

# New Acne Tx Approaches

Supplement to Aesthetic Buyers Guide® • July/August 2004

## Levulan Photodynamic Therapy Offers Effective Acne Treatment Alternative

The rapidly increasing interest in Levulan photodynamic therapy (PDT) from DUSA Pharmaceuticals, Inc. (Wilmington, Mass.) to treat acne and other medical conditions can largely be traced back to the efforts of Rox Anderson, M.D., research director of photomedicine at the Wellman Center, Massachusetts General Hospital, Boston. “I think light-activated drugs are extremely powerful,” Dr. Anderson said. “The use of topical 5-aminolevulinic acid (ALA) is one of the early examples of what I expect to become a growing number of diverse drugs in the near future. I believe we are near the beginning of this cycle of development — not the middle or the end.”

It was four years ago, at the 2000 annual meeting of the American Society for Laser Medicine and Surgery (ASLMS), that Dr. Anderson presented his seminal research on ALA PDT to treat acne. “This was the first paper to demonstrate that ALA would act as a light-activated drug against acne. There are basically two mechanisms involved at different doses. In the study, we were able to demonstrate that treatment inactivates the bacteria in the hair follicles that is part of the reason people develop acne. But much more exciting is that we were able to show that at high doses, treatment actually shuts down the sebaceous gland in the skin. This is great news because it has a long lasting effect. There was a strong effectiveness against even severe acne.”

Dr. Anderson’s original exposure to the novel compound was as an investigator for skin cancer. “When ALA enters the skin, it becomes metabolized. The skin cells turn it into a photosensitizer called porphyrin. Earlier, we had conducted a study showing that sebaceous glands were the most active part of the skin for producing porphyrins. Sebaceous glands are the root cause for the formation of acne.”

“Although there are many different treatments for acne, we have no cures,” observed Dr. Anderson. “We really need a cure, something that has a very long-term effect and treats the activity of the sebaceous gland. Drugs like isotretinoin (Accutane) are the only proven therapy to markedly impact the sebaceous gland. However, Accutane has fairly toxic side effects. We felt with our 2000 meeting presentation that we were on to something that could be used with a better safety profile and would have a long lasting effect against the disease.”

A separate study of ALA, around the same time, was conducted in Japan by Yoshiyasu Itoh, M.D., Ph.D. “Those results were similar to ours,” Dr. Anderson conveyed. “However, back in 2000, ALA was not approved for anything. It was an experimental drug. Since then, the drug is on its way to being embraced by the aesthetic community. ALA is now FDA approved for the treatment of actinic keratoses. Because the drug is approved, physicians can actually order it and many have begun off-label use to treat

*“This is great news because it has a long lasting effect. There was a strong effectiveness against even severe acne.”*

*- Rox Anderson, M.D.*



acne. I'm also optimistic about the recent work of looking at different light sources to activate ALA. The potential to use flashlamps, which are very fast treatment sources, with ALA to treat acne is certainly exciting."

As a physician, Dr. Anderson considers himself somewhere in the middle when it comes to implementing a wide range of applications for new technologies. "I

***"Because Levulan PDT has shown that it can be very effective in treating acne, physicians are now starting to incorporate this therapy creatively into their practices."***

like to undertake experiments and come up with new approaches to things. But it takes awhile before we really understand where it fits into the whole picture. Because Levulan PDT has shown that it can be very effective in treating acne, physicians are now starting to incorporate this therapy creatively into their practices.

There is a kind of clinical creativity going on. ALA PDT actually treats a number of aspects of chronic sunlight injury to the skin. But I don't ever expect ALA to be able to remove blood vessels. PDT therapy really is meant to be used synergistically with lasers and other modalities of treatment."

**Overall, Dr. Anderson** believes that the use of Levulan PDT will continue to grow. "I think it will be useful for acne and other follicular disorders of the skin. My guess is that it will be used in two different modes. One is a low dose maintenance mode. I can even imagine combining ALA with sunscreens and letting the sun do the work for you. This would be a totally different approach. The other mode would be a high dose, office-based procedure. I predict this approach will someday be used for severe acne. I also believe ALA has the potential to be as effective as oral retinoids. So ALA will likely become a very popular approach. But I don't think we will see ALA replacing our use of creams, topical retinoids, antibiotics and benzoyl peroxide." ■

## Clinical Roundtable: Levulan PDT Acne Tx

**Editors Note:** For this news article, we interviewed a select group of leading researchers to elicit their views and clinical experience regarding the use of Levulan PDT to treat acne.

