Patient-Centered Approach to Biologics in the Treatment of Psoriasis

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Background: With a growing number of psoriasis treatments options, making a decision can be daunting to patients. Biologics offer a less toxic and more effective alternative to people who have moderate-to-severe psoriasis, particularly those who have tried and failed other therapies. Objective: To provide a patient-centered approach to the decision to start on biologic treatment of psoriasis with an overview of pharmacology. Methods: An electronic literature search was performed in the PubMed and Medline databases using keywords with “biologics” or “biologic therapy,” “treatment,” and “safety.” Pharmaceutical package inserts and reference lists were also reviewed. Results: Though new advancements in psoriasis care have improved treatment options for patients, widespread treatment dissatisfaction and under- treatment occurs. Biologic agents are generally well-tolerated and effective for managing moderate-to-severe psoriasis. Lifetime risks of serious adverse events from biologic treatment are less than risks patients face on a daily basis. Current data suggests biologics are not predictors of serious adverse events. Rates of major adverse cardiovascular event and death are lower in biologic cohorts compared to non-biologic cohorts. The minimal risk and potentially protective effects of biologics may outweigh the consequences of undertreated or non-treated moderate-to-severe psoriasis. Limitations: Long-term data on biologic treatment safety is growing and this review will only encompass current data. Conclusions: Treating psoriasis with biologics can reduce overall risk of bad outcomes of psoriasis and its treatment and improve patient quality of life. Optimizing treatment adherence, accommodating patient preferences, emphasizing strong patient-physician communication, and conceptualizing treatment risk can improve patient satisfaction and clinical outcomes. Successful psoriasis care is a long-term, collaborative, and complete commitment on behalf of both the patient and physician. Journal of Nature and Science, 1(3):e53, 2015.

Introduction
Psoriasis is a chronic, immune-mediated, inflammatory skin condition that impacts quality of life through physical, psychological, and social distress and is associated with systemic consequences including arthritis and cardiovascular disease. Despite advances in psoriasis care, effective long-term treatment of psoriasis remains a challenge to both patients and physicians. Treatments for moderate-to-severe psoriasis often do not meet patient and physician expectations due to adverse effects, lack of long-term efficacy, and inconvenient administration schedules. Biological agents offer hope to psoriasis patients who are on treatment regimens with very little or no improvement and who experience quality of life impairment.

The management of psoriasis is complex and remains a challenge for patients and providers. Finding a suitable medication for each patient based on individual definitions of “treatment success” can be difficult. Psoriasis requires long-term maintenance and strict adherence to treatment regimens during both remission and flare-up periods; however, this concept is often not internalized in patients. Additionally, treatment goals differ between patients and physicians. While physician treatment goals focus on improvement and better quality of life, patient treatment goals focus on achieving visible results in treatment safety, and doctor-patient communication the most important attributes of disease management. From this perspective, biologic therapy is promising. Conceptualizing treatment efficacy and safety data and maintaining effective doctor-patient communication can enhance patient-centered biologic treatment strategies. Evaluating available data on biologics from a patient’s perspective has the potential to improve treatment adherence and satisfaction, and optimize clinical outcomes. The purpose of this paper is to provide an overview of psoriasis treatment from this perspective.

Methods
An electronic literature search was conducted in PubMed using the keywords “psoriasis” combined with “biologics” or “biologic therapy,” “treatment,” and “safety.” Fifty-one articles written in English published between 2001 and 2015 were evaluated and 41 were used in this review. Pharmaceutical package inserts of biologic medications and reference lists were also utilized.

