefits (due to, for example, contraindications). The EULAR guidelines offer slightly different recommendations, indicating that individuals with polyarthritis (≥5 swollen joints)—with or without dactylitis—should start DMARD therapy, but patients with mono/oligoarthritis should try NSAIDs and/or local glucocorticoid injections first, unless poor prognostic factors are present.[10] In real-world practice, if and when a patient chooses to begin DMARD therapy will often depend on how they feel about their PsA symptoms and about starting this type of treatment, as well as input from their provider.

Although early, effective therapy is important for all patients with PsA, prompt treatment is especially critical for those at high risk of joint damage. In addition to individuals with polyarthritis, this group includes individuals with poor prognostic factors, such as existing joint structural damage; high erythrocyte sedimentation rates/C reactive protein levels, which are indicative of inflammation; dactylitis; or nail involvement.[10]

Where to Start with Treatment

Today, a wide variety of DMARDs are available to treat PsA (Table 2). These include conventional synthetic DMARDs such as methotrexate; biologic DMARDs, including TNF inhibitors, IL-12/23 inhibitors, IL-17A inhibitors, and the CTLA4-Ig fusion protein abatacept; and targeted synthetic DMARDs, such as the Janus kinase (JAK) inhibitor tofacitinib and the PDE-4 inhibitor apremilast. With so many options, selecting a patient's first treatment can feel overwhelming. To complicate this choice further, current clinical practice guidelines differ regarding which class of medication to prescribe first.

The ACR/NPF guidelines recommend starting most patients on a TNF inhibitor; for patients with severe psoriasis or contraindications to TNF inhibitors, they recommend IL-17 inhibitors and IL-12/23 inhibitors as alternatives, in that order.[5] The EULAR guidelines, by contrast, recommend starting most patients on a conventional synthetic DMARD.[10] For patients with PsA that manifests primarily as peripheral arthritis, GRAPPA guidelines straddle those two guidelines by recommending patients start with either a conventional synthetic DMARD or a TNF inhibitor.[12]

Table 2 *Key Similarities and Differences in Clinical Practice Guidelines for the Treatment of PsA*

	ACR/NPF	EULAR	GRAPPA
Year updated	2018	2019	2015
Recommended first-line DMARD	TNF inhibitor	Conventional synthetic DMARD	Conventional synthetic DMARD or TNF inhibitor
Specificity of recommendations for therapy choices (ie, one class of drugs over another)	High	Low	Low
Specificity of recommendations for domain with active disease (eg, peripheral arthritis, axial disease, skin, nails)	Low	Medium	High
Recommends treat to target?	Yes, but with no target specified	Yes, with target of remission or low disease activity	Yes, but with no target specified
Recommendations for assessment frequency	No	No	Yes
Different recommendations for individuals with polyarthritis vs mono/oligoarthritis	No	Yes	No

Abbreviations: ACR, American College of Rheumatology; DMARD, disease-modifying antirheumatic drug; EULAR, European League Against Rheumatism; GRAPPA, Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; NPF, National Psoriasis Foundation

Why the difference in recommendations? The ACR/NPF guidelines recommend first-line treatment with a TNF inhibitor due to the more compelling evidence for the efficacy of this class of drugs over conventional synthetic DMARDs. This decision was supported by findings from a recent phase 3 clinical trial that showed more treatment-naïve patients with PsA achieve a 20% improvement on a TNF inhibitor than on a conventional synthetic DMARD (61% vs 51%). The same holds true of achieving an MDA response (36% vs 23%).[24] There is also little evidence to suggest that conventional synthetic DMARDs ameliorate symptoms for many of the domains affected in PsA, such as enthesitis.[25] By contrast, current evidence indicates that all biologics are more effective than placebo at alleviating the array of common symptoms of PsA, including domains such as enthesitis, skin, and axial disease.[26,27]

The EULAR guidelines take a different approach, extrapolating from the favorable benefit-to-risk ratio demonstrated for conventional synthetic DMARDs in RA and taking into consideration that this class of medications is less expensive than biologic DMARDs.[10,12] However, there are some circumstances in which even the EULAR guidelines recommend starting treatment-naïve patients on a biologic. For example, if a patient is experiencing entheseal or axial inflammatory involvement, first-line treatment with a biologic is recommended, as conventional synthetic DMARDs are ineffective for these conditions.[10]

All three clinical practice guidelines emphasize the need for patients to be engaged in selecting an initial treatment. For example, the ACR/NPF guidelines state that if a patient prefers oral medication and does not have severe PsA or psoriasis, conventional synthetic DMARDs or apremilast should be considered as a first treatment, notwithstanding the general recommendation to start patients on a TNF inhibitor.[5] In the end, the success of any course of treatment will depend on whether it helps a patient meet their unique treatment goals without sacrificing their quality of life due to tolerability issues, inconvenience, or cost.

