

PDT with Levulan Omnilux LED Pro and Effective

By Mark B. Taylor, M.D., and Inna Prokopenko, R.N.

Photodynamic therapy (PDT) with 5-aminolevulinic acid (ALA, Levulan® Kerastick®, Dusa Pharmaceuticals, Inc., Wilmington, Mass.) and activation with a red or blue LED panel (Photo Therapeutics Ltd., Boldmere, U.K.) offers a safe and efficacious treatment option — with a good cosmetic outcome — for patients who respond poorly to conventional treatments of actinic keratosis (AK), acne, photoaging, actinic cheilitis, or other common dermatologic conditions.

PDT Evolves in Dermatology

In PDT, a photosensitizer is activated by light to produce singlet oxygen and other free radicals that selectively destroy abnormal cells. Early photosensitizers were given systemically and patients had to avoid sun exposure for one month after treatment.

The introduction of topically applied ALA as a photosensitizing agent² reduced the duration of photosensitivity to several days. In ALA-PDT, the photosensitizing agent is absorbed more quickly by abnormal skin than normal skin and converted to photosensitive protoporphyrin IX (PpIX). Phase II and Phase III studies of ALA with blue light activation³ showed that ALA-PDT safely removed non-hypertrophic AKs on the face and scalp. Burning and stinging during treatment resolved within a week and post treatment erythema resolved within four weeks. Another study⁴ showed excellent cosmetic results and low recurrence rate of AKs four years after treatment. In 1999, the U.S. Food and Drug Administration (FDA) cleared Levulan Kerastick



Figure 1. Patient W.T. before, during, and after ALA-PDT with red light activation. Improvement is 75% to 100% in extensive actinic keratoses and 100% in BCC on the left side of the nose.

(5-aminolevulinic acid HCl, Dusa Pharmaceuticals, Inc.) for the treatment of multiple AKs on the head and scalp. A year later, the BLU-U® Blue Light Photodynamic Therapy Illuminator (Dusa Pharmaceuticals) was FDA cleared for the treatment of AKs.

ALA-PDT has also been used to treat basal cell carcinoma (BCC), Bowen's disease, sebaceous disorders (including acne), photorejuvenation, and other cutaneous conditions.¹ Researchers used a variety of laser and non-laser light sources. In 2003, a light emitting diode (OmniLux Blue; Alderm, N.A. [Irvine, Calif.] and Photo Therapeutics Ltd.) was cleared by the FDA for the treatment of moderate inflammatory acne. The

and ves Safe

Table 1. Treatment parameters and results for patients with AK (red light activation unless blue indicated)

Patient	Diagnosis	Treated Areas	ALA contact time (hr)	OmniLux exposure time (min)	Fluence (J/cm ²)	Improvement (%)	Follow-up time (mo)
D.K.	AK	Face	2	20	97.56	50/75	6
C.M.	AK	Face Hands	Overnight Overnight	5 20	24.39 97.56	50/75 50/75	8 8
W.T.	AK BCC	Face/scalp Nose	2 2	20 20	97.56 97.56	75/100 75/100	6 6
D.B.	AK	Face/scalp Arms	Overnight 1.5	16.7 16.7	80 80	75/100 75/100	6 6
K.W.	AK/photoaging	Face/scalp Hands Arms	3 Overnight Overnight	17 20 20	83 97.56 97.56	75/100 75/100 75/100	9 9 9
H.R.	Photoaging/AK	Face	Overnight	16.7	80	75/100	8
D.J.	AK/photoaging	Face Arms Hands Neck/chest	Overnight Overnight Overnight Overnight	16.7 20 20 10	80 80 80 80	75/100 75/100 75/100 75/100	6 6 6 6
K.M.	AK/photoaging	Face Arms Back Chest	Overnight Overnight Overnight Overnight	20 20 20 20	97 97 97 97	75/100 75/100 75/100 75/100	12 12 12 12
SL.	AK BCC	Arms Back Chest Nose	Overnight Overnight Overnight Overnight	20 20 20 20	97 97 97 97	75/100 75/100 75/100 100	8 8 8 8

AK = actinic keratoses.

