RHEUMATOLOGY NURSE
PRACTICE

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New **INSIGHTS** into the Treatment of the Spondyloarthropathies

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ACTIVITY SUMMARY

In this issue of *Rheumatology Nurse Practice*, we will explore trends in the management of 2 of the most common spondyloarthropathies: psoriatic arthritis and ankylosing spondylitis. With the recent availability of new biologics and additional therapies on the horizon, this issue will examine how biologics and small molecule therapies are shaping the treatment of these disorders.

LEARNING OBJECTIVES

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

- List the characteristics that differentiate the most common spondyloarthropathies
- Assess the role of pharmacologic and nonpharmacologic therapy in the treatment of both psoriatic arthritis (PsA) and ankylosing spondylitis (AS)
- Discuss the current targets of new agents under investigation for the treatment of PsA and AS
- Analyze the efficacy and safety of specific biologic therapies commonly used to treat acute anterior uveitis
- Review the nursing-related abstracts presented at the recent American College of Rheumatology annual conference

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New **INSIGHTS** into the Treatment of the Spondyloarthropathies

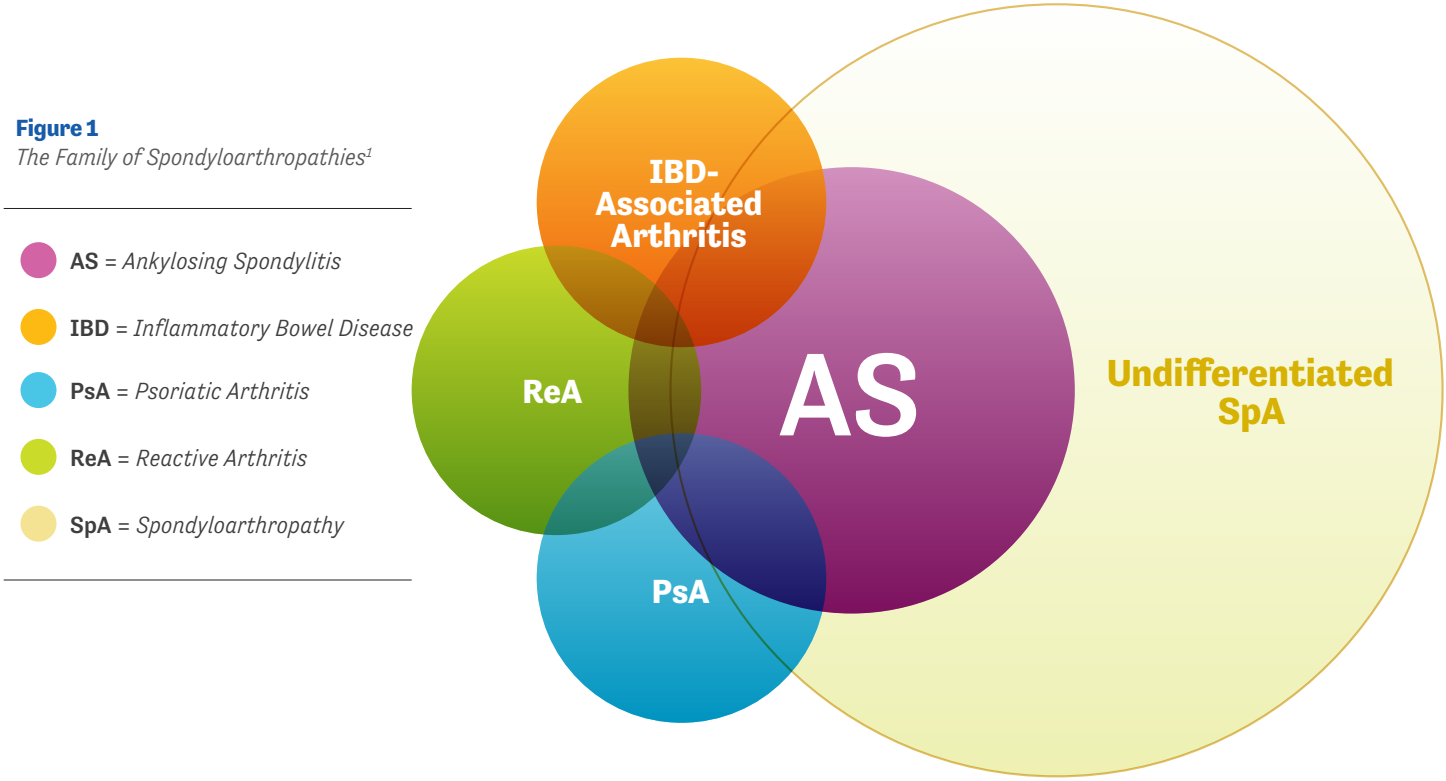
The spondyloarthropathies (also called spondyloarthritis or abbreviated as SpA) are a family of systemic inflammatory disorders affecting the axial and peripheral joints as well as extraarticular structures.[1] The SpAs share a common pathology that leads to overlapping clinical manifestations (Figure 1), often making it challenging to differentiate the individual disorders. The SpAs include the following:

- Axial spondyloarthritis and its advanced form, ankylosing spondylitis (AS)
- Enteropathic arthropathy, a form of arthritis associated with inflammatory bowel diseases (IBDs) such as Crohn's disease and ulcerative colitis
- Psoriatic arthritis (PsA)
- Reactive arthritis (ReA)
- Undifferentiated SpA, which includes disorders that do not fulfill the diagnostic criteria of the other SpAs

It is important to note that the SpAs are distinct from rheumatoid arthritis (RA), another common form of chronic inflammatory joint disease, in ways that influence both diagnosis and treatment (Table 1).[2]

In this issue of *Rheumatology Nurse Practice*, we will explore trends in the management of 2 of the most common SpAs: PsA and AS. With the recent availability of new biologics and additional therapies on the horizon, this issue will examine how biologics and small molecule therapies are shaping the treatment of these disorders.

Figure 1
The Family of Spondyloarthropathies[1]



Spondyloarthropathies 101

Evolving SpA Classification Criteria

To aid in the differential diagnosis of SpAs, classification criteria were updated in 2011 to divide the SpAs into 2 subgroups: those that were predominantly **axial** (such as AS), and those that were predominantly **peripheral** (such as PsA) (Figure 2).[3] For patients who present with symptoms of possible SpAs, the first step toward diagnosis is recognizing peripheral and axial features. For additional details on the diagnostic criteria for the SpAs, refer to the *Core Curriculum for Rheumatology Nursing* available on the Rheumatology Nurses Society website.

In 2014, an international task force of rheumatology experts outlined a treat-to-target (T2T) strategy for the SpAs, including PsA and axial spondyloarthritis.[4] The general principles of T2T for patients with SpAs may be familiar to many rheumatology nurses, as they follow the same structure as those used in RA management:

- The role of combination regimens and biologic agents as initial RA treatment
- The relative strengths and limitations of novel therapies
- Optimal dosing of biologic DMARDs
- Use of imaging and biomarkers to guide treatment choices

The specific treatment targets and disease activity measures recommended for patients with PsA and AS will be discussed in brief in subsequent sections of this issue and will be expanded upon in future issues of *Rheumatology Nurse Practice*.

PSORIATIC ARTHRITIS

PsA is a chronic, systemic inflammatory condition that occurs in patients with psoriasis. The clinical course of PsA is highly heterogenous, with different patients experiencing different effects on the peripheral joints, axial joints, skin, tendons, fingers, toes, and nails. In most—but not all—patients with PsA, the skin manifestations of psoriasis appear before joint symptoms occur.[1] Although the prevalence of PsA is low in the general population (0.05% to 0.25%), up to 40% of patients with psoriasis will develop PsA.[5]

Given the variability of PsA, diagnosis can be difficult. Among patients with pronounced skin involvement, for example, the diagnosis of PsA is often delayed or missed altogether.[6] One study found that up to 15.5% of patients with psoriasis have undiagnosed PsA.[6] To improve the timely diagnosis of PsA and access to treatment, some experts have called for annual PsA screening in patients with psoriasis.[7]

Several tools can be used to measure PsA disease activity and monitor treatment response. The American College of Rheumatology (ACR) 20, 50, and 70 responses indicate at least 20%, 50%, or 70% improvement, respectively, in tender and swollen joint counts, as well as improvement in ≥3 of the following 5 individual domains: pain, disability, patient global assessment, physician global assessment, and acute phase reactants (C-reactive protein [CRP] or erythrocyte sedimentation rate [ESR]). The Psoriasis Area Severity Index (PASI) 75 response indicates a 75% improvement in psoriasis skin involvement and is a primary endpoint in many psoriasis trials.

Setting Treatment Goals in PsA

Following a T2T strategy to achieve tight control of disease activity significantly improves joint and skin outcomes in patients with PsA. The Tight Control of Psoriatic Arthritis (TICOPA) study assessed the benefits of tight disease control in patients with early PsA, defined as a symptom duration of <24 months.[8] The study enrolled 206 patients with early PsA who had not started treatment with disease-modifying antirheumatic drugs (DMARDs), biologics, or other disease-modifying agents. Patients were randomly assigned to treatment with a tight control strategy (n=101) or standard care (n=105). Patients in the standard care group were managed at the discretion of their treating clinician, with a review of disease activity every 12 weeks. The protocol for tight control involved a review of PsA disease activity every 4 weeks and step-wise treatment escalation if the target of minimal disease activity (MDA) had not been achieved. Treatment in the tight control group started with methotrexate (MTX) monotherapy and escalated via the addition of sulfasalazine, additional DMARDs, and/or anti-TNF agents when MDA was not reached. Patients were classified as achieving MDA when at least 5 of the following 7 criteria were met:

- Tender joint count ≤1
- Swollen joint count ≤1
- PASI ≤1
- Patient pain visual analogue score (VAS) ≤15 mm
- Patient global disease activity VAS ≤20 mm
- Health assessment questionnaire score ≤0.5
- ≤1 tender entheseal points

After 48 weeks, patients in the tight control group were nearly twice as likely as those in the standard care group to achieve the primary endpoint of ACR20 response (62% vs 44%, respectively; odds ratio, 1.91). Moreover, patients in the tight control group were significantly more likely to achieve every measure of response to PsA therapy than those managed with standard care.[8]

Table 1
Differences between Rheumatoid Arthritis and Spondyloarthropathies[2]

Feature	Rheumatoid Arthritis	Spondyloarthropathies
Pattern of affected joints	Primarily symmetrical polyarthritis	Oligo/polyarthritis, more often asymmetrical
Axial joint involvement	Rare	Characterized by axial disease of the sacroiliac joints and spine
Gender	More common in women	More common in men
ACPA and RF antibodies	Commonly present	Absent
Genetic association	HLA-DR	HLA-B27
Predominant proinflammatory cytokine	TNF	IL-17
Predominant immune cell involvement	B cells and T cells	Innate immune cells (macrophages, PMN cells, mast cells)
Synovial involvement	Synovitis is central feature	Some synovial involvement
Additional pathologic features	Hyperplasia of the synovial lining	Increased vascularity, angiogenesis
Tissue repair/ formation	Little or no signs of tissue repair with joint damage	Joint damage leads to new cartilage and bone formation (remodeling)
Extra-articular features	Rheumatoid nodules, vasculitis, pneumonitis, scleritis	IBD, psoriasis, uveitis, aortitis

ACPA, anti-citrullinated protein antibody; HLA, human leukocyte antigen; IBD, inflammatory bowel disease; IL, interleukin; PMN, polymorphonuclear; RF, rheumatoid factor; SpA, spondyloarthritis; TNF, tumor necrosis factor.

