



Treatment recommendations for psoriatic arthritis

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Treatment Recommendations for Psoriatic Arthritis

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Running Footline: Psoriatic Arthritis Treatment Recommendations

ABSTRACT

Objective: To develop comprehensive recommendations for the treatment of the various clinical manifestations of PsA based on evidence obtained from a systematic review of the literature and from consensus opinion.

Methods: Formal literature reviews of treatment for the most significant discrete clinical manifestations of PsA (skin and nails, peripheral arthritis, axial disease, dactylitis, and enthesitis) were performed and published by members of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA). Treatment recommendations were drafted for each of the clinical manifestations by rheumatologists, dermatologists, and PsA patients based on the literature reviews and consensus opinion. The level of agreement for the individual treatment recommendations among GRAPPA members was assessed with an on-line questionnaire.

Results: Treatment recommendations were developed for peripheral arthritis, axial disease, psoriasis, nail disease, dactylitis, and enthesitis in the setting of PsA. Nineteen recommendations were drafted, and over 80% agreement was obtained on 16 of them. In addition, a grid that factors disease severity into each of the different disease manifestations was developed to help the clinician with treatment decisions for the individual patient from an evidenced-based perspective.

Conclusion: Treatment recommendations for the cardinal physical manifestations of PsA were developed based on a literature review and consensus between rheumatologists and dermatologists. In addition, a grid was established to assist in therapeutic reasoning and decision-making for individual patients. It is anticipated that periodic updates will take place using this framework as new data become available.

INTRODUCTION

The articular and dermatologic manifestations associated with psoriatic arthritis (PsA) are remarkably heterogeneous in both the extent and type of tissue involvement. Patients with PsA, a chronic systemic inflammatory disorder, may develop not only peripheral arthritis but also axial disease, dactylitis, enthesitis, and skin and nail psoriasis, with consequent adverse impact on function and quality of life (QOL).(1, 2) Heterogeneity is observed not only in disease manifestations but also in severity and course, which can vary from very mild psoriasis or enthesitis to widespread psoriatic plaques, disfiguring nail disease, and severe joint inflammation with destruction that can result in disability and increased mortality.(3, 4) Moreover, comorbidities associated with psoriasis such as the metabolic syndrome can contribute to damage in multiple end-organs and often leads to markedly impaired QOL as well as early mortality.(5-7)

Recent progress in understanding the immunopathogenesis of PsA has been accompanied by treatment advances that have accelerated rapidly over the last decade.(8) Despite these advances, therapeutic decisions for an individual patient with PsA can be challenging due to the diversity of clinical characteristics and the simultaneous involvement of multiple different tissues, often with varying degrees of severity. To address the need for evidence-based treatment recommendations and assist the practitioner, members of GRAPPA published systematic reviews of the literature to identify the best available evidence regarding treatment of the various manifestations of PsA.(1, 9) Herein, we present treatment recommendations that were formulated by rheumatologists and dermatologists in GRAPPA in conjunction with PsA patients, based on evidence from these systematic reviews and consensus opinion. These recommendations were developed to provide the best care for patients with PsA, regardless of economic or political considerations.

METHODS

The target audience for these treatment recommendations is all clinicians who care for PsA patients. First, formal literature reviews were performed by members of GRAPPA. To capture data regarding the varied areas of involvement characteristic of PsA, articles were selected that provided evidence supporting the treatment of peripheral arthritis, spinal disease, skin and nail disease, enthesitis, and dactylitis in the setting of PsA (**Figure 1**). These articles were reviewed and graded, and the results have been published.(10-16) The evidence was graded using the approach of the Institute of Medicine.(17) Wherever possible, effect sizes were calculated to quantify the extent of efficacy or toxicity. Effect size is the mean difference in effect between treatment and control, divided by the standard deviation of the difference.(18) Effect sizes of 0.2 or less are considered small and unimportant in terms of efficacy, whereas effect sizes greater than 0.8 are considered large and suggest high efficacy.

Reviewers graded the evidence and treatment recommendations for PsA in accordance with recommendations from the Agency for Health Care Policy Research (AHCPR), as shown in **Table 1**.

Table 1. Grading of Evidence Sources and Recommendations

| Grade | Evidence Source as Recommended by AHCPR |
|--------------|---|
| 1a | Meta-analysis of randomized controlled trials (RCT) |
| 1b | One or more RCT |
| 2a | One or more controlled trials (without randomization) |
| 2b | Other well designed studies (quasi-experimental) |
| 3 | Non-experimental studies (descriptive studies such as comparative or correlation studies, or case-control studies) |
| 4 | Expert committee opinions, clinical experience |
| | |
| Grade | Preliminary Recommendations for Treatment of PsA (using the best available evidence extracted from published literature) |
| A | Category 1 evidence |
| B | Category 2 evidence, or extrapolation from Category 1 evidence |
| C | Category 3 evidence, or extrapolation from Category 1 or 2 evidence |
| D | Category 4 evidence or extrapolation from Category 2 or 3 evidence |

To address the nuanced and complex application of the results of these studies to the heterogeneous situations that arise in the clinic, focus groups were assembled, comprising experts in rheumatology and dermatology with specific experience in the care of PsA and psoriasis, and patients with PsA. Next, subcommittees were formed for each of the five domains, and recommendations were drafted based on evidence and consensus between rheumatologists, dermatologists, and patients for psoriasis, peripheral arthritis, axial disease, dactylitis, and enthesitis. Each of these subcommittees developed a definition of mild, moderate, or severe for their individual domains. Finally, the subcommittee chairs met with Artie Kavanaugh and Chris Ritchlin to refine the recommendations (mild-moderate-severe categories) in each domain. The recommendations for each domain and the grid with the three categories were voted on by the entire membership of GRAPPA. Note that the grid was designed as a tool to assist in making treatment decisions for individual patients and as such is largely expertise-based. Data that became available after the systematic reviews were published were also considered by the various subcommittees.

Nineteen items covering the diagnosis, assessment, and treatment of the five PsA clinical manifestations were submitted for a vote using a web-based interface (Survey Monkey™). Each item was rated on a 5-point scale (1=strongly agree to 5=strongly disagree). The Disagreement Index (DI) was derived from the 30th and 70th percentile of the respondents' ratings, adjusted for symmetry between the central point of the interpercentile range and the mid-point of the rating scale. The adjustment factor was derived from experimental work that compared different definitions of what constituted "disagreement" among panels of various sizes. The number of respondents, percentage respondents in the 30th and 70th percentile, percentage respondents in category 1 or 2, and the mean and standard deviation were calculated.

RESULTS

The results of the survey are shown in **Supplementary Appendix I** (published online only). Seventy rheumatologists and dermatologists responded to the questionnaire. For 16 of the 19 items, 80% of the respondents agreed or strongly agreed. The three areas where agreement was not as strong included the use of the Bath Ankylosing Spondylitis Disability Activity Index (BASDAI) to measure axial disease activity over time (75.7%) and to assess axial treatment response (78.7%) and the algorithm for the treatment of psoriasis (69.2%). The strength of each recommendation (Grades A-D) is included.

Peripheral Arthritis

Diagnosis and assessment

Diagnosis of PsA should follow the CASPAR (ClAsSification criteria for Psoriatic ARthritis) criteria.⁽¹⁹⁾ We consider inflammation to include such features as pain involving joints, spine, and/or entheses associated with erythema, warmth, and swelling; prominent morning and rest stiffness.

Preferably, diagnosis of psoriasis should be confirmed by a dermatologist, and inflammatory musculoskeletal disease by a rheumatologist, or either one by an appropriately qualified health professional.

