Biologics and Pediatric Psoriasis

Though data has been lacking in recent years, the use of biologics in pediatric and adolescent patients deserves more consideration.

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Over the past 15 years, the therapeutic toolbox for the treatment of adult moderate-to-severe psoriasis has yielded many effective and relatively safe agents. In some cases, 50 percent of patients can become clear within 12 weeks. However, patient satisfaction with therapy is very low. In fact, more than half of patients with moderate to severe psoriasis are receiving no treatment or topical treatment only.¹

One subset of psoriatic patients that often does not receive optimal care is adolescents. Approximately 30 percent of psoriasis onset occurs before age 18,² and the emotional impact of psoriasis is comparable to that of asthma, arthritis, or diabetes. One recent study found that pediatric patients with psoriasis had an increased risk of developing psychiatric disorders, including depression and anxiety.³ Moreover, incidence appears to be occurring with increased frequency in this age category.⁴

But therapeutic options for adolescents with moderate to severe psoriasis are thin, particularly for those under the age of 18. In fact, there are no biologic agents approved in the US for the treatment of moderate to severe psoriasis under the age of 18. Conversely, biologics are approved with indications for younger ages in other disease states. For example, several biologics are approved down to the age of four for the treatment of juvenile idiopathic arthritis (JIA), a condition that some rheumatologists believe is a category for psoriatic arthritis under the age of 18. Additionally, infliximab (Remicade, Janssen) has been approved for the treatment of Crohn’s disease and ulcerative colitis down to age 6. Last year, adalimumab (Humira, AbbVie) was also approved for patients with Crohn’s disease down to age 6. Meanwhile, in Europe some biologic agents are approved for children with psoriasis down to the age of 8 years old.

For the treatment of adolescent and pediatric psoriasis in the US, however, all biologic treatment is off label. Therefore, we depend on published research to guide our therapeutic selections for these individuals. Ahead I will recap notable studies on the off label use of biologics for pediatric and adolescent psoriasis.

BIOLOGICS FOR PEDIATRIC PSORIASIS

One of the most significant studies evaluating biologics for the treatment of pediatric psoriasis was published in The New England Journal of Medicine in 2008.⁵ For the Phase III study, investigators evaluated 211 patients between the ages of four and 17 with psoriasis who were treated with etanercept (Enbrel, Amgen) for 48 weeks. The average patient age was 13 years old, and 36 percent were under the age of 11. Of note, average BSA was 20 percent. All patients had previously been on or were on systemic or phototherapy, and all washed out before entering clinical trial.

The first twelve weeks were double blind. Researchers administered etanercept was administered 0.8 mg/kg sc once weekly up to a max dose of 50 mg. The next 24 weeks was open labeled, followed by a 12 weeks withdrawal and retreatment period.

At week 12, PASI 50/75/90 response was 75, 57, and 27 percent, respectively, for those in the placebo group. At 24 weeks, 62 percent of patients who were on placebo through week 12 achieved PASI 75, as compared to 69 percent of people who were on it continuously for 24 weeks. These results were maintained through 36 weeks. Additionally, of those who continued with etanercept through 48 weeks, 80 percent maintained their PASI scores.

There were no increases overall in adverse events between placebo and etanercept-treated groups. Additionally, all serious adverse events in the etanercept-treated groups resolved without sequelae. They included removal of an ovarian cyst, pneumonia in an asthmatic patient, and gastroenteritis. No deaths, malignancies, opportunistic infections, tuberculosis, or demyelination were reported.
Patients who obtained at least at PASI 50 at week 48 entered a 264-week long-term open label extension. At week 96, the PASI 50/75/90 was 85, 58, and 29 percent, respectively. Common adverse events were URIs, strep pharyngitis, headache, and sinusitis. Two patients withdrew from the study—one due an incidence of Crohn’s disease, the other due to sinusitis.