OmniLux Blue emits spectrally pure 415 nm light that attacks *Propionibacterium acnes*. Light of 633 nm wavelength (red), which penetrates deeper into the dermis to reach glandular tissue, is also available on the OmniLux.

In the following paragraphs, we describe how we evaluated the safety and efficacy of PDT using Levulan Kerastick with 415 or 633 nm diode light activation (OmniLux) for the treatment of skin conditions commonly encountered in a dermatology practice.

Patients Fail or Fear Conventional Therapy

Our 31 patients aged 15 to over 70 had mild, moderate, or severe skin conditions and had either not responded to traditional therapies — isotretinoin for acne and cryotherapy and surgery for sun damaged skin and BCC — or preferred to avoid the adverse effects of these therapies. Diagnoses included severe

acne, sebaceous hyperplasia, AK, photoaging (with and without wrinkles), sun damage, actinic cheilitis, BCC, folliculitis, and rhinophyma. Some patients had two of these skin conditions. We excluded pregnant patients, those having skin infections, with a history of keloid scarring or post-inflammatory hyperpigmentation, receiving other treatment therapies, or unwilling to follow protocol or protect their skin from bright sunlight for 48 hours after application of ALA. We also excluded patients with Fitzpatrick skin types IV to VI because of their perceived higher risk for temporary hyperpigmentation with PDT.

Levulan Contact Time Varied

Our first step was to apply ALA to each area to be treated. We made at least two consecutive applications before exposing these areas to light. For the face, one Levulan Kerastick was usually enough for one treatment session on an area the size of the face. ALA contact time varied from 30 minutes to 18 hours (overnight) and duration of exposure to light varied from 53 seconds to 20 minutes. For most patients, ALA contact time was one to three hours. For topical anesthesia, analgesia, and sedation we used a mixture of lidocaine and tetracaine (Photocaine, University Pharmacy, Salt Lake City, Utah) applied 30 to 45 minutes before light treatment, acetaminophen and oxycodone (Percocet 10/650 mg, p.o., Novartis), and diazepam (Valium, 10 mg, p.o., Hoffman-LaRoche), respectively. We gave anesthetics approximately 30 minutes before applying ALA.

Red Light Used for Most Patients

We gave most patients a single treatment. For all but three patients (Tables 1-4) we activated ALA with

Table 2. Treatment parameters and results for patients with photoaging (red light activation)

Patient	Diagnosis	Treated Areas	ALA contact time (hr)	OmniLux exposure time (min)	Fluence (J/cm ²)	Improvement (%)	Follow-up time (mo)
D.E.	Photoaging/wrinkles	F			97.56	50/75	10
K.L.	Photoaging/wrinkles	Face	2	16.7	80	75/100	7
L.W.	Photoaging/wrinkles	Hands Arms Neck/chest Face	Overnight Overnight Overnight Overnight	17 17 5 2	83 83 24.39 97.56	25/50 75/100 75/100 25/50	7 7 7 7
S.H.	Photoaging/wrinkles/ large pores	Face	2	10	48.78	75/100	5
S.S.	Wrinkles/photoaging	Face	1.5	16.7	80	75/100	12
Cd.M.	Photoaging sun damage	Face	2	20	97.56	75/100	10

IPL = intense pulsed light; RF = radiofrequency
*Treated with Aurora DSR™ (Syneron Medical Ltd., Yokneam Illit, Israel), a combination of intense pulsed light and radiofrequency, before treatment with OmniLux (633 nm). Both treatments were given on the same day.

intense 633 nm light (OmniLux) with air cooling (Zimmer Elektromedizin Corp.) because long wavelength light penetrates deeper into the skin than short wavelength light. Fluences varied from 14 to 97 J/cm² (Tables 1-4). We used 415 nm blue light with the remaining three patients (Tables 1, 3).

The duration of light exposure varied with the disease (Tables 1-4). If multiple treatments were required, we gave them at one month intervals. We instructed patients to avoid exposure to the sun, and all other bright light sources for 48 hours after ALA application.