Baseline evaluations of PsA should include the following domains (consensus on core set of domains for psoriatic arthritis assessment established at OMERACT 8).⁽²⁰⁾

Peripheral joint assessment (68 joints for tenderness; 66 joints for swelling)

Pain (patient-reported on a visual analogue or category rating scale)

Patient global assessment of disease activity

Physical function (e.g., as measured by the Health Assessment Questionnaire [HAQ])

Health-related QOL, as assessed by a general measure (e.g., Short Form 36 [SF-36]) or a PsA-specific measure (e.g., Psoriatic Arthritis QOL [PsAQOL])

Fatigue, measured by patient self-report or a general instrument (e.g., Functional Assessment of Chronic Illness Therapy [FACIT])

Acute phase reactants (e.g., C-reactive protein [CRP] or erythrocyte sedimentation rate [ESR]).

Radiographic assessment is encouraged according to clinical manifestation and physician discretionary judgment.

Factors associated with a poor prognosis related to the progression of peripheral joint disease and damage in patients with PsA include: the number of actively inflamed joints (i.e., polyarticular disease, as opposed to monoarticular disease); elevated ESR; failure of previous medication trials; the presence of damage, either clinically or on x-rays;⁽²¹⁾ a loss of function as assessed by HAQ; and diminished QOL as assessed by SF-36, Dermatology Life Quality Index (DLQI), or PsAQOL.

A patient should be considered a treatment failure when in spite of therapy for a length of time appropriate to the pharmacokinetic/pharmacodynamic profile of the individual agent at an appropriate dose, the patient fails to demonstrate acceptable clinical improvement. Response to treatment of peripheral arthritis in patients with PsA may be assessed using criteria initially developed for rheumatoid arthritis (RA), such as the Disease Activity Score₂₈ (DAS₂₈,

shown to be reliable and discriminative in PsA, even though it uses only 28 joints) and the EULAR response criteria, which categorize levels of disease and changes to assess response. The American College of Rheumatology (ACR) response criteria (e.g., ACR20/50/70) may also be used in PsA.(22) In a recent analysis of PsA and RA outpatient cohorts,(23) the utility of the DAS28 for PsA was questioned with regard to its applicability in settings outside of clinical trials, where patients receive therapies of varying efficacy. Response may also be considered inadequate if there is evidence of progression of joint damage on radiographs.

Treatment

Treatment recommendations for peripheral arthritis include nonsteroidal anti-inflammatory drugs (NSAIDs), intra-articular glucocorticoid injections, disease-modifying antirheumatic drugs (DMARDs), and TNF inhibitors (see **Table 2**).

Systemic corticosteroids are not typically recommended in the treatment of psoriasis and are only advisable in discrete circumstances and not for chronic use, due to the potential to cause post-steroid psoriasis flare and other adverse effects (D). Gold salts, chloroquine, and hydroxychloroquine also are not recommended for use in PsA.

DMARDs have the potential to reduce or prevent joint damage, and preserve joint integrity and function (although none have been shown to do this in PsA). Many factors influence the choice of DMARD for the individual patient: its relative efficacy, convenience of administration, requirements of the monitoring program, costs of the medication and monitoring (including physician visits and laboratory costs), time until expected benefit, and the frequency and potential seriousness of adverse reactions. Input from a rheumatologist is often essential when initiating DMARD therapy.

A patient should be considered a DMARD-failure if at least one DMARD has been failed individually or in combination in an adequate therapeutic trial, defined as treatment for ≥ 3 months, of which ≥ 2 months is at standard target dose (unless significant intolerance or toxicity limits the dose). Intolerance/toxicity is defined as treatment for < 2 months, where treatment is withdrawn because of drug intolerance or toxicity. When treatment is withdrawn because of intolerance or toxicity after > 2 months therapy, at least 2 months should have been at therapeutic doses.

Although there is no evidence for the use of combination therapy, a combination of two or more agents could be used in those patients who fail to respond to a single agent, or who present joint damage progression in spite of treatment.

Axial Disease

Diagnosis and assessment (based on ankylosing spondylitis [AS] criteria)

Diagnosis of axial disease should be based on the presence of 2 of 3 of the following criteria:

1. Inflammatory back pain (features including onset age < 45 years, symptoms > 3 months, morning stiffness > 30 minutes, insidious onset, improved with exercise, alternating buttock pain).
2. Limitation of motion of cervical, thoracic, or lumbar spine in both sagittal and frontal planes; noted differences from AS include less pain, less limitation in movement, and less symmetry. The International SPondyloarthritis Interrater Reliability Exercise (INSPIRE) has shown assessments of spinal disease in AS are also reliable in axial PsA.(24)

3. Radiological criteria (e.g, plain x-ray [unilateral sacroiliitis Grade 2 or more], syndesmophytes, MRI changes in sacroiliac joints of bone marrow edema, erosions, joint space narrowing). Criteria modified from AS based on data from Helliwell et al.(25)

Based on experience in AS, disease activity in the spine can be reliably measured by the BASDAI, where active disease has been defined by a BASDAI score ≥ 4 . The BASDAI can be used to measure disease activity over time; assessment should take place after 6 weeks of treatment. A treatment response, based on definition of response in AS, is defined as a BASDAI score < 3 or a reduction by 2.

Treatment

See **Table 2** for treatment recommendations based on evidence derived in AS. Traditional oral DMARDs such as methotrexate, leflunomide, and sulfasalazine, have not been shown to be effective in axial manifestations of AS(26) and by extrapolation, they are not considered to be of adequate efficacy for PsA axial disease, until further data are available.

Enthesitis

Diagnosis and assessment

The diagnosis of enthesitis is challenging; currently three approaches have been described: clinical examination, including pain/tenderness/swelling at tendon, ligament or capsule insertion site by palpation and pressure; ultrasound with power Doppler; and MRI.

Several instruments proposed for clinical assessment of enthesitis have been tested in the INSPIRE study and were reliable in both AS and PsA, but no single instrument has gained widespread acceptance.(24) Another assessment modality is the visual analogue pain scale.

Treatment

See **Table 2** for treatment recommendations for mild, moderate, or severe enthesitis.

Skin and Nails

Diagnosis and assessment (for selection of topical vs systemic therapy)

For patients with mild psoriasis, candidates for topical therapy alone must meet all of the following criteria: generally asymptomatic; minimal impact on QOL; amenable and responsive to localized therapy; less than 5% for plaque psoriasis; and no incapacity and/or disability. For patients with moderate to severe psoriasis, candidates for an addition or change to systemic and/or phototherapy should meet at least one of the following criteria: symptomatic, i.e., pain, bleeding, itching; more than minimal impact on QOL; inadequate response to localized therapy; body surface area generally greater than 5% for plaque psoriasis; patients with guttate, erythrodermic, or pustular psoriasis; psoriasis in vulnerable areas (face, genitals, hands/feet, nails, scalp, or intertriginous areas); or varying degrees of incapacity and disability from psoriasis.

Treatment

See **Table 2** for a list of first-line, second-line, and third-line systemic therapies for treatment of psoriasis.

It is important to note that the clinician should consider all agents in a treatment level before proceeding to “lower” level. Situations rendering a specific therapy as “not appropriate” include: lack of response, adverse events, and poor access to therapy.

Unusual clinical subsets of psoriasis can co-occur with arthritis; thus, treatment may vary from that used in psoriasis vulgaris. For erythrodermic/generalized pustular psoriasis, consider acitretin as first-line therapy, although more research is needed. For palmoplantar pustulosis, acitretin and oral PUVA appear to result in improvement (no evidence for either one being superior), with combination of the two providing superior response. Cyclosporine and tetracycline appear to be of modest benefit. No strict recommendations can be given, due to lack of definition of treatment response, lack of controlled studies in this area.(27) For treatment of hand/foot psoriasis, consider topical PUVA, soriatane, efalizumab as preferable first-line agents although more research is needed in this area.