When Frontline Treatment Does Not Work

Unfortunately, most patients with PsA do not achieve sustained success on their first treatment. Research shows, for example, that among patients with PsA who have initiated their first TNF inhibitor, only 47% are still using the same medication 5 years later.[28] Therefore, clinicians must be ready to switch to a second-line therapy when it becomes apparent that a patient is not adequately responding to their first-line therapy.

"In the end, the success of any course of treatment will depend on whether it helps a patient meet their unique treatment goals without sacrificing their quality of life due to tolerability issues, inconvenience, or cost."

How does a provider know when it is time to switch a patient to a new therapy? The EULAR guidelines specify that if a patient's improvement does not exceed 50% within 3 months using the chosen composite measure for PsA, or if the treatment target is not reached within 6 months, a change in therapy is warranted.[10] This is because research shows that a patient's response to their therapy at 3 months is an excellent predictor of their response at 6 months and even 1 year.[29]

If a patient does not respond adequately to a TNF inhibitor—the first-line treatment for PsA recommended by ACR/NPF guidelines—the guidelines recommend switching them to a different TNF inhibitor unless the patient has severe psoriasis, in which case an IL-17 inhibitor or IL-12/23 inhibitor is recommended (in that order).[5] Of note, no compelling differences in efficacy between available TNF inhibitors have been demonstrated.[30] GRAPPA guidelines are less specific. They recommend that if a patient with PsA manifesting primarily as peripheral arthritis does not respond adequately to first-line therapy with a TNF inhibitor, they should be switched to another biologic or to the PDE-4 inhibitor apremilast.[12] The EULAR guidelines are even more general, recommending that if patients fail to respond adequately to any biologic DMARD, they should be switched to another biologic DMARD or to a targeted synthetic DMARD.[10]

If a patient does not respond adequately to a conventional synthetic DMARD—the first-line treatment for PsA recommended by the EULAR guidelines—ACR/NPF guidelines recommend a switch to a TNF inhibitor, an IL-17 inhibitor, or an IL-12/23 inhibitor (in that order). The EULAR guidelines recommend switching to a biologic but do not differentiate between TNF, IL-12/23, or IL-17 inhibitors.[10] An exception is when there is relevant skin involvement, in which case both the ACR/NPF and EULAR guidelines state that an IL-17 inhibitor or IL-12/23 inhibitor may be preferable to other treatment options.[5,10]

What if a patient fails to respond to first-line therapy with a different class of biologics? If a patient does not respond adequately to an IL-17 inhibitor, the ACR/NPF guidelines recommend switching to a TNF inhibitor, an IL-12/23 inhibitor, or a different IL-17 inhibitor, in that order.[5] If they do not respond to an IL-12/23 inhibitor, the guidelines recommend switching to a TNF inhibitor or an IL-17 inhibitor, in that order.[5] The EULAR guidelines recommend switching to another biologic DMARD or a targeted synthetic DMARD, and the GRAPPA guidelines recommend switching to a different biologic.[10,12]

Where Do Targeted Synthetic DMARDs Fit In?

Research shows that, when considering a DMARD, patients with PsA place high priority on route of administration, and tend to prefer oral medications over injections or infusions.[31,32] This may rule out biologics for some patients. Other patients have contraindications to biologics or find the side effects or need for laboratory monitoring intolerable. For all of these patients, targeted synthetic DMARDs can be an important treatment option. These oral agents currently fall into two classes, JAK inhibitors and PDE-4 inhibitors.

Tofacitinib is the only approved JAK inhibitor for the treatment of PsA. The ACR/NPF guidelines recommend tofacitinib instead of a TNF inhibitor for patients who have active PsA despite treatment with a conventional synthetic DMARD or apremilast, prefer oral medications, and do not have severe psoriasis.[5] The EULAR guidelines recommend tofacitinib be considered in patients with peripheral arthritis and an inadequate response to at least one conventional synthetic DMARD and at least one biologic, or when a biologic is not appropriate.[10]

Apremilast is the only approved PDE-4 inhibitor for the treatment of PsA, and it requires no routine laboratory monitoring.[25] The ACR/NPF guidelines group apremilast with the conventional synthetic DMARDs, such as methotrexate, so according to these recommendations, apremilast could potentially be used as first-line therapy in patients with mild disease, a preference for an oral medication, or contraindications to TNF inhibitor therapy.[5] In addition, the ACR/NPF guidelines recommend apremilast after TNF inhibitor failure if a patient is experiencing recurrent or serious infections and does not have severe psoriasis. The EULAR guidelines recommend apremilast be considered in patients with mild disease (≤4 joints affected, lower disease activity as rated by composite scores, and/or limited skin involvement) after an inadequate response to at least one conventional synthetic DMARD, if neither a biologic nor a JAK inhibitor is appropriate.[10]

Third-line Therapy and Beyond

Many patients with PsA end up trying multiple DMARDs during their lives, most often switching from one to another because of a lack or loss of efficacy.[9] For example, in one recent 2-year study of patients who initiated a biologic therapy for PsA, only 20% remained on that medication throughout the study period, with 40% of those who discontinued their medication initiating another biologic.[33] It is important to offer new therapies to patients who are not adequately responding to their current regimens; research shows that individuals whose therapies are not controlling their PsA symptoms have poorer health-related quality of life and physical functioning, as well as higher levels of work and activity impairment, than individuals who are experiencing treatment success.[9] Unfortunately, once a patient moves beyond second-line therapy, the evidence base available to help guide clinicians' decisions about which therapy to try next—an agent from a different class or one from the same class?—is limited.

