Psoriasis is a chronic, inflammatory skin condition that affects approximately three percent of the adult population in the US. Physical symptoms of psoriasis include red, scaly, itchy, and painful skin lesions, which can have a detrimental effect on the physical, emotional, and psychosocial well-being of the patient, particularly for patients with more extensive disease.

The etiology of psoriatic disease is rooted in the immune system, and psoriasis has been associated with a higher prevalence of several other comorbidities, including myocardial infarction, diabetes mellitus, chronic pulmonary disease, peptic ulcer disease, peripheral vascular disease, renal disease, and rheumatologic disease, and an increased overall risk of death in patients with psoriasis has been suggested. Due to the systemic nature of psoriatic disease, management requires systemic treatment, and the selection of the optimal therapeutic agent should be dependent on disease severity and overall impact on the patient’s wellbeing.

Many patients with psoriasis experience loss of efficacy, side effects, or insufficient response to therapy, necessitating consideration of alternative or combination therapy. However, optimal approaches to switching therapies in patients with psoriasis continue to be investigated.

This review provides an overview of psoriatic therapies and available data with practical approaches to support switching strategies in patients with psoriasis.

PSORIASIS TREATMENTS

Topical therapies. Topical therapies are recommended for most patients with mild-to-moderate psoriasis, defined as disease affecting less than five percent of the body surface area and sparing the genitals, hands, feet, and face. They are also a consideration for patients who are candidates for localized therapy, and many patients with less severe disease experience skin clearance and good tolerability. However, topical therapies may not be practical as monotherapy for most patients who are candidates for systemic therapy and/or phototherapy. Thus, topical treatments are often used concomitantly in patients who are on systemic medications as adjunctive therapy.

Topical agents include corticosteroids, tacrolimus and other calcineurin inhibitors, tazarotene, alpha hydroxyl acids, vitamin D analogs, and combination vitamin D/corticosteroid preparations. Multiple topical medications are often used...
and combined with ultraviolet light treatment. Targeted phototherapy, including with excimer lasers, may also be considered for patients with limited skin involvement (ie, an affected body surface area of less than 10 percent). In the event that topical therapy is not effective or practical, systemic therapy needs to be considered.

**Nonbiologic systemic therapies.** Nonbiologic systemic therapies, including methotrexate, cyclosporine, acitretin, and apremilast, are indicated for patients with moderate-to-severe psoriasis, which is defined as disease affecting ≥5% of the body surface area or involving the genitals, hands, feet, or face. When a patient presents with psoriasis and joint pain, we recommend initiation of systemic therapy.

The most commonly prescribed nonbiologic systemic therapy for psoriasis, methotrexate is an oral inhibitor of dihydrofolate reductase, which has over 50 years of clinical use in the treatment of psoriasis. Methotrexate has the potential for hepatotoxicity, which necessitates monitoring of patients dependent on individual risk factors for liver toxicity. It is also contraindicated in individuals who are pregnant or breastfeeding; have renal or hepatic impairment or active infectious disease; those with alcohol dependency, alcoholic liver disease, or other chronic liver disease; and those with bone marrow hypoplasia, leukopenia, thrombocytopenia, or significant anemia. Folic acid supplementation with methotrexate therapy may reduce the frequency of side effects.

Cyclosporine is an inhibitor of T-cell activation and is considered a highly effective and rapidly active psoriatic therapy. However, long-term use is limited by the development of renal toxicity (ie, glomerulosclerosis) in a notable proportion of patients. Cyclosporine also has the potential to cause hypertension and has been associated with the development of cutaneous and lymphoproliferative malignancies with long-term use and in association with a history of extensive phototherapy. Cyclosporine is metabolized by the cytochrome P450 3A4 system, and several potential drug interactions with cyclosporine use have been noted; a thorough drug history and patient education regarding drug interactions are recommended. Cyclosporine is typically used as a rescue treatment for one year or less.