All three TNF inhibitors have shown efficacy in phase 3 randomized controlled trials, but no head-to-head trials have been published to directly compare efficacy and safety. Some data, however, suggest that etanercept may not be as effective in patients with high BMIs.(15) In psoriasis studies, etanercept efficacy was dose-dependent, with doses as high as 100 mg per week (double the typical dose for RA and PsA patients) providing the most benefit.(28)

The efficacy of therapies for psoriatic nail disease is not well studied; see **Table 2** for existing evidence.(29) Specific recommendations cannot be made due to size of studies and lack of appropriate controls.

At this time, no recommendation can be given regarding efficacy and side effect profiles of systemic corticosteroids because clinical trial data are not available. In general, monotherapy with systemic corticosteroids is to be avoided in psoriasis because skin disease can flare during or after taper. Further studies, however, are needed to evaluate the role of short-term corticosteroids in severe, pustular, and erythrodermic psoriasis.

Dactylitis

Diagnosis and Assessment

Dactylitis, defined as uniform swelling of a digit, is due to synovitis, tenosynovitis, and enthesitis together with soft-tissue edema. Dactylitis occurs in 16-48% of cases of PsA, and acute dactylitis has been shown to be a clinical indicator of disease severity in PsA.(30) Conversely, chronic, non-tender diffuse dactylitic swelling may be less clinically significant, although MRI appearances differ only quantitatively from acute dactylitis. Recurrent isolated dactylitis, often in the same digit(s), may be the only clinical manifestation of PsA.

Treatment

The treatment of dactylitis is largely empirical. See **Table 2** for treatment recommendations of initial and more resistant cases.

Table 2. Treatment Recommendations

| | Disease Status | Treatment Recommendation | Level of Evidence * | Level of Agreement † | Comments |
|----------------------|-----------------------|---|--|-----------------------------|---|
| Peripheral arthritis | Mild | NSAIDs | A | 90.9% | For control of joint but not skin symptoms. |
| | N/A | Intra-articular glucocorticoid injections | D | | May be given judiciously to treat persistently inflamed joints, if care is taken to avoid injection through psoriatic plaques. Injections to any one joint should be repeated with caution according to clinical judgment. |
| | Moderate or severe | DMARDs (specific recommendations follow): Sulfasalazine Leflunomide Methotrexate Cyclosporine | A | | No evidence supporting DMARDs ahead of TNF inhibitors, although the effect size for TNF inhibitors is much larger than that for traditional DMARDs. |
| | | | A B B | | |
| Moderate or severe | TNF inhibitors | A | For patients who fail to respond to at least one DMARD therapy. The 3 currently available TNF inhibitors (etanercept, infliximab, and adalimumab) are equally effective for the treatment of peripheral arthritis and for the inhibition of radiographic progression. Patients with poor prognosis could be considered for TNF inhibitors even if they have not failed a standard DMARD. | | |
| Skin disease | Moderate to severe | Phototherapy | A | 69.2% | <u>First-line therapies</u> Phototherapy includes UVB/nbUVB, oral PUVA, bath PUVA, with or without acitretin. An initial trial of phototherapy should be made, unless it is not appropriate or if psoriasis is in areas that preclude phototherapy (i.e., scalp, groin, axilla). All forms of phototherapy are considered as a group, although many consider that PUVA therapy carries increased risk of skin cancer |

| | Disease Status | Treatment Recommendation | Level of Evidence * | Level of Agreement † | Comments |
|--------------------------|----------------|--------------------------|---------------------|----------------------|---|
| Skin disease (continued) | | | | | <p>compared with other UV modalities. Aggressive immunosuppression should not follow extensive phototherapy (especially PUVA), given the increased risk of melanoma and nonmelanoma skin cancer in this scenario.</p> <p>TNF inhibitors include etanercept, adalimumab, and infliximab.</p> <p>Cyclosporine should be limited to less than 12 consecutive months because cumulative toxicity, i.e., multiple courses, is not well studied.</p> <p style="text-align: center;"><u>Second-line therapies</u></p> <p style="text-align: center;"><u>Third-line therapies</u></p> |
| | | Methotrexate | A | | |
| | | Fumaric acid esters | A | | |
| | | TNF inhibitors | A | | |
| | | Efalizumab | A | | |
| | | Cyclosporine | A | | |
| | | Acitretin | A | | |
| | | Alefacept | A | | |
| | | Sulfasalazine | A | | |
| | | Hydroxyurea | C | | |
| | | Leflunomide | A | | |
| | | Mycophenolate mofetil | C | | |
| Thioguanine | C | | | | |
| Nail disease | N/A | Retinoids | C | 69.2% | TNF inhibitors include infliximab and alefacept. |
| | | Oral PUVA | C | | |
| | | Cyclosporine | C | | |
| | | TNF inhibitors | C | | |

| | Disease Status | Treatment Recommendation | Level of Evidence * | Level of Agreement † | Comments |
|----------------|--------------------|---|---------------------|----------------------|---|
| Spinal disease | Mild to Moderate | NSAIDs | A | 86.4% | |
| | | Physiotherapy Education, analgesia, and injection of sacroiliac joint | A | | |
| | | | A | | |
| | Moderate to Severe | TNF inhibitors | A | | For patients who fail therapies for mild to moderate disease. Infliximab, etanercept, and adalimumab have all demonstrated efficacy in AS; the consensus was that similar treatment responses reported in AS were also likely to be observed in axial PsA. |
| Enthesitis | Mild | NSAIDs, physical therapy, corticosteroids | D | 87.9% | |
| | Moderate | DMARDs | D | | |
| | Severe | TNF inhibitors | A | | |
| Dactylitis | N/A | NSAIDs | D | 90.2% | Usually employed initially. |
| | N/A | Corticosteroids | D | | Many clinicians rapidly progress to injected steroids. |
| | Resistant | DMARDs | D | | Nearly always in the context of co-existing active disease. |
| | N/A | Infliximab | A | | Some evidence available. |

AS = ankylosing spondylitis; DMARD = disease-modifying antirheumatic drug; N/A = not applicable or not specifically defined; NSAID = nonsteroidal anti-inflammatory drug; PsA = psoriatic arthritis; PUVA = psoralen-ultraviolet-light; TNF = tumor necrosis factor; UVB = ultraviolet B light

* See Methods section of manuscript for description of categories and levels of evidence.

† Percentage of survey responders who agreed or strongly agreed (see Part B of **Supplementary Appendix I** for complete results).

Severity Assessment in PsA

Patients may be roughly stratified in categories of “mild,” “moderate,” or “severe” for peripheral arthritis, skin disease, spinal disease, enthesitis, and dactylitis according to presence of criteria noted in **Table 3**. This table is designed to be used as a tool to assist in decision making, and rigorous adherence to the proposed stratification is not appropriate. Until numeric thresholds for mild, moderate, and severe for the various instruments are validated, physician judgment is required to appropriately stratify individual patients. Some patients may have multiple manifestations, and treatment decisions may be determined by the most severe clinical presentation. The synergistic impact of multiple simultaneous manifestations may be assessed with the patient global, HAQ, and disease-specific instruments (DLQI, PsAQOL). Two case illustrations are provided in **Table 4**.

