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Efficacy of Lasers and PDT for the Treatment of Acne Vulgaris

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Topical 5-aminolevulinic acid with photodynamic therapy (ALA-PDT) has a US FDA approved indication for the treatment of nonhyperkeratotic actinic keratoses (AKs) of the face and scalp with a blue light source for 16 minutes and 40 seconds. ALA is known to accumulate in actinically damaged skin cells, nonmelanoma skin cancer cells, and in the pilosebaceous unit. In the US, the only ALA currently available is Levulan®Kerastick™ (DUSA Pharmaceuticals). The European equivalent, which is the methyl ester of ALA, is marketed as Metvix® (PhotoCure ASA/ Galderma). ALA has US FDA clearance for the treatment of nonhyperkeratotic AKs of the face and scalp. In the US, this drug will be known as Metvixia® and will be available for the treatment of nonhyperkeratotic AKs. PhotoCure ASA will be distributing the methyl ester ALA for the treatment of acne vulgaris.

The first reported clinical trial using ALA in the treatment of acne vulgaris was reported by Hongcharu, et al.[5] The investigators studied 22 individuals treated with ALA, which was incubated for 3 hours, in combination with a 550nm-700nm broad band light source. Significant clinical clearance was evident after 4 weekly ALA-light treatments. The PDT effect (downtime experienced during the healing process) consisted of acneiform folliculitis, post-inflammatory hyperpigmentation, superficial peeling, and crusting. Partial destruction of the sebaceous glands was implicated as the major contributing factor in explaining the mechanism of action. In a case study, Itoh, et al.[25] reported using a 635nm pulsed excimer dye laser and a 4-hour ALA drug incubation in a single patient with intractable acne vulgaris on the face. The treated area remained disease free over the 8-month follow-up period. The patient did experience a PDT effect and exhibited erythema, edema, and crusting immediately after the therapy. In a subsequent study, Itoh, et al.[26] treated 13 acne vulgaris patients with ALA-PDT and a 600nm-700nm light from a halogen light source. All patients showed improvement in their inflammatory lesions, with new lesions reduced at 1, 3, and 7 months post-therapy. Once again, a PDT effect was seen and some recurrence was noted 6 months following therapy.

Goldman used short-contact, full-face ALA-PDT to treat acne vulgaris and sebaceous gland hyperplasia utilizing a 1-hour ALA incubation and therapy with either an IPL or blue light

activation. Relative clearing of the inflammatory acne vulgaris lesions was seen after 2-4 once-weekly ALA-PDT treatments. Treatments were noted to be pain free and no PDT effect was observed.

Gold28 used 30-60 minute ALA drug incubation times and a high-intensity blue light source to evaluate the effects on moderate-to-severe inflammatory acne vulgaris lesions. ALA-blue light treatments were administered once-weekly and patients were evaluated at 1 and 3 months following their final therapy session. Study findings included a response rate of 60%, treatments were well tolerated, and no PDT effects were observed in any of the patients.

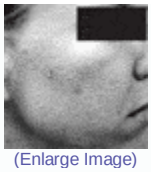
Goldman, et al.[29] treated 22 patients with moderate-to-severe inflammatory acne vulgaris using blue light, with and without the ALA. There was a greater response in the ALA-PDT blue light group than in the blue light group alone, and no adverse events were seen. Taub30 treated 18 patients with short-contact, full-face therapy utilizing blue light sources (ClearLight™ or Blu-U®) or an IPL with radiofrequency (Aurora®, Syneron). The patients received 2-4 treatments over a 4-8 week time period. Improvement was noted at 4 months following the last treatment: 11 out of 18 patients showed 50% improvement, and 5 exhibited >75% improvement.

Gold, et al.[31] reported their experience with short-contact, full face therapy utilizing ALA and an IPL, the Harmony® device (Alma Lasers). Patients received once weekly ALA-IPL treatments and were tracked for up to 3 months following their final treatment. A 72% reduction in acne lesions was seen and no PDT effects were observed.

Two split-face IPL treatments with ALA-PDT were recently reported in the literature. Santos, et al.32 explored the effectiveness of ALA-PDT in moderate-to-severe inflammatory acne vulgaris lesions utilizing ALA-PDT and the Quantum™ IPL device (Lumenis Ltd.). Thirteen patients were treated with short-contact, full face therapy. The IPL was used with a 560nm filter, double pulsed with 2.4/6.0msec, a 25msec pulse delay, and fluences of 26-34J/cm^2. In this split-face analysis, 10 out of 13 patients showed a marked response in the ALA-IPL treated side vs. the IPL side alone after a single treatment. A second split-face clinical trial, performed by Rojanamatin, et al.,[33] confirmed the results described by Santos, et al. They evaluated 14 patients in a split-face fashion with an IPL and found that the ALA-IPL combination was superior to treatment with the IPL alone.

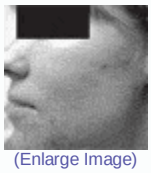
A study by Alexiades-Armenakas34 reported that an average drug incubation time of 45 minutes, and an average of three PDL treatment sessions produced clearance in all 14 patients. Miller and Van Camp[35] also reported on the successful use of ALA and the potassium titanyl phosphate

(KTP) laser in patients with inflammatory acne vulgaris. Clinical examples of acne vulgaris treated with ALA-PDT are shown in Figures 1-3.



(Enlarge Image)

Clinical example of ALA-PDT for the treatment of acne vulgaris. Before treatment (A) and after 2 treatments (B).



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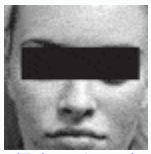
Clinical example of ALA-PDT for the treatment of acne vulgaris. Before treatment (A) and after 3 treatments (B).



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Clinical example of ALA-PDT for the treatment of acne vulgaris. Before treatment (A) and after 3 treatments (B).

At the time of this writing, a large multicenter controlled clinical trial is underway in the US, which is further evaluating the use of ALA in the treatment of moderate-to-severe inflammatory acne vulgaris. The study is investigating the effectiveness of the blue light source in an FDA phase II trial to determine what future role ALA might have in the US.

In Europe, the methyl ester form of ALA has been evaluated in several small clinical trials for the treatment of inflammatory acne vulgaris. In the first report, Wiegell and Wulf36 studied 21 patients with moderate-to-severe inflammatory acne vulgaris. Two treatments were given to these individuals 2 weeks apart. The areas treated were prepared, as is standard practice, for the use of the methyl ester of ALA, by being gently curetted prior to the application of the medication, which was occluded for 3 hours before exposure to a red light source. Twelve weeks after the treatments, there was a 68% reduction in inflammatory acne lesion counts, whereas a control group showed no change in their lesions. All patients in the study experienced a PDT effect consisting of severe erythema, pustular eruptions and exfoliation of the skin. Moderate-to-severe pain during the treatments was also noted. A second European clinical trial, by Horfelt, et al.,[37] looked at 30 individuals with moderate-to-severe inflammatory acne vulgaris lesions. This was a split-face analysis, with a 3-hour under-occlusion drug incubation and exposure to red light; two more treatments were given at 2 week intervals. At the end of the clinical trial, 12 weeks after

the last treatment, there was a statistical reduction in acne lesions of 54% vs. 20% in the control group. Pain and a PDT effect were once again seen in the patients treated. Additional clinical trials are underway in Europe to further evaluate what role the methyl ester of ALA will have in the treatment of moderate-to-severe inflammatory acne vulgaris.