Acitretin is a vitamin A derivative, which is thought to modulate the proliferation of the epidermis and to have immunomodulatory and anti-inflammatory effects. Acitretin is considered the least effective nonbiologic systemic monotherapy and, thus, is often used in conjunction with phototherapy or biologic agents. However, because of a lack of significant immunosuppression, acitretin is generally considered effective in the treatment of HIV-positive patients with severe psoriasis. Acitretin is teratogenic and should not be used in men or women of child-bearing potential, in women who are pregnant or breastfeeding, or in women who may become pregnant within three years of discontinuing treatment.

Apremilast is an oral small-molecule inhibitor of phosphodiesterase 4 that downregulates inflammatory responses within T-helper 1, T-helper 17, and type 1 interferon pathways and affects production of anti-inflammatory cytokines that was recently licensed for use in patients with moderate-to-severe psoriasis who are candidates for phototherapy or systemic therapy. Diarrhea, nausea, and upper respiratory tract infection were the most commonly reported side effects with apremilast in psoriasis clinical trials, and treatment with apremilast is also associated with an increased risk of depression and weight decrease.

**Biologic therapies.** Patients with moderate-to-severe psoriasis may also be candidates for therapy with biologic agents. The first biologic medication was approved for psoriasis in 2003 and ushered in a new era of clearance potential and symptom improvement for patients with psoriasis. Three classes of approved biologics are currently available for the treatment of psoriasis: tumor necrosis factor-alpha (TNF-α) inhibitors (adalimumab, etanercept, and infliximab), interleukin-12 (IL-12)/IL-23 inhibitors (ustekinumab), and IL-17A inhibitors (secukinumab). A summary of key efficacy and safety data from phase 3 studies of approved biologic therapies in psoriasis is provided in Table 1.

Systemic therapy with biologics is increasingly common in the management of moderate-to-severe psoriasis. These agents have considerably improved the prognosis of patients by providing greater efficacy than conventional systemic therapies due to their activity on specific therapeutic targets. However, notable safety considerations exist with biologics, including antidrug-antibody development, infections, demyelinating disorders, exacerbation of cardiac failure, hepatic dysfunction, lupus-like syndrome, and risk of malignancies (including nonmelanoma skin cancer, lymphoma, and solid-organ cancer).

Newer biologic therapies may offer a more favorable safety profile, although long-term safety data are not available. The efficacy of IL-17A inhibitors has been demonstrated to be superior compared with other biologic agents and these new agents may provide a more favorable benefit–risk profile compared to existing biologic therapies. The landscape of treatment options will continue to change as there are multiple newer biologics currently under development.

**Patients with psoriasis may be insufficiently treated**

Despite the increasing availability of a number of treatment options, patients with psoriasis may not be receiving the necessary care to adequately manage their cutaneous symptoms and to improve their quality of life.
conducted by the National Psoriasis Foundation, many individuals with psoriasis reported that they were not receiving adequate treatment, and up to 36 percent and 30 percent of patients with moderate and severe psoriasis, respectively, were reported to not be receiving any treatment. Similarly, undertreatment was also reported in patients with severe psoriasis, with 22 percent of respondents reporting receipt of topical therapies alone and levels of patient dissatisfaction were high with approximately 52 percent of patients reported to be unhappy with their current psoriasis treatment. Consistent with these findings, a large population-based survey from North America and Europe also reported that many patients with psoriasis are undertreated or are not being treated systematically, which may have a detrimental effect on patient outcomes due to the associated comorbidities. In our experience, the patient’s primary goal with therapy for psoriasis is to obtain clear skin.