Table 3. Disease Severity

| | Mild | Moderate | Severe |
|----------------------|--|--|--|
| Peripheral arthritis | <5 joints No damage on x-ray No LOF QOL-minimal impact Pt. evaluation mild | ≥5 joints (S or T) damage on x-ray IR to mild Rx Mod LOF Mod impact on QOL Pt. evaluation mod | ≥5 joints (S or T) Severe damage on x-ray IR to mild-mod Rx Severe LOF Severe impact on QOL Pt. evaluation severe |
| Skin disease | BSA <5, PASI <5, asymptomatic * | Non-response to topicals, DLQI, PASI <10 † | BSA >10, DLQI >10 PASI >10 |
| Spinal disease | Mild pain No loss of function | Loss of function or BASDAI >4 † | Failure of response |
| Enthesitis | 1-2 sites No loss of function | >2 sites or loss of function | Loss of function or >2 sites and failure of response * |
| Dactylitis | Pain absent to mild Normal function | Erosive disease or functional loss | Failure of response |

S = swollen; T = tender; LOF = loss of physical function; IR = inadequate response; BSA = body surface area; BASDAI = Bath Ankylosing Spondylitis Disability Activity Index; PASI = Psoriasis Activity Severity Score; QOL = quality of life; DLQI = Dermatology Life Quality Index

* See Case Illustration #1 in **Table 4**

† See Case Illustration #2 in **Table 4**

Table 4. Case Illustrations

| Case | History / Symptoms | Recommendation |
|--|---|---|
| #1 | 19-year-old male student: | This patient has severe enthesitis and mild skin disease (see Table 3), and he has failed therapies for mild and moderate enthesitis; a TNF inhibitor should be considered. |
| | <ul style="list-style-type: none"> • History of psoriasis. | |
| | <ul style="list-style-type: none"> • Presented with disabling bilateral Achilles tendonitis and right plantar fasciitis. | |
| | <ul style="list-style-type: none"> • Unable to bear weight. | |
| | <ul style="list-style-type: none"> • Initial treatment (without sustained relief) included 2 different NSAIDs, a 10-day course of oral corticosteroids, physiotherapy, and plantar fascia injection. | |
| | <ul style="list-style-type: none"> • Symptoms have been present for 10 weeks. | |
| #2 | 34-year-old male: | This patient has moderate axial disease and moderate skin involvement (see Table 3). For his axial disease, it is recommended that he have education, analgesia, and sacroiliac injection. For his skin disease, a systemic agent is warranted. If the combination of axial and skin disease is severely impairing QOL and/or function, a TNF inhibitor may be considered |
| | <ul style="list-style-type: none"> • Moderate to severe psoriasis since childhood. | |
| | <ul style="list-style-type: none"> • 2-year history of inflammatory back pain with unilateral grade 2 sacroiliitis on a plain film of the AP pelvis; his BASDAI is 5.6. | |
| | <ul style="list-style-type: none"> • Used topical agents and phototherapy for psoriasis; has been treated with 2 different NSAIDS and an exercise program with no change in the BASDAI. | |
| | <ul style="list-style-type: none"> • No loss of function but mild impairment in QOL. | |
| | <ul style="list-style-type: none"> • Percentage of BSA with plaque is 5%, which is having a significant negative impact on QOL, more than the back pain. | |
| <ul style="list-style-type: none"> • DLQI is 7.2. | | |

DISCUSSION

The array of disease manifestations coupled with the wide range in disease severity and course observed in PsA present formidable challenges to the treating clinician. Therapeutic decisions must be based on thorough assessments of the different areas of involvement including the skin and nails. Of note, the cumulative negative impact of widespread inflammation at various sites can be multiplicative, leading to profound impairment of patient quality of life and function. Further complicating treatment decisions are the paucity of adequately powered placebo-controlled clinical trial data for some of the most common agents used in the treatment of PsA, most notably methotrexate. Certainly, the development of improved trial design that incorporates relevant and measurable outcomes favors biologic agents since many of the older studies conducted on DMARDs are under-powered and suffer design flaws. Lastly, management of PsA often requires input from both rheumatology and dermatology: any treatment recommendations must be developed based on input from both groups of physicians as well as their patients.(31, 32)

The GRAPPA organization was founded with the mission to improve the care of PsA patients based on input from all physicians and health professionals who care for PsA patients.(1) The GRAPPA Treatment Recommendations Committee received expert opinion from over 16 dermatologists; indeed, the psoriasis treatment section of this paper was developed entirely by these physicians. Of note, however, these dermatologists focused on the treatment of psoriasis in the setting of PsA; therefore, their recommendations should not be extrapolated to psoriasis alone. The section on psoriasis treatment was also broadened to include some unusual subsets that can be particularly vexing for the treating physician with regard to both diagnosis and management.

The therapeutic strategies outlined in this manuscript represent the first treatment recommendations based on a thorough review of the literature, followed by a consensus exercise among international dermatology and rheumatology experts who care for PsA patients. Input from PsA patients provided the physicians with a deeper understanding and appreciation of how treatment options and decisions are viewed by individuals who suffer from this disease. The weaknesses of these recommendations center primarily on the lack of studies with high levels of evidence. It should be noted that many of the agents mentioned in these guidelines are not necessarily approved by appropriate regulatory agencies for these indications; for example, fumarates are neither FDA nor EMEA approved (they are approved only in Germany) for the therapy of plaque psoriasis, but there is sufficient high grade evidence to warrant their inclusion as a first-line therapy. In addition, while the sample size of participating GRAPPA members seems robust, this number represents less than half of the registered members in the organization. Although patient-reported outcomes (physical function, QOL, and fatigue) have been measured and have shown positive results, particularly with TNF inhibitors, they were not the focus of our guidelines, except as part of composite scores, e.g., the HAQ and patient global in the ACR scoring system. Finally, considerable differences persist among the members regarding how to assess severity for the various manifestations of PsA. While the group did have over 80% agreement regarding the content of the disease grid (**Table 3**), it was with the understanding that this tool represents a starting point that will be modified as new trial data are published. The core domains and instruments for use both in clinical trials and in the care of PsA patients have been identified by GRAPPA, and preliminary validation was obtained through the OMERACT process.(33-35)

Assessment and treatment of axial manifestations of PsA is very challenging because of the paucity of data. By consensus, it was agreed that ASAS guidelines be used.(36) The cut-off point for the definition of moderate to severe disease activity in AS was chosen by ASAS to be a BASDAI score ≥ 4 . For BASDAI response criteria, a 50% relative change or absolute

change of 2 (0-10) with expert opinion of significant improvement was chosen. However, this cut-off was formally validated by Cohen et al(37) and Pavy et al(38) and represents an appropriate criterion to borrow from AS for axial disease in PsA until further testing can be done prospectively in clinical trials.

Recent studies have shown that dermatologists and rheumatologists can assess skin and joint disease with a surprising degree of agreement and accuracy.(39) Similar studies have been published for axial disease.(24) Efforts to develop instruments for assessment of dactylitis and enthesitis are underway, and it is anticipated that these will be tested for validity in the near future.(24, 40) Ultimately, a composite assessment tool that can be applied in the office setting will allow clinicians to formulate more informed treatment decisions for individual patients.

Interest in PsA has greatly intensified over the past several years due to several factors including a better understanding of disease mechanisms, improved clinical trial design, and perhaps most importantly, the arrival of effective and relatively safe biologic agents that have dramatically altered the treatment paradigm. Currently, a host of new treatments are in the pipeline, many of which will offer new and possibly less expensive therapeutic options. It is anticipated that the treatment recommendations outlined in this study will be refined and serve as a template for the development of revised PsA treatment updates as new data are released.