After a patient has an inadequate response to one agent, it makes sense that prescribing an agent from a different class might yield better results. However, available evidence does not necessarily support this hypothesis. The ACR/NPF guidelines recommend that, in most cases, a patient who does not adequately respond to one TNF inhibitor should be switched to a different TNF inhibitor rather than to a DMARD from a different class.[5] However, EULAR guidelines observe that while switching within class is a viable option, it would be logical to change class after a second failure within that class.[10]

Clinicians should also be aware that rates of treatment failure increase with each successive DMARD. One study found that whereas only 13% of patients with PsA did not respond to their first therapy, 27% did not respond to their third-line or later therapy.[9] Therefore, providers must be especially alert to a lack of adequate response as patients move to third-line therapy and beyond.

Setting Patients Up for Success

Whatever the regimen, clinicians should help patients optimize their chances of treatment success. Undergoing PsA therapy tends to be a difficult experience for patients. In a 2014 study, 45% of patients with PsA taking biologics and 57% of those taking conventional synthetic DMARDs reported being dissatisfied with their therapy and eventually discontinued it.[7] Strikingly, 46% of respondents said they thought currently available therapies for PsA were worse than the disease itself. Although the treatment

Figure 2 *Resources for Patients with PsA*

Free educational materials for patients

- 1-page fact sheet on PsA from the American College of Rheumatology
  www.rheumatology.org/Portals/0/Files/Psoriatic-Arthritis-Fact-Sheet.pdf
- PsA 101 video series available on the Johns Hopkins Medicine website
  www.hopkinsarthritis.org/arthritis-info/psoriatic-arthritis/psa-101/
- "Psoriatic arthritis (beyond the basics)" article from UpToDate
  www.uptodate.com/contents/psoriatic-arthritis-beyond-the-basics

Patient websites with educational information and community forums

- National Psoriasis Foundation website: Includes information about treatments for PsA, a patient navigation center, and peer connection opportunities
  www.psoriasis.org
- Arthritis Foundation website: Includes educational articles about pharmacologic and non-pharmacologic therapies for PsA, as well as information about local educational and support groups
  www.arthritis.org

landscape has changed somewhat in the intervening years, patients still cite many of the same reasons for discontinuing therapy, including lack of tolerability, needle anxiety, and cost/insurance issues. Thus, it is essential for providers to cultivate a strong therapeutic alliance in which patients feel comfortable discussing any barriers to treatment.

Improving a patient's knowledge of PsA and available treatments may improve their adherence to the treatment plan, as has been shown for many conditions.[34] Such knowledge also allows patients to make informed decisions about their care. Providers can help patients acquire essential knowledge of PsA by directing them to high-quality patient education materials, which can be accessed online, or, in the case of handouts, provided during office visits (Figure 2) . Providers can also direct patients to advocacy organizations such as the National Psoriasis Foundation and Arthritis Foundation that offer reliable information and support through online forums or live meetings.[11]

With regard to tolerability, clinicians can warn patients about what types of side effects to expect and give pointers about how to respond when they arise. For example, many of the most common side effects of methotrexate such as nausea, stomach pain, stomatitis, and anemia result from the medication's inhibition of folate acid metabolism, so counseling patients to take daily folic acid supplements can help maximize tolerability and safety.[35] Infections are among the most common side effects of biologics, so providers should make sure that patients are up-to-date on their vaccinations either before initiating treatment in the case of live attenuated vaccines, or after initiating treatment in the case of killed vaccines.[5] If a patient's side effects on their current regimen cannot be tolerated, adjusting a patient's dose or switching them to another medication may be necessary. It is important that providers and patients work together to find a treatment plan that is both effective and tolerable, and trial and error is likely to be involved.

It is also essential to discuss a patient's preferences regarding route of therapy administration. Some patients prefer to avoid needles and instead want to take a pill once or twice a day. Other patients may have trouble remembering to take pills and prefer less frequent injections or infusions. Some patients may prefer to receive infusions at a facility while others may prefer the convenience of administering injections themselves at home. This is especially true given many people's desire to avoid unnecessary visits to healthcare facilities during the COVID-19 pandemic. Fortunately, a variety of administration options are available from which to choose.

