Among patients with Hurley stage II, significantly more adalimumab-treated patients had an abscess and inflammatory nodule count of 0, 1, or 2 (adalimumab 51.8% vs placebo 32.2%; $P \leq .01$). The effect was seen at week 2 and sustained throughout time.

Among patients with a baseline numeric rating scale for pain ≥3, significantly more adalimumab-treated patients had a 30% reduction and ≥1 unit reduction in the Patients' Global Assessment of Skin Pain numerical rating scale based on 24-hour recall of worst pain (adalimumab 45.7% vs placebo 20.7%; $P < .001$). Adalimumab-treated patients also achieved a significantly greater mean reduction from baseline in modified Sartorius score (adalimumab –28.9 vs placebo –9.5; $P < .001$).

At least 1 treatment-emergent adverse event (TEAE) was reported by 57.7% of adalimumab-treated patients and 66.9% of placebo-treated patients. TEAEs reported by ≥5% of adalimumab-treated patients were headache (12.9% of patients) and nasopharyngitis and diarrhea (5.5% each). There were no deaths. Prof Jemec concluded that AEs were comparable to the placebo group and consistent with the safety profile of adalimumab.

DL-PDT Not Inferior to c-PDT in Patients With AK

Written by Jill Shuman

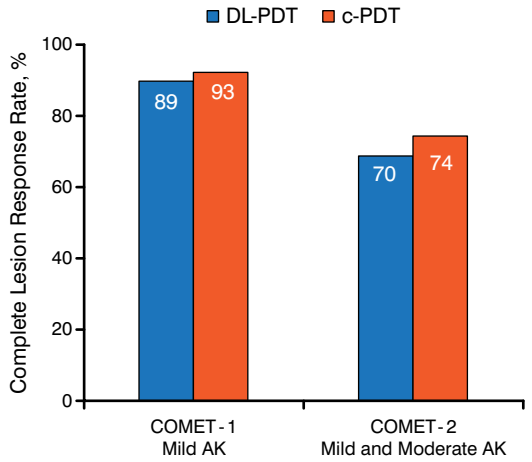
Rolf-Markus Szeimies, MD, PhD, Klinikum Vest Academic Teaching Hospital, Recklinghausen, Germany, discussed the rationale for using methyl aminolevulinate cream (MAL) and exposure to sunlight (daylight photodynamic therapy [DL-PDT]) as an alternative for MAL and conventional photodynamic therapy (c-PDT) to treat actinic keratoses (AKs). Although AKs of the scalp and face respond very well to c-PDT, the procedure is associated with pain and inconvenience [Rubel DM et al. *Br J Dermatol.* 2014; Kennedy JC, Pottier RH. *J Photochem Photobiol B.* 1992]. Previously published data from a series of studies [Wiegell SR et al. *Br J Dermatol.* 2012; Wiegell SR et al. *Br J Dermatol.* 2011; Wiegell SR et al. *Br J Dermatol.* 2009; Weigell SR et al. *Br J Dermatol.* 2008] and an international consensus paper [Wiegell SR et al. *J Eur Acad Dermatol Venereol.* 2012] all suggest that even in Scandinavian countries, DL-PDT is an effective, safe, and more convenient alternative to MAL-PDT as a treatment for many people with AKs.

Prof Szeimies reviewed data from the Intra-individual Comparison of Efficacy and Safety of Metvix Natural Daylight Photodynamic Therapy Versus Conventional Metvix Photodynamic Therapy in Subjects With Mild Actinic Keratoses trial [COMET-1; Rubel DM et al. *Br J Dermatol.* 2014] and the Phase 3b Study of Metvix NDL-PDT Versus Metvix c-PDT in Subjects With Actinic Keratoses [COMET-2; NCT01821391]. Both were randomized, phase 3, noninferiority studies of patients with mild (COMET-1) or mild-to-moderate (COMET-2) AKs.

COMET-1 included 100 Australian adults, and COMET-2 included 108 European patients. In both trials, patients were randomized to a single treatment of DL-PDT to either side of the face and c-PDT plus sunscreen to the other side. They were all followed for an initial 12 weeks; lesions that responded completely after the first 12 weeks were then followed for an additional 12 weeks. The primary efficacy outcome was complete AK lesion response rate per side at week 12. The primary safety end point was the self-reported pain assessment using the Visual Analog Scale (VAS) just after the treatment session at the baseline visit.

In both trials, the majority of patients were men. All were white with a mean age ranging from 67 to 73 years. The mean number of lesions on both sides at baseline in COMET-1 was 14, and it was 9 in COMET-2. At week 12, DL-PDT was noninferior to c-PDT in either trial (Figure 1). In COMET-1, 97% of the lesions that had completely responded at week 12 remained clear after 24 weeks; data were not presented for COMET-2. Prof Szeimies noted that DL-PDT was effective in either sunny or cloudy weather, with a similar rate of complete lesion response at 3 months after 1 session, but emphasized that the procedure will not be successful in rainy weather.

Figure 1. Primary Efficacy End Point at Week 12



AK, actinic keratosis; c-PDT, conventional photodynamic therapy; DL-PDT, daylight photodynamic therapy.

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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

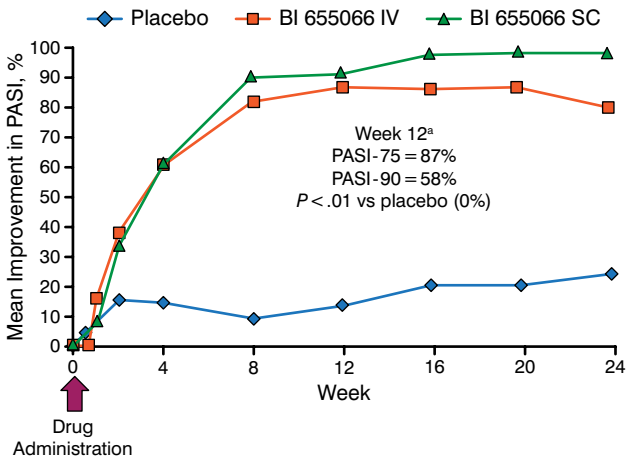
Written by Emma Hitt Nichols, PhD

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.

Reproduced with permission from J Krueger, MD, PhD.

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