SKIN

Clinical Management Recommendations

Topical Cycling: The Obstacles to Moving Forward with Systemic Psoriasis Therapies and How to Characterize the Systemic Ready Patient

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ABSTRACT

Background: Psoriasis is a chronic, inflammatory disease with numerous negative physical and psychosocial impacts. Topicals are a mainstay of treatment, particularly for disease with minimal skin involvement, but they are limited due to an inability to target systemic symptoms and a lack of convenience, patient adherence, and patient satisfaction. Given its systemic implications, many patients with psoriasis are undertreated including those with limited body surface area (BSA) involvement. With a growing role in providing dermatological services, physician assistants and nurse practitioners can benefit from additional guidance on how to appropriately treat these patients, as the current clinical recommendations require further expansion, and the criteria for what qualifies as adequate treatment and response are incomplete.

Methods: Two comprehensive literature searches of PubMed, Scopus, and Google Scholar were completed for English-language original research articles on the use of topical versus systemic medications for psoriasis and its comorbidities. A panel of 11 dermatology physician assistants and nurse practitioners with expertise in managing psoriatic disease gathered to review the selected literature and form consensus statements with clinical recommendations for treating psoriasis. A modified Delphi process was employed to approve each statement and a strength of recommendation was assigned to each statement using the Strength of Recommendation Taxonomy (SORT) criteria.

Results: The two literature searches produced 98 and 76 articles, respectively, that met search criteria. After screening the articles for relevance to the discussion topic, 19 articles were distributed to the panelists for review prior to the roundtable discussion. The panel unanimously voted to adopt 10 consensus statements and recommendations, 4 of which were given a strength of "A", 1 of which was given a strength of "B", and 5 of which were given a strength of "C".
Conclusion: Psoriasis is a systemic disease with cutaneous manifestations and should be considered as such for adequate treatment. The 10 consensus statements created by the experts provide clinical recommendations on the systemic effects of psoriasis and important treatment considerations that can help guide clinicians on how to appropriately treat psoriasis of all severities. Furthermore, an emphasis is placed on recognizing treatment goals and making the next appropriate clinical decision for patients with mild to moderate disease who fail topical therapy.

INTRODUCTION

Psoriasis is a chronic inflammatory and autoimmune disorder of the skin mediated by T cell induced keratinocyte hyperproliferation.[1] It typically presents as erythematous plaques with superimposed silvery scales on the extensor surfaces and scalp, however it can also affect the joints, heart, and eyes.[1] Psoriasis impacts an estimated 2% of the population of the United States (US) and can be a debilitating condition causing substantial psychosocial impairment and significantly worsened quality of life (QOL).[1,2] In addition, psoriasis is associated with psoriatic arthritis, Crohn's disease, uveitis, metabolic syndrome, and cardiovascular disease.[3] Early and appropriate treatment is paramount to controlling the disease and mitigating the incidence of these comorbidities.[3]

There are numerous modalities for the treatment of psoriasis, including topical medications, systemic agents, and phototherapy.[4] The initial strength of treatment is generally predicated on the disease severity determined by the Psoriasis Area and Severity Index (PASI), the body surface area (BSA), and/or the Physician Global Assessment (PGA).[4-6] Topical medications, such as topical corticosteroids, calcineurin inhibitors, and vitamin D analogues, are the standard first-line therapies employed in mild to moderate psoriasis and are the most common medications used for disease with limited skin involvement.[4,5] Topical therapies are efficacious but their practical use is often limited by convenience and patient adherence.[4,5] Phototherapy is another effective and relatively safe modality for treating mild to moderate plaque psoriasis, although there is a risk of dyspigmentation and carcinogenesis of the skin.[7] Systemic therapies are immunosuppressive or immunomodulatory in nature and include oral systemic agents and biologics.[4] While systemic therapies provide more widespread impact, many of these treatments carry a more severe side effect profile compared to that of topicals and phototherapy and require various degrees of laboratory monitoring.[4,6] Indications for use include: a PASI greater than 10, psoriasis symptoms recalcitrant to topical therapy, presence of psoriatic arthritis, or a significant decrease in QOL secondary to psoriasis.[4,6] For patients whose condition falls outside of these domains, the use of systemics is subject to the discretion of the clinician.

