A Growing Biologics Armamentarium for Psoriasis and Atopic Dermatitis

An overview of effective and safe treatment options that continue to come to market to target these chronic conditions.

There has been a significant amount of research and development in atopic dermatitis and psoriasis in the last couple of years, bringing new drugs to market and leaving a robust pipeline of drugs in development. Since 2014, five potential blockbuster drugs have been approved in the dermatology therapy area, forecast to achieve aggregate annual revenue of $12.4 billion by 2023, according to business intelligence provider GBI Research.

Four of these five market-driving drugs—secukinumab (Cosentyx, Novartis), apremilast (Otezla, Celgene), crisaborole (Eucrisa, Pfizer), and ixekizumab (Taltz, Eli Lilly)—were approved to treat psoriasis, and one, dupilumab (Dupixent, Celgene/Sanofi Genzyme), became the first and, to-date, the only biologic approved for the treatment of atopic dermatitis.

Biologics that have been available for more than 10 years have proven safety and efficacy data, and newer, more targeted biologics continue to be introduced for psoriasis, and now for atopic dermatitis. The continuing evolution of biologics is allowing dermatologists to offer more targeted treatments with outcomes of almost clear to clear skin, giving patients and physicians new hope in the battle against these chronic conditions.

**ATOPIC DERMATITIS**

Dupixent was FDA approved in March as an injection to treat adults with moderate to severe atopic dermatitis not controlled adequately by topical therapies, or those for whom topical therapies are not advisable. Dupixent was evaluated by the FDA with Priority Review, which is reserved for medicines that represent potentially significant improvements in safety or efficacy in treating serious conditions.

Dupixent is a human monoclonal antibody designed to specifically inhibit overactive signaling of two key proteins—IL-4 and IL-13—which are believed to be major drivers of the persistent underlying inflammation in AD. Dupixent comes in a pre-filled syringe and can be self-administered as a subcutaneous injection every other week after an initial loading dose.

The safety and efficacy of Dupixent were established in three placebo-controlled clinical trials with a total of 2,119 adult participants with moderate-to-severe atopic dermatitis not adequately controlled by topical medication(s). Overall, participants who received Dupixent achieved greater response, defined as clear or almost clear skin, and experienced a reduction in itch after 16 weeks of treatment.

Dupixent can cause side effects, such as serious allergic reactions and eye problems, such as conjunctivitis and keratitis. Patients who experience new or worsening eye symptoms such as redness, itching, pain or visual changes, should be encouraged to report their side effects to their physician. The most common side effects include injection site reactions; cold sores in the mouth or on the lips; and eye and eyelid inflammation, including redness, swelling, and itching.

Dupixent can be used with or without topical corticosteroids, and according to the one-year results of the LIBERTY AD CHRONOS study, combination treatment with dupilumab and topical corticosteroids (TCS) significantly improved measures of overall disease severity. The phase 3 study involved a total of 740 adult patients with moderate to severe AD that was inadequately controlled with topical medications. Dupilumab with TCS was compared to TCS alone.
At week 16, 39 percent of patients who received either dupilumab 300mg weekly with TCS or dupilumab 300mg every two weeks with TCS achieved clearing or near-clearing of skin lesions (IGA 0 or 1), compared to 12 percent of patients receiving placebo with TCS. Sixty-four percent of patients who received dupilumab 300mg weekly with TCS, and 69 percent of patients who received dupilumab 300mg every two weeks with TCS achieved a 75 percent reduction on the Eczema Area and Severity Index (EASI-75), compared to 23 percent of patients receiving placebo with TCS.

At the 52-week mark, 40 percent of patients who received dupilumab 300mg weekly with TCS, and 36 percent of patients who received dupilumab 300mg every two weeks with TCS achieved clearing or near-clearing of skin lesions (IGA 0 or 1), compared to 12.5 percent of patients receiving placebo with TCS. This was a secondary endpoint.

The study also found that patients were less likely to discontinue therapy in the dupilumab with TCS groups compared to placebo with TCS group (15 percent in both dupilumab groups; 33 percent placebo).