General Considerations
Psoriasis causes a broad spectrum of symptoms of varying severity. While there is no cure for psoriasis, several treatments are available that can temporarily relieve or eliminate disease symptoms. The treatment pathway for psoriasis differentiates those patients who have having few enough lesions that it is feasible to apply a topical to all the spots (termed localized or mild-to-moderate psoriasis) from those whose disease is too extensive for topicals to be practical or those who have affected areas where topicals do not penetrate well such as palm and sole (generally corresponding to moderate-to-severe psoriasis, Figure 1). Disease severity may also be defined, particularly for clinical trials, by percent of body surface area affected, with 0-3% BSA as mild, 3-10% BSA as moderate, and >10% BSA as severe (though many clinical trials of treatments for moderate-to-severe psoriasis enroll patients with >10% BSA). In clinical practice, disease severity is evaluated not only by objective matters such as location, extent of disease, and presence of psoriatic arthritis, but also by the impact on patient quality of life.

Sixty-five percent of psoriasis patients have limited disease extent and are considered mild cases (the percentage of people in the population whose psoriasis is mild is even higher). Mild cases that do not involve palms or soles are amenable to topical treatment and generally do not require biologics. Assuring good adherence to topical treatment may help address perceived efficacy limitations of topical options. Localized phototherapy is another approach for localized psoriasis.

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An estimated 30% of patients have moderate-to-severe psoriasis with more than 5%-10% body surface area affected or disabling involvement of palms or soles. Ultraviolet phototherapy and systemic therapies can be used with or without topical agents to achieve disease control in patients with moderate-to-severe psoriasis. Combining phototherapy with systemic therapies can enhance efficacy and lower systemic treatment doses needed. Non-biologic systemic therapies, taken orally or by injection, can be used for patients with moderate-to-severe psoriasis who have not improved from other methods of treatment.

Figure 1. Psoriasis Diagnosis and Initial Assessment. The treatment pathway for psoriasis depends on the patient's severity of disease, treatment preferences, and impact on quality of life. Biologics offer a solution to patients who suffer from moderate-to-severe psoriasis or who have failed to improve from other interventions.

Efficacy

Non-biologic systemic treatments have various limitations to consider when constructing treatment plans (Table 1). While non-biologic systemic therapies may be effective, they are associated with both short-term and long-term serious adverse events (SAE), including hepatotoxicity, nephrotoxicity, hypertension, dyslipidemia, malignancy, and teratogenicity. Phototherapy is considered one of the safer options for psoriasis treatment, but requires good compliance and is relatively costly and time-consuming (particularly when done in the medical office setting). Some cases of psoriasis are nonresponsive or do not achieve adequate responses to one or more of these therapies. As a result, many psoriasis patients express dissatisfaction with these treatment approaches.

Biologics offer a solution to patients who suffer from moderate-to-severe psoriasis or who have failed to improve from other interventions. These therapies target specific steps in the pathogenesis of psoriasis, involving T cells and cytokines such as TNF-alpha, IL 12/23, and IL17A. The available biologics approved for psoriasis include etanercept (Enbrel®), adalimumab (Humira®), and infliximab (Remicade®), which act on TNF-alpha pathways, ustekinumab (Stelara®), which acts on IL-12/23 pathways, and secukinumab (Cosentyx®), which acts on IL-17A pathways. Compared to older oral therapies (methotrexate, cyclosporine and acitretin), biologics have lower toxicity, and lower number of side effects.

Data, biologics offer patients an excellent chance to reach their treatment goals.

The overall efficacy of biologic agents in the treatment of moderate-to-severe plaque psoriasis is evidenced by the disease response in clinical trials and in post-marketing studies. The Psoriasis Area and Severity Index Score (PASI) is a measure of the overall psoriasis severity of four body surface areas (head and neck, upper extremities, trunk, and lower extremities) along with characteristics of lesions in each body area including erythema (redness), induration (thickness) and scaling. The efficacy of the biologic agents to sustain long-term psoriasis skin clearing has been demonstrated in trials using a 75% improvement in PASI score as a measure of treatment success (Table 2).