Patients See Results Quickly

We used digital photography and clinical observation to evaluate and document improvement (Tables 1-4). Independent observers graded improvement as worse, 0-25%, 25-50%, 50-75%, or 75-100%. Follow-up times ranged from three months to over a year.

Improvement was marked in lesions of the face, scalp, hands, and arms. In most cases, improvement was noticeable — even impressive — within one to two weeks after treatment.

Photorejuvenation and AK Removal Excellent for Most Patients

Improvement was 75% to 100% in two of four patients (three of six treated areas, Table 1) with AK only, in four of four patients with both AK and photoaged skin (14 of 14 treated areas, Table 1), in five of six patients with photoaging combined with wrinkles or sun damage (six of ten treated areas, Table 2), and in two patients with AK and BCC (W.T. [Figure 1] and



Figure 2. Patient D.J. before, during, and after ALA-PDT with red light activation. Improvement is 75% to 100% in extensive actinic keratoses and photoaged skin.

Table 3. Treatment parameters and results for patients with acne (red light activation unless blue indicated)

Patient	Diagnosis	Treated Areas	ALA contact time (hr)	OmniLux exposure time (min)	Fluence (J/cm ²)	Improvement (%)	Follow-up time (mo)
K.C.	Cystic acne	Face	1.5	20 (Each side)	97.56	75/100	9
B.J.	Cystic acne	Face	2	20: Turn from side to side	97.56	Worse	6
A.W.	Cystic acne	Face	Overnight	5	14.25	50/75	3
J.H.	Cystic acne	Face	Overnight	7	33.5	75/100	9
J.R.	Inflammatory acne (grade 3)	Face	2.5	20 (each side)	97.56	75/100	8
S.J.	Cystic acne	Face	2	10	48.78	0/25	7
J.M.	Acne (grade 3)/sebaceous hyperplasia	Face	2	17	83	75/100	9
L.R.	Cystic acne/AK	Face	2	16.7	80	0/25	8
L.L.	Cystic acne	Face	0.5	10 (Blue)	28.7	75/100	12
J.D.	Acne (grade 3)/melasma	Face	1.5	8 (Blue)	23	50/75	3.5

AK = actinic keratosis.

S.L., Table 1). In one patient with AK and photoaged skin (D.J., Table 1), blue light activation resulted in 75% to 100% improvement in the face (Figure 2), arms, hands, neck, and chest. Overall, results were excellent in non-facial areas treated; we obtained 75% to 100% improvement in five of six patients. Figures 3a and 3b show the cosmetic improvement in the arms and back, respectively, of one patient (K.M.).

In two patients with AK only (Table 1), improvement in three treated areas was 50% to 75%. In three patients with photoaging and wrinkles (Table 2), improvement was 50% to 75% in one patient (one treated area) and 25% to 50% in two patients (two treated areas).

After treatment, the skin of patients with AK was soft and smooth with no evidence of residual lesion. Excellent cosmetic outcomes were maintained for at least one year in a limited number of patients.

In earlier reports, the use of ALA-PDT with red light activation has produced complete response (CR) rates of 91% to 100% with laser^{5,6} and 71% to 100% with non-laser⁶⁻⁸ light sources. Adverse effects of patients in our study were similar to those of previous studies — burning or stinging during treatment, erythema, edema, and occasional blistering.

In our study, improvement was 75% to 100% in nine of ten patients with photoaged skin, even in non-facial areas. Our results are consistent with those of an earlier study⁹ in which the authors used ALA-PDT with intense pulsed light (IPL) activation for the simultaneous photorejuvenation and AK removal.



Figure 3. Patient K.M. before and after ALA-PDT with red light activation. Improvement is 75% to 100% in extensive actinic keratoses and photoaged skin of the arms (a) and back (b).

Using a 615 nm cutoff filter in the non-coherent light source and applying ALA for four hours, these researchers cleared 33 of 38 AKs with two treatments, and cosmetic results were excellent.