Of course, the reality is that many patients' treatment choices are governed, at least in part, by their insurance coverage. Some insurers may grant certain agents a "preferred" status that can result in much lower out of pocket costs for the patient. In addition, many insurers specify which therapies must be tried for what period of time before prescribing a given biologic or targeted synthetic DMARD. Because many biologic and targeted synthetic DMARDs are expensive, a critical part of setting a patient up for treatment success involves making sure that the selected therapy is covered by insurance and will not cause them undue financial stress.

Finally, clinicians should discuss non-pharmacologic therapies with patients to complement the pharmacologic therapies in their treatment plan. The ACR/NPS guidelines recommend exercise, weight loss, and smoking cessation among other possible non-pharmacologic therapies. A combination of these activities can be tailored to an individual patient's needs and preferences (Figure 3).

Figure 3 *Non-pharmacologic Therapies for PsA Recommended in the ACR/NPF Clinical Practice Guidelines*

- Low-impact exercise (tai chi, yoga, swimming)
- Physical therapy
- Occupational therapy
- Weight loss
- Massage therapy
- Acupuncture
- Smoking cessation

Sustained Remission: What Now?

When a patient achieves sustained remission (defined by EULAR as complete remission for at least 6 consecutive months[10]), they may wonder if it is possible to stop or modify their PsA therapy. The ACR/NPF guidelines remain silent on this matter. However, EULAR guidelines state that in this scenario, cautious tapering of a patient's DMARD may be considered.[10] Rather than being aimed at stopping the patient's treatment, this recommendation encourages providers to find the smallest effective dose for their patients, either through dose reduction or interval lengthening. This approach makes it more likely that a patient will find a treatment plan that is sustainable over the long term.

Conclusion

Today, patients have access to a wide range of PsA therapies, offering them unprecedented opportunities to control their disease. Choosing among all of these therapies can feel overwhelming for many providers, especially when decisions about how to sequence these medications must be made. The existence of three different sets of clinical practice guidelines, with recommendations that sometimes differ, does not make matters easier. In this complex clinical environment, clinicians can provide quality care by focusing on key recommendations most relevant to their practice. Although PsA is a challenging disease to manage, improving a patient's symptom control has a meaningful effect on their ability to live life on their own terms, making the trial-and-error process of PsA treatment worthwhile for both provider and patient.[9]

The future will no doubt yield additional therapeutic options for PsA, which may well add further complexity to the clinical decision-making process. In fact, a new IL-23 inhibitor, guselkumab, was just approved by the FDA for the treatment of PsA in July 2020. However, the future will also likely bring important information that can be used to guide treatment decisions, and in the next decade, it may become more clear which agents work best for which patients. This, in turn, would allow more patients with PsA to meet their treatment goals, allowing them to live fuller, more satisfying lives.

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The *Hidden* Hurdles in Our Way

by Linda Grinnell-Merrick, NP-BC

The patients that come through the doors of our rheumatology practice every day often arrive with a unique set of beliefs regarding their disease and preferences regarding treatment. As healthcare providers, our experience and training has instilled us with a different, and sometimes conflicting, set of beliefs. It's not that either party is necessarily right or wrong, but merely that these beliefs can sometimes clash, especially in patients with psoriatic arthritis (PsA), and that it takes time and patience to reconcile these differences before a communal approach can be reached that best serves each individual patient.

Let me share two recent cases with you, each highlighting a different set of challenges. You will probably recognize many aspects of these cases in some of your own patients.

I'll start with Regina, a woman in her mid-50s. Regina is a pediatrician who was forced to retire due to a variety of underlying medical conditions. She was referred to our office with multiple painful and swollen joints affecting her hands. On exam, she had obvious dactylitis of the right 2nd digit of her left hand, along with multiple swollen and tender distal interphalangeal joints. Given these two findings, initial signs certainly seemed to point to a diagnosis of PsA.

But where was her psoriasis? There wasn't any, she told us, and never had been any. Neither was there any family history of psoriasis. That certainly piqued our curiosity. Nevertheless, we proceeded to order X-rays, which showed a pencil-and-cup deformity, a classic finding among patients with PsA. With the sum of this evidence, we concluded that Regina must be one of the approximately 15% of patients who have PsA without skin involvement.[1] Given the severity of her joint involvement, we suggested an aggressive course starting with a biologic disease modifying anti-rheumatic drug (DMARD).

Not only was Regina resistant to this suggestion, but she fought us over any treatment we recommended. It took seveal months and multiple appointments before she would even agree to a low dose of methotrexate. For 2 years, every time Regina came into our office, it was the same story. There was pain and swelling in her hands, getting progressively worse each time. Eventually, she was barely able to make a fist. She told us that any activity involving her hands was painful. And yet, anything more than a short course of prednisone was a non-starter. Regina asked us time after time, "How can you be sure this is PsA? I don't have psoriasis, and I know that almost every patient with PsA has psoriasis. What if you

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“We would point to the evidence in front of us—her joint involvement and X-ray findings—but that was never enough. She simply did not believe us.”

got this wrong?” We would point to the evidence in front of us—her joint involvement and X-ray findings—but that was never enough. She simply did not believe us.

