end point of mean change in PASI score was maintained at 1 year. This trial was not powered to evaluate efficacy end points, however. The effect of BI 655066 is being evaluated in an ongoing phase 2b study.

Safety and Efficacy of Dupilumab in Adults With Chronic AD

Written by Jill Shuman

Marius Ardeleanu, MD, Regeneron Pharmaceuticals Inc, Tarrytown, New York, USA, reviewed safety and efficacy results from the phase 2b Study of Dupilumab Administered to Adult Patients With Moderate-to-Severe Atopic Dermatitis [NCT01859988].

Atopic dermatitis (AD) is a common, chronic skin condition induced by a type 2 helper (Th2) T cell–mediated response to various environmental antigens. These cells release cytokines that promote occurrence and recurrence of AD. Two Th2 cytokines thought likely to be involved in the pathogenesis of AD are interleukin (IL)-4 and IL-13 [Lebwohl MG et al. *J Clin Aesthet Dermatol*. 2013]. Dupilumab is a monoclonal antibody that targets the IL-4 receptor α subunit, blocking intracellular signaling of both IL-4 and IL-13. Data from early clinical trials have suggested that dupilumab is safe and efficacious for adults with moderate-to-severe AD [Beck LA et al. *N Engl J Med*. 2014].

The multicenter, international, double-blind, placebo-controlled, randomized, dose-ranging study was designed to test the safety and efficacy of subcutaneous injections of dupilumab in 380 adults with chronic moderate-to-severe AD poorly controlled on current topical medications. Patients were divided into 5 treatment groups. On day 1 of the 16-week study, patients received a loading dose of either 400 or 600 mg. The 5 groups of patients then received dupilumab in doses ranging from 100 mg every 4 weeks to 300 mg every week. All groups were followed for an additional 16 weeks.

The primary end point was percent change in the Eczema Area and Severity Index (EASI) from baseline to week 16. Key secondary end points included the proportion of patients who achieved a reduction of 50%, 75%, or 90% in the EASI (EASI-50/75/90); changes in various measurements of pruritus and skin condition; and safety.

All patients had chronic AD for ≥3 years (EASI≥16), with a documented inadequate response to topical treatments for at least 6 months prior to the screening visit. Patients who had received prior treatment with dupilumab, had an active infection, or had used topical medications for AD within 1 week of baseline were excluded from the trial. Mean patient age was 37 years, and mean duration of time with AD was 31 years.

Patients who received any regimen of dupilumab achieved a significantly greater mean percent change in the EASI compared with placebo (all $P<.0001$); the 300-mg dose given every week produced the greatest percent change. According to Dr Ardeleanu, most of the response was evident within 4 to 6 weeks.

Relative to the secondary end points, almost every dose regimen was statistically more likely to achieve EASI-50/75/90 throughout 16 weeks compared with placebo (P range, $<.05$ to $<.0001$); the only exception was the 100-mg dose once weekly, which did not reach statistical significance for EASI-50. Although patients who took any dose of dupilumab achieved an improved Investigator's Global Assessment response as well as self-reported reductions in pruritus, the 300-mg weekly and every 2-week doses showed the most consistent benefits among all the outcomes.

The most common adverse events were nasopharyngitis, headache, and injection site reactions, all of which were higher in the dupilumab groups. There were no dose-limiting toxicities. Based on these results, Dr Ardeleanu noted that the 2 highest dose regimens will be further tested in a phase 3 trial and that a maintenance study will be done to test whether lower doses of dupilumab can maintain the improvements sustained with higher doses.

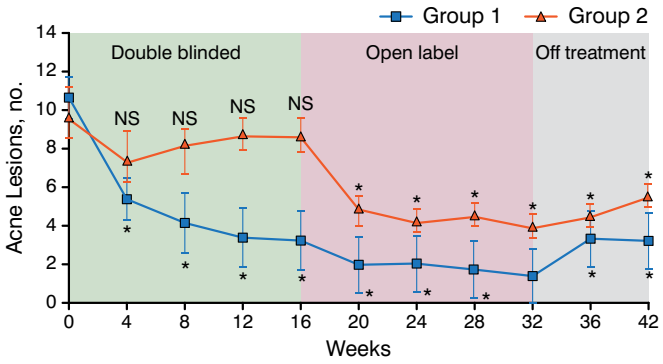
Low-Dose Isotretinoin Is Effective in Adult Acne Vulgaris

Written by Emma Hitt Nichols, PhD

Low-dose isotretinoin reduced the number of acne lesions in adult patients with acne vulgaris beginning at 4 weeks and continuing through 32 weeks, with 40% of patients remaining acne free for 3 years. Marius Rademaker, MD, Waikato Hospital, Hamilton West, New Zealand, presented data from an unpublished follow-up study that evaluated low-dose isotretinoin for the treatment of adult acne.