***Why did you add Levulan to your practice for the treatment of acne?***

**Macrene Alexiades-Armenakas, M.D.** – Following the discovery that ALA in combination with the long pulsed pulsed dye laser (LP PDL) was safe and effective in the treatment of actinic keratoses (*Alexiades-Armenakas and Geronemus, Arch Derm, October 2003*), we noted improvement in sebaceous hyperplasia and acne rosacea as well. We followed this up with the first study on the treatment of acne using ALA with the LP PDL vs. ALA PDL, which was published in abstract form and which I presented at ASLMS in 2003 (*Alexiades-Armenakas, et al, American Society for Laser Medicine and Surgery Abstracts, Anaheim, April 2003*). It has reproducibly shown to be effective in the treatment of both comedonal and inflammatory and cystic acne.

***"We needed an aggressive treatment for acne patients who did not feel comfortable taking antibiotics or Accutane."***



- Dore Gilbert, M.D.

**Gerald Bock, M.D.** – We had the BLU-U lamp (from DUSA) available and wanted alternative options for our acne patients.

**Dore Gilbert, M.D.** – We needed an aggressive treatment for acne patients who did not feel comfortable taking antibiotics or Accutane. Many patients don't want to take Accutane due to the numerous systemic side effects – dryness, scaling, achy joints, the birth control pill issue for women, and so on. If patients are given an option, they will usually choose a less complicated route.

In addition, a recent report in the *Journal of the American Medical Association (JAMA)* implicates prolonged use of antibiotics with invasive breast cancer.

Until that study is proven to be a faulty study, I have an obligation to my patients, particularly my female patients, to make them aware and allow them to choose which course of treatment they are most comfortable with. Frankly, anytime there is an alternative to an existing treatment that is riddled with as many side effects as the current traditional acne regimens, I feel obligated to investigate it. As it turns out, Levulan and PDT are proving to be exceptional alternatives for treating acne.

**Flor Mayoral, M.D.** – There have been several reports that show ALA PDT to be effective. Even though Accutane has been the gold standard for the treatment of severe acne, its cost, potential teratogenicity and the side effect of depression in rare patients have made some parents unwilling to allow their teenagers to take this medication. Levulan provides me a viable treatment option for these patients.

**Mark Nestor, M.D., Ph.D.** – Some standard treatments for acne have significant limitations. For cystic acne, in particular, the two treatments that are somewhat effective are long-term oral antibiotics and Accutane. However, as mentioned, a recently published study indicates that long-term oral antibiotics may be associated with breast cancer in women. Similarly, Accutane is becoming harder and harder to prescribe. So we have limited ability to treat cystic acne patients. Studies seem to suggest that PDT may hold the key. In my experience, I've had some wonderful results treating cystic acne with Levulan PDT along with either the pulsed dye laser or the BLU-U lamp.

**Donald F. Richey, M.D.** – I became very interested in Levulan when I realized that its primary function was to reduce the size and activity of the sebaceous oil

*“Studies seem to suggest that PDT may hold the key. In my experience, I’ve had some wonderful results treating cystic acne with Levulan PDT along with either the pulsed dye laser or the BLU-U lamp.”* - Mark Nestor, M.D., Ph.D.



gland. Also, when I heard that it was increasing the protoporphyrin destruction of the bacteria, I realized that it had a dual effect. We initially began Levulan as a secondary treatment in our practice. This was for people who had already had two or three treatments of Accutane and were frustrated. They did not want to deal with the side effects of the drug. We felt that the Levulan worked in a similar fashion to Accutane. We also have a number of people in our practice who are holistically committed and refuse any type of oral medication, including antibiotics or Accutane. Yet, they have severe cystic scarring acne, and need advanced treatment beyond the traditional topical treatments.

We also find that Levulan is a wonderful treatment for adult acne. Many of these patients have tried every topical and oral medication, but remain frustrated. We are now beginning to use Levulan as a frontline treatment for acne when anticipating prolonged treatment with either systemic antibiotics and/or Accutane. The results have been marvelous.

### ***How does Levulan fit into your acne treatment regimens?***

**Dr. Alexiades-Armenakas** – For patients who have failed systemic antibiotics, topical treatments, and are not candidates or are unwilling to take Accutane, laser options are recommended, including PDT.

**Dr. Bock** – We are still evaluating ALA PDT, but it appears that the BLU-U lamp with Levulan is much more effective than the blue light alone.

**Dr. Gilbert** – Levulan PDT has become the primary treatment modality of choice for pustular or cystic acne.

*“We are now beginning to use Levulan as a frontline treatment for acne when anticipating prolonged treatment with either systemic antibiotics and/or Accutane.”*

- Donald F. Richey, M.D.



If patients have mild acne, then I am inclined to use the BLU-U lamp by itself.

**Dr. Mayoral** – Levulan is a great alternative for those who have failed Accutane and also for those patients who fail treatments because of non-compliance. It is simple, effective and has minimal side effects.