Our study differs from earlier studies in our use of the OmniLux system as a source of red light. In previous studies, fluences of lamps and dye lasers ranged from 10 to 300 J/cm². In our study, fluences were lower, ranging from 24 to 97 J/cm². Touma *et al.*¹⁰ applied ALA one, two, and three hours respectively before activation with blue light. In this study, AK lesions were significantly reduced and photodamaged skin was significantly improved. The results of Touma *et al.* are consistent with the 75% to 100% improvement in one of

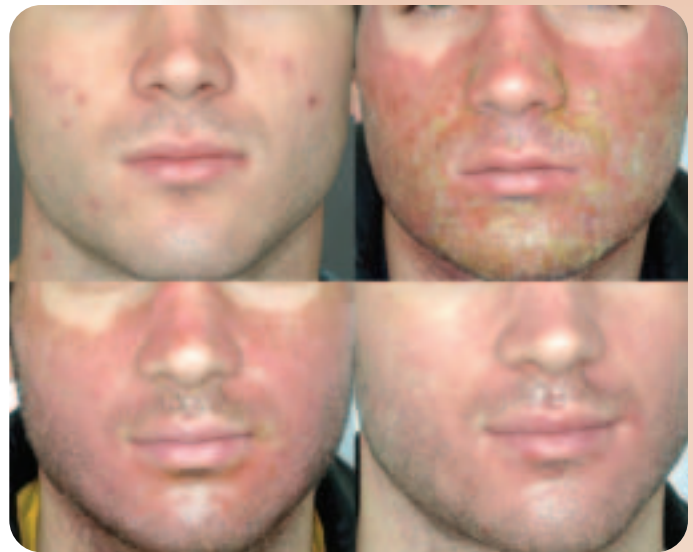


Figure 4. Patient (J.H.) with cystic acne before (upper left) and three days (upper right), five days (lower left), and ten days (lower right) after ALA-PDT with red light activation. The upper right photo shows the acute folliculitis that can occur a few days after activation with red light. Improvement is 75% to 100% in lesions.

our patients having both AK and photoaged skin, in which circumstances blue light activation was used.

Improvement Variable in Acne

Our results for ten acne patients (Table 3) were encouraging. Seven of the ten patients had cystic acne. Improvement was 75% to 100% in three patients. ALA contact times and light exposure times were short in two of these three greatly improved patients with cystic acne. Among the remaining four patients, ALA-PDT with red light activation produced 50% to 75% improvement in one patient (A.W.) without further treatment after an initial flare. ALA-PDT resulted in only slight improvement (0-25%) in two patients (S.J., L.R.).

Figure 4 shows one patient (J.H.) with cystic acne at different stages of treatment and improvement. Figures 5 and 6 show the 75% to 100% improvement in lesions of cystic acne in two additional patients, one with red light activation (K.C.) and the other (L.L.) with blue light activation, respectively. One teenaged patient (B.J.) with severe cystic acne had a sustained flare of the acne that persisted for several months after treatment. The patient had been in contact with ALA for two hours and exposed to 633 nm red light for 20 minutes. The patient was subsequently treated successfully with isotretinoin. For the three patients with Grade 3 inflammatory acne, improvement was 75% to 100% in two, and 50% to 75% in the remaining patient.

The use of blue rather than red light for ALA activation has recently shown encouraging results. In one

patient with cystic acne, 30 minute contact time with ALA and blue light activation produced 75% to 100% improvement. The use of blue light for ALA activation of ALA in patients with acne has been reported by Goldman and Boyce.¹¹ In a patient with Grade 3 inflammatory acne, improvement was less at 50% to 75% with 1.5 hours ALA contact time and eight minute activation with blue light.

Our experience has shown that improvement in acne is greater (e.g., 75%-100%) when ALA contact time is short (e.g., 30 minutes), 415 nm blue light (OmniLux) exposure time is short (e.g., eight minutes), and multiple treatments are given. In a few patients with longer ALA contact time and longer light exposure time, acne lesions flared up, not unlike the acute eruptions described in patients in which ALA contact time was three hours.¹² We chose not to give these patients additional aggressive treatments.