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FIGURE LEGEND

Figure 1. GRAPPA treatment guidelines for psoriatic arthritis, categorized by disease characteristics and distinct organ involvement.(1)

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Treatment Recommendations for Psoriatic Arthritis: Supplementary Appendix I

(in 2 parts: Part A = Online Questionnaire; Part B = Questionnaire Results)

Part A: Online Questionnaire

Subject 1. Diagnosis of PsA

A patient should be considered to have PsA when fulfilling the CASPAR (CIASsification criteria for Psoriatic ARthritis) criteria:

inflammatory musculoskeletal disease, with at least 3 points from the following features: current psoriasis (assigned a score of 2; all other features assigned a score of 1), a history of psoriasis (unless current psoriasis is present), a family history of psoriasis (unless current psoriasis is present or there is a history of psoriasis), nail changes, dactylitis, juxta-articular new bone formation on radiographs, and rheumatoid factor negativity.⁽¹⁾ We consider inflammation to include such features as pain involving joints, spine, and/or enthesium associated with erythema, warmth, and swelling; prominent morning and rest stiffness.

The diagnosis of psoriasis should preferably be made and/or confirmed by a dermatologist or appropriately qualified health professional.

The diagnosis of inflammatory musculoskeletal disease should preferably be made and/or confirmed by a rheumatologist or appropriately qualified health professional.

Question 1. The criteria outlined above are appropriate for identifying psoriasis arthritis patients.

1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Subject 2. Peripheral arthritis in PsA patients

Baseline evaluation of patients with psoriatic arthritis as regards peripheral arthritis should include the following domains (consensus on core set of domains for psoriatic arthritis assessment established at OMERACT 8):

Peripheral joint assessment, including 68 joints for tenderness and 66 joints for swelling.

Pain.

Patient global assessment of disease activity.

Physical function, measured by the Health Assessment Questionnaire (HAQ).

Health related quality of life as assessed by a general measure such as the Short Form 36 (SF-36) or a PsA-specific measure such as the Psoriatic Arthritis Quality of Life measure (PsAQOL).

Fatigue as measured by patient self report or use of a measure such as the Functional Assessment of Chronic Illness Therapy (FACIT) instrument.

Acute phase reactants such as CRP or ESR.

Radiographic assessment is encouraged according to clinical manifestation and physician discretionary judgment.

Question 2. The criteria outlined above are appropriate for baseline evaluation of peripheral arthritis in PsA patients.

1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Subject 3. Stratification of PsA patients

Prognosis

Factors that are associated with a poor prognosis as regards the progression of peripheral joint disease and damage in patients with PsA include: 1) an increased number of involved joints (i.e. polyarticular disease, as opposed to monoarticular disease); 2) elevated erythrocyte sedimentation rates; 3) failure of previous medication trials; 4) the presence of damage on x-rays; 5) a loss of function as assessed by HAQ; and 6) diminished quality of life as assessed by SF-36 or PsAQOL.

Patients may be roughly stratified in categories of “mild”, “moderate,” or “severe” peripheral arthritis according to presence of some of the criteria noted in the following table. Until numeric thresholds for mild, moderate, and severe for various instruments are defined, physician judgment as regards the predominance of prognostic factors is required to define these levels.

| | Mild | Moderate | Severe |
|----------------------|--|---|---|
| Peripheral arthritis | <p><5 joints S or T, none of which are critical to pt. function or QOL</p> <p>No damage on X-ray</p> <p>No LOF (measured by HAQ)</p> <p>Min impact on QOL</p> <p>Pt. evaluation mild (measured by patient global)</p> <p>Little or no fatigue</p> | <p><u>Inadequate response to therapies judged typically used for mild disease</u></p> <p>≥5 joints (S or T)</p> <p>damage on xray</p> <p>Mod LOF</p> <p>Mod impact on QOL</p> <p>Pt. evaluation mod</p> <p>Moderate fatigue</p> | <p>Inadequate response to mild-mod Rx</p> <p>≥5 joints (S or T)</p> <p>Severe damage on xray</p> <p>Severe LOF</p> <p>Severe impact on QOL</p> <p>Pt. evaluation severe</p> <p>Severe fatigue</p> |

S - swollen, T - tender: LOF - loss of physical function

Failure to respond to therapy

A patient should be considered to have failed to respond to therapy when in spite of treatment for a length of time appropriate to the pharmacokinetic/pharmacodynamics of the individual therapy, at an appropriate dose, the patient failed to demonstrate acceptable clinical improvement. Response to treatment of peripheral arthritis in patients with PsA may be assessed using criteria initially developed for rheumatoid arthritis, such as the Disease activity score (DAS), the DAS using 28 joints (DAS), and the EULAR response criteria, which categorize levels of disease and changes to assess response. The ACR response criteria (eg ACR20/50/70) may also be used to assess changes with treatment in peripheral arthritis among patients with PsA. Response may also be considered inadequate there is evidence of progression of joint damage on radiographs.

Question 3. The criteria outlined above are appropriate for stratifying peripheral arthritis in PsA patients

1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Subject 4. Treatment of peripheral arthritis

Pharmacological treatment

Nonsteroidal anti-inflammatory drugs (NSAIDs), may be considered for control of symptoms (evidence grade 1B, recommendation grade A).

Systemic corticosteroids are not typically recommended in the treatment of psoriasis and are only advisable in discrete circumstances and not for chronic use, due to the potential to cause post-steroid psoriasis flare and other adverse effects (evidence grade 4, recommendation grade D).

Intra-articular glucocorticoid injections may be given judiciously to treat persistent mono- or oligoarthritis, if care is taken to avoid injection through psoriatic plaques. Intra-articular injections to any one joint should be repeated with caution according to clinical judgment (evidence grade 4, recommendation grade D).

All patients with severe or moderate peripheral arthritis should be started on DMARDs. Patients with mild disease should be considered for DMARDs if they do not respond to NSAIDs or intra-articular steroids.

DMARDs

DMARDs have the potential to reduce or prevent joint damage, preserve joint integrity and function. Many factors influence the choice of DMARD for the individual patient. Patients and their physicians must select the initial DMARD based on its relative efficacy, convenience of administration, requirements of the monitoring program, costs of the medication and monitoring (including physician visits and laboratory costs), time until expected benefit, and the frequency and potential seriousness of adverse reactions. The physician should also assess patient factors, such as likelihood of compliance, comorbid diseases, severity and prognosis of the patient's disease, and the physician's own confidence in administering and monitoring the drug. Because of these many considerations, input from a rheumatologist is often essential when initiating DMARD therapy.

According to evidence the DMARDs recommended as first line therapy are sulfasalazine (evidence grade 1A, recommendation grade A), leflunomide (evidence grade 1B, recommendation grade: A) methotrexate (evidence grade 3, recommendation grade B), and cyclosporine (evidence grade 1B, recommendation grade B). Gold salts, chloroquine and hydroxychloroquine are not recommended for use in PsA. Although there is no evidence for the use of combination therapy, combination of two or more DMARDs could be used in those patients that fail to respond to a single agent, or who present joint damage progression in spite of treatment.

Patients who fail to respond to at least one standard DMARD therapy should be considered for anti-TNF α therapy.

Patients with poor prognosis could be considered for anti TNF α therapy even if they have not failed a standard DMARD

In order to fail standard DMARD therapy patients should have failed adequate therapeutic trials of at least 1 of the above standard DMARDs individually or in combination.

An adequate therapeutic trial is defined as:

Treatment for at least 3 months, of which at least 2 months is at standard target dose (unless significant intolerance or toxicity limits the dose).