Adalimumab was approved by the Food and Drug Administration in 2002 and for plaque psoriasis in 2008. In cross-sectional analyses of post marketing data, 47.7% of patients treated with adalimumab had clear or minimal skin disease. PASI 75 rates ranged from 14 to 48% for etanercept compared to placebo. A recent meta-analysis of adalimumab PASI 75 at 63 weeks showed 70.1% (95% CI 65.8, 74.3) while the 90 mg dose was associated with a PASI 75 of 75.7% (95% CI 72.1, 79.3). In clinical trials at doses of 25 to 50 mg weekly to biweekly, PASI 75 rates ranged from 14 to 48% for entanercept compared to placebo at 3.9%. A meta-analysis shows that adalimumab 50 mg biweekly had a PASI 75 of 43.5 (95% CI 40.0, 47.1).

Entanercept was approved by the FDA for plaque psoriasis 2004. Gelfand and colleagues compared efficacy of the biologics in outpatients with moderate to severe plaque psoriasis and reported 34.2% treated with entanercept had clear or minimal skin disease. In clinical trials at doses of 25 to 50 mg weekly to biweekly, PASI 75 rates ranged from 14 to 48% for entanercept compared to placebo at 3.9%. A meta-analysis shows that entanercept 50 mg biweekly had a PASI 75 of 43.5 (95% CI 40.0, 47.1).

Infliximab has been FDA approved for psoriasis since 2006 and is used for a wide variety of other inflammatory conditions. Remicade was highly effective in Phase 3 clinical trials (Table 2). PASI 75 rates were 70% of placebo compared to 2.6% for placebo. Meta-analysis data indicate infliximab had a PASI 75 of 75.7% (95% CI 72.1, 79.3).

Ustekinumab was approved for plaques psoriasis by the FDA 2013. Outpatient cross-sectional data (n=73) show 36.1% of patients with clear or minimal skin disease at 4 months. The 45 mg dose of ustekinumab by meta-analysis shows a PASI 75 of 70.1% (95% CI 65.8, 74.3) while the 90 mg dose was associated with a PASI 75 of 65.5% (95% CI 60.2, 72.9).
While these black box warnings state “Patients treated with entanercept/infliximab are at increased risk for developing serious infections that may lead to hospitalization or death.”

Likewise, more than half of patients who responded inadequately to etanercept, methotrexate, or narrow-band UVB therapy switched to adalimumab and achieved cleared or minimal disease extent.6

Apremilast has less efficacy than biologics, but offers an alternative to patients who prefer an oral agent or who do not respond adequately to topicals.6

<table>
<thead>
<tr>
<th>Table 1. Topical, Phototherapy, and Non-biologic Systemic Treatment Considerations</th>
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<tr>
<td><strong>Treatment</strong></td>
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<tr>
<td>Topical Treatment</td>
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<tr>
<td>Phototherapy</td>
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<tr>
<td>Methotrexate</td>
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<td>Cyclosporin</td>
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<td>Acitretin (Soriatane®)</td>
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**Table 2. Biologic Agent Mechanism and Efficacy**