Finally, 2 years after she first came to our office, Regina came in for a visit and showed me a small, dime-size patch of scaly skin behind her ear. “Is this psoriasis?" she asked me. It turns out that this patch of scaly, occasionally itchy skin behind her ear had been there all along, but since it was covered up by her hair, we couldn’t see it, and Regina never said a word about it. At this visit, she told us that she simply didn’t think it was a big deal. It was always something she would treat with hydrocortisone and it would go away.

Now that I had the smoking gun—“See, you do have psoriasis!”—everything changed. Regina finally believed in our diagnosis and, that day, agreed to start on biologic therapy. I’m happy to report that, several years later, she is doing well. We see her every 6 months just to check in, but there haven’t been any urgent calls or unscheduled appointments to treat a disease flare. Yes, she has some residual damage in several joints, but she has regained function in her hands, and her pain and swelling have both resolved.

That’s one avenue that some patients with PsA follow.

And then there are those patients like Laurie, who I first met when she was 39 years old. A married woman with two school-aged children, Laurie had been treated by one of our practice’s rheumatologists for years and consistently struggled to adhere to her agreed-upon treatment regimens. At our first visit, Laurie arrived in a wheelchair due to the pain and swelling in her knees and ankles. She also had swelling that affected numerous joints in her hands. Frankly, based on my first impression, I had no idea how she was caring for her family at all.

But that wasn’t even the worst of things. Laurie had thick, red plaques covering the majority of her body, including her scalp, arms, trunk, and legs. Her face was somehow spared, but that was about the only noticeable area without visible psoriatic lesions.

At this time, Laurie was only being treated with methotrexate. Clearly, she needed more, but every time another provider in our practice tried to introduce a biologic, there would invariably be an insurance issue or another unclear problem, and Laurie would be lost to follow up. Despite providing her regularly with information on patient assistance programs that were available to her, Laurie rarely completed the forms or showed up for scheduled follow-up visits. The problem was never quite clear.

On my first visit with Laurie, I brought in one of our administrative assistants to help complete the patient assistance forms to get her back on biologic therapy. She was able to restart adalimumab and seemed to be doing OK. On her initial follow-up 2 months later, Laurie was out of her wheelchair and used a walker to enter the office. Her skin was visibly clearing. I felt so happy to see her doing better that I went up and gave her a teary-eyed hug. Over the course of next year, Laurie

continued to improve. She was soon walking without any assistive devices and her skin was almost completely clear.

Alas, the chronic nature of her disease unfortunately meant that the good times would not last. Her adalimumab stopped working as well as it once did, and we were forced to look at other biologic options. That meant another round of forms and another round of coaxing. Unfortunately, Laurie reverted back to her previous routine. For unknown reasons, the forms went uncompleted, and Laurie stopped responding to our calls and emails.

I last saw Laurie a year ago. The plaques on her abdomen, back, upper arms, and legs were back in full force. She was using a walker again due to numerous painful joints. I again urged her to complete the financial assistance forms we provided to her and set up regular appointments with our office to control her disease. Unfortunately, she's been a no-show to her last several scheduled visits and I remain unsure how she is doing, though I fear the worst. My heart breaks for Laurie and her family, but I remain hopeful and undeterred. Hopefully, whatever factors brought Laurie back to our practice last time will re-emerge, and she'll give us a chance to help her again.

What these dual cases demonstrate is that despite our best efforts, intentions, education, and compassion, there are times when we need to accept that there are some hurdles we can't overcome in the short term and simply hope for the best. Not all our cases are "instant wins," and there will likely be some long-term losses, but with persistence and patience, we can usually break through our patients' defenses to get them the help they need.

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Omics Research: *Its Role in the Future of Rheumatology*

by Laura P. Kimble, PhD, RN, FNP-C, CNE, FAHA, FAAN

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As healthcare professionals specializing in rheumatology, we know the importance of seeing patients as individuals as we interact with them and hear about their experiences managing their chronic illness. Clinicians treating patients with psoriatic arthritis (PsA) frequently note that patients present with highly variable signs and symptoms, trajectories of disease, and response to treatment. This heterogeneity observed in PsA as well as other rheumatic diseases is what makes rheumatology so challenging.[1] In a recent article, Fitzgerald and Ritchlin reiterated how perplexing it is when some patients have an excellent response to pharmacologic treatment while others who present with similar symptoms do not respond at all.[2] They advocated for additional research to better tailor treatments based on a patient's unique clinical characteristics, otherwise known as "precision medicine." In this article, I'll talk about the current state of precision medicine and why omics research is important to help fill the gap between where we are today and where we need to be in the future.