Given the subjective nature of many of the clinical guidelines for appraising psoriasis severity (presence of subjective symptoms, degree of impact on QOL, etc.), it can be difficult to determine the initial optimal treatment, especially in patients with minimal cutaneous disease. There are a number of patients with limited BSA involvement suffering from other aspects of the disease who would benefit from systemic therapy, including many who are included and excluded by the currently described clinical guidelines. However, many clinicians default to topical treatments for every patient with minimal skin involvement, are uncomfortable initiating systemic therapies for these patients, and/or may lack an understanding of the clinical sequence involved in escalating a patient from topical therapies to systemics. With a continuously expanding role in the field of dermatology, physician assistants and nurse practitioners play a crucial and growing role in treating patients with psoriatic disease. Their grasp and employment of key clinical recommendations in dermatologic practice are integral to holistically improving the quality of care for psoriasis patients. Thus, the purpose of this expert consensus was for a panel of dermatology physician assistants and nurse practitioners with advanced expertise in managing psoriatic disease to provide literature-based consensus statements and guiding clinical recommendations about appropriate psoriasis treatment and goals of care, including when to consider topical versus systemic therapy.

METHODS

Literature Search and Study Selection

Two comprehensive literature searches of PubMed, Scopus, and Google Scholar with individual search terms were completed on November 7th, 2023, and November 12th, 2023. The first search used the keywords “psoriasis,” “topicals” and “systemics” and the second “psoriasis”, “quality of life”, and “comorbidities” along with the Boolean term “AND” for English-language original research articles, systematic reviews, and meta-analyses without date restrictions. Articles were screened for relevance to the topics of initiation of systemic treatment in psoriasis and topical psoriasis treatment satisfaction and impact of psoriasis on quality of life and comorbidities associated with psoriasis. The literature searches were treatment independent, and articles that mentioned specific therapies by name in the title were excluded. The articles that met inclusion criteria were distributed to the eleven-person consensus panel for each member of the panel to review the selected studies and assign them a level of evidence based on the Strength of Recommendation Taxonomy (SORT) criteria.[8] These levels include level 1 (good-quality patient-oriented evidence i.e. systematic review and meta-analyses of high-quality studies), level 2 (limited-quality patient-oriented evidence i.e. retrospective cohort studies), or level 3 (all other evidence including consensus guidelines, expert opinions, or disease-oriented evidence).[8] For clarification, a level 2 or 3 designation, such as for retrospective studies or basic science articles, does not necessarily imply that a study is of inferior quality or value, but rather, it is an objective assignment for specific study types.

Development of Consensus Statements

The panel consisted of 9 dermatology physician assistants and 2 dermatology nurse practitioners with expertise in diagnosing and managing psoriasis. The panel convened on December 9th, 2023, to review and discuss the relevant literature and form consensus statements with clinical

recommendations on considering topical versus systemic therapies for psoriasis treatment. The panel followed a modified Delphi process to reach a consensus on each statement.[9] This process requires supermajority approval to adopt a recommendation through multiple rounds of real-time voting and is an accepted and frequently used method for creating expert recommendations in dermatology.[10-13]

RESULTS

Literature Search and Study Selection

The initial literature searches resulted in 98 and 76 articles that met the search criteria, respectively. After a thorough screening, 19 articles that were relevant to the research questions were selected and distributed to the panelists for review and assessment prior to the roundtable discussion.

Levels of Evidence Designation

Out of the 19 articles reviewed, the panel assigned level 1 evidence to three articles[14-16], level 2 evidence to three articles[17-19], and level 3 evidence to 13 articles[20-32] (**Table 1**).

Consensus Statements

The panel formulated 10 consensus statements regarding the risk factors associated with psoriasis and recommended guidelines for appropriate treatment. All ten of the statements were unanimously (11/11) voted for adoption. Each statement and recommendation was assigned a strength of recommendation using the SORT criteria. (**Table 2**).