<table>
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<tr>
<th><strong>Generic (Brand)</strong></th>
<th><strong>Mechanism</strong></th>
<th><strong>Dose &amp; Route</strong></th>
<th><strong>Efficacy Phase 3 Studies</strong></th>
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<tbody>
<tr>
<td>Adalimumab (Humira®)</td>
<td>Human monoclonal antibody against TNF to neutralize its effects.</td>
<td>80 mg SC on day 1, then 40 mg every other week beginning on day 8 for moderate to severe plaque psoriasis</td>
<td>2 trials (n=1212, 655 treatment) 16 week PASI 75 was 71 to 78% vs. placebo 4 to 19%. 52 week subjects from PASI 75 responders maintained response in 68% (n=250) vs. placebo 28% (n=240)</td>
</tr>
<tr>
<td>Etanercept (Enbrel®)</td>
<td>Human fusion protein of the TNF receptor to Fc portion of IgG1. Blocks TNF to neutralize its effects.</td>
<td>50 mg SC twice weekly for 3 month then maintenance 50 mg weekly for moderate to severe plaque psoriasis</td>
<td>2 trials (n=1283) PASI 75 at 12 week with 50 mg SC twice weekly was 47% (n=79) vs. placebo 4% 24 week 54% vs. placebo 33%</td>
</tr>
<tr>
<td>Infliximab (Remicade®)</td>
<td>Chimeric (murine-human) antibody against TNF-α. Blocks TNF to neutralize its effects.</td>
<td>IV infusion, 5 mg/kg over 2-3 hours at 0, 2 and 6 weeks, then every 8 weeks for moderate to severe plaque psoriasis</td>
<td>3 trials (n=1462) 10 week PASI 75 was 75 to 90% compared to placebo 1 to 10%</td>
</tr>
<tr>
<td>Secukinumab (Cosentyx®)</td>
<td>Human monoclonal antibody against TNF to neutralize its effects.</td>
<td>150 or 300 mg SC for moderate to severe plaque psoriasis</td>
<td>3 trials with 931 in treatment groups, PASI 75 response at 12 weeks was 59 to 84% with 150 to 300 mg. PASI 90 was 39 to 59%. 52 week subjects from PASI 75 responders maintained response in 81 to 84% for 300 mg dose and 72 to 82% at 150 mg over 2 trials</td>
</tr>
<tr>
<td>Ustekinumab (Stelara®)</td>
<td>Immuno modulator, Human monoclonal antibody against the p40 subunit of IL-12 &amp; IL-23 from human immunoglobulin transgenic mice. Blocks the actions of IL-12 and IL-23.</td>
<td>45 mg at week 0 &amp; 4 if weight is ≤100 kg, 90 mg at week 0 &amp; 4 if weight is &gt;100 kg, then every 12 week afterward for moderate to severe plaque psoriasis</td>
<td>PASI 75 response at week 12 was 49 to 74% using 45 to 90 mg doses with higher dose response rate at 90 mg doses (Pl)</td>
</tr>
<tr>
<td>Golimumab (Simponi®)</td>
<td>Human monoclonal antibody against TNF to neutralize its effects.</td>
<td>50 mg SC once monthly for psoriatic arthritis</td>
<td>Patients had psoriatic arthritis with skin lesions at least 2cm in diameter. In combination with MTX (n=405) at week 24: ACR 20 was 52%, ACR 50 was 32%, ACR 70 was 19%</td>
</tr>
</tbody>
</table>

**ACR** = American College of Rheumatology Criteria, **IL** = Interleukin, **IV** = intravenous, **MTX** = Methotrexate, **PASI** = Psoriasis Area and Severity Index, **Score**, **TNF** = Tissue Necrosis Factor, **SC** = subcutaneously, *Designed to take continuously to maintain improvement

Secukinumab is the newest biologic recently approved by the FDA for plaque psoriasis in doses of 150 and 300 mg (Table 2). Comparative data post-marketing is not yet available for this biologic. Another TNF inhibitor, golimumab, is not approved for plaque psoriasis but is approved for psoriatic arthritis and has been used in clinical practice for plaque psoriasis.6

Overall, biologics had excellent efficacy in both Phase 3 and in clinical practice. All routes of administration for the biologics are by injection and require continuous therapy to maintain effectiveness. For patients who do not achieve adequate responses with a biologic treatment, trying another biologic agent is an option.25 Two thirds of patients who had an inadequate response to etanercept switched to infliximab, and achieved either cleared or minimal disease extent after 10 weeks of treatment.25 Likewise, more than half of patients who responded inadequately to etanercept, methotrexate, or narrow-band UVB therapy switched to adalimumab and achieved cleared or minimal disease extent.26

