TNF Inhibitors a Top Choice Among Biologics For Psoriasis

• Bruce E. Strober, MD, PhD, Assistant Professor of Dermatology and Director of Clinical Trials, University of Connecticut, Farmington, Conn.

Among biologic drugs for psoriasis, the safety profile and ability of tumor necrosis factor (TNF) inhibitors in treating psoriatic arthritis (PsA) make them a first-line choice for most patients who need biologic therapies, said Dr. Strober. He prescribes them when patients with moderate-to-severe psoriasis have not responded to topical therapies or when severe psoriasis justifies starting treatment with these agents immediately.

“That’s acceptable under American Academy of Dermatology guidelines for psoriasis—you don’t have to make a person fall topical therapy” before prescribing biologics, he said.

Biologic drugs that have been approved for psoriasis include etanercept (Enbrel, Amgen/Pfizer), alefacept (Amevive, Astellas U.S. Inc. Pharma), infliximab (Remicade, Janssen Biotech Inc.), adalimumab (Humira, Abbott), and ustekinumab (Stelara, Janssen Biotech Inc.). In selecting biologic therapies, Dr. Strober commented:

“I believe drugs that treat psoriatic arthritis should be put ahead of drugs that don’t. Psoriatic arthritis is present in many patients with moderate-to-severe psoriasis, and the ability to treat psoriatic arthritis provides a surrogate measure of the drug’s ability to reduce systemic inflammation.”

He said that systemic inflammation is a poorly understood but highly consequential issue in psoriasis because it leads to cardiovascular risk.

“In essence, drugs that can reduce cardiovascular risk associated with psoriasis would provide an additional benefit to patients,” he added.

To that end, he explained that TNF inhibitors not only treat PsA symptoms (swelling, pain, and joint tenderness) but also inhibit progression of joint destruction. He said that TNF inhibitors are unique in their ability to do that but added that ustekinumab is unproven in PsA. Although one pilot study indicated a degree of response,1 “the jury is still out,” he claimed. In his own experience, he said that ustekinumab did not perform as well as the TNF blockers—or methotrexate—at PsA.

Regarding cardiovascular risk, one study showed that TNF inhibitors could increase amounts of the protective cytokine adiponectin.2 Similarly, in a retrospective analysis of patients with psoriasis, TNF inhibitor therapy corresponded with a decreased risk of myocardial infarction (MI).3

Conversely, Dr. Strober said that a meta-analysis he co-authored suggests that the interleukin (IL)-12 and IL-23 inhibitors ustekinumab and Abbott’s briakinumab (ABT 874) showed a small numerical imbalance, indicating a possible risk for a major adverse cardiovascular event (AE), namely stroke, MI, or sudden cardiac death.4

“The TNF inhibitors do not appear to carry this risk,” he said.

Because of the potential for cardiovascular AEs, he said that Abbott has withdrawn its application for the FDA’s approval of briakinumab.

He said, “The issue arises now whether ustekinumab poses a very small yet real risk to certain patients—we cannot yet define who they are—of major adverse cardiovascular events, especially in the first six months of therapy.”

Because ustekinumab might carry a risk that TNF inhibitors don’t, “it may mean that we want to use TNF inhibitors before ustekinumab unless there’s a contraindication to using a TNF blocker,” he said.

Another factor that guides the choice of a biologic therapy is efficacy. In this regard, said Dr. Strober, the proportions of patients who show 75% improvement in Psoriasis Area and Severity Index scores (PASI 75) with infliximab, adalimumab or ustekinumab, etanercept, and alefacept are 80%, 70%, 50%, and 25%, respectively. Moreover, he said that physicians also must recognize that patients tend to lose their response to all of these drugs over the long term, which may necessitate switching them to another biologic agent.

As for ease of use, Dr. Strober pointed out that patients require subcutaneous injections of etanercept, adalimumab, and ustekinumab, performed weekly, every other week, or every 12 weeks, respectively. Conversely, the intravenous infusion required for infliximab and the intramuscular injections needed for alefacept often prove difficult for patients.

Regarding the FDA’s warning in September about a risk of Legionella and Listeria infections for patients taking TNF inhibitors, he said:

“I don’t believe it changes anything. When you’re monitoring patients on TNF inhibitors, you’re always thinking about infection risk. This warning [was] just added to the list of possible pathogens.”

Takaharu Kato is a freelance health care journalist based in White Plains, New York. Mr. Sonnenreich, based in Washington, D.C., is the editor of the Maruho Derma Report.
An Intralesional Strategy for Nail Psoriasis

Richard K. Scher, MD

Physicians have very few treatments for nail psoriasis, which affects up to half of patients with psoriasis, according to Dr. Scher. In treating the condition, he said, topical agents, including steroids and vitamin D analogues, cannot effectively penetrate the nail bed and matrix. Phototherapy works somewhat better than intralestional steroid injections, he added, but not as well as systemic drugs (such as cyclosporine and methotrexate) and biologic drugs. However, he commented that systemic medications carry many side effects and should be considered only in special situations. Insurers are reluctant to pay for biologic therapies unless patients also have extensive skin disease.

Intralestional corticosteroids injected around the sides of the nail and the cuticle area provide effective treatment by allowing the steroid to penetrate into the nail bed and matrix. However, Dr. Scher acknowledged that the injections are “sometimes painful and uncomfortable. And none of our psoriasis treatments give a permanent cure.”