Intolerance/ toxicity is defined as:

- Treatment for <2 months, where treatment is withdrawn because of drug intolerance or toxicity.
- When treatment is withdrawn because of intolerance or toxicity after >2 months therapy, at least 2 months should have been at therapeutic doses

Question 4. The criteria outlined above are appropriate for treatment of peripheral arthritis in PsA patients

1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Subject 5. Diagnosis of axial disease

Diagnosis of axial disease should be based on presence of 2 out of 3 of the following clinical criteria:

1. Inflammatory back pain features including
 - (a) onset age <45 years
 - (b) symptoms >3 months
 - (c) >30 minutes morning stiffness
 - (d) insidious onset
 - (e) improved with exercise
 - (f) alternating buttock pain

2. Limitation of motion of cervical, thoracic, or lumbar spine in both saggital & frontal planes
 - (a) noted differences from AS - less pain, less limitation in movement, less symmetry,
 - (b) INSPIRE study has shown assessments of spinal disease in AS are also reliable in axial PSA.
3. Radiological criteria.
 - (a) Plain x-ray - unilateral sacroiliitis Grade 2 or more
 - (b) non-marginal and symmetric syndesmophytes
 - (c) MRI changes of bone marrow edema, erosions, joint space narrowing

Question 5. The diagnostic algorithm outlined above is appropriate for the diagnosis of axial disease in PsA.

1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Subject 6. Disease activity assessment of axial disease

Active disease is defined as BASDAI >4.

Question 6. The BASDAI should be measured to determine disease activity of axial disease over time.

1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Subject 7. Treatment assessment of axial disease

Evaluation at 6 weeks, BASDAI <3 or a reduction by 2:

- (a) Expert opinion required to ensure symptoms are related to underlying disease process.
- (b) Responder/nonresponder criteria to physical therapy and NSAIDs (use BASDAI to assess response).

Question 7. The BASDAI should be used to assess axial response to treatment in PsA.

1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Subject 8. Treatment algorithm for axial disease

- (a) NSAIDs.
- (b) Physiotherapy.

- (c) Education, analgesia, inject sacroiliac joint as indicated a, b, c for mild to moderate disease.
- (d) Non-responders – Anti-TNF therapy. For moderate to severe patients who fail the therapies outlined above.

Question 8. The treatment algorithm outlined above is appropriate for the treatment of axial disease in PsA.

1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Subject 9. Diagnosis of enthesitis

- (a) Clinical: pain/tenderness/swelling by palpation and pressure
- (b) Ultrasound with power Doppler
- (c) MRI

Question 9. These tools are important for the diagnosis of enthesitis.

1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Subject 10. Treatment goals for enthesitis

- (a) Reduction in signs and symptoms: pain, stiffness, tenderness, swelling.
- (b) Disease modification: Stop bone resorption and formation.

Question 10. The treatment goals as stated are appropriate for psoriatic enthesitis.

1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Subject 11. Treatment assessment of enthesitis

- (a) MANDER/MASES.
- (b) Visual analogue pain scale.
- (c) Ultrasound with power Doppler.
- (d) MRI.

Question 11. The measures outlined above, either alone or in combination, are appropriate for assessment of psoriatic enthesitis.

1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Subject 12. Treatment of enthesitis

- (a) Mild disease: NSAIDS, physical therapy, injections.
- (b) Moderate disease: DMARDs.
- (c) Severe disease: Anti-TNF agents.

Question 12. The therapies outlined above are indicated for treatment of psoriatic enthesitis.

1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Subject 13. Skin and nails (psoriasis): Identifying patients for systemic therapy

Background

The Skin and Nails recommendations are a result of two consensus meetings. The first meeting was part of the GRAPPA meeting at ACR where a breakout group composed of dermatologists, patient advocates and a psoriasis patient discussed priorities for this section. The second meeting was the focus of the GRAPPA meeting at AAD where a larger group of dermatologists, patient advocates and industry representatives discussed content for this section. A number of ground rules were established for the discussion. Treatment recommendations were to be considered for patients with psoriasis, irrespective of psoriatic arthritis. Recommendations were to be evaluated and ranked in terms of efficacy and safety, patient-care driven, and although cost-effectiveness was considered an important factor in ranking recommendations, the group focused on safety and efficacy for this set of recommendations primarily.

Selecting patients appropriate for systemic therapy

Candidates for topical therapy alone (mild psoriasis; all criteria should be fulfilled)

1. Generally asymptomatic, and
2. Minimal impact on quality of life, and
3. Amenable and responsive to localized therapy, and
4. Less than 5% for plaque psoriasis, and
5. No incapacity and/or disability.

Candidates for addition/change to systemic and/or phototherapy (moderate-severe psoriasis)

1. Symptomatic, i.e., pain, bleeding, itching, or
2. More than minimal impact on quality of life, or
3. Inadequate response to localized therapy, or
4. Body surface area generally greater than 5% for plaque psoriasis, or
5. Patients with guttate, erythrodermic, or pustular psoriasis, or

6. Psoriasis in vulnerable areas (face, genitals, hands/feet, nails, scalp, or intertriginous areas), or
7. Varying degrees of incapacity and disability from psoriasis.

Question 13. The criteria outlined above are appropriate for identifying psoriasis patients that are candidates for systemic therapy.

1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Subject 14. Appropriately defining severity in psoriasis

Using these criteria, we suggest the following definitions of severity:

1. Mild
 - (a) Generally asymptomatic, and
 - (b) Minimal impact on quality of life, and
 - (c) Amenable and responsive to localized therapy, and
 - (d) Less than 5% for plaque psoriasis, and
 - (e) No incapacity and/or disability.
2. Moderate
 - (a) Inadequate response to localized therapy, or
 - (b) More than minimal impact on quality of life, or
 - (c) Symptomatic, or
 - (d) Body surface area generally greater than 5% for plaque psoriasis, or
 - (e) Moderate degree of disability or incapacity.
3. Severe
 - (a) Severe impact on quality of life, or
 - (b) Symptomatic, or
 - (c) Body surface area generally greater than 10% for plaque psoriasis, or
 - (d) Patients with erythrodermic or pustular psoriasis, or
 - (e) Severe degree of incapacity or disability.

Question 14. The above definitions of mild, moderate, and severe are appropriate for patients with psoriasis.

1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Subject 15. Establishing severity definitions in psoriasis

Using these criteria, we suggest the following definitions of severity:

- 1) **Mild:** Generally asymptomatic, and (a) minimal impact on quality of life, and (b) amenable and responsive to localized therapy, and (c) less than 5% for plaque psoriasis, and (d) no incapacity and/or disability.
- 2) **Moderate:** (a) Inadequate response to localized therapy, or (b) more than minimal impact on quality of life, or (c) symptomatic, or (d) body surface area generally greater than 5% for plaque psoriasis, or (e) moderate degree of disability or incapacity.
- 3) **Severe:** (a) Severe impact on quality of life, or (b) symptomatic, or (c) body surface area generally greater than 10% for plaque psoriasis, or (d) patients with erythrodermic or pustular psoriasis, or (e) severe degree of incapacity or disability.

Comment: When evaluating patients with psoriasis, clinicians tend to lump therapy in two broad categories (topical and systemic therapy) rather than the three categories that FDA labelling uses (mild, moderate, and severe). More research is required to define instruments that measure quality of life, even for mild and moderate patients, and are responsive to patients' changing perception of quality of life.

Question 15. Accept the above definitions of psoriasis severity.

- 1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Subject 16. Psoriasis treatment algorithm

(For patients appropriate for systemic therapy)

Plaque-type/guttate (strength of recommendation)

First Line

Phototherapy (UVB/nbUVB, oral PUVA, bath PUVA) (+/- acitretin) (A)

Methotrexate (A)

Fumaric acid esters (A)

TNF inhibitors (etanercept /adalimumab/infliximab) (A)

Efalizumab (A)

Cyclosporine* (A)

Second Line

Acitretin (A)

Alefacept (A)

Third Line

Sulfasalazine (A)

Hydroxyurea (C)

Leflunomide (A)

Mycophenolate mofetil (C)

Thioguanine (C)

* limit therapy to less than 12 consecutive months. Cumulative toxicity of therapy (i.e., multiple courses) is not well studied.