**Safety Considerations**

Psoriasis patients on biologics experience greater quality of life and show greater improvement than patients on phototherapy, topicals, or systemic agents.27 Despite this, general side effects and risk of serious side effects (Table 3)28-29 can impact patients’ and physicians’ treatment decisions. Black box warnings for biologics include immunosuppression as a potential effect. Adalimumab warning states there is “Increased risk of serious infections leading to hospitalization or death, including tuberculosis, bacterial sepsis, invasive fungal infections (such as histoplasmosis), and infections due to other opportunistic pathogens.”15 Etanercept and infliximab warnings state “Patients treated with etanercept/infliximab are at increased risk for developing serious infections that may lead to hospitalization or death.”16,17 While these black box warning highlight potential serious adverse effects and may terrify potential biologic candidates, less serious side effects are commonly reported with biologics use (Table 3).
The relative risks of developing these severe adverse events attributable to TNF-alpha therapy are lower than the risks that patients face on a daily basis. The lifetime risks of developing cancer, stroke, heart disease, and even dying in a car accident are more common than the lifetime risks of developing lymphoma, demyelinating disease, or tuberculosis with anti-TNF-alpha biologics. The lifetime risk of demyelinating disease and lymphoma with TNF-alpha inhibitors are 0.1 to 1.7% and .5 to 4.8% respectively, offering a potentially protective to marginally increased risk compared to that of the general population.

Although patients may be concerned that biologics can double or triple the risk of SAE, explaining the absolute and attributable risks may be reassuring. Since the baseline risk of SAE is small, a 2 to 3-fold relative risk may not amount to much, and in some cases (such as lymphoma) the elevated risk may be due to the severe immune disease, not to the treatment. The risk attributable to TNF-alpha and other biological therapies may be outweighed by the beneficial consequences of treating the psoriasis, depending on disease severity.

Relative risk data for biologics are often presented in statistical descriptions that are difficult for patients to grasp. Patients tend to weigh risks based on salience. Rare opportunistic events that may or may not be due to biologic therapy stand out in patients’ (and doctors’) minds and may make it difficult to make rational choices, discouraging patients from using the treatment, even when the overall death rate of psoriasis patients on biologics is lower than that of patients not on biologics. Conceptualizing the magnitude of risks can help patients relieve anxiety and make well-balanced treatment decisions. The Lifetime Risk (LTR) model for biologic therapy created by Kaminska and colleagues is a helpful tool that visually compares lifetime risks of developing lymphoma, anemia, lower respiratory tract infection, thrombophlebitis, leukaemia lymphadenopathy, and the death rate in psoriasis patients not on biologics.

The estimated total annual costs of methotrexate range from $1,200 to $1,400, including post-hoc analyses. Biologics are more expensive than oral systemic therapies and may not be due to biologic therapy stand out in patients’ (and doctors’) minds and may make it difficult to make rational choices, even when the overall death rate of psoriasis patients on biologics is lower than that of patients not on biologics. Conceptualizing the magnitude of risks can help patients relieve anxiety and make well-balanced treatment decisions. The Lifetime Risk (LTR) model for biologic therapy created by Kaminska and colleagues is a helpful tool that visually compares lifetime risks of developing lymphoma, anemia, lower respiratory tract infection, thrombophlebitis, leukaemia lymphadenopathy, and the death rate in psoriasis patients not on biologics.

Available data suggest the current biologics are not predictors of serious adverse events. Based on the over 12,000 patients enrolled in the PSOLAR registry thus far, the death rate in the biologic cohort is numerically lower than that of the non-biologic cohort, and no psoriasis biologic treatment has been identified as a predictor of death. Rates of malignancies are generally comparable among all biologic treatments; the most frequently reported malignancies include breast, prostate, lung, melanoma, and lymphoma. Patients receiving TNF alpha show no increased risk of malignancy compared with psoriasis population not receiving biologics. Ustekinumab exposure has no evidence of cumulative toxicity. While exposure to anti-TNF biologics is a predictor of serious infection, ustekinumab exposure is not a predictor of infections compared to non-biologics. Disease state should be considered when assessing safety data, as patients with severe psoriasis are already at a greater risk for infection compared to those without psoriasis.