PsA Treatment Guidelines

Treatment guidelines are continuously evolving to reflect best practices in patient care. Two international organizations published PsA guideline

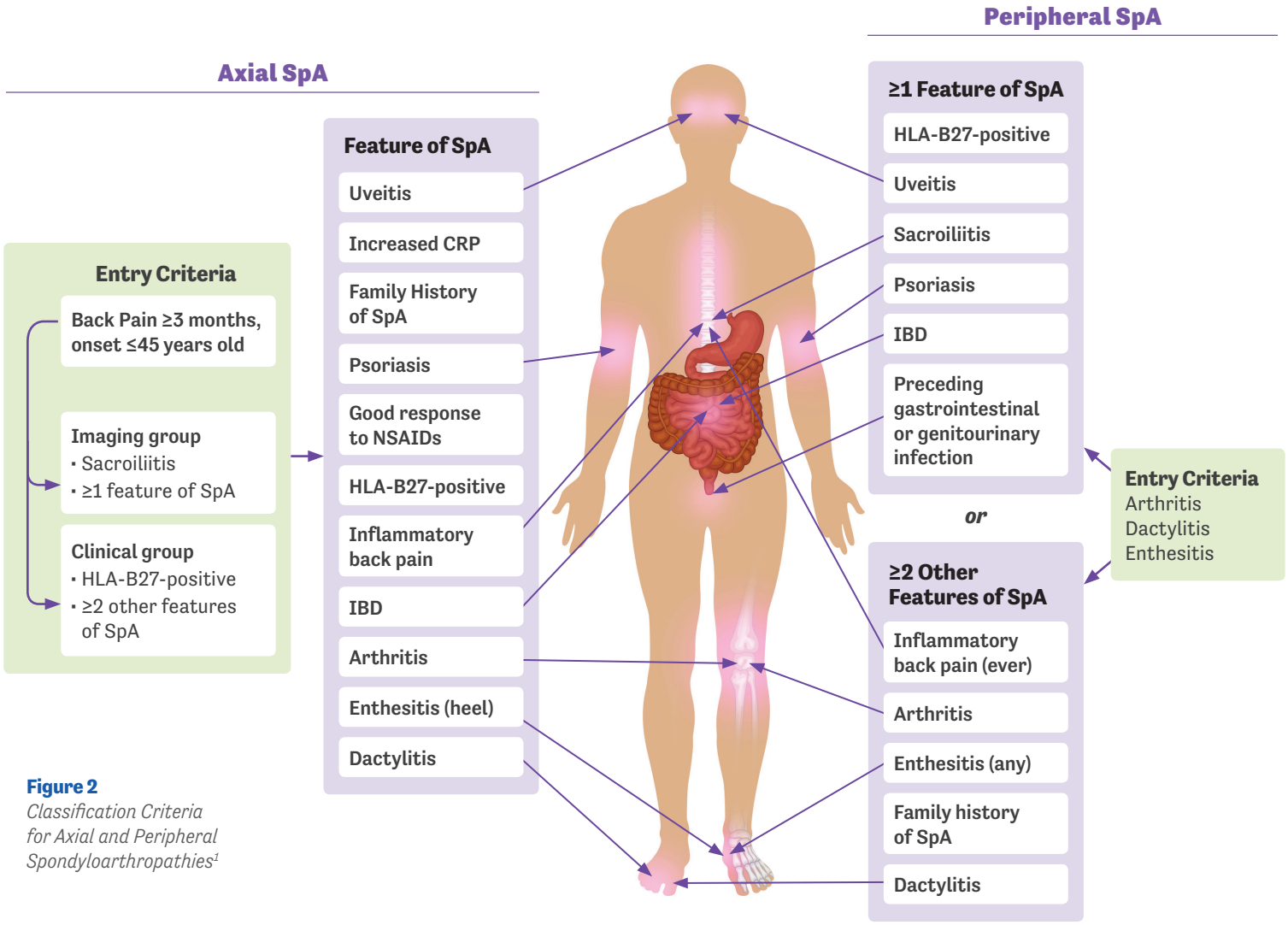


Figure 2
Classification Criteria for Axial and Peripheral Spondyloarthropathies[1]

CRP, C-reactive protein; HLA, human leukocyte antigen; IBD, inflammatory bowel disease; NSAID, nonsteroidal antiinflammatory drug; SpA, spondyloarthropathy.

updates in 2015: the European League Against Rheumatism (EULAR) and the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA).[9,10] While EULAR is a Europe-based organization, GRAPPA involves an international consortium of more than 600 rheumatology experts, with 55% practicing in the United States. The EULAR and GRAPPA recommendations stress the importance of treating both the psoriatic (skin) and arthritic (joint) manifestations of PsA with a combination of nonpharmacologic and pharmacologic therapies.[9,10] The American College of Rheumatology (ACR) is in the process of drafting new PsA guidelines in collaboration with the National Psoriasis Foundation (NPF), with final publication scheduled for 2018.[11]

Nonpharmacologic Management

Exercise and physical therapy are standard nonpharmacologic interventions for patients with PsA.[1] For those patients who are overweight or obese, weight loss is an especially important strategy to minimizing disease burden.[12] One recent meta-analysis of PsA studies identified obesity (body mass index [BMI] ≥30 kg/m^2) as a significant predictor of worse treatment outcomes. Among patients with PsA treated with anti-TNF therapy, obesity predicted a lower likelihood of achieving and maintaining MDA, a worse skin response, and a higher rate of treatment discontinuation. Obesity also increased the risk of liver toxicity during conventional DMARD therapy. Among patients treated with MTX, obese patients had a higher risk of developing increased transaminase levels.[12]

Patients with PsA can be reassured that even modest weight loss can improve their prognosis. One study examined outcomes among 126 overweight or obese patients with PsA who were starting both a dietary intervention and anti-TNF therapy.[13] After 6 months, patients who lost more weight were more likely to achieve MDA: weight losses of <5%, 5% to 10%, and >10% were associated with

MDA rates of 23%, 45%, and 60%, respectively.[13] Another study of obese patients with PsA who underwent bariatric surgery illustrates the effects of dramatic weight loss on disease burden.[14] The retrospective study involved 128 patients with psoriasis, including 21 patients (24%) with PsA. After undergoing bariatric surgery (mean preoperative BMI, 45.8 kg/m^2), patients lost 46% of their excess body weight over a mean follow-up of 6.1 years. In the PsA group, the mean duration of PsA at the time of surgery was 16.9 years, and 62% of patients had been treated with biologic therapy. Within 1 year of surgery, 62% of patients with PsA reported a subjective improvement in their disease. Furthermore, the mean PsA disease-severity score (self-rated on a scale from 0 to 10) decreased from 6.4 prior to surgery to 4.5 at 1 year post-surgery (p=0.01).[14]

Pharmacologic Management

Patients with PsA typically experience a range of clinical manifestations, yet have one aspect of their disease that they report to be most prominent or bothersome. Some patients may feel most limited by joint tenderness, while others feel that their skin symptoms most severely affect their quality of life. Each patient's most prominent feature, or disease domain, will drive the selection and sequence of optimal pharmacologic treatment (Figure 3).[10]

Initial treatment with nonsteroidal antiinflammatory drugs (NSAIDs) and/or glucocorticoids provides effective symptom management for some patients, although these therapies do not slow underlying disease progression. Conventional DMARDs are often used early in the management of patients with peripheral joint and skin manifestations, whereas initial biologic therapy is appropriate for patients with prominent enthesitis, dactylitis, or nail disease. Following a step-wise treatment algorithm will lead most patients to biologic DMARDs and small-molecule therapy, regardless of disease domain.[9,10]

Current biologic DMARDs used in the treatment of PsA include TNF inhibitors and agents that target the IL-12/23 and IL-17 signaling pathways (Figure 4). Given their different mechanisms of action and pharmacokinetic properties, these agents have a range of treatment schedules that may influence treatment selection.[15]

Anti-TNF Agents

As a class, the anti-TNF agents significantly improve the clinical signs and symptoms of PsA. All 5 TNF inhibitors used in the treatment of RA are also approved in PsA, including intravenous (IV) infliximab and subcutaneous (SC) etanercept, adalimumab, golimumab, and certolizumab pegol.[1] The TNF inhibitors demonstrate similar clinical efficacy in terms of controlling PsA disease activity, slowing structural damage, and improving function and quality of life.[15] The safety profiles are also similar across agents, with risk of infection due to immunosuppression being an important concern during anti-TNF therapy.[15]