Statement 1: *Due to the systemic inflammatory nature of the disease, psoriasis contributes to numerous comorbidities including cardiometabolic disease and psoriatic arthritis, even in new-onset disease and/or limited skin involvement. (SORT Level A)*

Psoriasis is known to be associated with numerous comorbidities including psoriatic arthritis, uveitis, Crohn's disease, metabolic syndrome, and cardiovascular disease.[3,18,19,24,25] It was previously thought that the comorbidities of psoriasis were secondary to behavioral risk factors, such as obesity and smoking, precipitated by the psychosocial burden of the disease.[19,24] While these factors certainly contribute, the systemic elevation of proinflammatory cytokines in psoriasis promotes a chronic inflammatory state that leads to comorbidity progression.[18,19,24,25] Studies have demonstrated increased rates of occlusive vascular disease, myocardial infarction, and coronary artery disease in patients with psoriasis even when controlling for known cardiovascular risk factors including hypertension, diabetes, smoking, obesity, and atherosclerosis.[18,19,24] Similarly, cytokine mediated inflammatory pathways are hypothesized to cause the enthesitis and osteitis responsible for psoriatic arthritis.[33]

Psoriasis is mediated by the stimulation of plasmacytoid dendritic cells which result in the overproduction of tumor necrosis factor (TNF)-α, interferon (IFN)-γ, interleukin (IL)-17, IL-22, and IL-23.[19,25] This process causes a chronically accelerated feedback loop, as the IL-12 and IL-23 produced by dendritic cells activate T helper cells that release TNF-α, further creating a proinflammatory state.[19] The progressive cytokine release stimulates keratinocytes responsible for the development of cutaneous psoriasis.[18,19,23] Additional research has demonstrated that inflammation induced dysfunction of vessel walls allows for the release of inflammatory molecules into the

Table 1. SORT criteria level of evidence for articles pertaining to the systemic treatment of psoriasis and its associated comorbidities.

Article	Level of Evidence
Alinia H, Moradi Tuchayi S, Smith JA, et al. Long-term adherence to topical psoriasis treatment can be abysmal: a 1-year randomized intervention study using objective electronic adherence monitoring. *Br J Dermatol*. 2017;176(3):759-764. doi:10.1111/bjd.15085	1
Armstrong AW, Robertson AD, Wu J, Schupp C, Lebwohl MG. Undertreatment, Treatment Trends, and Treatment Dissatisfaction Among Patients With Psoriasis and Psoriatic Arthritis in the United States: Findings From the National Psoriasis Foundation Surveys, 2003-2011. *JAMA Dermatol.* 2013;149(10):1180–1185. doi:10.1001/jamadermatol.2013.5264	3
Belinchón I, Rivera R, Blanch C, Comellas M, Lizán L. Adherence, satisfaction and preferences for treatment in patients with psoriasis in the European Union: a systematic review of the literature. *Patient Prefer Adherence*. 2016;10:2357-2367. Published 2016 Nov 17. doi:10.2147/PPA.S117006	2
Boehncke WH, Boehncke S. Research in practice: the systemic aspects of psoriasis. *J Dtsch Dermatol Ges*. 2008;6(8):622-625. doi:10.1111/j.1610-0387.2008	2
Gupta S, Garbarini S, Nazareth T, Khilfeh I, Costantino H, Kaplan D. Characterizing Outcomes and Unmet Needs Among Patients in the United States with Mild-to-Moderate Plaque Psoriasis Using Prescription Topicals. *Dermatol Ther (Heidelb)*. 2021;11(6):2057-2075. doi:10.1007/s13555-021-00620-x	3
Hedemann TL, Liu X, Kang CN, Husain MI. Associations between psoriasis and mental illness: an update for clinicians. *Gen Hosp Psychiatry*. 2022;75:30-37. doi:10.1016/j.genhosppsych.2022.01.006	1
Henkemans S, de Jong P, Luime J, Kok M, Tchetverikov i, van der Helm-van Mil A, vis m. The Window of Opportunity in Psoriatic Arthritis: Similar to Rheumatoid Arthritis? [abstract]. *Arthritis Rheumatol.* 2023; 75 (suppl 9). https://acrabstracts.org/abstract/the-window-of-opportunity-in-psoriatic-arthritis-similar-to-rheumatoid-arthritis/. Accessed December 20, 2023.	1
Kerdel F, Zaiac M. An evolution in switching therapy for psoriasis patients who fail to meet treatment goals. *Dermatol Ther*. 2015;28(6):390-403. doi:10.1111/dth.12267	3
Kim J, Bissonnette R, Lee J, et al. The Spectrum of Mild to Severe Psoriasis Vulgaris Is Defined by a Common Activation of IL-17 Pathway Genes, but with Key Differences in Immune Regulatory Genes. *J Invest Dermatol*. 2016;136(11):2173-2182. doi:10.1016/j.jid.2016.04.032	3
Kimball AB, Gladman D, Gelfand JM, et al. National Psoriasis Foundation clinical consensus on psoriasis comorbidities and recommendations for screening. *J Am Acad Dermatol*. 2008;58(6):1031-1042. doi:10.1016/j.jaad.2008.01.006	3
Korman NJ. Management of psoriasis as a systemic disease: what is the evidence?. *Br J Dermatol*. 2020;182(4):840-848. doi:10.1111/bjd.18245	2
Martin G, Young M, Aldredge L. Recommendations for Initiating Systemic Therapy in Patients with Psoriasis. *J Clin Aesthet Dermatol*. 2019;12(4):13-26.	3
Merola JF, Ogdie A, Gottlieb AB, et al. Patient and Physician Perceptions of Psoriatic Disease in the United States: Results from the UPLIFT Survey. *Dermatol Ther (Heidelb)*. 2023;13(6):1329-1346. doi:10.1007/s13555-023-00929-9	3
Mukhtar R, Choi J, Koo JY. Quality-of-life issues in psoriasis. *Dermatol Clin*. 2004;22(4):389-viii. doi:10.1016/j.det.2004.03.016	3