Recent studies found numerically lower rates of major adverse cardiovascular events (MACE) in biologic cohorts compared to non-biologic cohorts. No biologic agents, including anti-TNF alpha and anti-interleukin12/23, were associated with MACE. Whereas, some anti-TNF trials indicate no increased risk of MACE, other findings suggest that anti-TNF therapy may reduce risk of MACE by preventing plaque rupture and improving endothelial function. More studies testing the long-term effect of anti-TNF therapy on MACE will help explain this relationship.

With all safety considerations for biologic treatments the disease state, disease history, and risk of serious adverse events from therapy should be considered. In all, no new safety signals for adalimumab, infliximab, entercept, and ustekinumab have been reported. Understanding common side effects of biologic therapy and setting a plan to effectively manage them can improve patient adherence and clinical outcomes. The continued collection of longitudinal data on the spectrum of available biologics will provide important information on treatment efficacy and safety.

Cost Considerations

While biologics are effective, cost-considerations may limit their use. Biologics are more expensive than oral systemic therapies and have increased in cost over time. The estimated total annual costs of methotrexate range from $1,200 to $1,400, including post-hoc analyses.

Table 3. Biologic Treatment Serious Adverse Events and Common Adverse Events (While black box warning highlight potential serious adverse effects, less serious side effects are commonly reported with biologics use.)

<table>
<thead>
<tr>
<th>Biologic Treatment</th>
<th>Serious Adverse Events</th>
<th>Most Common Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab (Humira®)</td>
<td>TB, opportunistic and other serious infections; hepatitis B reactivation, malignancies, serious allergic reactions, demyelinating disease, heart failure, hematologic cytopenias, immune reactions.</td>
<td>Upper respiratory or urinary infections, abdominal pain, headache, rash, and injection site reactions.</td>
</tr>
<tr>
<td>Etanercept (Enbrel®)</td>
<td>Infections, neurologic events, CHF, hematologic events</td>
<td>Upper respiratory infections, dizziness, sore throat, cough, stomach pain, injection site reactions, headache, rhinitis.</td>
</tr>
<tr>
<td>Infliximab (Remicade©)</td>
<td>Infections, allergic reaction, edema, pancytopenia, hypotension, constipation, intestinal obstruction, dizziness, bradycardia, hepatitis, dehydration, thrombocytopenia, lymphoma, Anemia, lower respiratory tract infection, thrombophlebitis, leukaemia lymphadenopathy.</td>
<td>Infusion reactions, upper respiratory infections, headache, rash, cough, stomach pain.</td>
</tr>
</tbody>
</table>

*Secukinumab was approved on January 21, 2015, and lacks long-term safety data. The available data on secukinumab is acquired from Phase 3 studies of short duration. **Golimumab is currently not approved for treatment of plaque psoriasis, but is approved for treatment of psoriatic arthritis.

Cost Considerations

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components of medication cost, monitoring cost, and office visit costs.\textsuperscript{38} Estimated acitretin total annual costs range from $9,200 to $17,600, but can be lowered if medication is purchased outside the U.S.\textsuperscript{39} First year costs of ustekinumab, etanercept, and adalimumab have been estimated at $54,000, $46,000, and $39,000 respectively.\textsuperscript{40} While the cost of biologic therapy is greater than the cost of non-biologic therapy, most of this increased cost is related to drug costs.

