Prof Szeimies went on to discuss the primary safety end point. The VAS scores were 0.8 and 7.7 ($P<.001$) with DL-PDT and c-PDT, respectively, in COMET-1 and were 0.7 and 4.4 ($P<.001$), respectively, in COMET-2. In COMET-1 and COMET-2, 82% and 91% of patients respectively treated with DL-PDT did not report any pain. In COMET-1, patients were more highly motivated to consider retreatment with DL-PDT than the conventional treatment (93% vs 63%); data were not available for COMET-2.

In summary, data from Australia and Europe suggest that DL-PDT is noninferior to c-PDT in treating mild and moderate AK and that the efficacy is sustained throughout at least 24 weeks for either procedure. Patients reported less pain when they underwent DL-PDT, expressed satisfaction with the procedure, and were motivated to seek out retreatment if necessary.

## IL-23 Blockade With BI 655066 Improves PASI in Psoriasis

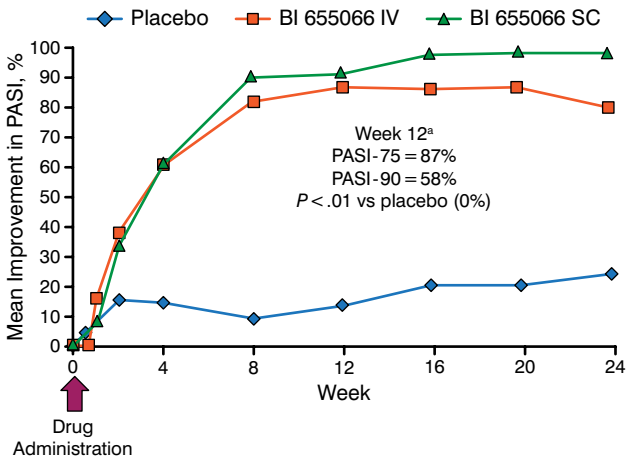
Written by Emma Hitt Nichols, PhD

Interleukin (IL)-23 blockade with a single dose of the monoclonal antibody BI 655066 was safe and well tolerated in the Single Rising Dose Study of BI 655066 in Patients With Moderate and Severe Psoriasis [NCT01577550] presented by James Krueger, MD, PhD, Rockefeller University, New York, New York, USA.

Secretion of IL-23 by myeloid dendritic cells plays a role in the initiation of psoriasis [Lowes MA et al. *Ann Rev Immunol.* 2014]. In addition, chronic psoriasis is maintained, at least in part, by the continued secretion of IL-23, which promotes the secretion of chemokines and antimicrobial peptides by keratinocytes, resulting in amplification that causes further IL-23 secretion. BI 655066 is a monoclonal antibody that selectively targets the p19 subunit of IL-23 to prevent IL-23 activity. The purpose of this first-in-human study was to evaluate the safety and tolerability of BI 655066 in patients with moderate to severe plaque psoriasis.

In this study of 39 patients with moderate to severe plaque psoriasis with a Psoriasis Area and Severity Index (PASI) score ≥12, patients were randomly assigned to receive a single intravenous (IV) dose (0.01, 0.05, 0.25, 1.00, 3.00, or 5.00 mg/kg) of BI 655066 (n=18) or placebo (n=6), and 15 patients were randomly assigned to receive a single 0.25 mg/kg or 1.00 mg/kg dose of subcutaneous (SC) BI 655066 (n=13) or placebo (n=2). End points included safety; PASI at 0, 2, 4, 12, or 24 weeks; and skin biopsies for histology and next-generation RNA sequencing analysis at 0 and 8 weeks.

Figure 1. Effect of BI 655066 on PASI Score




IV, intravenous; PASI, Psoriasis Area and Severity Index; SC, subcutaneous.

[a]IV and SC BI 655066 groups combined.

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The mean change in PASI score was significantly higher among patients who received IV or SC BI 655066 compared with patients who received placebo, in a pooled analysis ($P<.01$; Figure 1).

In patients who received SC BI 655066, the mean improvement in PASI score was about 90% at week 12 and 100% at week 16; PASI-100 was maintained by 66% of patients who entered an optional long-term follow-up period for up to 66 weeks. In addition, immunohistochemical analysis of a skin biopsy sample harvested from a patient who received 0.25 mg/kg of SC BI 655066 demonstrated a decrease in markers associated with psoriasis at 8 weeks, including K16, K167, S100A7, Lipocalin, β-defensin, CD3, CD11c, and DC-lamp. Furthermore, next-generation sequencing analysis found that treatment with BI 655066 resulted in normalization of psoriatic lesions similar to that of nonlesional skin.

Any adverse event (AE) occurred in 20 of 31 (65%) patients who received BI 655066 and in 7 of 8 (88%) of patients who received placebo. Serious AEs, including recurrent alcoholic pancreatitis, recurrent stroke, transient ischemic attack, and myositis, occurred in 13% of patients who received BI 655066 compared with none of the patients who received placebo. Common AEs included nasopharyngitis, headache, and upper respiratory tract infection.

The results of this study show that the novel drug BI 655066 appears to be safe and well tolerated in patients with moderate to severe plaque psoriasis. In a subset of the study patients, the improvement in the secondary

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.