Ninosu N, Hoelker S, Kappenstein M, Buettner S, Peitsch WK, Schaarschmidt ML. Treatment satisfaction of patients with psoriasis with topical therapy in a real-world setting: unmet need for higher effectiveness. *J Dermatolog Treat*. 2023;34(1):2200570. doi:10.1080/09546634.2023.2200570	3
Ogdie A, Strober B, Lebwohl M. Relationship between skin involvement and disease burden in patients with mild to moderate plaque psoriasis: Real-world findings From CorEvitas' Psoriasis Registry. September 2022. Accessed November 14, 2023. https://www.jaad.org/article/S0190-9622(22)01492-X/pdf.	3
Reich A, Mędrek K, Szepietowski JC. Interplay of Itch and Psyche in Psoriasis: An Update. *Acta Derm Venereol*. 2016;96(217):55-57. doi:10.2340/00015555-2374	3
Schaarschmidt ML, Herr R, Gutknecht M, et al. Patients' and Physicians' Preferences for Systemic Psoriasis Treatments: A Nationwide Comparative Discrete Choice Experiment (PsoCompare). *Acta Derm Venereol*. 2018;98(2):200-205. doi:10.2340/00015555-2834	3
Strober B, Ryan C, van de Kerkhof P, et al. Recategorization of psoriasis severity: Delphi consensus from the International Psoriasis Council. *J Am Acad Dermatol*.	3

Table 2. Consensus statements and clinical recommendations for the treatment of psoriasis with topicals versus systemics.

Consensus Statement/Recommendation	Strength of Recommendation	Consensus Vote
Due to the systemic inflammatory nature of the disease, psoriasis contributes to numerous comorbidities including cardiometabolic disease and psoriatic arthritis, even in new-onset disease and/or limited skin involvement.	A	11/11
Psoriasis has a significant impact on mental and psychosocial health, including addictive behaviors, insomnia, depression, anxiety, and suicidality.	A	11/11
Delays in initiating systemic therapy in patients with psoriasis can result in worsened clinical outcomes and life course impairment.	A	11/11
Psoriasis correlates with an increased risk of morbidity and mortality.	A	11/11
Failure of topical treatment of psoriasis would be defined by inadequate disease control.	C	11/11
Patients may be hesitant to begin systemic therapy due to perceived safety concerns and convenience, laboratory requirements, expense, and a lack of awareness of the systemic impact of psoriatic disease.	B	11/11
Providers may be hesitant to begin systemic therapy due to lack of education and training, insurance/access barriers, clinical time constraints, ongoing management of systemics or unrealized patient QOL burden.	C	11/11
Providers play a crucial role engaging patients hesitant to move beyond topical therapy.	C	11/11