Precision medicine is an approach to healthcare that takes individual variation into account.[3] It is not a new concept, having grown from the theory of "personalized medicine" popularized a decade ago. Assuring that the blood administered to a patient matches that patient's blood type is an example of precision medicine that has been in place for decades. That's a more straightforward example. In rheumatology, along with many other medical specialties, we are faced with more complex questions. But at its essence, precision medicine is poised to answer the following question:

> ***What if rheumatology providers could use a biomarker (or set of biomarkers) to prescribe medications for patients with PsA or other diseases based on an understanding of their genetic characteristics, the relative composition of certain types of immunologic cells, or the metabolic processes that are disrupted in their body?***

In the field of oncology, this type of decision-making is increasingly becoming a part of routine clinical practice.[3] Omics is a growing area of research that may ultimately make this type of precise decision-making possible in other areas such as rheumatology.

Broadly speaking, omics is a term used to describe the study of biological systems and their interactions.[4] Systems biology and omics research have emerged as key methods for elucidating biologic mechanisms across multiple health conditions. Systems biology is a multidisciplinary field that examines

complex biological systems at the cell, tissue, organ, or organism level. Clinicians study physiology and pathophysiology as part of their training; however, systems biology takes the understanding of these concepts to a higher level by integrating molecular biology and biochemistry, examining how molecules within the body undergo chemical changes and interact with each other.[5] Advances in bio-computational methods have made "high throughput analyses" possible wherein thousands of different biological molecules can be measured simultaneously in relatively small samples of blood, tissue, or other biological samples.[6] The information from these analyses can help scientists understand molecular mechanisms of health and disease within a single cell, tissue, or organ. Omics research is used to characterize individuals with and without certain disease manifestations, as well as molecular responses to tissue damage and disruptions in physiological pathways.

Multiple different types of omics approaches are reported in the literature; however, the four major areas frequently identified within molecular biology are those measuring genes, transcripts (messenger RNA), proteins, and metabolites.[7] These areas, sometimes described as the "omics cascade," represent different levels at which biological systems operate and influence each other.[8] Research in different parts of the omics cascade can inform clinicians about multiple aspects of clinical practice.[7] The information provided in genetics studies relates to what might happen in a specific patient; for example, having a genetic predisposition for particular types of rheumatic diseases increases an individual's risk of developing that disease. Metabolomics, which are at the farthest end of the cascade, are the closest to "real-time" measurement of what is happening within individuals as their genetic predisposition and environmental exposures interact. Metabolomics is also the closest biological reflection of the clinical phenotype, or the outward signs and symptoms of disease that are found during a patient encounter. In some clinical situations, biomarkers which objectively measure normal biological processes or a pathological process in patients may not be available to optimally manage patients. Omics investigations can lead to identification of new and improved biomarkers, which ultimately strengthens clinical practice.[6]

As omics research advances and new discoveries are used in clinical practice, patient care should be enhanced. Rheumatology providers should be prepared for these advances as well as helping patients understand the complex nuances of the different approaches to their treatment.

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THE LITTLE DIFFERENCES

That Can Have a Big Impact

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"She's flaring again. She had a hard time even going to school this week and hasn't been able to play at all for her basketball team this season. She wants to know why the medicine isn't working, and I don't know what to say to her anymore!"

When mom or dad calls after a rough weekend, it's a tough conversation. I wish it were uncommon, but it does seem to happen from time to time. It is difficult for the patient, the family, and the care team as we all want our patients to improve and feel better.

This particular conversation took place approximately 18 months ago and concerned Jessica, a 11-year-old female who was diagnosed with juvenile idiopathic arthritis (JIA) as a toddler. Jessica was initially treated at an out-of-state practice where she spent her early childhood. At that practice, she was diagnosed with oligoarticular JIA and received treatment that consisted of intra-articular joint injections and daily NSAIDs. When this did not alleviate her symptoms, she was ultimately started on methotrexate (MTX) as a 7-year-old. Jessica's mom relocated for work to the Chicago area (where our practice is located), and after a 4-month lapse in care following her move, she ended up in our office in 2019.

During her initial clinical exam with our team, Jessica had swelling of her left knee and right ankle, as well as tenderness in her 2nd and 3rd left proximal interphalangeal (PIP) joints. Jessica's mother expressed some concerns about an intermittent rash she had noticed on her daughter's scalp, although it was not apparent on the day of this initial visit. There was some nail pitting.

Jessica did not have a family history of psoriasis, although several members of her family had been diagnosed with other autoimmune conditions such as inflammatory bowel and thyroid disease.

After our physical exam and review of Jessica's medical history, we ordered a routine lab panel as well as Quantiferon-TB Gold (in case we might need to consider introducing a tumor necrosis factor [TNF] inhibitor) and HLA-B27 testing. The TB test came back negative, but the HLA-B27 result was positive. We also suggested to Jessica's mom that she take her daughter for an eye exam with slit lamp. Fortunately, there was no evidence of uveitis. Based on this evidence, we felt Jessica's JIA subtype was more consistent with psoriatic JIA than our previous suspicion of oligoarticular disease.