Adult acne affects up to 50% of the population. Conventional treatment of adult acne is frequently ineffective or unacceptable to patients, however; there is a high dissatisfaction rate due to a slow response, poor total clearance of acne, and a high relapse rate [Rademaker M et al. *J Eur Acad Dermatol Venereol.* 2013]. In addition, few studies have evaluated topical retinoids, systemic antibiotics, or isotretinoin in adults. The purpose of this study was to evaluate the effect of low-dose isotretinoin on low-grade adult acne vulgaris.

Figure 1. Low-Dose Isotretinoin Treatment for Adult Acne



NS, not significant.

*$P < .0001$ from baseline.

Adapted from Rademaker M et al. Isotretinoin 5 mg daily for low-grade adult acne vulgaris—a placebo-controlled, randomized double-blind study. *J Eur Acad Dermatol Venereol*. 2013;28:747–754. With permission from European Academy of Dermatology and Venereology.

In this double-blind, parallel-group study, 60 patients aged 25 to 55 years with low-grade adult acne vulgaris were randomly assigned to receive 5 mg/d of isotretinoin or placebo for 16 weeks, followed by an open-label period of isotretinoin treatment for 16 weeks. Follow-up continued for an additional 10 weeks after treatment ended. The primary end point of the study was difference in acne lesion count and disability score at week 16. The secondary end points included the differences in acne lesion count and disability score at week 32 and at the final follow-up visit.

The number of acne lesions significantly decreased in the isotretinoin arm beginning at week 4 and peaked at week 32 ($P < .0001$), and it was maintained throughout the study, including during the off-treatment follow-up period (Figure 1).

In a follow-up study, 60% of patients reported recurrence of at least one acne lesion at a mean time of 9.1 months. Their acne, however, was less severe at recurrence than what they had experienced prior to isotretinoin treatment. As a result, 60% of patients received further treatment for their acne, including topical retinoids, doxycycline, or isotretinoin. Isotretinoin was restarted by 48% of patients for a median of 6 months, and they continued the medication for a mean of 12.4 months. At the time of the follow-up study, 21% of patients were still taking isotretinoin with a median dose of 10 mg twice per week.

In conclusion, Prof Rademaker stated that, in his opinion, the data from this study suggest that treatment of adult acne with low-dose isotretinoin is effective, because it improves acne by week 4 with continuous improvement up to week 32. In addition, 40% of patients remained acne free by 3 years, and patients reported a very high level of satisfaction. Isotretinoin was well tolerated with few adverse events.

Azithromycin Improved FD Symptoms

Written by Emma Hitt Nichols, PhD

Azithromycin treatment in patients with folliculitis decalvans (FD) resulted in a significant decrease in the number of papules and pustules on the scalp and improved the global subjective score. Rui Oliveira-Soares, MD, CUF Descobertas Hospital, Lisbon, Portugal, presented data from a study that evaluated the effect of azithromycin monotherapy on FD.

Characterized by neutrophilic inflammation of the scalp, FD has an unknown etiology and results in painful, recurrent purulent follicular exudation. The typical treatment for FD includes systemic antimicrobial agents, such as tetracycline antibiotics. However, some tetracyclines may cause hyperpigmentation, particularly in response to sunlight; in contrast, azithromycin is less likely to cause hyperpigmentation and it has been successfully used to treat acne [Hasibur MR, Meraj Z. *Mymensingh Med J.* 2013; Antonio JR et al. *J Dermatolog Treat*. 2008; Innocenzi D et al. *Acta Dermatovenerol Croat.* 2008]. The purpose of this study was to evaluate the safety and efficacy of azithromycin for the treatment of FD.

In this single-arm study, 19 patients with a first diagnosis of FD were enrolled at least 6 months after discontinuing any prior medication. The study treatment was azithromycin monotherapy administered as 500 mg/d for 3 consecutive days every 2 weeks for 6 months. All patients had persistent disease that was either stable or not responsive to prior therapy. The primary end point of the study was the change in the number of intact or crusted papules, or pustules present on the scalp. The secondary end point was change in a global subjective symptoms, including pain, burning sensation, and pruritus.

Treatment with azithromycin resulted in a significant decrease in the number of papular and pustular lesions over 6 months compared with baseline ($P < .0001$). In addition, the patient-reported symptoms decreased at 1 month and had not increased by 6 months.

In conclusion, Prof Oliveira-Soares stated that, in his opinion, the data from this study suggest that azithromycin treatment of FD resulted in a decrease in the number of papular and pustular lesions, as well as improvement in global subjective symptoms. As a result, Prof Oliveira-Soares suggested that azithromycin may be a reasonable alternative to tetracycline therapy, particularly during the summer months.