Ustekinumab

Ustekinumab is a human monoclonal antibody that binds a common subunit shared by IL-12 and IL-23 to disrupt the proinflammatory effects of these cytokines. Ustekinumab was initially approved by the FDA in 2009 for the treatment of moderate to severe plaque psoriasis. In 2013, the indication was expanded to include PsA based on findings from the phase 3 PSUMMIT trials.[16,17] In the PSUMMIT 1 trial, 615 patients with active PsA despite conventional DMARD therapy were randomly assigned to treatment with ustekinumab (45 mg or 90 mg) or placebo.[16] At week 24, 42.4% and 49.5% of patients treated with ustekinumab 45 mg or 90 mg, respectively, achieved ACR20 responses, compared with 22.8% of patients treated with placebo. Patients in the ustekinumab groups maintained treatment responses through week 52.[16]

The PSUMMIT 2 trial evaluated ustekinumab in patients with active PsA despite treatment with conventional DMARDs or anti-TNF therapy (n=312).[17] At 24 weeks, 43.8% of patients treated with ustekinumab (45 mg or 90 mg) achieved ACR20 responses, compared with 20.2% of those in the placebo group.[17] In a pooled analysis of the PSUMMIT trials, treatment with ustekinumab also significantly reduced the risk of radiographic progression of joint damage compared with placebo.[18] Safety outcomes were similar between the ustekinumab and placebo groups.[16,17]

Secukinumab

Secukinumab, a monoclonal antibody that blocks IL-17A, is the most recently approved biologic therapy for PsA. In 2016, the FDA approved secukinumab for the treatment of active PsA on the basis of findings from the phase 3 FUTURE 1 and FUTURE 2 trials.[19,20] In the FUTURE 1 trial, 606 patients with PsA were randomly assigned to treatment with secukinumab given via IV induction (10 mg/kg) at weeks 0, 2, and 4, followed by SC maintenance dosing (75 mg or 150 mg) every 4 weeks, or placebo.[19] After 24 weeks, the ACR20 response was 50.5% and 50.0% for patients treated with secukinumab 75 mg and 150 mg, respectively, compared with 17.3% in the placebo group. Secukinumab also significantly improved the individual measures of physical functioning, disability status, dactylitis, enthesitis, and structural joint damage compared with placebo.

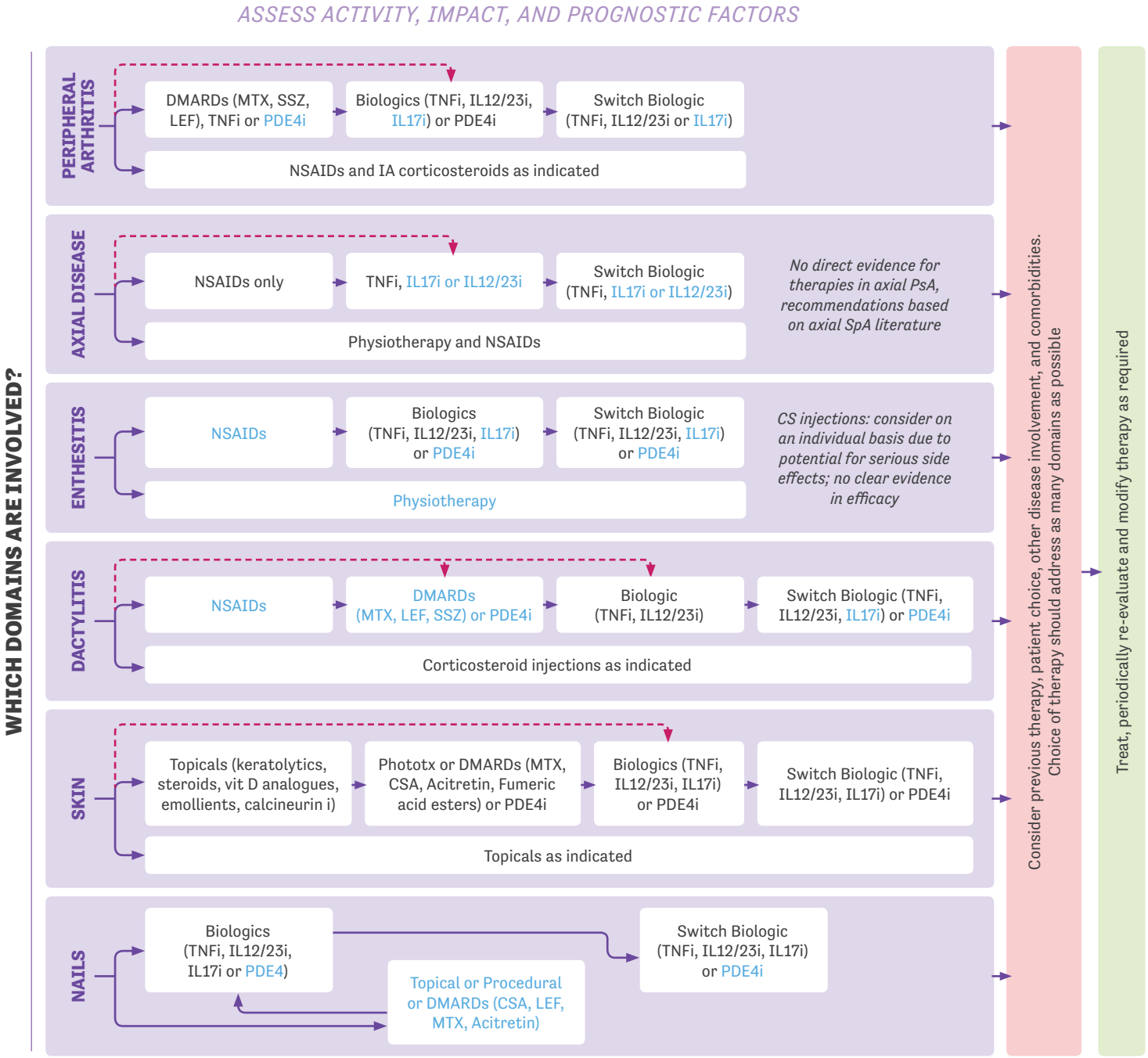


Figure 3
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) Algorithm for the Treatment of PsA[10]

CS, corticosteroid; CSA, cyclosporin A; DMARDs, disease-modifying antirheumatic drugs; IA, intraarticular; IL-12/23i, interleukin-12/23 inhibitor (ustekinumab); IL-17i, interleukin-IL inhibitor (secukinumab); LEF, leflunomide; MTX, methotrexate; NSAIDs, nonsteroidal antiinflammatory drugs; PDE-4i, phosphodiesterase 4 inhibitor (apremilast); phototx, phototherapy; SpA, spondyloarthritis; SSZ, sulfasalazine; TNFi, tumor necrosis factor inhibitor; vit, vitamin.

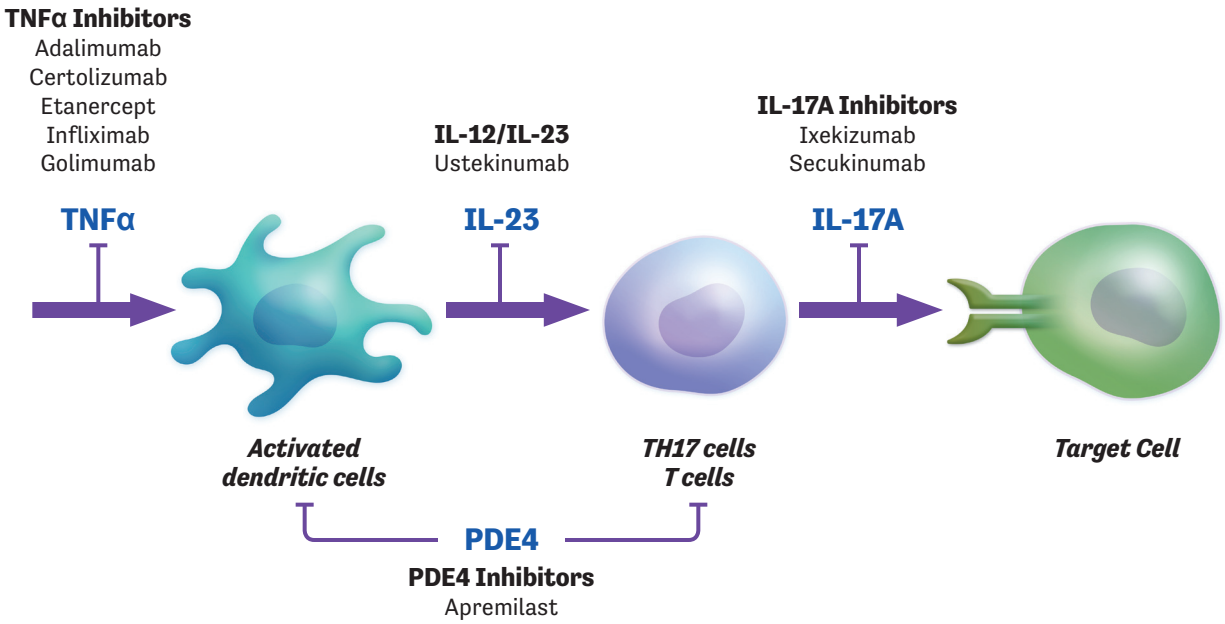


Figure 4
Biologic Agents in the Treatment of PsA[15]

IL, Interleukin; PDE4, phosphodiesterase-4; Th17, t-helper cell 17; TNFα, tumor necrosis factor alpha.

The benefits of IV loading with secukinumab followed by SC maintenance were sustained through 52 weeks of treatment.[19]

The FUTURE 2 trial evaluated 3 doses of SC secukinumab in patients with active PsA despite treatment with conventional DMARDs and/or anti-TNF therapy.[20] In total, 397 patients with PsA were randomly assigned to SC secukinumab (75 mg, 150 mg, or 300 mg) or placebo given once weekly for the first 4 weeks of treatment and then every 4 weeks thereafter. At week 24, the ACR20 rates in the secukinumab 75 mg, 150 mg, and 300 mg groups were 29%, 51%, and 54%, respectively, compared with 15% in the placebo group. The most common adverse events in the secukinumab groups were upper respiratory tract infections and nasopharyngitis.