JIA is typically classified into different subtypes, including a psoriatic subtype. At the time of diagnosis, some children with the psoriatic subtype may present with symptoms similar to adults, including dactylitis, psoriasis, and nail pitting. Joint distribution is often asymmetrical and involves both small and larger joints, which can differentiate the condition from other JIA subtypes such as oligoarticular or polyarticular disease.[1,2] In some cases, such as Jessica's, juvenile psoriatic arthritis can present with symptoms that seem to mimic other JIA subtypes, with bilateral joint involvement.[3]

It is currently unclear whether the disease course of children with juvenile psoriatic arthritis differs significant from other JIA subtypes. Some studies have found that children with juvenile psoriatic arthritis have more progressive and persistent disease courses than other JIA subtypes, while other studies have found no differences.[3]

Distinguishing juvenile psoriatic arthritis from other JIA subtypes can have an important influence on treatment decisions. As an example, methotrexate—which is a common DMARD used to treat JIA—is not as effective in treating adults with PsA as it is in adults with RA.[3] Additionally, some of the newer biologic DMARDs, including interleukin-17 inhibitors, have shown to be particularly efficacious in adults with PsA, although they are not currently approved for use in the pediatric population.

Now back to our story.

Following our comprehensive workup and conclusion that Jessica had juvenile psoriatic arthritis, we decided to start her on a combination of methotrexate and etanercept, along with her twice-daily NSAID. Six months later, there was no notable improvement in her disease activity, so we switched her to adalimumab while continuing the methotrexate. Unfortunately, Jessica went through a significant disease flare. We stopped the adalimumab and switched her to abatacept.

Three months later, I got the Monday morning phone call.

"We're all just so tired and frustrated," Jessica's mother told me. "Isn't there something that is going to make things better?"

Treatment availability for kids and teens can be particularly challenging. We see some options that seem to work in older patients, but can't get access to them for our younger patients. And when families such as Jessica's see a poor response to the medications we can utilize, it can be discouraging as our options seem to dwindle.

Jessica came in a few days after I heard from her mother and she indeed was in a flare, with swelling in her knee and ankle. Since she had only been on abatacept for 3 months, we wanted to give it a bit more time to potentially work, so we kept her on the biologic while also recommending a series of intra-articular joint injections. Fortunately, these quieted her active joints, and Jessica was able to get back into school and rejoin the basketball team. She's determined, along with the support of her family and our team of providers, to push through, tackling each hurdle as it is put before her. I suspect this isn't the last time I'll be hearing from Jessica's mother on a Monday morning, but hopefully we'll be able to figure out the best answers together.

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AUTHOR BIO

Leanne Donaldson

Leanne Donaldson writes about her experiences as a mom and parent with a chronic illness on her blog, ***Smiles and Sundays****.*

Walking a Mile in My Painful Shoes

by Leanne Donaldson

When providers attempt to identify and eliminate some of the barriers to successful treatment of psoriatic arthritis (PsA), they quickly realize that there is no shortage of hurdles to overcome. Some of the barriers that patients encounter are reasonably within the control of providers and patients, such as education, lifestyle choices, and the ability to foster positive, mutually-respectful relationships. Others, such as insurance coverage, cost of medications, and medication efficacy/safety, are not so easy to remedy. It is an unfortunate fact that some patients with PsA have limited support systems and are forced to manage their pain on their own. In many cases, there are multiple comorbid conditions to manage as well. It's a lot, and it can be overwhelming for many patients.

However, that doesn't mean that rheumatology practices should simply throw up their hands and say, "I give up," when dealing with patients who arrive with a slew of challenging barriers to successful care. There is a lot that providers can do to help even the neediest of patients, and it doesn't always require a tremendous amount of effort. In my experience, the core issue for providers is the inability to identify and communicate realistic expectations of successful treatment for each patient.

Why do I feel that way? And more importantly, what can be done about it? Let's take a look.

What is "Success" in Treating PsA?

No one wants to be the bad guy. Having honest, difficult conversations about anything—whether it's at home, at work, or in the exam room—isn't anyone's idea of a good time. I truly believe that most people in the medical field try their best to remain positive for their patients. My rheumatologist fights for me at every turn, reminding me not to give up and that we have other options we can try if what I'm currently taking stops working. She continues to make changes to my treatment plan based on my feedback and the ever-changing landscape of PsA medications.

And yet, at the same time, I've learned that I should have had a realistic and honest conversation with my rheumatologist about what a "successful" treatment would look like for me right at the beginning of my healthcare journey. It would most certainly have changed many aspects of my treatment choices, especially in those precious first few years immediately after diagnosis.