Though the drug cost of biologic therapy is high, patients do not face this cost. Their copay may be large or small depending on their insurance plans. From a patient’s perspective, cost may be only what they pay out of pocket; this may be zero for some patients using patient assistance and copay coverage from the drug manufacturer. From a patient’s perspective, effectiveness in the cost-effectiveness calculus is measured not only by a treatment’s ability to clear the disease, but also by the patient’s subjective assessment of aspects of dermatology-related quality of life, such as productivity or mental health.\textsuperscript{39} With these factors in mind, biologics may serve as a cost-effective approach for many people with moderate-to-severe psoriasis. Biologics may also improve medical resource use and other health care costs. Biologics reduce costs associated with major changes in the pattern of healthcare delivery, reduce the number of inpatient admissions by more than half and reduce the mean number of inpatient days by more than 75%.\textsuperscript{40}

Despite better safety and efficacy than drugs like methotrexate and cyclosporine, insurance companies often require patients to have failed less expensive oral treatments before covering biologics. Depending on the specific requirements of the insurance plan, patients with moderate-to-severe-psoriasis may be eligible for reimbursement if they are nonresponsive to, intolerant of, or have a contraindication to phototherapy and/or systemic agents.

In the current healthcare landscape, cost-considerations heavily influence treatment decisions. Physicians are faced with an ethical issue when considering costs for biologics versus other treatments for psoriasis. They have the decision of prescribing an expensive, safer and more effective treatment versus a less expensive, less safe and less effective medication. Ultimately it is the responsibility of the physician to offer patients the best opportunity to meet their treatment goals within the constraints set by government regulators and insurer rules. At the same time, physicians can work to improve societal influences that drive these costs, and ensure their patients are receiving the care they need. Patient assistance programs and patient assistance foundations are options to help with out-of-pocket costs of biologic treatments. The cost of these drugs can be a serious financial obstacle for some psoriasis patients, and may contribute to high rates of under-treatment and non-treatment.

Treatment Considerations

Patients want effective therapies that maintain clearance of psoriasis, provide rapid response, are safe enough for long-term use, and result in a minimal disruption to their daily lives.\textsuperscript{33} Biologics offer patients an opportunity to reach this goal. Many articles present an approach to choosing biologic treatments from a physician’s perspective. However, a patient-centered approach to psoriasis care is systematically different, and just as important for treatment success. While physicians can offer guidance and education about available treatment options, patients generally prefer more autonomy and want to play a more active role in decision-making.\textsuperscript{41} Optimizing treatment, adherence, accommodating patient preferences, emphasizing strong patient-physician communication, and conceptualizing treatment risk can improve patient satisfaction and clinical outcomes.

Choosing and adhering to a treatment can be challenging for patients due to the unpredictable nature of psoriasis. Studies demonstrate up to 50% of individuals with psoriasis do not comply with recommended treatment regimens.\textsuperscript{42} Maintenance treatment is vital for chronic disease management. However, this concept isn’t well understood by patients, as many admit to using treatment only when deemed necessary, primarily during initial treatment and flare-ups, and do not see a need for treatment during psoriasis remission.\textsuperscript{41} Non-adherence to biologic treatment regimens can lead to anti-drug antibody formation that can prevent psoriasis patients from receiving full medication responses. In-office or clinic scheduled biologic treatments can improve adherence rates compared to at-home biologic injection treatments. Advising patients to incorporate their treatment regimen into their normal routines, but allowing them to decide the specifics can give patients a sense of autonomy. Giving patients the opportunity to take the initiative can help them achieve optimal adherence and receive the full benefit from biologic treatment.

Adherence to treatment can also be improved by considering and incorporating individual treatment preferences, such as mode of administration and access.\textsuperscript{33,44} Dosing frequency and route of administration may affect preferences for one biologic treatment over another; less frequent dosing is preferred for both physicians and patients.\textsuperscript{45} Some patients may prefer self-administered subcutaneous injection to intravenous infusions; with this in mind, infliximab may be the least desirable biologic as it requires infusion, as all other biologics for psoriasis are available in self-injection form.\textsuperscript{46} New oral medications in development may appeal to psoriasis patients who are hesitant to take injectable treatment.\textsuperscript{47}