DEFINING TREATMENT FAILURE IN PSORIASIS
A generally accepted consensus definition of treatment success or failure in psoriasis has been lacking, but it would be an essential tool in patient care that would aid in treatment decision making. A European consensus statement acknowledged that while the ultimate goal of psoriasis treatment is complete clearance of cutaneous lesions, a definition of treatment success or failure needs to be based upon the results achievable with current therapies. The consensus recommended defining treatment success in patients undergoing induction and maintenance therapy as a reduction in the Psoriasis Area and Severity Index (PASI) of at least 75 percent compared to disease severity at the time of treatment initiation. An intermediate response was considered to be achievement of PASI ≥50 and <75, with a Dermatology Life Quality Index score of ≤5. The consensus recommended recommending treatment modification if an intermediate response is not achieved at the end of the induction phase or during bimonthly follow-ups for safety monitoring during the maintenance phase. However, the utility and clinical relevance of this guidance is limited because PASI measurements are rarely performed outside of research trials.

Due to the efficacy of current agents and the high level of clearance currently attainable, we often find that patients become upset or frustrated when even small amounts of psoriasis return. A component of this may be psychologically manifested due to patient fear that the disease might be recurring. As such, there is a need for patient education and expectation management in the identification and subsequent approach to treatment failure. It is our experience that because treatment failure in psoriasis is a combination of subjective and objective measurements that are specific to each patient, identification of treatment failure needs to be a collaborative consideration between the provider and patient to determine the need for intervention. In accordance with this, the use of numerical cutoffs to measure response has been discouraged by the National Psoriasis Foundation, and they advise that the patient’s perception of psoriasis and its burdens should guide treatment decisions.

PRACTICAL CONSIDERATIONS IN SWITCHING PSORIASIS TREATMENTS
Switching psoriatic therapies is generally considered necessary when the therapeutic benefit of an agent has been maximized, when safety concerns mandate the change, or when the therapeutic improvement begins to wane. It is our recommendation that switching therapies should be considered when the level of skin clearance is not acceptable for the patient or provider, with the patient being actively involved in the decision to switch therapies. To help determine if a switch should occur, the provider could ask patients if they are satisfied with their current level of disease control or if they desire more clearance, for example, by asking “Are you satisfied with how your skin looks?”

Loss of treatment response can be a significant setback for patients with psoriasis, as their potential treatment options become limited. It is our experience that patients are generally amenable to switching to a new therapy after they have achieved success with previous treatment. At this point, trust and a good rapport have likely been established between the patient and provider, and an open dialog is possible. In our experience, nurse practitioners and physician assistants are often able to develop a close relationship with patients as they are able to spend considerable time with the patient during an office visit. This relationship enables the nurse practitioner or physician assistant to more easily detect nonverbal cues indicating dissatisfaction with the patient’s current level of disease clearance.

While specific treatment goals vary for each patient, the ultimate goal is to maximize the percentage of clear skin so their disease does not impact daily activities or increase morbidity in the future. The common goal of patients with psoriasis is having “normal skin,” which translates to a wish to have complete clearance. Therefore, assuming similar safety profiles, providers should choose agents to maximize efficacy that will best lead to clear skin for an individual patient. Providers should set realistic goals for the patient, which may be approached through the establishment of reasonable patient expectations with respect to clearance rates and onset of action. For instance, in our experience, patients typically experience a decrease in pruritus, followed by scaling, and finally erythema after initiation of a new agent.

