Tumor necrosis factor-alpha (TNF-α) inhibitors and anti-interleukin 12/23 (IL-12 and IL-23) therapies are the two classes of biologic drugs currently approved by the FDA for psoriasis.1 Among the other biologics in development, there are several anti-interleukin 17 (IL-17) agents that have shown significant promise in recent Phase II trials.1

IL-17 is produced by neutrophils, mast cells and CD4+ and CD8+ T cells, and the two isoforms of IL-17, IL-17A and IL-17F, are expressed as homodimers and IL-17A/17F heterodimeric proteins by T cells.1 All three cytokines have similar functions and transduce their signals via the same IL-17 receptor complex.1

The three anti-IL-17 agents in development are all monoclonal antibodies (mAbs).1

**IXEKIZUMAB (LY2439821)**

This humanized IgG4 mAb neutralizes IL-17.2 A recent Phase II trial of ixekizumab randomized patients to receive subcutaneous injections of placebo or 10 mg, 25 mg, 75 mg or 150 mg of ixekizumab at 0, 2, 4, 8, 12 and 16 weeks.2 Patients were allowed to use topical moisturizers or emollients, bath oils, oatmeal bath preparations or topical salicylic acid preparations for skin conditions during the study, as well as weak corticosteroids.2 In addition to a placebo group of 27 patients, 28 were randomized to the 10-mg dose, 30 to the 25-mg dose, 29 to the 75-mg dose and 28 to the 150-mg dose.2

The primary endpoint – to test if ixekizumab resulted in a reduction of the Psoriasis Area and Severity Index (PASI) score of at least 75% over baseline at 12 weeks – was achieved by 8% of patients in the 10-mg group, 77% of patients in the 25-mg group, 83% of patients in the 75-mg group and 82% of patients in the 150-mg group.2
ekizumab also resulted in significant improvements in nail and scalp psoriasis. No serious adverse events (AEs) were reported.2

In the New England Journal of Medicine article on the study, the researchers write: “Taken together, these data suggest that inhibition of interleukin-17 may be an effective and targeted therapy for psoriasis. Patients with chronic moderate-to-severe plaque psoriasis treated with ixekizumab had significant improvement in clinical measures during the 12-week treatment period that were rapid and sustained through 20 weeks with continued treatment.”

**BRODALUMAB (AING827)**

Brodalumab, a human, anti-IL-17RA mAb that antagonizes the IL-17 pathway,3 binds to IL-17RA with high affinity and blocks the biologic activity of IL-17A, 17E, 17A/F heterodimer and 17E (interleukin-25).

The results of a Phase II randomized study revealed that brodalumab was significantly more efficacious than placebo as measured by an improvement in PASI scores of 50%, 75%, 90% or 100%. Patients were randomized to receive placebo or brodalumab at doses of 70 mg, 140 mg or 210 mg, administered subcutaneously at day 1 and weeks 1, 2, 4, 6, 8 and 10, or at a dose of 280 mg at day 1 and weeks 4 and 8.3 The placebo was given to 38 patients, while 39 received the 70-mg dose, 39 received the 140-mg dose, 40 received the 210-mg dose and 42 received the 280-mg dose.3

The greatest improvement in PASI scores was seen in patients receiving the higher doses of brodalumab (36.5% in the 140-mg group, 86.3% in the 210-mg group and 76% in the 280-mg group).3 According to the abstract on the study in NEJM, the clinical response was rapid, “with improvements relative to placebo observed in all brodalumab groups as early as 2 weeks,” which is when the first measurements were taken.3 Other indicators of treatment efficacy, such as the extent of body surface area affected, the Physician’s Global Assessment score, Dermatology Life Quality Index scores and skin biomarker measurements, all also improved in patients receiving brodalumab.3

There were more AEs reported in the study of brodalumab than in the study of ixekizumab. The most common AEs were nasopharyngitis, upper respiratory tract infection, arthralgia and erythema at the injection site.3 One patient in the 280-mg dose group had to discontinue treatment because of mild urticaria.3 Three serious AEs were reported: renal colic (1 patient), ectopic pregnancy (1 patient) and neutropenia (2 patients).3 Only the patients with neutropenia had to discontinue treatment, after which laboratory tests returned to normal.3

The researchers conclude: “In this phase II study, brodalumab showed a high level of efficacy in patients with moderate-to-severe plaque psoriasis with a rapid onset of action. These findings also support the important role of interleukin-17RA in the pathogenesis of psoriasis.”3

**SEKINUMAB (AIN457)**

This fully human mAb specifically and rapidly binds to and neutralizes IL-17A.4 In a series of three Phase II trials, this biologic produced quick, significant improvement in patients with moderate-to-severe plaque psoriasis.4

Results were presented at the annual Congress of the European Academy of Dermatology and Venereology (EADV).5 The primary endpoints of the studies, which were designed to evaluate safety and efficacy at different dose and administration regimens, were met for one or more of the doses (25, 75 or 150 mg subcutaneously; 3 mg/kg, 10 mg/kg and 3 x 10 mg/kg intravenously) and regimens (early, monthly and single) studied in each trial.5 In one study, the 150-mg subcutaneous dose once a month resulted in an improvement of at least 75%, as measured by PASI scores, for 81% of patients.4 The second study showed that 83% of patients given an intravenous starting dose of secukinumab experienced at least a 75% improvement of symptoms compared to 10% on placebo.4 In the last study, at week 12, secukinumab was shown to be efficacious in the first month for 55% of patients compared to 2% receiving placebo.4

In all three studies, 60% of patients experienced AEs with secukinumab in the first 12 weeks compared to 61% of with placebo.4 Serious AEs were reported in 3% of patients receiving secukinumab compared to 1% on placebo.4

“These data suggest that AIN457 could potentially bring about a considerable improvement in the lives of patients with moderate-to-severe plaque psoriasis by producing a rapid response and a substantial relief of symptoms,” explains Kim Papp, MD, a dermatologist and one of the investigators on the studies.

**ADDITIONAL INFORMATION**

In the same issue of NEJM that discusses ixekizumab and brodalumab, there is an editorial about those two biologics from Ari Waisman, PhD, of the Institute for Molecular Medicine at the Johannes-Gutenberg University of Mainz in Germany. Dr. Waisman discusses the efficacy of both agents and the significant potential they have for improving the treatment of psoriasis. The article, “To Be 17 Again – Anti-Interleukin–17 Treatment for Psoriasis,” can be found here: http://www.nejm.org/doi/full/10.1056/NEJMe1201071.

The IL-17 agents are also discussed briefly in the April 2012 Biologics in Practice column in this journal. To read more, please visit http://www.thedermatologist.com/content/immunopathogenesis-psoriasis-and-mechanism-biologics.

**References**


5. Probity Medical Research. Novartis phase II data show AIN457 provided rapid and significant relief of symptoms in up to 81% of patients with psoriasis. Available at: http://www.probitymedical.com/?resourceID=995&articleView=individual&articleID=55. Accessibility verified May 3, 2012.