Apremilast

Apremilast is an oral small-molecule inhibitor of phosphodiesterase-4 (PDE4) that significantly improves the signs and symptoms of PsA across multiple patient groups, including patients who are DMARD-naïve and those who are refractory to DMARDs and/or biologic therapies. The FDA approved apremilast for the treatment of active PsA in 2014 based on positive results from the phase 3 PALACE studies. In the first 3 PALACE trials (PALACE 1-3), patients who were treated with apremilast 20 mg twice daily or apremilast 30 mg twice daily were significantly more likely than those treated with placebo to achieve ACR20 responses by week 16, with responses maintained through week 52.[21-23] Apremilast also significantly improved individual domains of PsA such as skin involvement, enthesitis, and dactylitis.[21-23] The PALACE 4 trial demonstrated the long-term benefits of PDE4 inhibition among DMARD-naïve patients with active PsA.[24] Among patients treated with apremilast 30 mg twice daily, 57% maintained an ACR20 response through 104 weeks of treatment.[24] Apremilast is generally well tolerated, although dose titration is recommended to minimize GI side effects.[1]

Future Directions in PsA Treatment

Several agents are currently under evaluation for the treatment of PsA, including familiar medications used to treat RA and other autoimmune diseases (abatacept, tofacitinib), biologics with established mechanisms of action in PsA (IL-17 and IL-23 inhibitors), and agents that utilize novel mechanisms of action.

Abatacept

Activated T cells play a central role in the pathogenesis of PsA. Abatacept is a selective T-cell inhibitor that is currently approved for the treatment of inflammatory conditions including RA and juvenile idiopathic arthritis. By targeting T-cell activation, abatacept offers a mechanism of action that is distinct from the available biologic therapies in PsA.

The phase 3 ASTRAEA trial enrolled 424 patients with active PsA and an inadequate response or intolerance to prior DMARD therapy.[25] This included 60% of patients who failed prior treatment with anti-TNF therapy. Patients were randomly assigned to treatment with SC abatacept 125 mg

once weekly or placebo. After 24 weeks, the ACR20 response rates were 39.4% in the abatacept group and 22.3% in the placebo group. Among those treated with abatacept, ACR20 rates were higher in patients with no prior exposure to anti-TNF therapy compared with those who tried and failed prior TNF-targeted therapy (44.0% vs 36.4%). Responses persisted throughout the 52-week follow-up period. The safety profile was similar in the abatacept and placebo groups.

Tofacitinib

The Janus kinase (JAK) signaling pathway mediates the proinflammatory mechanisms that drive the pathogenesis of PsA.[26] Tofacitinib is an oral small-molecule inhibitor of JAK1 and JAK3 that exhibits more modest effects on JAK2. Treatment with tofacitinib 5 mg twice daily is currently approved for patients with RA who are unresponsive to conventional DMARD therapy.[1]

Given the importance of the JAK signaling pathway in chronic inflammatory diseases, tofacitinib is now being evaluated for the treatment of psoriasis and PsA. A recent phase 3 study assessed the safety and efficacy of tofacitinib 5 mg BID and 10 mg BID in Japanese patients with psoriasis (n=87) or PsA (n=12), including 5 patients with both diagnoses.[27] Among those with psoriasis, the PASI75 response rates were 62.8% and 72.7% after 16 weeks of treatment with tofacitinib 5 mg BID and 10 mg BID, respectively. In the PsA group, 100% of patients achieved an ACR20 response by week 16. All psoriasis and PsA responses were maintained through 52 weeks of tofacitinib therapy. The most common adverse events across tofacitinib dosing groups were nasopharyngitis and headache. During the 52-week study, 16 patients (17%) developed herpes zoster infection.[27]

Anti-IL-17 Therapy

Ixekizumab is an investigational IL-17A inhibitor that shows promising activity in patients with PsA. In the phase 3 SPIRIT-P1 trial, 417 patients with PsA who were naïve to biologic DMARDs were randomly assigned to 1 of 4 treatment groups: adalimumab 40 mg once every 2 weeks; ixekizumab 80 mg once every 2 weeks; ixekizumab 80 mg once every 4 weeks; or placebo. The primary endpoint was the superiority of ACR20 responses among ixekizumab-treated patients compared with placebo-treated patients.[28] After 24 weeks, the SPIRIT-P1 trial met its primary endpoint. Significantly more patients treated with ixekizumab every 2 or 4 weeks achieved an ACR20 response (62.1% and 57.9%, respectively) than with placebo (30.2%). The ACR20 response rate was 57.0% in the adalimumab group at 24 weeks. Ixekizumab was also associated with significant improvements in enthesitis, dactylitis, and physical functioning compared with placebo, as well as a significant reduction in radiographic progression of joint damage.[28] Treatment-emergent adverse events were more common in the ixekizumab and adalimumab groups (66% and 64%, respectively) than in the placebo group (47%). The most common AEs in the ixekizumab and adalimumab groups were injection-site reactions, injection-site erythema, and nasopharyngitis.[28]

Findings from the SPIRIT-P1 trial support the role of IL-17A inhibition in biologic-naïve patients with PsA.[28] The phase 3 SPIRIT-P2 trial will evaluate the safety and efficacy of ixekizumab in patients with PsA and prior exposure to biologic therapy. The primary endpoint is ACR20 response after 24 weeks of treatment with ixekizumab or placebo.[29]

Additional IL-17-directed therapies include **brodalumab**, a human monoclonal antibody that blocks the anti-IL-17 receptor A (IL-17RA) to inhibit IL-17A, IL-17F, and other IL-17 subtypes.[30] In February 2017, brodalumab was approved for the treatment of moderate to severe plaque psoriasis.[31] The brodalumab label includes a black box warning for an increased risk of suicidal ideation and behavior, and brodalumab is available only through a risk evaluation and mitigation strategy (REMS) program that trains providers on patient education, counseling, and options for mental health referrals.[31] Brodalumab is also under evaluation in patients with PsA. In a phase 2 trial, the ACR20 response rates were 37% and 39% for patients treated with brodalumab 140 mg and 280 mg, respectively, and 18% for patients treated with placebo.[32]

Bimekizumab is a dual inhibitor of IL-17A and IL-17F that shows activity in patients with psoriasis and PsA.[33,34] A phase 2 study of bimekizumab in patients with PsA, including those with and without prior exposure to anti-TNF therapy, is currently enrolling.[35]

Anti-IL-23 Therapy

Guselkumab is an investigational monoclonal antibody that selectively binds to IL-23. In a phase 2 study, 149 patients with active PsA despite standard treatment (including anti-TNF therapy) were randomly assigned to SC guselkumab 100 mg or placebo given at baseline and week 4, then every 8 weeks. At week 24, treatment with guselkumab significantly improved joint symptoms as well as physical function, skin involvement, enthesitis, dactylitis, and quality of life compared with placebo. The ACR20 responses rates were 58.0% and 18.4% in the guselkumab and placebo groups,

respectively. The risks of adverse events, including common infections, were similar in both groups.

Another selective IL-23 inhibitor, **risankizumab**, is also being studied in a range of autoimmune disorders, including Crohn's disease, psoriasis, and PsA.[30] The phase 3 UltMMa-1 and UltMMa-2 trials are underway to compare risankizumab and ustekinumab in patients with moderate to severe plaque psoriasis.[36,37] Results from these trials are expected in late 2017 and should provide more insight on the clinical implications of selective IL-23 inhibition versus dual IL-23/IL-12 blockade.

Anti-VEGFs

The creation of new blood vessels is a critical pathogenic feature of psoriasis.[38] Among many cytokines and growth factors that contribute to angiogenesis, vascular endothelial growth factor (VEGF) is a key target of anti-angiogenesis therapies. One case report described a patient who experienced complete remission of psoriasis and PsA during treatment with bevacizumab for renal cell cancer.[39] This hypothesis-generating observation supports additional research into the role of VEGF-targeted therapy in psoriasis and PsA.

ANKYLOSING SPONDYLITIS

Axial spondyloarthritis (axial SpA) is a chronic systemic inflammatory disease characterized by enthesitis, new bone formation, and fusion (ankylosis) of the sacroiliac joints and spine.[1] In 2009, the classification system around AS was adjusted to recognize earlier manifestations of the same underlying disease process.[40] According to the current naming convention, the umbrella term "axial SpA" covers the earlier and later stages of disease, both before and after any structural damage to the sacroiliac joints or spine is visible on radiographs. More precisely, these stages are classified as the following:

- Nonradiographic axial SpA; also called preradiographic SpA
- Radiographic axial SpA; also called ankylosing spondylitis

In patients with axial SpA, inflammation often begins at the entheses (ie, the insertion site of ligaments and tendons into bones). Ligament and tendon inflammation can occur throughout the skeletal system, but the joints of the axial skeleton and lower extremities are the most frequently and severely involved. Signs and symptoms of axial SpA include redness, swelling, and warmth that extends above and/or below the affected joints. Inflammation may also affect extraarticular structures such as the eye (uveitis), GI system, skin, and aortic valve.[1]

Setting Treatment Goals in AS

Current guidelines endorse a T2T strategy for AS management.[4,41] As with PsA, clinical remission is the preferred treatment goal for most patients with AS, with low disease activity regarded as a secondary target.[4] The most commonly used composite measures of disease activity in AS are the Ankylosing Spondylitis Disease Activity Score (ASDAS) and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI).[4] Using these tools, clinical remission is defined as ASDAS <1.3 or BASDAI <3.6 as well as a normal CRP level. The Bath Ankylosing Spondylitis Functional Index (BASFI) can provide additional information about functional status to guide treatment decisions.