Question 16. The treatment algorithm outlined above is appropriate for the treatment of plaque psoriasis for patients appropriate for systemic therapy.

1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Comments

- Clinician should consider all agents in a treatment level before proceeding to “lower” level. Situations rendering a specific therapy as “not appropriate” include: lack of response, adverse events, unavailability of therapy.
- Within first-line treatments, consideration for a trial of phototherapy as initial therapy should be made, unless this is not appropriate or if psoriasis is in areas that preclude this therapy (i.e., scalp, groin, axilla).
- Acitretin can be considered as first-line therapy if psoriasis is moderate in nature and driven by patient preference.
- Alefacept can be considered as first-line therapy if the patient has already demonstrated adequate response to this therapy in the past.

Special situations

Erythrodermic/generalized pustular psoriasis

Consider acitretin as first-line therapy (need more research).

Anti-TNF failures (need more research)

The value of switching between anti-TNF therapies (versus choosing a medication with a different mode of action) after failure of one specific anti-TNF agent has not been formally studied.

Palmoplantar pustulosis

Acitretin and oral PUVA appear to result in improvement (no evidence for either one being superior), with combination of the two providing superior response. Cyclosporine and tetracycline appear to be of modest benefit. No strict recommendations can be given, due to lack of definition of treatment response, lack of controlled studies in this area (see Marsland AM et al, Cochrane Review, 2006, issue 1).(2)

Psoriatic nail disease (needs more research)

Evidence exists for retinoids (C), oral PUVA (C), cyclosporine (C), infliximab (C), and alefacept (C). Recommendations cannot be made due to size of studies and lack of appropriate controls.

Large BMI/heavy patients (needs more research)

Recent evidence suggests that etanercept and acitretin may not be as effective in large patients, while infliximab and efalizumab appear to maintain efficacy. No official recommendations can be made due to paucity of data.

Hand/foot psoriasis

Consider topical PUVA, soriatane, efalizumab as preferable first-line agents (need more research)

The role of systemic corticosteroids (need more research)

At this time no recommendation can be given due to lack of good studies evaluating the efficacy and side effect profile of systemic corticosteroids. Further studies are needed to evaluate the role of short-term corticosteroids in severe, pustular and erythrodermic psoriasis.

Subject 17. Defining lack of response to psoriasis therapy

Lack of success to a systemic therapy is defined by:

- 1) Continued presence of sufficient disease to continue to classify the patient as “moderate” or “severe” AND lack of continued improvement in both objective and subjective measures, despite an adequate time of use (consistent with the known onset of response of each agent); OR
- 2) Unacceptable toxicity seen with the agent.

Comments

- Objective measures: can include physician global assessment, body surface area, or PASI.
- Subjective measures: should be based upon quality-of-life measures and/or measures of cutaneous itch and/or pain.
- Guidelines for length of therapy: 12 weeks, with exceptions including alefacept (16 weeks) and acitretin (16-18 weeks). Length of time may be shorter than 12 weeks in urgent situations (i.e., erythroderma, generalized pustular psoriasis) as deemed appropriate by the physician.
- Unacceptable toxicity includes any persistent, newly abnormal lab value deemed clinically significant by the physician; or, side effects that the patient finds subjectively intolerable.

Question 17. The definition of treatment response outlined above is appropriate for use in managing therapy of patients with psoriasis.

1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Subject 18. Dactylitis treatment algorithm

Background

Dactylitis is a hallmark clinical feature of spondyloarthritis and is particularly seen in psoriatic arthritis and reactive arthritis. Dactylitis occurs in 16-48% of cases of psoriatic arthritis; according to some authors, dactylitis is predominantly due to swelling and inflammation in the flexor tendon sheaths although other groups have recorded joint synovitis as well as tenosynovitis. The CASPAR database has shown that people with current dactylitis or a history of dactylitis have greater swollen and tender joint counts, in keeping with the concept that dactylitis is a marker for disease activity (data not yet published).

The treatment of dactylitis is largely empirical. NSAIDs are usually employed initially but many clinicians will rapidly progress to treatment with injected corticosteroids. In resistant cases disease modifying drugs are used but this is nearly always in the context of co-existing active disease. There is good evidence for the efficacy of biological drugs in the peripheral arthritis and spondylitis of psoriatic arthritis but for dactylitis there is only good (level II) evidence for infliximab.

Treatment algorithm for dactylitis

Mild disease:

- a) NSAIDS
- b) Physiotherapy
- c) Corticosteroid injection

Moderate disease (unresponsive to above treatments): DMARD (sulfasalazine, leflunomide, methotrexate, cyclosporine)

Moderate-to severe disease and failure to above regimens: Anti-TNF agent

Question 18. The dactylitis treatment algorithm outlined above:

1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Subject 19. Treatment grid for psoriatic arthritis

| | Mild | Moderate | Severe |
|----------------------|--|--|--|
| Peripheral arthritis | <5 joints | ≥5 joints or LOF Rx failure plus damage | Failure of response |
| Skin disease | BSA <5, PASI <5, asymptomatic | Non-response to topicals, DLQI, PASI <10 | BSA >10, DLQO >10, PASI >10 |
| Spinal disease | Mild pain No loss of function | Loss of function or BASDAI >4 | Failure of response |
| Enthesitis | 1-2 sites No loss of function | >2 sites or loss of function | Loss of function or >2 sites and failure of response |
| Dactylitis | Pain absent to mild Normal function | Erosive disease or functional loss | Failure of response |

Question 19. The treatment grid outlined above:

1) Strongly Agree 2) Agree 3) Neither Agree or Disagree 4) Disagree 5) Disagree Strongly

