Psoriasis treatment options have broadened over the last decade to include some of the most revolutionary treatments ever developed for this condition: biologics. Biologic agents developed for the treatment of psoriasis can be classified by their mechanisms of action. T-cell modulating agents interact with T cells, key mediators in the immunopathogenesis of psoriasis (Alefacept/Amevive, Astellas; Efalizumab/Raptiva, Genentech). Anti–tumor necrosis factor (anti-TNF) agents interfere with TNF receptor interaction, eliminating the inflammatory and immune responses involved in generating symptoms of psoriasis (Adalimumab/Humira, Abbott; Etanercept/Enrel, Amgen and Wyeth; Infliximab/Remicade, Centocor).

Both types of treatments have provided psoriasis patients the ability to manage their disease and maintain an improved quality of life. Anti-TNF agents are the most commonly used biologic agents in the United States for moderate to severe
psoriasis. Unfortunately, nearly 25 percent of patients treated with anti-TNF agents experience treatment failure. Determining which psoriasis patients will respond or are responding poorly to an anti-TNF requires several considerations.

Primarily, it is most important to base this decision on the patient’s level of satisfaction with the treatment. If the patient feels that his/her response is inadequate, that alone may be reason to seek alternative options. Additionally, some key attributes may indicate ahead of time that a patient might respond better to one biologic agent rather than to another. Two such clinical features are obesity and increased involvement of the hands and/or feet.

Because biologic treatments for psoriasis tend to be as—if not more—efficacious than other systemic and topical agents, it is extremely useful for healthcare professionals to monitor their patients’ responses and consider alternative biologic therapy as well as non-biologic therapy for their psoriasis patients.

**Types of Poor Responders**

The various types of patients who respond poorly or who are “inadequate responders” can be divided into three distinct categories that I will describe in greater detail below:

1. Patients who respond to treatment and then relapse,
2. Patients who never respond to treatment; and
3. Patients whose psoriatic arthritis symptoms respond but whose psoriasis symptoms do not.

**Patients who respond and then lose their response.** After about 12 to 18 months of treatment, some patients begin to lose their initial response. While this relapse can be extensive, with patients experiencing a return of as much as 50 percent of their psoriasis, it may be less severe, with a patient gaining back perhaps only 10 percent of their psoriasis. However, depending upon the location of the relapse, even a 10 percent return can be significant and deemed a failure to the patient or the doctor. For example, recurrence of psoriasis on the hands or feet can severely affect a patient's function, self-image, and quality of life, thus eclipsing any benefit seen on the rest of their body.

Consider the case of a 34-year-old man with a 19-year history of plaque psoriasis who presented with 10 percent affected BSA with moderately thick, red, scaly plaques on his trunk, scalp, and extremities. After failing on previous treatments, etanercept (50mg, twice weekly along with cyclosporine initially) treatment was initiated. At 12 weeks, the patient experienced 50 percent improvement, and after six months the patient experienced 75 percent improvement. At nine months, though, the patient experienced a significant flare (to 15 percent BSA) in his psoriasis and expressed a desire to try an alternate therapy. Efalizumab (1mg/kg/wk) was initiated one week after discontinuation of etanercept, and the patient experienced a steady improvement in skin disease and achieved a 50 percent improvement at 12 weeks. Psoriasis symptoms were clear by 24 weeks.

**Patients who never respond.** In addition to patients who relapse, another inadequate responder would be a patient who never receives a response from a treatment. Generally, patients on etanercept (50mg, twice daily) see reasonable results in 12 weeks. If after 12 weeks there is no noticeable improvement it should be considered a failure.

A 29-year-old female patient illustrates this point. She had a five-year history of plaque psoriasis and presented with a 15 percent BSA with psoriasis on the trunk, scalp, arms, and legs, and mild psoriatic arthritis. After initial treatment with methotrexate, the patient was then treated with etanercept (50mg/wk) for 12 weeks. After this time, there was still no improvement in symptoms and efalizumab treatment (1mg/kg/wk subcutaneously with concomitant fluocinonide cream 0.05% twice daily) was started. Within three months the patient experienced a decrease in BSA to less than 10 percent. After seven months, the patient achieved 0 percent affected BSA.

**Patients whose PsA symptoms respond while their psoriasis symptoms do not.** The third type of inadequate responder includes patients who achieve success in treating
their psoriatic arthritis but continue to experience the symptoms of psoriasis. While there is some precedent to maintain patients on both anti-TNF agents and T-cell modulators simultaneously, this treatment strategy has not yet been widely researched or accepted by the medical community. A recent poster presentation showed that patients with psoriatic arthritis and psoriasis can be successfully treated with a combination of etanercept (25mg, one to two times/wk) and efalizumab (1mg/kg/wk). In these cases, combination therapy with efalizumab and etanercept effectively controlled both skin disease and arthritis for patients who previously responded poorly to either treatment alone. The complementary yet differing mechanisms of action of these two treatments most likely contributed to the positive results.