I remember sitting in my doctor's office very clearly on the day of my initial diagnosis of PsA. More than anything, more than shock or fear, I felt relief. It wasn't necessarily relief because I finally had a diagnosis after years of traversing from specialist to specialist, but relief that I was finally, FINALLY going to get better.

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And then I took my medicine, starting with methotrexate and then following down a path of biologic agents. Each time, month after month rolled by as I waited to get better. I reminded myself to be patient and just follow my rheumatologist's instructions. That's the only way, I told myself, that things would get better. That's the whole point of healthcare, right? You get sick, you go to the doctor, you get a prescription, and you get better.

It never occurred to me that the pain and stiffness I felt as a result of my PsA wouldn't go away once I started taking medication. I knew enough by then to understand that my disease would never be "cured"—at least not with what we currently have available to treat it—but I was also quite certain that the treatment my rheumatologist had prescribed would at least be somewhat helpful.

But here's the problem—I had no idea what "better" was supposed to mean. My interactions with healthcare providers earlier in my life were much simpler. Something was wrong—a fever that wouldn't go down, a rash that suddenly appeared—so you went to the doctor. They figured out the problem, sent you home with a prescription, and a few days or weeks later, all better!

PsA, as I learned, is a very different animal, but no one at my rheumatology practice had spelled out for me the fact that I may only see a certain percentage of improvement in my symptoms, or even no improvement at all. Yes, I knew there was no cure. But I had no idea how far short of my expectations my treatment would fall. Even if someone had told me that, "The average patient with PsA will see a XX% of improvement in their symptoms from their initial treatment with a biologic," I could have been better prepared. I would have known what to truly expect. Instead, the only thing I had to go on were the smiling faces on the medication advertisements and the assurance from my rheumatology that we would find something that "made me better." If only I'd known what was coming…

Taking Our "Failures" Personally

Months went by, and yes, on some days, I did feel marginally better. I spent those early months hoping that as long as I remembered to take my prescribed medicine every day, I'd be able to start putting the pieces of my life back together again. Unfortunately, it felt like a personal failure when things didn't get better after 6 months, then 12, then 18. It became more and more difficult to pick myself up and keep going every day. It wasn't just the physical aspect of my condition that was difficult, but also the mental turmoil of managing the emotions that come with failing medicine after medicine. I began to notice major changes in my emotional well-being and mental health that I did not like.

But here's the kicker—to my rheumatologist, I was "getting better." Because I told her that my pain was slightly improved and my morning stiffness lasted only 1 hour each day instead of 2, she thought I was happy with how I was doing. But that wasn't how I was thinking. At all.

So then what can rheumatology practices do to address this mismatch in perception?

1. **State and adhere to realistic expectations for treatment**

   Every patient will base their expectations on their previous healthcare experiences. Because I had been a reasonably healthy individual prior to being diagnosed with PsA and had interactions with healthcare providers that typically resulted in alleviation of all of my symptoms, I was expecting that my treatment would essentially make me "all better." Obviously, that isn't the case for most patients with rheumatic disease, but my rheumatologist didn't prepare me for that likelihood. Letting patients know exactly what to realistically expect can break down one of the main barriers to achieving a clinician-defined, "successful" treatment.

2. **Clearly outline parameters for improvement**

   If they are honest with you, most patients will tell you that those checklists and pain scales you have us fill out at the beginning of every office visit are a total joke (sorry to burst your bubble). They don't even begin to tell the story of the previous 3 months. They often don't include symptoms that are unique to any of us. For example, one of the ways that I can tell if my medicine is helping or not is by fluctuations in my hearing. That isn't tracked by any pain scale and yet, it is a major part of my identification of successful treatment.

3. **Show patients how to clearly track the symptoms that are important to them**

   Whether it is journaling, charting, or simply checking boxes, having patients track specific symptoms can make all the difference when it comes to making informed decisions about the success or failure of any given treatment regimen. Patients who are able to take some ownership of their health are more likely to adhere to treatment plans, seek the help of support systems, and make the necessary lifestyle changes for better outcomes.

4. **Make fostering the constantly-evolving doctor-patient relationship a priority**

   Like it or not, we are all held solidly in the grip of insurance companies. We know that it affects your decisions too. The clinician-to-patient ratio is astronomical in many areas of the United States, and especially within rheumatology. As much as many providers may want to sit with every patient for as long as is needed, we understand that there are limits. Honest, straightforward, open communication needs to be a priority. Without it, patient treatment will completely fall apart.

Patients know that there is a lot that falls outside the control of rheumatology offices that impacts the success or failure of treatment. As much as you may sometimes be frustrated when a patient stops taking their medication or doesn't show up for scheduled appointments, know that we are frustrated too. There are steps that both parties can take to proactively identify and prevent key barriers to successful treatment. Identifying and communicating realistic expectations of "successful" treatment is a great place to start.

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