The systemic-ready patient may be characterized by those using topical therapy with unsatisfactory response, QOL impairment, psoriasis in high impact sites, joint involvement, comorbidity considerations, and/or patient preference.	C	11/11
Due to the systemic nature of psoriasis, systemic therapies should be considered in all patients regardless of the extent of disease, severity, and/or previously attempted therapies.	C	11/11

surrounding area, which is thought to be the underlying pathogenesis for both atherosclerosis and psoriatic plaques.[18] In this way, the background inflammation responsible for psoriasis also causes its comorbidities.[18,19]

Preliminary evidence suggests that early systemic intervention in the treatment of psoriasis can help treat cutaneous disease and the associated symptoms and comorbidities.[19,25] Numerous studies have demonstrated a reduced risk of cardiovascular events in addition to symptom resolution for patients with psoriasis treated with TNF-α inhibitors.[25] While patients with moderate to severe psoriasis benefit from the anti-inflammatory aspects of systemic therapy, it is unclear what level of systemic inflammation exists in patients with limited cutaneous disease. Several studies have shown a positive correlation between cytokine levels and disease severity, suggesting the background inflammation is increased in more extensive disease.[23] However, Kim et al. revealed that cutaneous lesions in mild psoriasis exhibited higher levels of inflammatory cytokines and cells than those in more severe psoriasis.[23] Although the risk of comorbidities is greater in more severe psoriasis, inflammation likely stills plays a large role in milder disease, and these patients would likely still benefit from systemic therapy.[23,25,34]

The expert panel recommends that clinicians strongly consider systemic therapies for psoriasis patients with substantial comorbidity risk, regardless of the degree of cutaneous disease. Additionally, they recommend counseling patients with psoriasis on smoking cessation, drinking alcohol in moderation, and exercising at least three times a week for 30 minutes to manage cardiovascular risk factors.[24] Patients should also receive routine laboratory monitoring for their cholesterol levels, glucose levels, and hemoglobin A1C.[24] Of note, patients who are already predisposed with risk factors such as diabetes, a family history of cardiovascular disease, etc. should be followed more closely by their clinicians, with the primary goal of care being reduction of cardiovascular disease risk.[24]

Statement 2: *Psoriasis has a significant impact on mental and psychosocial health, including addictive behaviors, insomnia, depression, anxiety, and suicidality. (SORT Level A)*

The relationship between skin pathology and mental illness is well established.[35] Psoriasis is associated with significantly increased rates of depression, anxiety, schizophrenia, and suicidal ideation.[15] Psoriasis is one of the few skin conditions associated with suicidal ideation, and the prevalence of depression and anxiety seen with psoriasis is much greater than that seen with other dermatoses.[15,35] While the underlying pathogenesis is not yet understood, proinflammatory markers are elevated in patients with anxiety, depression, and schizophrenia, supporting the notion that the chronic inflammation responsible for

psoriasis may play a role in precipitating mental illness.[15] Appropriate treatment with systemic agents may help mitigate these symptoms, as multiple studies have shown patients treated with biologics demonstrate reduced depressive and anxiety symptoms.[15,36,37] The expert panel agrees that clinicians should thoroughly screen all patients with psoriasis for anxiety, depression, psychotic symptoms, and suicidal ideation.[15,24]

Psoriasis has a significant negative impact on psychosocial health.[27] One survey found that 44% of psoriasis patients felt physically unattractive, 33% avoided leaving their homes during a flare, and 46% felt moderately to extremely depressed during flares.[27,38] In addition, numerous patients report sleeping difficulties secondary to uncontrolled pruritus.[27] It is estimated that 70% of patients with psoriasis experience pruritus, and a study by Reich et al. found that itching has significant consequences on patients' functioning, emotions, and social status.[30] Psoriasis is linked to addictive behaviors including gambling and illicit substance use.[39] Zink et al. found that addiction was more prevalent in those with psoriasis[39], and another study showed that there was a positive correlation between self-reported psoriasis severity and rates of alcohol, cigarette, and antidepressant medication use.[27,40] While rating the degree of psychosocial impairment of a patient is subjective, the panel contends that clinicians should strongly consider the psychosocial ramifications of psoriasis and the patient's individual circumstances when determining treatment modality and strength.