Providers should provide comprehensive chronic disease state and compliance education. It is helpful to also explain that changes are not instantaneous and that once therapy...
## TABLE 1. PIVOTAL TRIALS OF APPROVED BIOLOGICS IN PSORIASIS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Treatment</th>
<th>Efficacy</th>
</tr>
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<tbody>
<tr>
<td><strong>TNF-α inhibitors</strong></td>
<td></td>
<td></td>
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<tr>
<td>Adalimumab&lt;sup&gt;43&lt;/sup&gt;</td>
<td>Subcutaneous adalimumab 80mg at week 0, 40 mg at week 1, and then 40mg every other week or placebo for the first 15 weeks of the 52-week study (N=1212)</td>
<td>Week 16 PASI-75: 71% of adalimumab patients and 7% of placebo patients</td>
</tr>
<tr>
<td>Etanercept&lt;sup&gt;44,45&lt;/sup&gt;</td>
<td>Trial A: Subcutaneous etanercept once weekly at 25mg or twice weekly at either 25mg or 50mg for 24 weeks, or placebo for the first 12 weeks and etanercept 25mg twice weekly for the second 12 weeks (N=652) Trial B: Subcutaneous etanercept twice weekly at 50mg or 25mg or placebo for first 12 weeks, then 25mg twice weekly for the second 12 weeks (N=583)</td>
<td>Week 12 PASI-75: Trial A: 49% (etanercept50 mg twice-weekly group), 34% (etanercept25 mg twice-weekly group), 4% (placebo) Trial B: 49% (etanercept 50 mg), 34% (etanercept 25 mg), 3% (placebo)</td>
</tr>
<tr>
<td>Infliximab&lt;sup&gt;46&lt;/sup&gt;</td>
<td>Infliximab 5 mg/kg or placebo at weeks 0, 2, and 6, and then every 8 weeks to week 46 (at week 24, placebo-treated patients crossed over to infliximab) (N=378)</td>
<td>Week 10 PASI-75: 80% (infliximab) and 3% (placebo)</td>
</tr>
<tr>
<td><strong>IL-12/23 inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ustekinumab&lt;sup&gt;47,48&lt;/sup&gt;</td>
<td>PHOENIX 1: Subcutaneous ustekinumab 45mg or 90mg or placebo at weeks 0 and 4 and then every 12 weeks; at week 40, those who achieved long-term response (PASI-75) were re-randomized to maintenance ustekinumab through week 76 or withdrawal until ≥50% of PASI improvement was lost (N=766) PHOENIX 2: Subcutaneous ustekinumab 45mg or 90mg or placebo at weeks 0 and 4 and then every 12 weeks; at week 28, partial responders (PASI ≥50 to &lt;75) were re-randomized to continue ustekinumab every 12 weeks or increase dosing every 8 weeks through week 52 (N=1230)</td>
<td>Week 12 PASI-75: PHOENIX 1: 67% (ustekinumab 45 mg), 66% (ustekinumab 90 mg), and 3% (placebo) PHOENIX 2: 67% (ustekinumab 45 mg), 76% (ustekinumab 90 mg), and 4% (placebo)</td>
</tr>
<tr>
<td><strong>IL-17A inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secukinumab&lt;sup&gt;50&lt;/sup&gt;</td>
<td>ERASURE: Subcutaneous secukinumab 300 mg or 150 mg or placebo once weekly for 5 weeks, then every 4 weeks, through week 48 (N=738) FIXTURE: Subcutaneous secukinumab 300 mg or 150 mg or placebo once weekly for 5 weeks, then every 4 weeks through week 48 or etanercept 50 mg twice weekly for 12 weeks, then once weekly, through week 51 (N=1306)</td>
<td>Week 12 PASI-75: ERASURE: 82% (secukinumab 300 mg), 72% (secukinumab 150 mg), and 5% (placebo) FIXTURE: 77% (secukinumab 300 mg), 67% (secukinumab150 mg), 44% (etanercept), 5% (placebo)</td>
</tr>
</tbody>
</table>

<sup>4</sup>Includes low-, medium, and high-dose etanercept groups.<br>
<sup>5</sup>Includes patients receiving etanercept at either 25 or 50 mg twice weekly.<br>
<sup>6</sup>Includes patients receiving either 45 mg or 90 mg of ustekinumab.<br>
<sup>7</sup>Includes patients receiving either 150 mg or 300 mg of secukinumab.<br>
AE, adverse event; IL, interleukin; PASI-75, 75% reduction in the Psoriasis Area and Severity Index; TB, tuberculosis; TNF-α, tumor necrosis factor-alpha.
**Safety**

**Week 16:**
- AEs: 62% (adalimumab) and 56% (placebo)
- Serious AEs: 1.8% of patients in each group
- Serious infections: ≤1% of patients in each group
- AEs occurring in ≥5% of patients in either group: upper respiratory tract infection (7.2% [adalimumab] and 3.5% [placebo]) and nasopharyngitis (5.3% and 6.5%)
- Incidences of malignancies and nonmelanoma skin cancer were ≤1% of patients in each group