In an interview with DermTube.com about new and emerging therapies for atopic dermatitis, Emma Guttman, MD said it’s a very exciting time for treating atopic dermatitis.

“In my mind, the body surface are is the most important,” Dr. Guttman said. “Patients who have more than 10 percent body surface area, it’s just not feasible to treat them just with topicals.”

The study found significant differences between before and after the switch to biological treatment, both at three to five months after the switch and also sustained over the entire observed timespan,” says Dr. Schmitt-Egenolf.

“Our results suggest that both the clinical effectiveness and the impressive effects on the quality of life under biological treatment as used in clinical practice are sustained over time. These results may support clinicians in initiating and continuing biological treatment for patients with poor outcomes under conventional treatment. This is an important finding from an international perspective, as data on real-life long-term outcomes of biological treatment is rare but crucial for treatment guidelines,” concludes Dr. Schmitt-Egenolf.

NEWEST BIOLOGICS FOR PSORIASIS

Since 2015, three new biologics have been FDA approved to treat psoriasis—secukinumab (Cosentyx), ixekizumab (Taltz), and brodalumab (Siliq). In addition, in 2016, the FDA approved the supplemental Biologics License Application (sBLA) for the expanded use of Amgen’s etanercept (Enbrel), making it the first systemic therapy to treat pediatric patients (ages 4-17) with chronic moderate to severe plaque psoriasis.

In January 2015, Cosentyx received FDA approval for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. Cosentyx was the first approved psoriasis medication to selectively bind to IL-17A and inhibit its interaction with the IL-17 receptor. Approval was based on the efficacy and safety outcomes from 10 Phase 2 and 3 studies, including more than 3,990 patients with moderate to severe plaque psoriasis, which demonstrated that Cosentyx resulted in clear or almost clear skin in the majority of patients and had an acceptable safety profile.


“Most studies in this area were initiated by the industry and conducted in controlled settings that are ultimately beneficial for their product. Consequently, those studies cannot really predict how a product will perform under real-life circumstances, with real-life patients.”

The study was based on data from repeated consultations of patients included in the Swedish psoriasis register and conducted by researchers at Umeå University and the Swedish Institute for Health Economics (IHE) in Lund.

Researchers analyzed three different measurements: the clinical measurement Psoriasis Area Severity Index (PASI), the DLQI, which measures the impact of skin diseases on the quality of life, and the EQ-SD measurement, which analyses the general health-related quality of life.

“In all three of these measures of treatment outcome, we found significant differences between before and after the switch to biological treatment, both at three to five months after the switch and also sustained over the entire observed timespan,” says Dr. Schmitt-Egenolf.

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PSORIASIS

Of course, biologics are not new to the treatment armamentarium for psoriasis—in the beginning of the century, the introduction of this new class of drugs transformed the treatment of moderate to severe psoriasis by providing better skin clearance rates, low toxicity, and improved quality-of-life. A recent study by researchers at Umeå University assessed long-term outcomes in clinical practice, where switching between biological agents is common. The Swedish study followed 583 individuals for up to 10 years showing satisfactory long-term effectiveness of biologic treatments. The findings were recently published in the British Journal of Dermatology.

“We employed a real-life patient perspective in this study,” says Marcus Schmitt-Egenolf, professor at the Department of Public Health and Clinical Medicine at Umeå University and senior author of the study.

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of secukinumab treatment on patient-reported health-related quality of life as assessed by the DLQI in patients with moderate to severe psoriasis. Of 1,470 patients, 1,144 received secukinumab and 326 received etanercept. DLQI score 0/1 response rates were significantly higher for secukinumab than for etanercept at week 24. The median time to DLQI score 0/1 response was significantly shorter for secukinumab versus etanercept (12 vs 24 weeks). The majority of secukinumab-treated patients achieved DLQI score 0/1 response at week 24 and sustained it through week 52 along with a 90 to 100 percent reduction in the PASI total score response.