Folliculitis, BCC, Actinic Cheilitis, and Rhinophyma Need Multiple Treatments

Severe folliculitis after treatment (J.H., Figure 4, upper right photo) sometimes caused acne flare-ups that continued for weeks. One patient (F.M.) was treated with ALA-PDT for scalp folliculitis, lower lip actinic cheilitis-leukoplakia type lesions, and BCC. One ALA-PDT treatment resulted in 0% to 25% improvement in the folliculitis and 100% improvement in the BCC, whereas two ALA-PDT treatments provided 25% to 50% improvement in the actinic cheilitis. This patient had 100% clearing (biopsy-proven) of actinic cheilitis with a subsequent treatment using vigorous microdermabrasion before overnight application of ALA. (Before receiving PDT, this patient had failed treatment with 5-



Figure 5. Patient (K.C.) with cystic acne before and after ALA-PDT with red light activation. Improvement is 75% to 100% in lesions.

fluorouracil, cryotherapy, and laser ablation. The small improvement after the first two ALA-PDT treatments may be attributable to scarring from previous treatments, thus preventing adequate absorption of ALA.)

In two other patients with actinic cheilitis (Table 4), ALA-PDT resulted in 75% to 100% improvement, although follow-up time was limited: one week in patient S.B. Conventional treatment options for actinic cheilitis include cryosurgery, 5-fluorouracil, electrocautery, carbon dioxide laser, and scalpel vermilionectomy.¹³ In 1996, Stender *et al.*¹⁴ used ALA-PDT with incoherent visible light to treat three AC patients who had failed conventional therapy. Patients reported burning during irradiation. The treatment was successful and 6 to 12 month follow-up revealed no recurrence. Our results are consistent with these.

Results of four patients with BCC were encouraging, with improvement for three patients with superficial BCC at 100% (Table 4). The fourth patient (C.H.) with nodular BCC chose to have the remaining tumor surgically excised, although additional PDT may have provided 100% improvement. In previous studies, the use of ALA-PDT has been more successful in the treatment of superficial BCC than nodular BCC, perhaps due to greater lesion thickness and limited penetration of ALA and light.¹ In one patient with mild rhinophyma (Table 4), a single ALA-PDT session resulted in 50% to 75% improvement, while a second session increased the level to 75% to 100%. To our knowledge, this is the first reported case of rhinophyma treated

Table 4. Treatment parameters and results for patients with actinic cheilitis, BCC, folliculitis, rhinophyma, photoaging, or combination (red light activation)

Patient	Diagnosis	Treated Areas	ALA contact time (hr)	OmniLux exposure time (min)	Fluence (J/cm ²)	Improvement (%)	Follow-up time (mo)
D.S.	Actinic cheilitis	Lower lip	2	12	58.54	75/100	9
S.B.	AK/actinic cheilitis	Upper, lower lip	1.5	20 each	97.56	75/100	0.25 (1 wk)
F.M.	Actinic cheilitis (2 Tx)*	Lower lip	Overnight (1 st Tx), 3 (2 nd Tx)	20 (each Tx)	97.56	25/50	9
	BCC	Nose	3	20	97.56	100	9
	Folliculitis	Scalp	3	20	97.56	0/25	9
I.B.	BCC	Nose	2	16.7	80	100	7
C.H.	BCC	Nose	2	20	97.56	0/25	8
S.L.	BCC	Scalp	Overnight	20	97	100	8
	BCC	Nose	Overnight	20	97	100	8
W.T.	BCC	Nose	2	20	97.56	75/100	6
C.O.	Rhinophyma/photoaging	Nose	3	20	97.56	50/75	8
	Rhinophyma	Nose Tx #2	3	20	97.56	75/100	4

BCC = basal cell carcinoma
*Treated with microdermabrasion before applying ALA on second treatment.

with ALA-PDT. Since ALA-PDT has efficacy in sebaceous gland disorders, it is reasonable that the technique would be an effective treatment of rhinophyma.

PDT Not Perfect

After PDT, the skin of patients had the appearance of mild to severe sunburn that healed within several days to more than one week. Pain, swelling, blisters, scabs, crusts, folliculitis, and post-inflammatory erythema were noted during some of the treatments. These effects were minimized by: (1) limiting the ALA contact time to 30 minutes to one hour, (2) spreading the treatment over several sessions, (3) Zimmer cooling during treatment, (4) limiting light exposure time, and (5) ice packing treated sites.