**Dr. Nestor** – We use Levulan to treat moderate-to-severe nodular papular and papular cystic acne, typically three sessions. We can use Levulan in combination with BLU-U light alone or in combination with topicals.

**Dr. Richey** – Levulan is increasingly becoming the primary a line of defense in our practice for treating acne.

### What light sources and treatment protocol do you typically use?

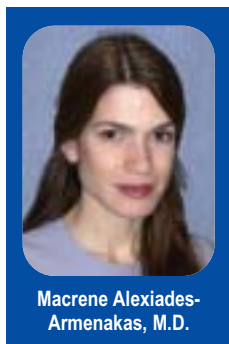
**Dr. Alexiades-Armenakas** – The Vbeam pulsed dye laser (Candela Corporation, Wayland, Mass.) for inflammatory acne and the BLU-U lamp for comedonal, each following a one hour incubation with Levulan.

**Dr. Bock** – We do an acetone preparation and leave the Levulan on for at least one hour. The BLU-U light exposure is between 8 and 20 minutes. Most of the time we use 15 minutes of BLU-U light with Levulan.

**Dr. Gilbert** – The light sources that we typically use for Levulan PDT are the BLU-U and intense pulsed light (IPL). The blue light treatment begins with a very mild scrub with acetone. We then evenly apply the Levulan to the affected areas of the face, neck or back. We allow approximately 30 minutes for incubation, and then expose the patient to the BLU-U for eight minutes.

The IPL protocol is the same, except of course for the light source. We use 3.0, 6.0 IPL treatment with an energy setting of 30 J/cm<sup>2</sup>. After we perform one pass with the IPL, the patient sits for two to four minutes in the BLU-U in order to expose the area or areas to an additional wavelength of light. This also ensures coverage of any areas that may have been missed by the IPL treatment.

**Dr. Mayoral** – I use the BLU-U or the Vbeam laser for my acne patients. The patients will first have a micro-



Macrene Alexiades-Armenakas, M.D.



Before Tx



One year after ALA PDT Tx

Photos courtesy of Mark Nestor, M.D., Ph.D.

dermabrasion, then the Levulan Kerastick is applied. We allow the Levulan to incubate for approximately 45 minutes. The patients that are receiving the BLU-U will be exposed to this light source for 12 minutes. For patients receiving treatment with the Vbeam, we use the following settings: two passes with 50% overlap, a 10 mm spot size, and a 6 ms pulse duration at 7 J/cm<sup>2</sup>.

**Dr. Nestor** – The most common treatment protocol is about three sessions, roughly three weeks apart, using Levulan anywhere from 30 minute to 60 minutes after microdermabrasion. This is followed by pulsed dye laser at low fluence and nonpurpuric doses. We especially use the BLU-U lamp in darker skinned individuals because the pulsed dye laser may have more of a problem getting through to the pigment. We can also substitute an IPL device, again at fairly low fluence, 24 to 26 J/cm<sup>2</sup>.

***“The most common treatment protocol is about three sessions, roughly three weeks apart, using Levulan anywhere from 30 minute to 60 minutes after microdermabrasion.”***

**Dr. Richey** – For acne, we also use the BLU-U with Levulan. We start with a 30 minute incubation after an acetone scrub. We typically give the patient 12 minutes of actual light exposure. We plan on four sessions at one week intervals. We sometimes increase the drug incubation period, depending on the erythema that develops after the treatments. We also sometimes use IPL, but that is only for our patients undergoing photorejuvenation.

***How do your patients respond? Please summarize your clinical results and observations.***

**Dr. Alexiades-Armenakas** – Typically, they are all cleared in two to four treatments, spaced three weeks apart.

**Dr. Bock** – We have only treated a limited number of patients. But we have seen a spectacular result in one adult male who was on continuous Accutane, antibiotics and anti-inflammatory agents for two and a half years, without clearing. He cleared dramatically after a single BLU-U lamp and Levulan treatment. He also remained clear for a month, when he had a second treatment, and still remains clear several weeks later.

**Dr. Gilbert** – Most of our patients have an immediate, minimal, erythematous reaction. Within two to twelve hours, most patients will develop more erythema. However, the amount of erythema is not predictable. Some patients may have only a mild degree of erythema, while others will have erythema followed by scaling for another three to four days.

Our clinical results have been very encouraging with about an 80% success rate. After two to four treatments, most patients are acne free, or have a significant improvement in their acne condition for six months to one year. However, some patients require maintenance treatments after about six months. Maintenance treatments follow the same protocol as the initial treatments, but they are only done on an ‘as needed’ basis.