Patients consider doctor-patient communication one of the most important factors of dermatology care.\textsuperscript{3} However, patient and physicians perspectives do not align on several aspects of communication. Patients desire more verbal and written information regarding disease information, causes, comorbidities, triggers for flare, current treatment options, curability, and prognosis.\textsuperscript{48} Patients also want to set treatment goals within a certain timeline, and discuss alternative approaches if the goal is not met.\textsuperscript{48} In addition, patients feel physicians should express more empathy and compassion, acknowledging the social and emotional impact of psoriasis. Biologic treatment regimens require the continuous collection and use of feedback from patients. Increasing communication with patients about goals of treatment and life circumstances can improve patient knowledge, ease anxiety, and guide treatment decisions.

Presenting the risk of biologics in a format patients can understand may be helpful. Weighing the risks of biologic therapy may be like choosing an airline ticket. Both of these paths require assessing options based on costs, convenience, and the ability to reach a final ‘destination’; safety, because risks are uncommon (and therefore relative risk differences have little impact on absolute risk), may not play much of a role in the decision. Though there are risks to flying, and different airlines may have varying levels of risk, people don’t consider airline safety when choosing a flight. After all, airline travel is relatively safe and differences in travel safety between airlines are extremely marginal. A similar rationale may be applied to biologics. Biologic therapy is relatively safe (apparently safer than not taking a biologic), and the risks are so small that it is hard to know if any of the biologics are safer than others. When risks and risk differences are that small they may play little role in treatment planning, beyond the enormous effects of emotionally charged anecdotes.

Black box warnings on biologic treatment package inserts indicate these agents carry serious, life-threatening adverse events. Though these risks may be rare, they often become patients’ focus. These warnings induce fear, and without placing these risks into proper perspective, patients can easily be dissuaded from use. These warnings do not convey the risks of psoriasis under-treatment or non-treatment and subsequent comorbidities. Approximately 25% of people with psoriasis are depressed and up to 30% of people with psoriasis develop psoriatic arthritis.\textsuperscript{48} Individuals with psoriasis are 58% more likely to have a major cardiac event, 43% more likely to have a stroke, and 46% more likely to have type 2 diabetes.\textsuperscript{49} Those individuals with severe psoriasis are 50% more likely to die. Given the tremendous impact of psoriasis on patients’ quality of life and the finding that death rates were higher in psoriasis patients not on biologics compared to those on biologics, perhaps there should be a black box warning for not adequately treating psoriasis.
Conclusion
Biologics provide a valuable option for people who suffer from moderate-to-severe psoriasis or who have tried and failed other therapies. Despite the growing number of available treatment options, non-treatment and under-treatment of psoriasis remain a problem in the U.S. Psoriasis has also been linked to cardiovascular disease, psychosocial distress, depression, and suicide. Treating psoriasis can reduce overall risk of these adverse events and improve patient quality of life.

Managing psoriasis is a complex, life-long process, and choosing a treatment can be daunting for patients. Great advances have been made in psoriasis care especially with the use of biologics. More efforts in patient education are needed to ensure that patients are aware of their options, have access to effective treatments, and can make informed decisions about choosing treatments. Data from recent registries can be shared with potential biologic candidates to convey marginal therapy risk and guide treatment decisions.

The National Psoriasis Foundation has an array of helpful educational material that patients and physicians can utilize to guide their collaborative decisions (materials are freely available at www.psoriasis.org). Psoriasis treatment is a long-term process that requires a collaborative and complete commitment on behalf of both patients and physicians. Assessing the available biological treatment options, conceptualizing the risk of developing serious adverse events from treatment, and maintaining regular and thorough communication can optimize adherence and contribute to an effective patient-centered approach to psoriasis care.

26. Strober BE, Poulin Y, Kerdel FA, Langley RG, Gu Y et al. Switching to adalimumab for psoriasis patients with a suboptimal response to