Part B: Questionnaire Results

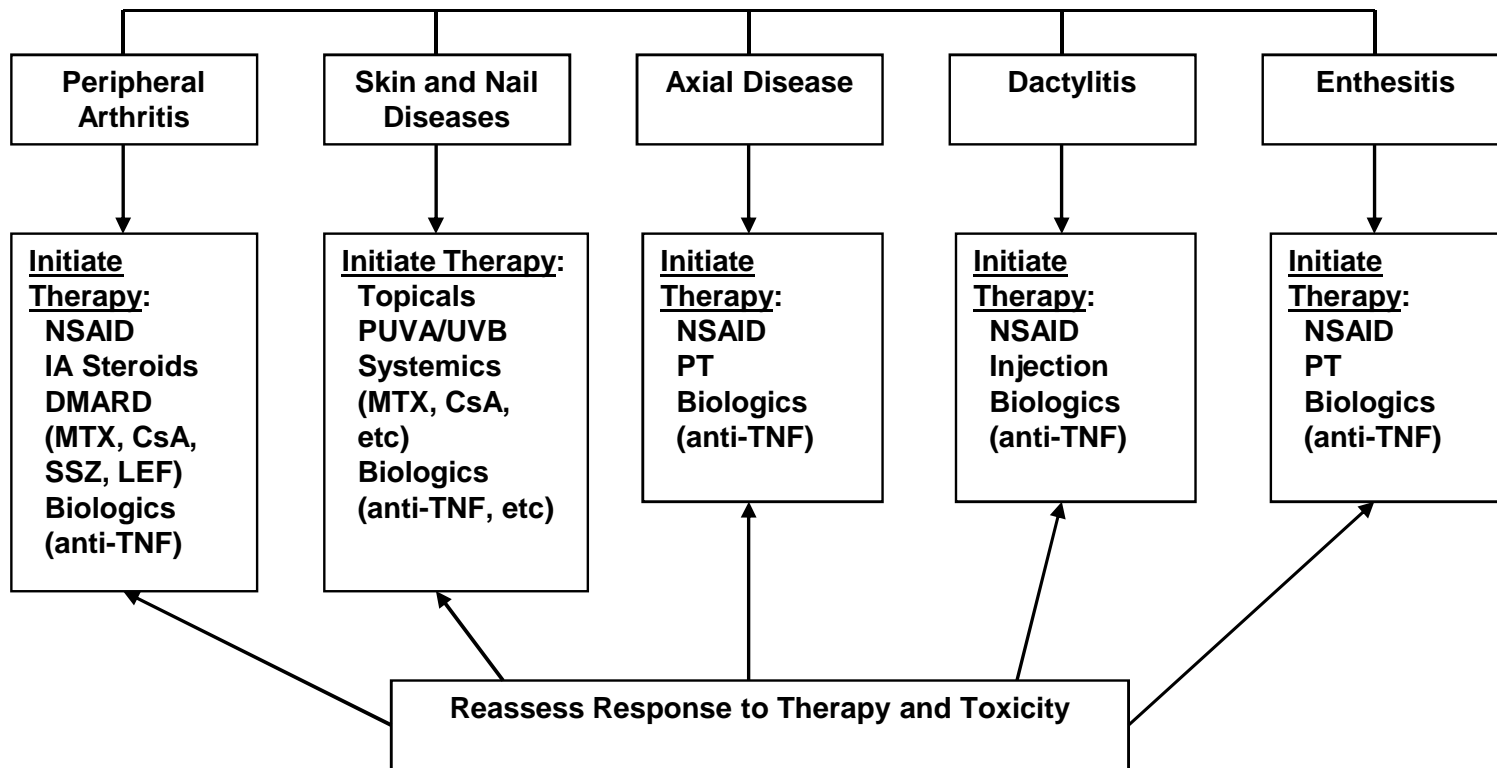
Each item was rated on a 5-point scale (1=strongly agree to 5=strongly disagree). The Disagreement Index (DI) is derived from the 30th and 70th percentile and is constructed so that values greater than 1 indicate disagreement. Although 70 persons commenced the online survey, not everyone completed every question. Question 15 was rephrased because there was uncertainty regarding the wording and sent out again for a revote, and 73 members participated. The only item in which there appeared to be disagreement concerned the use of PASI to define severity of skin disease.

| Question | N | Median | Interpercentile | | DI | %, 1 or 2 | Mean | SD |
|--|----|--------|-----------------|------|----------|-----------|----------|----------|
| | | | 30th | 70th | | | | |
| 1. The criteria outlined above are appropriate for identifying psoriatic arthritis (PsA) patients. | 70 | 1 | 1 | 2 | 0.217391 | 95.71429 | 1.471429 | 0.582882 |
| 2. The criteria outlined above are appropriate for baseline evaluation of peripheral arthritis in PsA patients. | 66 | 2 | 1 | 2 | 0.217391 | 86.36364 | 1.878788 | 0.850615 |
| 3. The criteria outlined above are appropriate for stratifying peripheral arthritis in PsA patients. | 66 | 2 | 1.5 | 2 | 0.118343 | 84.84848 | 1.893939 | 0.786984 |
| 4. The criteria outlined above are appropriate for treatment of peripheral arthritis in PsA patients. | 66 | 2 | 1 | 2 | 0.217391 | 90.90909 | 1.727273 | 0.713506 |
| 5. The diagnostic algorithm outlined above is appropriate for the diagnosis of axial disease in PsA. | 66 | 2 | 1 | 2 | 0.217391 | 90.90909 | 1.681818 | 0.682955 |
| 6. The BASDAI should be measured to determine disease activity of axial disease over time. | 66 | 2 | 1 | 2 | 0.217391 | 75.75758 | 1.909091 | 0.872267 |
| 7. The BASDAI should be used to assess axial response to treatment in PsA. | 66 | 2 | 2 | 2 | 0 | 78.78788 | 1.984848 | 0.754315 |
| 8. The treatment algorithm outlined above is appropriate for the treatment of axial disease in PsA. | 66 | 2 | 1 | 2 | 0.217391 | 86.36364 | 1.727273 | 0.83289 |
| 9. These tools are important for the diagnosis of enthesitis. | 66 | 2 | 1 | 2 | 0.217391 | 83.33333 | 1.772727 | 0.924794 |
| 10. The treatment goals as stated are appropriate for psoriatic enthesitis. | 66 | 1.5 | 1 | 2 | 0.217391 | 92.42424 | 1.590909 | 0.678857 |
| 11. The measures outlined above, either alone or in combination, are appropriate for assessment of psoriatic enthesitis. | 66 | 2 | 1.5 | 2 | 0.118343 | 80.30303 | 1.954545 | 0.830784 |

| Question | N | Median | Interpercentile | | DI | %, 1 or 2 | Mean | SD |
|--|----|--------|-----------------|------|----------|-----------|----------|----------|
| | | | 30th | 70th | | | | |
| 12. The therapies outlined above are indicated for treatment of psoriatic enthesitis. | 66 | 2 | 1 | 2 | 0.217391 | 87.87879 | 1.742424 | 0.750602 |
| 13. The criteria outlined above are appropriate for identifying psoriasis patients that are candidates for systemic therapy. | 65 | 2 | 1 | 2 | 0.217391 | 93.84615 | 1.692308 | 0.635489 |
| 14. The above definitions of mild, moderate, and severe are appropriate for patients with psoriasis. | 65 | 2 | 1 | 2 | 0.217391 | 87.69231 | 1.846154 | 0.887954 |
| 15. Accept the following definitions of psoriasis severity (mild, moderate, and severe; defined in Part A, questionnaire). | 73 | 2 | 1 | 2 | 0.217391 | 75.35425 | 2.115639 | 1.062642 |
| 16. The treatment algorithm outlined above is appropriate for the treatment of plaque psoriasis for patients appropriate for systemic therapy. | 65 | 2 | 2 | 2.8 | 0.246154 | 69.23077 | 2.107692 | 0.850057 |
| 17. The definition of treatment response outlined above is appropriate for use in managing therapy of patients with psoriasis. | 65 | 2 | 1.2 | 2 | 0.179775 | 85.2459 | 1.868852 | 0.694632 |
| 18. The dactylitis treatment algorithm outlined above. | 65 | 2 | 1 | 2 | 0.217391 | 90.16393 | 1.704918 | 0.691478 |
| 19. The treatment grid outlined above for manifestations of PsA. | 64 | 2 | 2 | 2 | 0 | 81.66667 | 2.016667 | 0.650728 |

References

1. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. *Arthritis Rheum.* 2006;54(8):2665-73.
2. Marsland AM, Chalmers RJG, Hollis S, Leonardi-Bee J, Griffiths CEM. Interventions for chronic palmoplantar pustulosis. *Cochrane Database of Systematic Reviews.* 2006; Issue 1. Art. No.: CD001433. DOI: 10.1002/14651858.CD001433.pub2.



Anti-TNF = tumor necrosis factor inhibitor; CsA = cyclosporin A; DMARD = disease-modifying antirheumatic drugs; IA = intra-articular; LEF = leflunomide; MTX = methotrexate; NSAID = nonsteroidal anti-inflammatory drugs; PT = physiotherapy; PUVA = psoralen plus ultraviolet light A; SSZ = sulfasalazine; UVB = ultraviolet light B.

(1) with permission