Results Encouraging, More Studies Needed

When traditional treatments fail or patients are concerned about prolonged systemic drug use, PDT with ALA and 633 nm light (or occasionally 415 nm with the OmniLux or 417 nm with the BLU-U blue light) appears to be an efficacious and safe alternative for the treatment of AKs, photoaging, and acne. Our encouraging results warrant additional studies on the use of ALA-PDT in the treatment of severe acne, sebaceous hyperplasia, actinic cheilitis, folliculitis, and rhinophyma. For acne patients, we currently use shorter ALA incubation times than those reported in this study. Our results are excellent, patient satisfac-



Figure 6. Patient (L.L.) with cystic acne before and after ALA-PDT with blue light activation. Improvement is 75% to 100% in lesions.

tion is high and we see fewer immediate and post treatment side effects. ■

Editor's Note: Dr. Taylor is a dermatologist in private practice at Gateway Aesthetic Institute and Laser Center, Salt Lake City, Utah. Ms. Prokopenko is a dermatology nurse in practice with Dr. Taylor. Dr. Taylor has received discounted equipment from Alderm, N.A., LLC, and Dusa Pharmaceuticals, Inc.. He has also received honoraria for speaking at seminars for Dusa Pharmaceuticals, Photo Therapeutics Ltd., and for Alderm. Ms. Prokopenko has no financial interest in any product in this study. Dr. Taylor and Ms. Prokopenko received no funding for this study.

All photos courtesy of Mark B. Taylor, M.D.

References

1. Taub AF. Photodynamic therapy in dermatology: history and horizons. *J Drugs Dermatol* 2004; 3(1 Suppl):S8-S25.
2. Kennedy JC, et al. Photodynamic therapy with endogenous protoporphyrin IX: basic principles and present clinical experience. *J Photochem Photobiol B* 1990; 6:143-148.
3. Jeffes EW. Levulan: the first approved topical photosensitizer for the treatment of actinic keratosis. *J Dermatolog Treat* 2002; 13 Suppl 1:S19-S23.
4. Fowler JF Jr, Zax RH. Aminolevulinic acid hydrochloride with photodynamic therapy: efficacy outcomes and recurrence 4 years after treatment. *Cutis* 2002; 69(6 Suppl):2-7.
5. Calzavara-Pinton PG. Repetitive photodynamic therapy with topical delta-aminolevulinic acid as an appropriate approach to the routine treatment of superficial non-melanoma skin tumours. *J Photochem Photobiol B* 1995; 29:53-57.
6. Jeffes EW, et al. Photodynamic therapy of actinic keratosis with topical 5-aminolevulinic acid. A pilot dose-ranging study. *Arch Dermatol* 1997; 133:727-732.
7. Fijan S, et al. Photodynamic therapy of epithelial skin tumors using delta-aminolevulinic acid and desferrioxamine. *Br J Dermatol* 1995; 133:282-288.
8. Szeimies RM, et al. Photodynamic therapy with topical application of 5-aminolevulinic acid in the treatment of actinic keratoses: an initial clinical study. *Dermatology* 1996; 192:246-251.
9. Ruiz-Rodriguez R, et al. Photodynamic photorejuvenation. *Dermatol Surg* 2002; 28:742-744.
10. Touma D, et al. A trial of short incubation, broad-area photodynamic therapy for facial actinic keratoses and diffuse photodamage. *Arch Dermatol* 2004; 140:33-40.
11. Goldman MP, Boyce SM. A single-center study of aminolevulinic acid and 417 NM photodynamic therapy in the treatment of moderate to severe acne vulgaris. *J Drugs Dermatol* 2003; 2:393-396.
12. Hongcharu W, et al. Topical ALA-photodynamic therapy for the treatment of acne vulgaris. *J Invest Dermatol* 2000; 115:183-192.
13. Dufresne RG Jr, Curlin MU. Actinic cheilitis. A treatment review. *Dermatol Surg* 1997; 23:15-21.
14. Stender IM, Wulf HC. Photodynamic therapy with 5-aminolevulinic acid in the treatment of actinic cheilitis. *Br J Dermatol* 1996 Sep; 135:454-6.