Relative to PsA and RA, current AS guidelines provide more flexibility for clinicians to personalize treatment goals for patients with AS.[4,42] This is due to the diversity of AS, as well as less robust evidence supporting one treatment target over another. Rheumatology providers are encouraged to collaborate with patients on a shared treatment target, taking into consideration features such as extraarticular manifestations, peripheral musculoskeletal features, axial inflammation on MRI, and radiographic progression.[1,4]

Nonpharmacologic Management

Regular physical activity is a cornerstone of nonpharmacologic treatment for AS.[1] According to recent consensus recommendations, exercise for patients with AS should focus on 3 domains:

- Exercises to address the primary musculoskeletal features of AS, including decreased spinal mobility and decreased peripheral joint mobility
- Exercises to address the secondary consequences of AS, such as impaired balance and decreased cardiopulmonary function due to impaired spinal mobility
- General health maintenance exercises, similar to exercise recommendations for the general population to improve well-being and functional outcomes

Several studies support the benefits of exercise in patients with AS, with outcomes including increased spinal mobility, increased chest expansion, increased lumbar flexibility, reduced

pain, and decreased disease activity.[43,44] Although structured physical therapy is preferred, home exercises are also effective.[1]

For patients with AS who smoke, smoking cessation is critical. Smokers with AS experience more severe disease activity, more structural damage, more pain, less mobility, and worse quality of life than non-smokers with AS.[45] Smoking also appears to interfere with therapeutic response in AS. In one study of 698 patients with AS, current smokers were less than half as likely as non-smokers to achieve a 40% improvement in the signs and symptoms of AS within 1 year of starting anti-TNF therapy (odds ratio, 0.43; P=0.004).[46] Quitting smoking should be encouraged as early as possible, as patients who accumulate a higher number of pack-years of smoking history have significantly worse AS outcomes.[47]

Pharmacologic Management

The ACR and EULAR published updated guidelines for the treatment of AS in 2015 and 2016, respectively, reflecting new standards in disease classification and management.[41,42] The recommendations are consistent in general treatment approaches, including the role of biologics targeting TNF and IL-17 (Figure 5).[48]

NSAIDs are recommended as first-line pharmacotherapy for all patients with AS. Even as other therapies are added, continuous use of NSAIDs is appropriate for patients who are otherwise symptomatic. Local glucocorticoid injections and conventional DMARDs are recommended only for those patients with AS who also exhibit peripheral disease manifestations such as enthesitis and dactylitis. Sulfasalazine is the preferred DMARD for managing peripheral arthritis in patients with AS.

Biologic therapy is recommended for all patients with persistent disease activity after an initial trial of at least 2 NSAIDs over a total of 4 weeks (and glucocorticoids/conventional DMARDs, if indicated, for peripheral symptoms). Current practice generally involves starting biologic therapy with an anti-TNF agent. If clinical remission or low disease activity is not achieved within 3 months, patients should switch to another TNF inhibitor or an anti-IL-17 agent. Consistent with T2T principles, treatment should be adjusted every 3 months until patients achieve clinical remission or low disease activity.[41,42]

Anti-TNF Agents

All 5 of the currently available anti-TNF agents (infliximab, etanercept, adalimumab, golimumab, and certolizumab) are indicated for the treatment of AS. In general, the TNF inhibitors demonstrate similar efficacy in patients with AS, yielding ASAS20 responses of 57% to 80% after 12 to 24 weeks of treatment.[49,50] New evidence, however, suggests differences among anti-TNF agents in the ability to control the risk of uveits.[51] Otherwise, the long-term safety profiles of TNF inhibitors are also similar.[50]

Acute Uveitis and Choice of Therapy in AS

Acute anterior uveitis (AAU) is the most common extraarticular manifestation of AS.[1] Approximately 40% of patients with AS will develop AAU during the course of their disease, with cases occurring more commonly in male patients and in young adults aged 20 to 40 years.[52] Patients with AAU are always symptomatic and typically present with a red, painful, photophobic eye and blurred vision. In many cases, the first attack of AAU is misdiagnosed as conjunctivitis. Once a patient with AS develops AAU, recurrences are likely but tend to become less frequent over time. In the first 5 years following an initial event, AAU recurs at a rate of 1.[1] events per year, but slows to 0.8 events per year after 5 years.[52] Standard treatment for an AAU flare includes a potent topical corticosteroid given in combination with drops to dilate the pupil. Systemic therapy and intraocular injections are also used, depending on the severity of the attacks and frequency of recurrence.[52]

Given the burden of uveitis in patients with AS, the potential interaction between AS therapy and AAU is an important consideration. Different TNF-targeted therapies appear to have different effects on the long-term risk of uveitis in patients with AS.[51] In a recent analysis from the Swedish biologics registry, uveitis rates were evaluated in 1365 patients with AS who started anti-TNF therapy (adalimumab, infliximab, or etanercept) between 2003 and 2010. In the 2 years prior to starting anti-TNF therapy, the average rate of AAU events was similar across treatment groups and ranged from 36.8 to 45.5 events per 100 patient years. Compared with pretreatment rates, the rates of AAU decreased significantly during treatment with adalimumab and infliximab (lowest rate, 13.6 events per 100 patient years). In contrast, the rate of AAU increased during treatment with etanercept (60.3 events per 100 patient years). Patients treated with etanercept were nearly 4-times as likely as those treated with adalimumab (hazard ratio [HR], 3.86) and twice as likely as those treated with infliximab (HR, 1.99) to develop AAU during the study period.[51]

In summary, the results suggest a protective benefit against AAU during treatment with adalimumab and infliximab, but no protection against uveitis when using etanercept. These findings also underscore how small differences in the molecular structures of different agents with similar mechanisms of action may influence clinical outcomes.

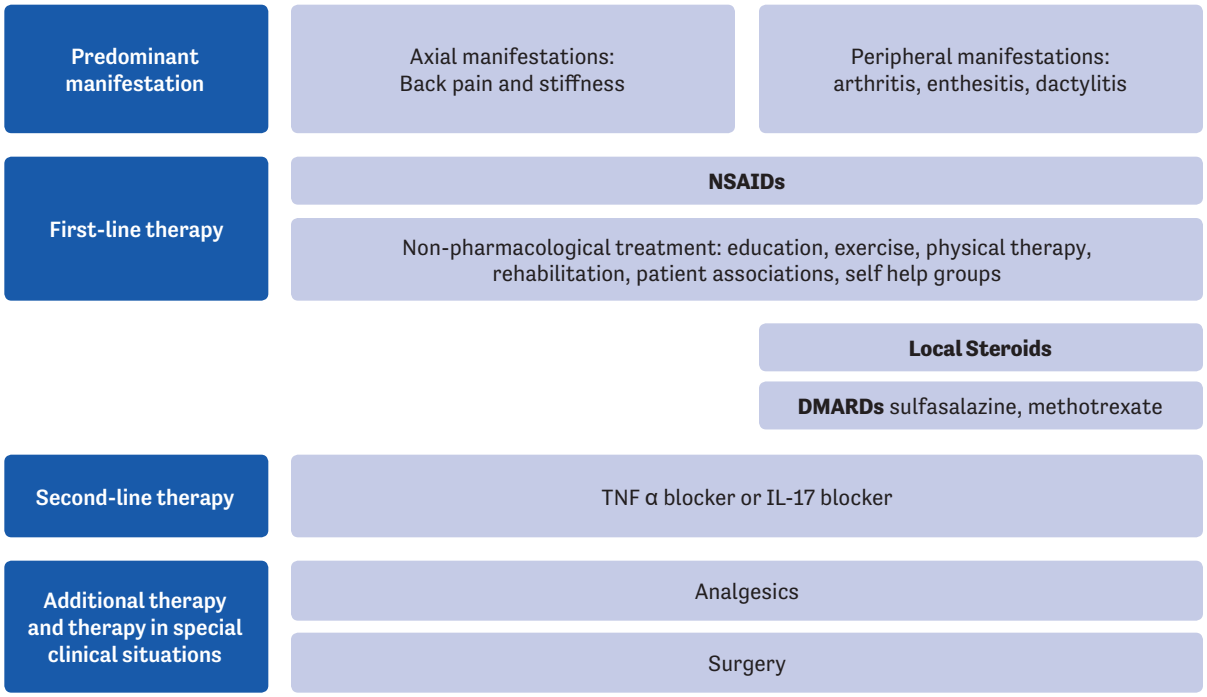


Figure 5
Management of Axial SpA[48]

DMARDs, disease modifying antirheumatic drugs; NSAIDs, nonsteroidal anti-inflammatory drugs; TNF, tumor necrosis factor.

Secukinumab

Up to 50% of patients with AS fail to achieve clinical remission or low disease activity with anti-TNF therapy.[53] As an IL-17 inhibitor, secukinumab is the first non-TNF biologic available for the treatment of AS, giving patients and providers another option to help control the signs and symptoms of AS.[53]

Secukinumab was approved for the treatment of AS in 2016 based on findings from the phase 3 MEASURE 1 and MEASURE 2 trials.[54] In MEASURE 1, 371 patients with AS were randomly assigned to either placebo or secukinumab administered via an IV loading dose (10 mg/kg) at weeks 0, 2, and 4, followed by SC maintenance (75 mg or 150 mg) every 4 weeks. In the MEASURE 2 trial, 219 patients with AS were randomly assigned to placebo or SC secukinumab (75 mg or 150 mg) given at weeks 0, 1, 2, and 3, and then every 4 weeks beginning at week 4.[54]

In the pooled efficacy analysis, the ASAS20 response rates at week 16 ranged from 41% to 61% in the secukinumab groups, compared with 28% to 29% in the placebo groups. Secukinumab also significantly improved physical functioning and health-related quality of life, and the clinical benefits of secukinumab were maintained throughout the 52-week study. Overall, treatment with SC secukinumab 150 mg, starting with either SC or IV loading doses, provided the greatest reductions in the signs and symptoms of AS relative to placebo. The most common adverse events across all secukinumab dosing groups were infections (especially candidiasis), neutropenia, and the development of Crohn's disease.[54]

In a long-term follow-up of the MEASURE 2 trial, the ASAS20 response rate at week 104 was 71.5% among all secukinumab-treated patients.[55] Secondary benefits related to functional status and quality of life were also maintained. These findings demonstrate a sustained improvement in the signs and symptoms of AS over 2 years of treatment with secukinumab. After a mean exposure duration of 735 days, the calculated incidence of serious infections/infestations, Crohn's disease, malignant/unspecified tumors, and major adverse cardiovascular events were 1.2, 0.7, 0.5, and 0.7 per 100 patient-years, respectively. No cases of suicidal ideation, tuberculosis reactivation, or opportunistic infections were reported.[55]

Future Directions in AS Treatment

Agents under evaluation for the treatment of AS include small molecules that are currently approved for other indications (tofacitinib, apremilast), novel biologics (ixekizumab), and other emerging therapies.[56]