Statement 3: *Delays in initiating systemic therapy in patients with psoriasis can result in worsened clinical outcomes and life course impairment. (SORT Level A)*

Given the progressive, systemic inflammatory nature of psoriasis, disease severity continues to advance and symptoms generally worsen without treatment over time.[41] Similarly, the burden of the comorbidities and associated psychosocial effects also become more severe over time with undertreated disease.[16,41] While the long term impacts of delaying treatment in isolated plaque psoriasis haven't been investigated, they have been studied for broader psoriatic disease. Henkemans et al. found that the median delay in starting patients on therapy following a new diagnosis of psoriatic arthritis was 42 weeks.[16] Those who were diagnosed and started on therapy early (<12 weeks) had improved outcomes and QOL compared to those who had a greater delay in receiving treatment.[16] Early treatment makes the disease easier to control and stops or slows the long term progression of the associated comorbidities.[16,23,25,41]

Cumulative Life Course Impairment (CLCI) is a term used to encapsulate the cumulative effect of a disease on a person's life when taking into consideration the associated physical, emotional, psychosocial, economic, and external factors.[42] Studies examining CLCI in psoriasis show that patients feel the disease greatly impacted their major life-changing decisions (education, career, relationships, etc.) and had a negative impact on their life course trajectory.[42,43] While additional research on the determinants of CLCI is needed, the initial studies support that many patients are inadequately treated and would benefit from earlier intervention.[42,43] The panel notes that there is clear evidence of the negative impacts of delayed treatment and recommends that once clinicians recognize the need for systemic therapy, they start treatment as soon as feasible to improve patients' long term outcomes.

Statement 4: *Psoriasis correlates with an increased risk of morbidity and mortality. (SORT Level A)*

The increased risk of cardiovascular disease is well described[3,18,19], but psoriasis also confers an increased risk of mortality from all causes.[44] Studies have found higher rates of mortality due to liver disease, kidney disease, infections, malignancies, dementia, chronic respiratory disease, and unknown causes in patients with psoriasis.[44,45] Furthermore, there is a positive correlation between the rate of all-cause mortality and disease severity.[44] Interestingly, the rates of mortality secondary to noncardiovascular factors were significantly increased regardless of the severity of psoriasis.[44] While the risks of several other comorbidities are elevated in psoriasis, cardiovascular disease remains the most prominent mortality factor for patients with psoriasis.[44,45] Clinicians should recognize that psoriasis, especially severe and/or uncontrolled disease, has substantial implications on the quality and quantity of life of patients and treatment escalation should be determined accordingly.

Statement 5: *Failure of topical treatment of psoriasis would be defined by inadequate disease control. (SORT Level C)*

Topicals are used as an initial treatment for mild psoriasis by many clinicians and can often be efficacious for limited disease. However, all 11 clinical experts on the panel support that if adequate disease control is not obtained with topical treatment, topical therapy has failed and management should be escalated. The expert panel agreed that inability to achieve clear or almost clear skin with topical treatment, lack of patient adherence to topicals, issues with topical tolerability and side effects, patient satisfaction or preference for an alternative therapy, continuation or escalation of symptoms despite topical treatment, and/or ineffectiveness in difficult-to-treat areas all constitute clinical failures of topical treatment. The goal of treatment should be to maximize the achievable skin clearance while also minimizing symptoms, and as such, the panel notes that switching to an alternative therapy should be considered in patients who fail topicals.[22]

Rates of topical failure are unclear, but in a survey of 175 patients with mild-to-moderate psoriasis treated with topicals, Gupta et al. found that 43.4% of respondents experienced no improvement in BSA.[21] Additionally, emotional distress secondary to psoriasis persisted despite treatment in 72.6% of respondents, and 49.7% of patients reported incomplete adherence with their medication.[21] Alinia et al. further demonstrated poor long term adherence (35% in the standard-of-care group over six months) in a randomized trial examining the use of topical treatment for psoriasis.[14] Failure from undertreatment and treatment dissatisfaction with topicals is also significant. Armstrong et al. found rates of undertreatment ranging from 36.6% to 49.2% in patients with mild psoriasis from 2003 to 2011, and 52.3% of patients with psoriasis were dissatisfied with their treatment regimen.[20] Another study assessing patients' impression of topical therapies using the Treatment Satisfaction Questionnaire showed that patients mean satisfaction score was highest for safety profile but lowest for efficacy.[28] In a systematic review, Belinchon et al. outlined multiple studies that demonstrated that patients were least satisfied with topicals when compared to phototherapy, systemics, and biologics.[17]