**Week 12:**
- Trial A: AEs occurring in ≥5% of patients in either group: injection-site reaction (11–17% [etanercept] and 7% [placebo]), headache (3–12% and 7%), upper respiratory infection (5–10% and 11%), injection-site ecchymosis (2–7% and 4%)
- Trial B: AEs occurring in ≥5% of patients in either group: injection-site reaction (13–18% [etanercept] and 6% [placebo]), upper respiratory infection 13% for etanercept and placebo groups), headache (11–12% and 8%), injection-site ecchymosis (8–12% and 11%), accidental injury (4–7% and 6%), flu syndrome (4–5% and 2%)

**Week 24:**
- AEs: 82% (infliximab) and 71% (placebo)
- Serious AEs: 6% and 3%
- Serious infections: 1% and 0%
- Most common AEs occurring in ≥5% of patients in either group included (but not limited to): upper respiratory tract infection (15% [infliximab] and 16% [placebo]), headache (14% and 12%), fatigue (8% and 4%), pruritus (7% in each group), and arthralgia (7% and 4%)
- Neoplasms: 1% and 0%
- There were no demyelinating events, TB, or serious opportunistic infections and no new onset congestive heart failure or hematological events of interest in either group; two patients in the infliximab group reported lupus-like syndrome

**Week 12:**

**PHOENIX 1**
- AEs: 51–58% (ustekinumab) and 48% (placebo)
- Serious AEs: 0.8–1.6% and 0.8%
- Serious infection: 0–0.8% and 0.4%
- AEs occurring in ≥5% of patients in either group: upper respiratory tract infection (6–7% [ustekinumab] and 6% [placebo]), nasopharyngitis (8–10% and 9%), and headache (5–6% and 2%)
- No cases of cutaneous or noncutaneous cancers were reported in any group; 1 patient (ustekinumab 45 mg) experienced a serious cardiovascular event

**PHOENIX 2**
- AEs: 48–53% (ustekinumab) and 50% (placebo)
- Serious AEs: 1–2% and 2%
- Serious infection: 0–0.2% and 0.5%
- AEs ≥5% in any group: nasopharyngitis (7% in each group) and headache (5% [ustekinumab] and 4% [placebo])
- Cutaneous cancer occurred in 2 patients (1 ustekinumab 90 mg, 1 placebo), noncutaneous cancer occurred in 1 patient (placebo), and serious cardiovascular event occurred in 1 patient (ustekinumab 90 mg)

**Week 12:**

**ERASURE**
- AEs: 55–60% (secukinumab) and 47% (placebo)
- Serious AEs: 2% in each group
- AEs occurring in ≥5% of patients in either group: infections and infestations (27–29% [secukinumab] and 16% [placebo]), nasopharyngitis (9% and 8%), headache (5% and 3%)

**FIXTURE**
- AEs: 56–58% (secukinumab), 58% (etanercept), and 50% (placebo)
- Serious AEs: 1–2%, 1%, and 2%
- AEs occurring in ≥5% of patients in either group: infection or infestation (27–31% [secukinumab], 25% [etanercept], 19% [placebo]), nasopharyngitis (11–14%, 11%, 8%), headache (5–9%, 7%, 7%), and diarrhea (4–5%, 3%, 2%)
is initiated and results are achieved, continued therapy is needed to maintain these results. Patients should understand that psoriasis can often wax and wane depending on environmental, physical, or emotional stressors. It is our experience that often small flares can be managed effectively by reinstituting a topical medication for a brief time.