Tofacitinib

The JAK signaling pathway influences intracellular signaling mediated by IL-17 and other key cytokines implicated in the pathophysiology of AS. Treatment with tofacitinib, a JAK inhibitor, shows promising activity in patients with AS.[57] In a phase 2 trial, 207 patients with active AS were randomly assigned to treatment with tofacitinib 2 mg, 5 mg, or 10 mg twice daily or placebo.[57] At week 12, tofacitinib 5 mg and 10 mg significantly reduced the signs, symptoms, and spinal inflammation of AS compared with placebo. Although responses in the tofacitinib 2 mg twice daily group were higher than those in the placebo group, the difference was not statistically significant. Overall, the ASAS20 response rates at 12 weeks were 51.9% with tofacitinib 2 mg BID, 80.8% with tofacitinib 5 mg BID, 55.8% with tofacitinib 10 mg BID, and 41.2% with placebo. The most common adverse events across the tofacitinib groups were nasopharyngitis and upper respiratory infection.[57]

Apremilast

Despite its efficacy in PsA, apremilast does not appear to have a role in the treatment of AS. In the phase 3 POSTURE study, 490 patients with AS were randomly assigned to apremilast 20 mg BID, apremilast 30 mg BID, or placebo. After 16 weeks, there was no difference in the ASAS20 response between patients in the apremilast 30 mg BID (32.5%) and placebo (36.6%) groups.[58] Based on these results, additional trials of apremilast in patients with AS are unlikely.

Ixekizumab

The investigational IL-17A inhibitor ixekizumab is also under evaluation in AS in 2 phase 3 trials. The COAST-V trial will assess the safety and efficacy of ixekizumab in patients with biologic-naïve AS, and the COAST-X trial will evaluate ixekizumab in patients who were previously treated with anti-TNF therapy. The primary endpoint in both trials is ASAS40 response rate at week 16.[59,60]

Anti-VEGF therapy

A disruption in the balance between bone resorption and bone formation, leading to the inappropriate formation of new bone, is a characteristic feature of AS. In addition to its role in promoting angiogenesis, VEGF also mediates osteoclast and osteoblast activity. Researchers have proposed anti-VEGF therapy as a strategy to prevent bone remodeling in patients with aggressive spondyloarthritis, including patients with AS.[61] This strategy remains hypothetical to date, but trials of anti-VEGF therapy in AS may be planned in the future.

Summary

Treatment options for patients with PsA and AS are evolving rapidly. New biologic therapies are now available to target the specific pathways of inflammation that are most active in SpAs—notably the IL-17 and IL-23/12 pathways—and several new agents with diverse mechanisms of action are on the horizon. Updated clinical practice guidelines provide a clear framework for incorporating biologic DMARDs and small molecule therapy into SpA management. At each stage of treatment, the T2T principles of routine disease activity monitoring and frequent treatment adjustments are critical for achieving clinical remission or low disease activity. As new treatments for PsA and AS reach the rheumatology practice setting, providers will have an unprecedented number of options for helping patients to reach their treatment goals.

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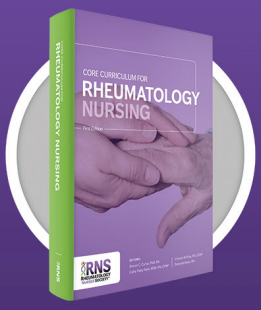

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The Long and Winding Road of a Young Athlete

by Iris Zink, MSN, NP, RN-BC

AUTHOR PROFILE:

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Iris Zink, MSN, NP, RN-BC is a nurse practitioner at Lansing Rheumatology in Lansing, Michigan, and President of the Rheumatology Nurses Society.

I recently saw a 17-year-old patient whose case caused a lot of people in our local healthcare community to scratch their heads. NJ is a high school senior, a sprinter who holds numerous school records. He had been a perfectly healthy kid until last year, when he began to battle painful plantar fasciitis. He spent a year trying various exercises and ice, bought several pairs of new shoes, and even tried prescription orthotics looking for something that relieved the pain.

Everything seemed futile, as his midfoot and plantar pain progressed to heel pain, which then led to swelling in his heel and Achilles. NJ and his mother assumed that between track, football, and year-round training that he must have injured his foot somewhere.

Frustrated with the lack of improvement, NJ tried physical therapy (no help) and went to see a podiatrist (nothing) before finally ending up in the office of an orthopedic surgeon.

The orthopedic surgeon first tried a series of cortisone injections (no relief) before coming to the conclusion that NJ's problems were most likely related to heel spurs. And so NJ was scheduled for surgery, where the surgeon moved his inflamed Achilles tendon and scraped the spurs off his heel.

Unfortunately, the surgery was unsuccessful in relieving NJ's pain, but with school sports season about to begin, NJ felt that he had no choice but to try to live with the pain. He regularly iced his foot after practices and games, and continued to search for that "perfect shoe" that would solve his problems.

A few weeks into his senior year, NJ started having knee and low back pain. NJ, his mother, and his school's athletic trainer felt that NJ's knee and low back pain must be due to his favoring his bad foot, and so the trainer tried to realign NJ's back on a number of occasions to no avail.

Despite all this, NJ managed to play in every football game during his senior season. His mother was convinced that his pain was mostly due to being pushed too hard by his coach and overdoing it on the field. Finally, though, when the pain and swelling had not subsided weeks after the football season ended, NJ went to a different orthopedic surgeon. This surgeon did not feel that an

MRI was needed and suggested exploratory arthroscopic surgery to fix what he was convinced would be a torn ligament in the knee.

During the surgery, however, the surgeon saw that something was not quite right. There were no tears in NJ's knee, but there was a thickened pannus and chronic synovitis. A subsequent biopsy revealed increased plasma cells consistent with inflammatory arthritis.

NJ got lucky. Although the approximate time for new patients in Michigan to see a rheumatology provider can be 6-to-9 months, we were able to get NJ into our office immediately after a desperate call from his surgeon's physician assistant.

We faced several challenges. NJ was adopted as a newborn, so his family history is limited. We were told that NJ's biologic mother had a likely family history of RA and possibly psoriasis or eczema.

I asked NJ about any history of rash, and was told that he shaved his head due to a dry flaking scalp. NJ denied any history of uveitis or inflammatory back pain at night. He also denied any regular diarrhea, constipation, inflammatory bowel symptoms, and gastrointestinal infection. He did tell me that he had regular morning stiffness in his foot and knee of at least 45 minutes, and that he constantly battled joint discomfort.

Armed with this information, his history of Achilles enthesitis, and his biopsy results, we diagnosed NJ with undifferentiated spondyloarthropathy. Labs were drawn, and I put NJ on prednisone 10 mg. I asked him and his mother to come back in a week.

At home, I told my teenaged daughters about this handsome young man I had seen in clinic and how worried I was that he had some type of inflammatory arthritis when it dawned on me that I missed an important question. I never thought to ask NJ about his sexual history, which was a huge oversight, a slap-yourself-in-the-forehead type of mistake. It is well documented that reactive arthritis can be caused by common sexually transmitted disease such as chlamydia or gonorrhea,[1] and I had missed asking NJ important questions to complete my differential diagnosis.

I called NJ's mom the next day. I told her that I was concerned about NJ, and that I realized that I forgot to ask if he was sexually active, explaining that that too can cause reactive arthritis. I informed her that most sexually transmitted diseases that lead to reactive arthritis would cause unusual penile discharge.[1] She did not seem shocked or offended, telling me she was pretty sure that her son was sexually active but that she would ask. We agreed to meet in a few days to review NJ's lab results and hopefully put the pieces together.

We got incredibly lucky!

While NJ's sexual activity turned out not to be linked with his pain, his labs revealed that he carried the HLA-B27 antibody, meaning that he is genetically predisposed to the spondyloarthropathies. While our eventual diagnosis of ankylosing spondylitis could have been made without this genetic clue, it certainly helped to make us more confident in our diagnosis. The flaking of his scalp, at least for now, is being attributed to either psoriasis or simply dry skin.

After we made our diagnosis, we started NJ on sulfasalazine 500 mg delayed release tablets and asked him to slowly taper the prednisone over the next 10 weeks. As there is limited evidence that methotrexate is effective in patients with ankylosing spondylitis[2]—and I remain concerned about the possibility of NJ getting someone pregnant or drinking excessively—our next option is a biologic.

The fact that we diagnosed NJ early in the disease process is a big plus. Many patients with ankylosing spondylitis remain undiagnosed for years and suffer while searching for answers. Our hope is that we can get NJ into remission and keep him there.

My lesson in this case involves education—both for myself and my fellow healthcare providers. NJ had two senseless knee surgeries, but we are fortunate that his second orthopedic surgeon was aware that there was nothing for him to "fix" when he recognized that the cause of NJ's swelling was Achilles enthesitis and not an injury or ligament damage.

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The Many Faces of Psoriatic Arthritis

by Jacqueline Fritz, RN, MSN, CNS, RN-BC

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Jacqueline Fritz, RN, MSN, CNS, RN-BC, is Owner and Coordinator of Education at the Medical Advancement Center in Cypress, CA. Her primary responsibility is working as an advanced practice nurse for a large rheumatology practice where she is involved in patient visits, research programs, and infusion center coordination. In addition, she enjoys speaking, teaching, and learning about immunology.

Two years ago, a 30-year-old woman (RB) came to our office for an initial consult. She was in a wheelchair, covered from head to toe with a knit hat, turtleneck top, long knit pants, and Ugg boots. She was reticent to make eye contact with our staff and visibly wincing in pain.

Our initial discussion revealed a 10-year history of psoriasis that had previously only been treated with topical medications. However, RB's disease had progressed to the point where she had been reduced to a wheelchair as a result of pain, swelling, and multiple joint stiffness, and she could no longer manage her condition on her own.

RB's primary care physician placed her on 40 mg of prednisone and morphine for pain, which provided some relief over the course of the eight months before we met. RB told us she had had a gastrointestinal bleed about 4 months after starting prednisone that required one unit of packed red blood cells. She denied use of alcohol or street drugs, but did report a pack-a-day smoking habit for the last 6 years.