The evidence shows that a substantial subsection of patients fail topical therapy, per the description outlined by the clinical experts. The panel stresses that the practical

applications of a therapy must be considered, as treatments with low patient adherence are ineffective regardless of its theoretical benefit. In addition, patient satisfaction with treatment should be a key guiding clinical milestone, as several aspects of the disease are subjective and can only be appreciated by the patient's experience. The panel recommends that escalation of care be the next step for these patients, and systemics are a viable treatment option.

Statement 6: *Patients may be hesitant to begin systemic therapy due to perceived safety concerns and convenience, laboratory requirements, expense, and a lack of awareness of the systemic impact of psoriatic disease. (SORT Level B)*

In a study by Schaarschmidt et al. examining patients' and physicians' preferences for systemic therapies, they found that patients were most concerned about potential mild and severe side effects associated with treatment.[31] Patients also expressed concern about delivery method, treatment frequency, cost, and laboratory monitoring, although these were secondary to efficacy and safety.[31] Armstrong et al. found that 18.6% of patients used topicals alone due to them having fewer side effects while 16.7% of respondents didn't believe that their disease required stronger treatment than topicals.[20] The expert panel notes that clinicians should discuss the safety profile and logistical implications of treatment escalation with patients, and treatment choices can be altered with patient preferences in mind. Patient education is crucial, as many patients lack an understanding of psoriasis as a systemic disease that impacts multiple organ systems. The panel recommends that patients should be informed of the additional actions of systemic therapies (i.e. cardiovascular risk, potential joint involvement, etc.) when discussing the risks and benefits of therapy.

Statement 7: *Providers may be hesitant to begin systemic therapy due to lack of education and training, insurance/access barriers, clinical time constraints, ongoing management of systemics or unrealized patient QOL burden. (SORT Level C)*

In the same study by Schaarschmidt et al., providers were most concerned about severe adverse events and the cost of treatment when prescribing systemics.[31] Physicians became more concerned with severe adverse events as their years of experience increased, but they also had an improved outlook on the cost effectiveness and safety profile of systemic therapies when they prescribed the therapies more often.[31] The panel notes that clinician comfort with systemic therapies is heavily influenced by previous training and clinical experience, as clinicians with inadequate experience will often defer to other treatment modalities. Similarly, physician assistants' and nurse practitioners' range of practice can be constrained by the training and practice structure of his/her supervising physician. Additionally, members of the panel mention that certain clinicians won't have the logistical bandwidth, such as the appointment time necessary to counsel patients, ability to follow up on laboratory values, or resources to attain insurance authorization, to treat psoriasis patients with systemics.

A large gap in initiating systemic therapies for psoriasis patients may be due to a lapse in provider realization of an increased need for care. Merola et al. found that more than half (56.2%) of patients with less than 3% BSA involvement, classified as mild disease, still rated their disease severity as moderate or severe, and across spectrums of skin involvement, 60.8% to 86.1% of patients

reported that their QOL was at least moderately impacted.[26] The panel recognizes that a gap between clinician and patient perceived disease severity exists and recommends that clinicians thoroughly assess patients for associated symptoms and QOL impairment. Despite having conventionally considered milder cutaneous disease, many of these patients may benefit from transitioning to systemic therapy.

Statement 8: *Providers play a crucial role engaging patients hesitant to move beyond topical therapy. (SORT Level C)*

In patients with psoriasis that is not adequately controlled with topicals, systemic therapies are a consideration for escalation of treatment. However, as detailed above, patients may be hesitant to initiate systemic treatment for a multitude of reasons. Members of the panel stressed that clinicians serve a crucial role in counseling and educating patients who are considering systemic therapies. They note that while the choice of treatment is ultimately dependent upon the patients' preferences, clinicians should engage patients on the subject and provide them with the risks and benefits necessary to make an informed decision. Furthermore, the panel emphasizes that patient-based evidence should be incorporated into patient interactions as much as possible.