**Dr. Mayoral** – My patients tolerate the BLU-U lamp and Levulan combination very well. They do not complain of pain and are careful to stay out of the sun for 48 hours after application of the Levulan. Their clinical response is good. To date, the response has been good in greater than 60% of patients.



The Vbeam also renders a great response, although some patients complain of pain. I have seen a couple of patients that became a little edematous for a couple of days when I combine this laser with the ALA. This resolves quickly without any problem.

**Dr. Nestor** – Overall, about 60% of our patients realize greater than 80% long-term reduction in their acne. We

have followed some patients close to two years who have remained clear. With three treatments, results are similar with Accutane. About 20% to 30% of patients require more than three sessions.

**Dr. Richey** – Our acne patients have responded very satisfactorily. We have had a few minimal responders, and we have had some almost miraculous responders. Some of our patients are absolutely thrilled that they have been able to clear their cystic scarring acne without having to take any type of systemic medication or spend months and months using topical preparations.

***“Levulan PDT could become a first line modality in the treatment of acne.”***

*- Gerald Bock, M.D.*



***What role will Levulan PDT fill in the treatment of acne versus systemic pharmaceuticals and topicals?***

**Dr. Bock** – If our initial experience is borne out, Levulan PDT could become a first line modality in the treatment of acne. Its low side effect profile combined with significant effectiveness could be very attractive.

**Dr. Gilbert** – In the future Levulan PDT will become one of the mainstay treatments for pustular and cystic acne. I’m very excited about adding Levulan PDT to my practice. It is proving to be a great option for my patients who don’t wish to, or cannot, take Accutane or antibiotics to treat their acne.

In addition, the process of Levulan PDT has numerous ancillary cosmetic benefits. For older patients, Levulan PDT therapy also treats actinic keratoses. The procedure can also diminish, if not eliminate, brown spots and even overall pigmentation. It can tighten pores, prevent further acne scarring, and smooth existing acne scars as well as fine lines.

**Dr. Mayoral** – The use of Levulan PDT for the treatment of acne has the potential for being very effective with less incidence of side effects than oral medications.

It could also be more economical for insurance companies and patients.

**Dr. Nestor** – Topicals can be used with Levulan PDT without a problem. The idea is to stay away from systemic medications when necessary. Levulan can also be used as augmentation for patients who are on systemic agents, but not responding well. Levulan PDT can fit in anywhere because there are no systemic effects.

Almost everything we do as physicians is really combination therapy. Whether it is PDT or merely BLU-U light, I have found that combination therapy works the best. For instance, the vitamin A related topical drug adapalene (Differin) is truly great for comedonal acne, and can help enhance all treatments. In fact, we're preparing to start a half-face study comparing Differin and BLU-U together versus the BLU-U lamp alone for mild to moderate acne.

**Dr. Richey** – I feel Levulan will be a very important part of acne treatment, and will be a very competitive product to systemic pharmaceuticals. The problems



Before Tx

After Tx

with Accutane are multiple, and with further restrictions from the FDA, this is going to be a difficult treatment program to orchestrate. We also feel that for the patient who takes oral antibiotics, the inherent problems of photosensitivity, yeast infections and the controversy over breast cancer must all be carefully weighed. I am thrilled that we can now offer an alternative topical treatment for treating mild through severe acne. Our patients have more choices, and we can customize our Levulan PDT treatments to their particular problems and preferences. ■

## ROUNDTABLE PARTICIPANTS:

**Macrene Alexiades-Armenakas, M.D., Ph.D.**

A dermatologist in private practice in New York City and a clinical instructor of dermatology at the Yale University School of Medicine.  
voice (212) 570-2067  
fax (212) 861-7964  
email: dralexiaades@nyderm.org

**Gerald Bock, M.D.**

A dermatologist in private practice in Stockton, Calif.  
voice (209) 957-0720  
fax (209) 957-0801  
email: gnbock@deltaderm.com

**Dore Gilbert, M.D.**

An associate clinical professor of dermatology at the University of California, Irvine. For the past 12 years, he has also served as chief of dermatology at HOAG Memorial Hospital in Newport Beach, Calif.  
voice (949) 718 1222  
fax (949) 718 1220  
email: drgilbert@oco.net

**Flor Mayoral, M.D.**

A dermatologist in private practice in Miami, Fla.  
voice (305) 665-6166  
fax (305) 662-4649  
email: flormayoral@aol.com

**Mark Nestor, M.D., Ph.D.**

A clinical associate professor of dermatology and dermatologic surgery at the University of Miami School of Medicine in Florida.  
voice (305) 933-6716  
fax (305) 933-3853  
email: nestormd@admcorp.com

**Donald F. Richey, M.D.**

A cosmetic dermatologist in private practice in Chico, Calif.  
voice (530) 342-3686  
fax (530) 342-4199  
email: drichey132@aol.com