After disrobing, RB's skin showed plaque and red scales on 90% of her total body surface area and severe alopecia on her scalp. Her Psoriatic Arthritis Severity Index (PASI) score was 6 (most severe on a scale of 1-6). The majority of RB's pain was focused on her lower extremities. Her hip and shoulder motion was restricted. She had no proximal or distal interphalangeal joint swelling, and no dactylitis or enthesitis.

Our initial diagnosis was psoriatic arthritis (PsA).

We ordered labs and x-rays to complete our clinical picture. Lab results showed that RB was hepatitis B and C negative, but HLA-B27 positive. Her C-reactive protein was 7.5 mg/L and erythrocyte sedimentation rate was 77 mm/hr, both indicating very high levels of disease activity. She also had severe anemia. X-rays revealed the presence of bamboo spine and sacroiliac joint fusion. RB had neither erosive disease nor pencil cup deformities, but mostly axial damage.

To add to the complexity, RB's Quantiferon test came back as "indeterminate." In these cases, it is commonly recommended to perform an alternate test before starting any tuberculosis medications,[1] so we performed a T-Spot TB test. It fortunately came back negative.

We initially started RB on daily methotrexate (MTX) 10 mg with folate, escalating to 15 mg after receiving her labs and serology report. We eventually increased the dose to 20 mg. After a few weeks with limited improvement in RB's symptoms, we added sulfasalazine and infliximab to her regimen, while slowly tapering the prednisone. RB remained on acetaminophen/oxycodone and clonazepam for her pain.

Four months after the latest switch, RB's PASI score had decreased to 3—a remarkable improvement in such a short amount of time. She had gone from a wheelchair to a cane and was now even beginning to walk. Her alopecia was improving as well, her hair growing back soft and curly.

RB started to smile and establish eye contact with our staff when she came to the clinic, making us all tingle with excitement at her progress. For St. Patrick's Day, RB colored her hair bright green, telling us that "I feel beautiful and I want people to notice me."

While for a short time we all felt good about our chances to reach remission, the heterogeneity of PsA—especially in patients who are HLA-B27 positive[2]—quickly put a damper on our optimism.

Six months after her initial response to infliximab, MTX, and sulfasalazine, RB's alopecia was back, along with worsening psoriasis. Because we were unsure whether these symptoms were due to worsening of her disease or a reaction to the MTX, we first cut back the MTX to a dose of 10 mg daily, which improved the alopecia but not the disease activity. This reduction also triggered a second GI bleed and subsequent anemia. We then transitioned RB from oral, daily MTX to weekly injections to try to take advantage of the benefits of MTX while minimizing the side effects.

The treatment of RB has been a seesaw of ups and downs in the last year. We've tried a variety of approaches. Infliximab monotherapy worked for a while (bright red hair for the holidays) but then its effects dampened. We added sucralfate for a short time along with a proton pump inhibitor. This too briefly helped but saddled RB with anemia of chronic disease.

The heterogeneity of PsA can make management of the disease a significant challenge. Patients who appear to be doing well can and often do develop new symptoms despite our best efforts to keep their disease at bay. Associated conditions such as ulcerative colitis, Crohn's disease, reactive arthritis, ankylosing spondylitis, and uveitis can all become involved.

RB's latest symptoms include dactylitis and enthesitis of the elbow, adding to the challenge of peripheral damage to the already axial disease she initially presented with. We're now waiting on her insurance to authorize a change to adalimumab.

Fortunately, RB's spirits have remained high throughout our time together. She changes her hair color with the seasons and keeps telling us, "Just keep fixing me" whenever we talk about trying something new. It's good to remind ourselves that when we first met, RB was confined to a wheelchair with horrible symptoms, so even her worst days now are better than those times.

Managing a patient with PsA such as RB is certainly frustrating because of the variability of the spondyloarthropathies, which makes it important to keep focused on the goal of remission (or, in some cases, low disease activity) through all the ups and downs. We're fortunate to be practicing in an era where we have options to cycle through to try to find combinations that work for long periods of time. It just takes patience.

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Digging Deep for Clues

by Linda Grinnell-Merrick, MS, NP-BC

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Linda Grinnell-Merrick, MS, NP-BC

Linda Grinnell-Merrick, MS, NP-BC, is a board-certified nurse practitioner at the University of Rochester Medical Center in Rochester, NY, and the incoming President of the Rheumatology Nurses Society.

A few months ago, our office received an urgent call from an anxious primary care provider (PCP) asking to speak with our clinic director. In his office, he had an 18-year-old female (JW) crying in pain.

A college freshman, JW said she had been experiencing severe right ankle pain and swelling for approximately 3 weeks before going to see her PCP. She was unaware of any specific injury that triggered the pain.

JW was initially evaluated at the university health clinic and discharged with a diagnosis of a sprained ankle after an X-ray revealed no fractures, only minor soft tissue swelling. JW was instructed to rest, ice the ankle regularly, and take ibuprofen to blunt the pain.

Two weeks later, the pain had gotten significantly worse, JW could not bear weight on her right leg, and the ankle had become very swollen, red, and warm. Sensing this was much more than a sprained ankle, JW reached out to her parents for help. Her parents immediately made an appointment with JW's PCP and picked up their daughter from college.

During JW's appointment with her PCP, she was examined and asked again about any specific injury to the ankle. X-rays were repeated, again revealing no obvious fracture or acute injury. Feeling there was something unusual going on, JW's PCP called our office before deciding upon any treatment. The primary concern he relayed to us was that he thought JW might have a septic joint.

Our team instructed JW and her parents to come right over (the beauty of having nurse practitioners in our rheumatology office to take urgent calls). When JW arrived, she was being pushed in a wheelchair by her parents. She could not bear any weight on the right ankle without experiencing excruciating pain.

Upon examination, JW's foot and ankle were very red, warm to the touch, and exquisitely painful on exam. A thorough history revealed no significant injuries, and no family or personal history of autoimmune disorders. The remainder of our exam was normal—no skin abnormalities or fever.

So in summary, we had an 18-year-old with a sudden onset of monoarthritic joint pain and swelling with no recent illness or infections who denied any sexual activity. This was just not adding up. I planned on ordering some labs, but I could just sense that there was something I was missing.

I asked JW's parents to step out into our waiting room so I could get her in a gown to do a full exam, feeling that I needed to talk to her alone. Once her parents left the room, I again asked JW about any sexual activity. Sure enough, once we were alone, she admitted that she had been sexually active with her current boyfriend but did not want her parents to know. I asked if she thought she could have contracted a sexually transmitted disease. She said she didn't think so (she had only been with her boyfriend), but admitted she didn't know about his past relationships. I told her we would do some testing and began treatment to get her ankle feeling better as quickly as possible.

Once we were able to rule out a septic joint, we started JW on prednisone. Laboratory results revealed she had chlamydia, which was the clue we needed to unravel this mystery.

Chlamydia affects people of all ages, but is most common in young women and is frequently asymptomatic. For this case, the important link is that chlamydia is a common case of reactive arthritis, an inflammatory arthritis that develops after certain infections of the gastrointestinal or genitourinary tracts. Symptoms of reactive arthritis are commonly acute, affect <4 joints (commonly in the lower extremities), and occur within several weeks of the initial infection. It is classified as one of the spondyloarthropathies. C-reactive protein (CRP) levels and erythrocyte sedimentation rates (ESR) are frequently elevated in patients with reactive arthritis. HLA-B27 positivity is seen in up to 50% of patients.[1]

Reactive arthritis is typically self-limiting, lasting from 3-5 months, though it can become chronic. Patients with HLA-B27 positivity, family history of spondyloarthropathies, and chronic bowel inflammation will typically fair worse than others.[1]

After we received back JW's lab report, we notified her PCP of the positive chlamydia result and allowed him to initiate treatment, which would typically involve either doxycycline or azithromycin. JW responded well and has not had any further inflammation. She continues to do well in college.

Reference

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Nurse-Focused Research at the ACR/ARHP Conference

by Sheree C. Carter, PhD, RN, RN-BC

The annual conference of the American College of Rheumatology (ACR)/Association for Rheumatology Health Professionals (ARHP) is typically the premier annual venue in the United States for the presentation of current and upcoming research topics in the field of rheumatology. In 2016, more than 3,000 abstracts were accepted for poster presentations for the 2016 ACR/ARHP Annual Conference.

While it is not possible to tell how many potential abstracts were submitted that focused on nursing or nurse-related research, there were a number of important peer-reviewed posters at the most recent conference that shine light on our daily practice. A conference online database search of "nurse" identified 24 abstracts with faculty from 11 countries that included nurse-related outcomes and interventions.

Table 1 includes a brief summary of these abstracts.

- Four abstracts from the United States, Brazil, Israel, and Canada explored the merits of the manufacturer Patient Support Program for adalimumab, which has differing nurse components in various countries.
- Two abstracts demonstrated positive results in tobacco cessation programs as precursors to pilot intervention programs
- Three abstracts from the United States and Canada assessed shared or collaborative care models that included various combinations of primary care physicians, NPs, psychologists, psychiatric nurses, and chaplains.
- Four abstracts from four different studies had positive patient outcomes in a nurse-led care environment.
- French researchers provided three abstracts from the COMEDRA study, which focuses on nurse-led care of patients with RA.
- Two abstracts – one from Japan and the other from the United States – focused on the impact of professional development opportunities for nurses on patient outcomes.
- A U.S.-based pilot study showed the benefits of nurse educators, specifically with patient self-management programs

A small number of studies also used rheumatology nurses as assessors and/or researchers to gather patient data for analysis. Several of these studies mentioned the need for a rheumatology nurse, certified medical assistant, physician assistant (PA), or "rheumatology extender." A review of these studies showed consistent statistical advantages utilizing the rheumatology nurse for early triage, performance of specific identification measures, targeted follow-up protocols, closing educational gaps of patients, and providing patient training with self-management techniques.

A small number of studies compared the ability of physicians vs. nurses and/or PAs to identify specific diseases such as spondyloarthropathies and assess the effectiveness of treatment. These studies showed no significant differences between the groups.