**TREATMENT OPTIMIZATION AND SWITCHING CONSENSUS GUIDELINES**

International consensus recommendations from the International Consensus Meeting on Progressive Psoriasis Initiative (PPI) Transitioning Therapies on treatment optimization and transitioning for patients with moderate-to-severe psoriasis were recently developed by dermatologists from 33 countries. These recommendations provide clinically relevant consideration of optimization of conventional systemic therapies, transitioning from conventional systemic therapies to biologic therapy, and transitioning from one biologic therapy to another. Fourteen questions were identified and answers were drafted based on systematic literature reviews and expert opinion. Dermatologists from 30 countries voted on their level of agreement (on a scale of 1 [strong disagreement] to 9 [strong agreement]) with each draft answer, with consensus defined as 75 percent or more of participants scoring within the 7–9 range. Note that no nurse practitioners or physician assistants participated in this consensus meeting.

In addition to detailed guidelines on switching between specific agents, general guidelines included consideration of using an increased dosage or reduced treatment interval prior to deciding to switch treatments. Unfortunately, insurance benefits and payer systems that regulate and reimburse restrictions on increasing doses will represent a major limitation to this approach.

**Switching from traditional systemic therapy to biologic therapy.** The PPI international consensus guidelines note that recommendations for transitioning from a traditional systemic therapy to a biologic agent differ according to the reason for the switch. For instance, when transitioning because of tolerability concerns, a treatment-free interval may be required, while switching due to low efficacy may require an overlap period. Approved induction doses should always be utilized.

Many patients could achieve greater clearance and greater tolerability by switching to newer biologic therapies, and it is important for providers to identify patients who could benefit from switching. The use of adjunctive therapies such as topical steroids and phototherapy could also be reduced or limited by switching to a more effective biologic agent, which would also minimize the side effects of adjunctive therapies.

Providers should discuss with patients why biologic therapy may be appropriate, as well as their perception of the efficacy of biologics. We have found that patients are generally satisfied with switching to potentially more effective agents with a similar or better safety profile. The primary discussion between provider and patient is often regarding treatment safety, especially because of what patients hear and see in direct-to-consumer advertising, and patients are concerned about the potential increased risk of side effects, including cancer. Having a comprehensive risk–benefit discussion, including how biologic therapy modulates the immune system and the need for safety monitoring of the rare, but serious, side effects with these therapies (eg, monitoring for tuberculosis [all agents] and reactivation of hepatitis B [TNF-α inhibitors], and assessment of hepatic function [TNF-α inhibitors]) is prudent. Similarly, highlighting the overall good, long-term safety profiles of these agents may be useful. Providers must take into account the patients’ past medical history, immune response, and personal schedule before initiating biologic therapy.

Another consideration is a common patient concern regarding self-administration of an injection when initiating a biologic. This underscores the need for patient education by providers or clinic staff, including the difference between subcutaneous, intramuscular, and intravenous injections and the availability of an auto-injector for many of the biological agents.

**Switching between biologic therapies.** The PPI international consensus guidelines recommend that when switching biologic therapies because of poor efficacy, switching should be considered without a washout period and the standard induction dose of the new biologic should be given at the time of the next scheduled dose. For tolerability reasons, a treatment-free interval may be necessary until the safety parameter is normalized or stabilized.

It is our experience that patients are open to switching to a new biologic therapy, especially if they are not satisfied with current levels of clearance. Switching between biologics is typically easier than initiating biologic therapy, as patients already understand the risks associated with these agents. Only recently have multiple classes (TNF-α, IL-12/23, and IL-17 inhibitors) of biologic therapies been available to allow for switching to a biologic therapy with a different therapeutic target.

Within the past few years, switch studies have been conducted and published. Table 2 presents a sampling of such studies. Regardless of the biologic being switched from or to, results suggest that switching agents can lead to improvement in psoriatic symptoms in patients who previously experienced no response, a suboptimal response, or a diminished response to biologic therapies, with no noted unexpected side effects or safety concerns. In a real-world retrospective analysis of 4,309 patients with moderate-to-severe psoriasis, switching to another biologic was observed in 12.5 percent of patients, and those receiving etanercept were most likely to switch.