The panel particularly wanted to communicate this point to their fellow dermatology physician assistants and nurse practitioners, as these clinician groups continue to increase in number of practitioners and serve a large subsection of psoriasis patients.[46] The panel encourages advanced dermatology practitioners to practice to the full scope of their capabilities, which includes counseling patients and treating those with more severe psoriasis with the appropriate systemics. In addition, they stress that clinicians should be aware that from a medicolegal perspective, if he/she is comfortable and has received adequate training, his/her range of practice should not be limited when treating complicated psoriasis patients, regardless of the scope of his/her supervising physician. However, if he/she is to encounter a clinical situation with which he/she is not comfortable, he/she should then refer that particular patient to another provider with further expertise. The panel concludes that much of this patient burden will be subject to the initiative of dermatology physician assistants and nurse practitioners, and they want to encourage these groups to feel empowered and prepared to treat this patient population.

Statement 9: *The systemic-ready patient may be characterized by those using topical therapy with unsatisfactory response, QOL impairment, psoriasis in high impact sites, joint involvement, comorbidity considerations, and/or patient preference. (SORT Level C)*

Strober et al. conducted an expert consensus panel where they proposed recategorizing psoriasis severity as either patients that require topical therapy or those that require systemic therapy.[32] They state that the need for systemic therapy should be determined after assessing several factors, including PASI, QOL, comorbidities, etc.[32] Similarly, Martin et al. notes that the decision to use systemic therapy should be based on the consideration of similar factors (disease severity, comorbidities, impact on QOL, etc.).[25] Patients characterized by one or several of these criteria would be candidates for receiving systemic therapy due to their clinical presentations.[25,32] Thus, the panel characterizes the systemic-ready patient as those resistant to treatment with topicals, patients with a significant QOL burden and/or

associated comorbidities, patient preference (issues with adherence, convenience, etc. with topicals), and/or patients with disease in areas that can't easily be treated with topicals (difficult to treat areas such as the scalp, nails, and palms). Additionally, as described above, a number of conditions constitute topical failure, and in many of these clinical conditions, the panel recommends that escalating to systemics would be an appropriate treatment to consider.

Statement 10: *Due to the systemic nature of psoriasis, systemic therapies should be considered in all patients regardless of the extent of disease, severity, and/or previously attempted therapies. (SORT Level C)*

As demonstrated above, psoriasis is a systemic disease with impacts on multiple organ symptoms, even in milder disease. Thus, the panel recommends that all patients be considered for systemic therapy in the appropriate circumstances given the potential benefit of reduced disease severity, disease progression, and risk of comorbidities. The clinical goal of therapy remains complete or near complete resolution of skin involvement and associated symptoms. The panel contends that treatment escalation, such as the use of systemics, should be considered until these criteria are met. Ogdie et al. found that even mild to moderate psoriasis confers a notable disease burden.[29] The panel notes that this supports the use of systemics for all degrees of severity of psoriasis. In addition, previous treatment with a systemic agent shouldn't preclude a patient from systemics as a class, as an alteration in agent, formulation, or vehicle may improve tolerability and efficacy.[25]

CONCLUSION

Psoriasis is a systemic disease that is associated with numerous comorbidities and can result in significant psychosocial burden and impaired QOL.[1-3,15,34-40,42-45] Consideration of these associated negative effects in addition to cutaneous involvement is necessary for adequate treatment. After a comprehensive review of the literature, our expert panel of dermatology physician assistants and nurse practitioners crafted these 10 consensus statements regarding the systemic impacts of psoriasis, important considerations for the patient-provider relationship, and the numerous benefits of systemic therapy for patients of all severities. Furthermore, many patients with limited skin involvement and mild to moderate psoriasis are undertreated and warrant consideration for treatment escalation. The clinical recommendations provided by the expert panel can help guide other clinicians on the appropriate use of systemic therapies and identify the patients for which these therapies should be considered in order to improve their care and clinical outcomes.

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