Lastly, there was one study from the United Kingdom that reported high levels of patient satisfaction with care that utilized an interdisciplinary team led by a physiotherapist that included nurses.

You can find out more details about any of the studies included here by visiting the ACR website and searching their conference data. Being involved in research as a rheumatology nurse is a terrific way to build your professional resume and show off the great work you do.

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Table 1 – *2016 ACR/ARHP Poster Presentations Focused on Nursing Components*

Title	Authors	Findings	Country
Impact of a Patient Support Program on Abandonment of Adalimumab Treatment Initiation in Patients with Rheumatoid Arthritis, Ankylosing Spondylitis, and Psoriatic Arthritis	Mease P, Mittal M, Skup M, et al	The manufacturer's patient support program (PSP) for adalimumab (ADA)-treated patients, which includes nurse support, was shown to reduce treatment abandonment among patients with RA, PsA, and AS	United States
Canadian Study of Outcomes in Adalimumab (HUMIRA®) Patients with Support for Adherence – Results from the Companion Study	Gerega S, Millson B, Bessette L, et al	Patients taking advantage of the manufacturer's PSP program showed higher rates of adherence and were less likely to cease therapy. In this program, nurses provided motivational interventions over the phone.	Canada
Is Patient Support Program (PSP) Participation Associated with Longer Persistence and Greater Adherence Among New Users of Adalimumab?	Srulovici E, Garg V, Ghilai A, et al	The manufacturer's PSP in Israel includes a home visit by an RN, telephone calls, and mail outreach. Use of the program led to improved patient persistence and adherence.	Israel
Patient Support Program for Adalimumab-Treated Patients in Brazil: Impact on Patients' Adherence and Persistence	Levy RA, Teich V, Fernandes R, et al	The manufacturer's PSP in Brazil includes nurse and telephone support. Use of the program led to improved patient persistence and adherence.	Brazil
Inter-Professional Satisfaction and Perceptions of Collaborative Practice of an Innovative Model of Care for the Early Detection of Axial Spondyloarthritis	Passalent L, Hawke C, Bidos A, et al	Community-based primary care physicians (PCPs), physiotherapists, chiropractors and nurse practitioners (NPs) involved in a collaborative, inter-professional care program designed to assist with the early detection of SpA were invited to participate via survey. This study did not list NPs as significant responders to the survey, but the model of care showed high levels of satisfaction with collaboration between providers.	Canada
Use of a Shared Medical Appointment for Patients with Fibromyalgia in a Rural, Academic Medical Center: A Process Improvement Initiative for the Development of a New Care Model	Orzechowski NM, Lloyd D, Tuthill K, Puttgen J, Bergeron R	One rheumatologist, two NPs, one chaplain, and one secretary implemented a new shared medical appointment model using the Plan-Do-Study-Act method. The model reduced wait times for fibromyalgia patients from 3 months to 1 month. The model also freed up consultation slots for new patient with other conditions.	United States
The Development of an Interdisciplinary Treatment Program for Fibromyalgia in a Tertiary Medical Center Focused Upon Rheumatology and Internal Medicine	Gehin J, Abril A, Rivera F, Wang B, Bruce B	Fibromyalgia patients were seen in an interdisciplinary model that included health psychologists and psychiatric nurses. Positive results were demonstrated after a 2-day course focusing on cognitive behavioral strategies and education.	United States
Online Consultation for Chinese Patients with Rheumatic Diseases Based on Smart System of Disease Management (SSDM) Mobile Tools: A Study of Medical Economics	Xiao F, Liu X, Li Z, et al	Rheumatologists and nurses developed and launched a series of Smart System Disease Management applications focusing on patient self-management. Patients were trained on performing DAS28 and HAQ evaluations, as well as entering medication and lab test data. The program reduced the need for in-person visits, thereby reducing overall patient costs.	China

(Table 1 Continued on next pages)

Table 1 – *(Continued)*

Title	Authors	Findings	Country
Feasibility of a Rheumatology Staff Protocol for Tobacco Cessation Counselling and Quit Line Electronic Referral	Bartels CM, Panyard D, Lauver D, et al	Evaluation of a pre-trained staff-led (medical assistants and nurses) tobacco cessation intervention program in 3 academic rheumatology clinics. Capture and documentation of tobacco use improved, as did 30-day assessment of patient readiness to quit smoking.	United States
Developing a Staff-Driven Electronic Smoking Cessation Referral Program in Rheumatology Clinics	Panyard D, Ramly E, Gilmore-Bykovskyi A, et al	Training and development of medical assistants and nurses within an academic rheumatology system on an Ask-Advise-Connect model to remove barriers in referring patients to tobacco cessation resources. Precursor to a pilot study.	United States
Improving Pneumococcal Vaccination Rates for Immunosuppressed Patients in an Academic Rheumatology Clinic	Bays A, Nayak RR, Murray S, et al	9 rheumatology fellows, 11 faculty members, 1 nurse practitioner, and 9 medical assistants participated in a QI project that increased the number of eligible patients receiving the 13-valent pneumococcal conjugate vaccine.	United States
Use of Electronic Medical Record to Identify Immunocompromised Patients in a Pediatric Rheumatology Clinic	Favier LA, Smitherman EA, Furnier A, et al	Evaluation of an EMR program aimed to identify immunocompromised pediatric patients. EMR performance steadily improved over 5 weeks as compared to human identification by pediatric rheumatologist and nurse.	United States
Nurse Scheduled Telephone Visit: The Right Rheumatology Care for the Right Patient at the Right Time	Butt S, Newman E, Smith N	Development of a new visit type within an EHR called a Nurse Scheduled Telephone Visit (NSTV). Bottom line suggested NSTV's will reduce office visits to allow approximately 300 hours more clinic time for new patients.	United States
How to Implement Cardiovascular Disease Risk Assessment for Patients with Inflammatory Joint Diseases in Daily Rheumatology Practice: An Overview of a Nationwide Norwegian Project	Ikdahl E, Rollefstad S, Wibetoe G, et al	Rheumatologists and rheumatology nurses performed and recorded CVD risk assessments and were taught how to perform brief smoking cessation and health/diet educational instruction	Norway
The Musculoskeletal Master Educator Training Program: A New Resource and Professional Development Opportunity for Leaders in Medical Education	Barker AM, Okuda Y, Bruno P, et al	Significant increases in confidence and competence after participation in a 2-day professional development workshop by 25 participants (15 MDs, 7 APRNs, 2 PAs, 1 nurse) at the Veterans Health Affairs SimLEARN Center	United States
Survey on the Understanding and Practice of T2T for Nurses Engaged in Medical Treatment of Rheumatoid Arthritis	Fusama M, Higashi K, Maeda K, Murata N, Nakahara H	Better patient outcomes in RA can be achieved by expanding the role of the rheumatology nurse. Specifically, knowledge of T2T concepts and the importance of DAS28 measurements can increase likelihood of achieving treatment goals for patients with RA	Japan
Promoting Self-Management Techniques for Osteoarthritis Pain: A Pilot Study of Nurse Practitioner Led Coping Skills Training	Stamatos CA, Bruckenthal P	Patients with OA and chronic pain enrolled in a 10-week group training program led by an NP to learn coping skills. Significant improvements in pain, depression, coping, and self-efficacy were seen.	United States

Table 1 – *(Continued)*

Title	Authors	Findings	Country
The Effect of Nurse-Led Follow-up in Rheumatoid Arthritis. a Systematic Review and Meta-Analysis of Randomized Controlled Trials	de Thurah A, Esbensen BA, Roelsgaard IK, Frandsen TF, Primdahl J	Review of 5 recent studies showing that routine monitoring from rheumatology nurses on stable-phase RA patients leads to no difference in disease activity over time compared to those monitored by a physician. Nurse monitoring does lead to an increase in patient satisfaction.	Denmark
Effects of an Educational Program Using Treat to Target Strategy in Korean Patients with Rheumatoid Arthritis	Paek S, Kim SH, Kim H, et al	Nurse-led educational interventions for patients with RA using T2T strategy showed statistically significant improvements in pain, fatigue, illness/ disease activity perception, and quality of life compared to those treated conventionally.	South Korea
Systematic Development of a Patient-Centered Strategy to Improve Tight Control in Daily Clinical Practice	de Jonge MJ, Manders SHM, Huis AMP, et al	Positive results reported from a 2-phase program to empower RA patients to take an active role in their disease control. Phase 1 involved an informational leaflet; phase 2 included consults and guidance from a specialized rheumatology nurse.	Netherlands
Is the Self-Assessment of Disease Activity (auto-DAS28) By Patients a Feasible and Acceptable Measure over the Long Term in Rheumatoid Arthritis (RA)? Three-Year Follow-up of a Nurse-Led Program in 771 Patients with Established RA	Gossec L, Foissac F, Soubrier M, et al	Patients were trained to perform auto-DAS by a nurse using a video to teach self-assessment of joints. Within 2-4 years after the end of the trial, patients were seen in a face-to-face interview with a nurse and the frequency of auto-DAS was assessed.	France
One Third of Patients with Established Rheumatoid Arthritis (RA) Are Correctly Vaccinated Against Influenza and Pneumococcus and This Is Increasing: 3 Year Longitudinal Assessment of 776 Patients	Gossec L, Foissac F, Soubrier M, et al	Patients in the COMEDRA study (nurse-led program) demonstrated increased levels of compliance with EULAR vaccination recommendations among patients with RA.	France
Screening for and Management of Comorbidities after a Nurse-Led Program: Results of a 3 Year Longitudinal Study in 776 Established RA Patients	Gossec L, Foissac F, Soubrier M, et al	Patients with RA had comorbidity counseling from a nurse. The nurse-led interventions led to improvements in vaccine adherence, CV risk screening, and bone density testing.	France
Minding the Gap: The Use of Nurse Practitioners and Physician Assistants in U.S. Rheumatology Practice to Affect Rheumatology Workforce Shortages	Smith BJ, Bolster MB, Ditmyer M, Jones KB, Monrad S, Battafarano D	Information presented from a survey of 19 NPs and 13 PAs in rheumatology practices. Respondents reported that the majority of patient visits are follow-ups. These professionals may not be utilized to the full potential of their license.	United States

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