**Consideration of antidrug antibodies.** Although antidrug antibodies (ADAs), which form due to an immune response...
## TABLE 2. SELECTED SWITCHING STUDIES OF BIOLOGIC THERAPIES IN PSORIASIS

<table>
<thead>
<tr>
<th>Switch From</th>
<th>Switch To</th>
<th>Dosage</th>
<th>N</th>
<th>Assessment Endpoint(s)</th>
<th>Efficacy</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etanercept</td>
<td>Adalimumab</td>
<td>40mg every other week for 12 weeks (no loading dose), followed by 40mg weekly for 12 weeks if PGA 0 or 1a not reached</td>
<td>85</td>
<td>12 and 24 weeks</td>
<td>PGA 0 or 1a: 31–34% at week 12; 46% at week 24</td>
<td>Total AEs: 154b • Serious AEs: 0b • No cancer, tuberculosis, congestive heart failure, or demyelination reported</td>
</tr>
<tr>
<td>Etanercept, MTX, or phototherapy</td>
<td>Adalimumab</td>
<td>80mg at week 0 and then 40mg every other week from week 1</td>
<td>152</td>
<td>16 weeks</td>
<td>PGA 0 or 1a: 52% overall (48–61% based on prior therapy)</td>
<td>% of patients: • AEs: 54.6% • Serious AEs: 3.3% • Infectious AEs: 21.7% • Serious infectious AEs: 0.7% • No malignancies, TB, demyelinating disease, congestive heart failure, lupus-like syndrome, or opportunistic infection reported</td>
</tr>
<tr>
<td>Etanercept</td>
<td>Infliximab</td>
<td>5mg/kg infusions at weeks 0, 2, 6, 14, and 22 (10 patients received concomitant immunomodulators)</td>
<td>215</td>
<td>10 and 26 weeks</td>
<td>PGA 0 or 1a: 65% at week 10 and 61% at week 26</td>
<td>% of patients: • AEs: 68.8% • Serious AEs: 3.7% • Infectious AEs: 33.0% • Serious infectious AEs: 0.5% • TB: 0 • Squamous cell carcinoma: 0.9% • Ischemic coronary artery disease: 0.5%</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>Etanercept</td>
<td>50mg twice weekly for 12 weeks, followed by 50mg once weekly for 12 weeks</td>
<td>10</td>
<td>12 and 24 weeks</td>
<td>Mean change in PGA score: from 2.6 (baseline) to 1.5 (week 12) and 1.4 (week 24)</td>
<td>AEs: 20% 1 AE of viral pharyngitis at week 12, 1 AE of exacerbation of female-pattern alopecia (seen on adalimumab, but worsened on etanercept [timing not reported])</td>
</tr>
</tbody>
</table>

*0=clear; 1=minimal

*Per 37.6 patient years

AE, adverse event; MTX, methotrexate; NS, not significant; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; QD, once daily; TB, tuberculosis; TNF-α, tumor necrosis factor-alpha.
to a therapeutic antigen, have been observed for all biologic drugs used to treat psoriasis—with drug-related, patient-related, and treatment-related factors playing a role in their development—not all patients develop ADAs.\textsuperscript{20,29,36,37} Clinical consequences of developing ADAs can include lack or loss of treatment response and acute or delayed infusion reactions, such as headache, pruritus, hypotension, nausea, fever, skin rash, and arthralgia; although the frequency of such infusion-related reactions appears to vary according to biologic agent.\textsuperscript{\textit{36}} In particular, neutralizing antibodies, which inhibit the activity of biologic agents, can develop in some patients and lead to loss of response. A clinical response can still occur in the presence of ADAs, as long as the concentration of unbound active drug remains at or above the therapeutic level.\textsuperscript{38} Of note, ADAs to etanercept and secukinumab do not appear to be associated with reduced clinical outcome or adverse events.\textsuperscript{20,29,36}