More recently, Novartis received approval in the EU for a Cosentyx label update, including long-term superiority data versus ustekinumab (Stelara) in treating psoriasis. The label updated from the Committee for Medicinal Products for Human Use (CHMP) includes 52-week data from the CLEAR study demonstrating the long-term superiority of Cosentyx versus ustekinumab in psoriasis. The updated label also includes use of Cosentyx to treat moderate to severe scalp psoriasis. The updated label is based on the proven efficacy and consistent safety profile of Cosentyx.

The 52-week data show that Cosentyx is superior in delivering long-lasting clear or almost clear skin over one year of treatment in adults with moderate to severe psoriasis, according to Novartis. Cosentyx remained consistently superior to Stelara in achieving and sustaining a PASI 90 response (76 vs. 61 percent) and significantly better in achieving a PASI 100 response (46 vs. 36 percent) at Week 52.

Cosentyx is currently the only fully human IL-17A inhibitor to demonstrate efficacy and safety in a dedicated Phase III study of scalp psoriasis. The CHMP approval is based on results from the 24-week study of moderate to severe scalp psoriasis where Cosentyx demonstrated superior efficacy compared to placebo. Psoriasis Scalp Severity Index (PSSI) 90 responses were achieved by a significantly greater percentage of patients receiving Cosentyx 300mg (53 percent) than placebo (2 percent) at Week 12.

The label update is applicable to all European Union and European Economic Area countries.

The IL-17A blocker Taltz was FDA approved in March 2016 for adults with moderate to severe plaque psoriasis. Given via 80mg/mL injection, Taltz’s active ingredient ixekizumab is an antibody that binds to the IL-17A protein that causes inflammation. It is intended for patients who are candidates for systemic therapy, phototherapy or a combination of both.

Taltz’s safety and efficacy were established in three randomized, placebo-controlled clinical trials with a total of 3,866 participants with plaque psoriasis who were candidates for systemic or phototherapy therapy. Results showed that Taltz achieved greater clinical response than placebo, with skin that was clear or almost clear, as assessed by scoring of the extent, nature, and severity of psoriatic changes of the skin. Taltz was approved with a Medication Guide to inform patients about risk of infection or allergic or autoimmune condition.

The IXORA-S study, which was presented earlier this year at the 2017 American Academy of Dermatology Meeting, found Taltz demonstrated superior efficacy at 24 weeks compared to patients treated with Stelara. In the IXORA-S study, patients were randomized to receive either Stelara (45mg or 90mg weight-based dosing per label) or Taltz (80mg every two weeks for 12 weeks followed by 80mg every four weeks), following a 160mg starting dose, for a total of 52 weeks. At 24 weeks, patients treated with Taltz achieved significantly higher response rates compared to patients treated with Stelara, including 83 percent of patients who achieved PASI 90—the study’s primary endpoint—compared to 59 percent of patients who achieved PASI 90 after treatment with Stelara.

The majority of treatment-emergent adverse events were mild or moderate. There were no statistically significant differences between treatment groups in overall treatment-emergent adverse events.

Newest to market is Valeant Pharmaceutical’s Siliq, which was approved in February for subcutaneous use for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies. Siliq works by binding to IL-17RA with high affinity, therefore blocking the inflammatory downstream activity of IL-17A, IL-17F, IL-17A/F heterodimer, and IL-17E. By targeting the IL-17 receptor, Siliq prevents skin cells from accumulating.

Siliq’s safety and efficacy were established in three randomized, placebo-controlled clinical trials with 4373 patients with moderate to severe plaque psoriasis who were candidates for systemic therapy or phototherapy. More patients treated with Siliq compared to placebo had skin that was clear or almost clear, as assessed by scoring of the extent, nature, and severity of psoriatic changes of the skin. In three clinical studies that have been completed, more than 50 percent of patients who used Siliq achieved total skin clearance within a year.

Siliq has a Boxed Warning for risks in patients with a history of suicidal thoughts or behavior. SILIQ was approved with a Risk Evaluation and Mitigation Strategy (REMS) involving a one-time enrollment for physicians and one-time informed consent for patients.

**A PROMISING FUTURE**

With so many new and effective existing treatments and more in the pipeline, patients with psoriasis and atopic dermatitis and physicians who treat these conditions now have many options that offer hope for clear skin.