In 2009, the FDA reported 48 pediatric malignancies in anti-TNF-treated patients (mostly treated for JIA) between the ages of zero and 18. Of these, 31 were treated with infliximab, 15 etanercept, and two adalimumab. In the etanercept group, five were lymphoma and four were leukemia. The average duration of exposure was 28 months, and 73 percent were treated concomitantly with methotrexate and steroids. Importantly, the rate of lymphomas treated in children was 11 per 100,000 patient years, five-fold over the background rate.

It is likely that this reported increase in lymphoma hindered further research in pediatric psoriasis and may explain why so little research has been conducted since then.

**RECENT DATA**

New data presented at the 2015 Annual Meeting of American Academy of Dermatology in San Francisco evaluated ustekinumab (Stelara, Janssen) in the treatment of adolescent psoriasis. Researchers evaluated 110 subjects between the ages of 12 and 18 years with moderate to severe psoriasis. Average PASI scores were greater than 12, PGA scores were greater than three, and BSA was greater than 10 percent. The average patient age was 15 years, with average age of onset nine years old, and most had a family history of psoriasis.

Patients were either treated with the standard dose (45 mg for patients less than 100 kg, 90 mg for patients greater than 100 kg), half the standard dose (22.5 mg for those less than 100 kg, and 45 mg for those greater then 100 kg), or placebo.

At 12 weeks, 80 percent of patients in the standard dose category achieved PASI 75, as compared to 78 percent in patients in the half-dose category, and 10 percent in the placebo group. In the half-dose group, 54 percent of patients achieved PASI 90, compared to 61 percent in the full dose group.

In the 52-week data (last dose at week 40), 65 percent of patients in the half-dose group maintained PASI 75, as compared to 78 percent in the standard dose group. Additionally, 60 percent of standard dose patients achieved PASI 90, compared to 50 percent in the half dose category.

These efficacy results are extremely compelling, particularly because of the overall lower weight of the patients and hence a more appropriate weight-based dosage. Although PASI scores were similar between the two groups, the duration of remission and improvement were not as long in the half dose group as they were in the full dose group. Adverse events were also similar to those seen in adult clinical trials, with a slight increased risk of infections but no serious infections were noted in this study.

**TREATMENT PEARLS**

When we are evaluating patients with psoriasis who are under the age of 18, particularly those in the adolescent years, we should consider that they are at a time in their lives in which they are developing a sense of self. Good treatment doesn’t just help them cope but helps to relieve all adolescent stresses with exceptional burdens that impacts their self esteem. Importantly, clinicians should continue to explore the possibilities of using biologic therapies in these patients. Safety is a key consideration, but the recent data indicate that, if used appropriately and with the proper precautions, these therapies can be use safely and yield good results.

While etanercept can be dosed according to each individual’s weight, ustekinumab is administered only at 45mg or 90mg depending on whether the patient is over or under 100kg. However, ustekinumab may offer an advantage when it comes to the number of treatments. Since patients in the pediatric population may be particularly resistant to shots, ustekinumab’s administration every 12 weeks may be more enticing than the higher frequency of treatments with etanercept.

For patients with more severe cases, limited case reports suggest that infliximab 5mg/kg given at weeks zero, two, six, and then every eight weeks thereafter can offer benefit in children who are refractor to other systemic and biologic therapies down to the age of three years. A review of the literature did not provide information concerning the use of adalimumab in pediatric psoriasis.

Also, when using biologics off label in pediatric patients, it is important that they are brought up to date with all immunizations prior to therapy. If patients are exposed to varicella, temporarily stop therapy and consider varicella zoster immune globulin (VZIG).

**CONCLUSION: HOPE FOR THE FUTURE**

Despite the lack of studies in recent years, the newest data suggest promising directions for harnessing biologics in the treatment of psoriasis in patients under the age of 18 years. Moreover, it’s quite possible that the FDA, now realizing the effect that psoriasis has on quality of life, may be more open to allowing clinical trials for the study of biologics in pediatric psoriasis.

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