The clinical implications for the development of ADAs in patients with psoriasis is poorly characterized, although a better understanding of this issue could allow a more rational approach to the management of patients experiencing treatment failure.\textsuperscript{36} Clinicians may be hesitant to take a patient off of a drug if neutralizing antibodies could develop, due to the possibility that the drug would not be as effective if restarted. In clinical trials, the presence of ADAs has been associated with failure to regain response when resuming treatment after discontinuation and relapse.\textsuperscript{39} Therefore, patients should be cautioned against discontinuing therapy when they have achieved the desired level of skin clearance because they may not be able to regain a similar response. It is our experience that if neutralizing antibodies have been detected, treatment should be considered a failure only if it has been addressed and the patient is still not achieving efficacy. One approach is to add additional therapeutic agents (such as methotrexate) to current therapy to maintain efficacy with a biologic agent,\textsuperscript{29} although switching to a different class of biologic therapy may be considered and this approach may be more acceptable to patients and providers.

\textbf{Safety monitoring.} Infection is a risk associated with all biologic agents used to treat psoriasis, although serious infections are uncommon. If an infection does develop, it should be monitored closely, and if the infection becomes serious, biologic treatment should be discontinued. If possible, biologic treatment with TNF-\(\alpha\) inhibitors should be avoided in patients with a history of chronic, serious, or recurring infections.\textsuperscript{1}

Due to the potential for reactivation of tuberculosis, patients should be screened for latent tuberculosis prior to initiation of biologics.\textsuperscript{1} If present, tuberculosis should be treated before administration of biologics. Patients should also be monitored for active tuberculosis during treatment even if latent tuberculosis was not present at initiation. The TNF-\(\alpha\) inhibitors have a boxed warning requiring monitoring for active tuberculosis.\textsuperscript{40-42}

Because TNF-\(\alpha\) may be involved in the pathogenesis of hepatocyte destruction in chronic hepatitis C infection, use of TNF-\(\alpha\) inhibitors in patients with chronic hepatitis C infection should be approached cautiously.\textsuperscript{1} Serum aminotransferases and hepatitis C viral load should be monitored throughout treatment in these patients. Due to the reported role of TNF-\(\alpha\) in viral clearance in hepatitis B infection in animals, screening patients for hepatitis B should be considered prior to initiation of TNF-\(\alpha\) inhibitor treatment. Of note, the FDA warns against treatment with TNF-\(\alpha\) inhibitors in patients with concurrent hepatitis B infection.\textsuperscript{1}

Table 3 reports our suggested best practices for monitoring safety and tolerability following treatment with biologic therapies, both as initial therapy or when switching between agents.

\textbf{CONCLUSION}

The goal of therapy for psoriasis should be to provide patients with clear skin in a manner that does not result in an increased risk of morbidity. To achieve this goal, it may be necessary for providers to change the type of treatment that a patient is receiving. Nurse practitioners and physician assistants are uniquely suited to identify patients who could benefit from switching therapies due to the collaborative relationship they commonly develop with patients.

When considering switching to a new psoriatic therapy, it is important for providers to have a candid conversation with the patient regarding realistic expectations for efficacy and the safety risks of the new agent. Patients are generally open to switching to a biologic agent from traditional systemic therapies, as biologics can provide high levels of skin clearance with good long-term safety.

There are currently three classes of biologic therapies available for the treatment of psoriasis (ie, TNF-\(\alpha\), IL-12/23, and IL-17A inhibitors), which allows for patients to be switched to a new biologic agent with a different therapeutic target. The risks between different biologics are similar but newer agents may offer a better safety profile in addition to greater efficacy. While all biologics are effective, the newer agents offer a much greater chance of achieving clear skin.

Psoriasis is a prevalent and chronic inflammatory condition that can have significant effects on the morbidity, mortality, and well-being of those affected. Effective management and improved outcomes for patients with psoriasis requires the appropriate use of existing therapies, rational approaches to treatment modification, patient education, and collaborative efforts between the patient and healthcare provider.

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