To minimize recurrences, he injects about once every 4 to 6 weeks. As the healthy nails start to come in, he injects less frequently. After the nails are under control, he stops the injections and advises the patient to return when the psoriasis starts to recur.

In one study, low-dose acitretin (Soriatane, Steifel Laboratories) was effective for nail psoriasis, particularly in combination with phototherapy. Another review indicated that cyclosporine A was better than acitretin for non-plaque psoriasis. Dr. Scher mentioned that the experimental topical agent indigo naturalis (Qing dai) clearly appears to help moderate-to-severe nail psoriasis.

A single-blinded, randomized study involving 34 patients also showed that methotrexate achieved a 43% decrease in Nail Psoriasis Severity Index (NAPSI) scores, compared with a 37% reduction for cyclosporine. Moreover, Dr. Scher said that in this study, “the nail matrix did better with methotrexate; nail bed psoriasis fared better with cyclosporine.”

Accordingly, he advised the following if a clinician is considering a systemic therapy for severe nail psoriasis in a patient with no contraindications for either drug:

“If the overwhelming involvement is in the matrix, the patient will be better off with methotrexate. If the overwhelming involvement is the nail bed, the treatment of choice would be cyclosporine.”

If the nail bed and matrix are equally involved, he said that it’s a matter of which product the clinician is more experienced in using.

Although some researchers have suggested modifying the NAPSI, Dr. Scher pointed out that it’s been available for 8 years. “Several thousand patients have been evaluated with it, and it has stood the test of time.”

Other advantages of the NAPSI include the fact that it’s reproducible, consistent, objective, quick, simple, and ideal for clinical trials. As such, said Dr. Scher, “NAPSI remains the gold standard for evaluating nail psoriasis.”

Finally, a controversy in the medical literature concerns whether onychomycosis occurs more commonly in psoriatic nails. Dr. Scher referred to a convincing 228-patient study showing that men with the condition had a higher prevalence of onychomycosis compared with men who did not. Overall, he said that cultures confirmed the presence of nail fungus in 62% of these patients. Therefore, these study authors recommended that physicians test dystrophic nails in psoriatic patients for fungal infection.

REFERENCES


Phototherapy for Psoriasis

Henry W. Lim, MD

American Academy of Dermatology guidelines state that when psoriasis affects more than 20% of a patient’s body surface area (BSA) or when it interferes with daily activities (such as palmar psoriasis), phototherapy is an appropriate choice. Physicians also consider it for patients with milder psoriasis that resists more conservative treatments, said Dr. Lim.

Typically, he said, phototherapy for psoriasis involves narrowband–ultraviolet B (NB–UVB, 311–313 nm), delivered to the entire body, or targeted light sources used to treat small areas, often in combination with topical agents.

With a response rate of 70% to 80% for NB–UVB, Dr. Lim said, “The advantage of phototherapy is that it’s quite effective. Because we have used it for many years, we know the long-term side effects of phototherapy very well. Based on cur-
REFERENCES


Recommendations for Vitamin D

- Henry W. Lim, MD, Chairman of Dermatology,
  Henry Ford Hospital, Detroit, Mich.

Institute of Medicine (IOM) guidelines regarding vitamin D intake rest upon research regarding bone health, because this is the only area in which the IOM found sufficient evidence to support specific intake recommendations, said Dr. Lim.

In a meta-analysis of 12 prospective clinical trials, 700 to 800 International Units (IU) of vitamin D, daily, compared with calcium or placebo, decreased the risk of hip fractures in 26% of subjects and the risk of nonvertebral fractures in 23% of subjects. Accordingly, in November 2010, the IOM recommended the following daily intake levels: 600 IU for adults, 800 IU for people older than 70 years of age, and 400 IU for infants younger than 1 year of age. However, the IOM has concluded that the currently available evidence of vitamin D’s impact is often inconclusive and sometimes conflicting for other health outcomes.

In the Health Professionals Follow-up Study, after adjustments were made for medical and other risk factors, African-Americans, who are known to have lower vitamin D levels than Caucasians, were found to have a higher total cancer incidence and mortality risk. African-Americans with few risk factors for hypovitaminosis D did not face higher risks of cancer incidence or mortality, said Dr. Lim, whereas those with risk factors for low vitamin D levels faced much higher risks.

As for rarer cancers, such as cancers of the endometrium and pancreas, however, a pooled analysis of several international cohort studies showed no impact of serum vitamin D concentrations above 75 nmol/L. In a somewhat similar fashion, in a prospective study involving more than 7 million U.S. military personnel, the risk of multiple sclerosis in Caucasians decreased significantly with increasing vitamin D levels. However, investigators observed no effect of higher vitamin D levels in African-Americans and Hispanic patients.

Likewise, in an analysis of all published reports regarding vitamin D and the prevention of cardiovascular disease and type-2 diabetes, the data were found to be inconsistent and insufficient to substantiate a cause-and-effect relationship, said Dr. Lim. As for sunscreen, a recent review showed that for the average user, applying it did not diminish serum vitamin D levels, probably because people rarely apply or reapply sunscreen adequately.

For people concerned that their vitamin D levels might be inadequate, Dr. Lim suggests oral supplementation. People at high risk of vitamin D inadequacy, such as older adults, people with darker skin types, and those who practice vigilant sun protection, could benefit from serum vitamin D measurements, he added.

REFERENCES