Consider a 53-year-old man with a 13-year history of moderate psoriasis who presented with 12 percent affected BSA, with thick plaques on his knees, elbows, dorsal surface of his hands, calves, upper back, and scalp. The patient was also obese and had diabetes and psoriatic arthritis. Previous treatment with etanercept reduced the symptoms of the psoriatic arthritis but had no effect on the symptoms of psoriasis. After receiving an inadequate response on etanercept (25mg twice weekly for one year), efalizumab therapy was initiated at 1mg/kg/wk. After four months of treatments, psoriasis improved, and after 20 months of treatment with efalizumab, the psoriasis was completely clear. After four months of treatment, the patient developed severe arthritis, but was successfully treated with valdecoxib. The patient remains totally clear at three years on efalizumab.

**Treatment Failure Rates.** Determining what constitutes a treatment “failure” can be tricky, and failure rates often vary greatly from practice to practice. Generally speaking, of course, the more psoriasis patients treated in a dermatology practice, the more “failures” that practice will see in terms of whole numbers. A certain percentage of patients do not respond to any drug, and each physician uses his or her own formula or pattern to determine approximate failure rates. Overall, I have found that about 20 to 25 percent of patients who were on etanercept, after about a year, start to have enough recurrence that they need to switch or add another therapy. Approximately five to 10 percent of the patients I treat with etanercept or adalimumab never respond, while five percent of patients I start on infliximab don’t respond.

**Course of Action**

Involving the patient in treatment decisions is crucial to maintaining a positive physician-patient relationship. Based on the nature of the disease, I find that patients want to be proactive in their treatment, and some may even express a specific desire to switch to another class of drug. It is important that the patient be given these choices. Very rarely do I tell a patient which treatment they should be using: Instead, I give them options. Involving the patient in this process allows him or her to share in the success or failure of the treatment, and this participatory model of treatment tends to increase compliance. Choice is essential and, unfortunately, not enough doctors always participate in this kind of dialogue with their patients.

Determining which treatment a patient should be switched to can be as difficult as determining which treatment to initiate when the patient first starts therapy. Fortunately, switching anti-TNF inadequate responders can be guided by breaking the responses down into subgroups. As a general rule, it is best to switch classes if a psoriasis patient is not responding to their anti-TNF treatment and they do not have significant psoriatic arthritis. Further insight into subgroups where this course of action is not appropriate include:

**Severe psoriatic arthritis.** For patients with severe, life-altering psoriatic arthritis, including such presentations as bad ankle pain or morning sickness, the best course of action is to switch to a different anti-TNF. The T-cell modulators do not target nor are they indicated for the treatment of psoriatic arthritis. For this reason alone, it would be important to maintain treatment for the psoriatic arthritis in severe cases.

**Mild psoriatic arthritis.** For patients with mild psoriatic arthritis, the best course of action is to control the arthritis with an over-the-counter or prescription anti-inflammatory pain medication and switch to a T-cell modulator, such as efalizumab. Alternatively, a different anti-TNF agent could be tried.
Failed T-cell modulator and failed one anti-TNF. While it is generally beneficial to switch to a different class once one anti-TNF fails, if the patient has also failed on a T-cell modulator, it is most beneficial to switch to another anti-TNF agent.

Once the decision is made to switch treatments, a couple of different courses of action can be taken. If the patient has maintained some level of improvement on their current anti-TNF, it may be fine to simply stop treatment with the one drug and switch to another. More frequently, though, the process of switching treatments occurs over several visits. For example, a recent patient was treated for 12 weeks with etanercept (50mg, twice weekly). After this time, it was decided that the treatment was not working. In this situation, I suggest that the patient be offered the opportunity to switch to a T-cell modulator, such as efalizumab. To make this transition smooth, the best process would be to wean down the frequency of the etanercept so that the patient will still have some etanercept left to use while starting the weekly efalizumab. This overlap would occur for a fairly short period of time, ranging from four weeks to two months.

For patients who have clearly not responded to an anti-TNF agent whose psoriatic disease is getting worse, consider a “bridge” drug—methotrexate or cyclosporine—while transitioning to efalizumab. The overlap can occur for as long as eight to 10 weeks.

Make a Change
Overall, it is important to remember that if a patient does not respond to anti-TNF therapy, there are many safe and effective options available that the dermatologist should consider with the patient. Neither the healthcare professional nor the patient should be content if results are not satisfactory. If it’s time to make a change, make the change. While it is never obvious which drug will work for which patient, do not hesitate switching if the patient or you are unsatisfied. While some doctors are averse to changing a psoriasis patient’s biologic therapy because of the involved process of switching treatments, it is important to remember that we can make an enormous difference in a patient’s life simply by making a change.

Guidelines for Switching Therapies (See text for full discussion.)

- Involve the patient in treatment decisions.
- It is important to give the patient choices.
- As a general rule, it is best to switch classes if patient is not responding to anti-TNF treatment and does not have significant PsA.

For anti-TNF non-responders...
- With severe, life-altering PsA, including such presentations as bad ankle pain or morning sickness: switch to a different anti-TNF. (T-cell modulators do not target PsA.)
- With mild PsA: control arthritis with an OTC or prescription anti-inflammatory pain medication and switch to a T-cell modulator.
- Who has also failed on a T-cell modulator: it is most beneficial to switch to another anti-TNF agent.