

Treatment of Acne Vulgaris With a Pulsed Dye Laser

A Randomized Controlled Trial

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ACNE VULGARIS IS AN EXCEEDINGLY common skin disorder that carries the potential for significant psychosocial morbidity.¹⁻³ Given that this condition occurs in the vast majority of individuals at some point during adolescence or adult life, effective treatment is of major importance. While conventional forms of therapy provide adequate control of the disorder for many patients, most medications used to treat acne have various drawbacks in terms of potential adverse effects or inconvenience for the patient.⁴⁻⁸

Several physicians have reported a positive response among acne patients treated with various forms of phototherapy.⁹ Exposure to blue, red, violet, and ultraviolet light sources has reportedly resulted in reductions in lesion counts.¹⁰⁻¹³ Absorption of light of specific wavelengths by endogenous porphyrins contained in *Propionibacterium acnes* is believed to produce phototoxic effects that kill the bacteria. In addition,

Context The high prevalence of acne vulgaris and its significant morbidity underscore the need for convenient, low-risk, and efficacious therapy. Treatment with various lasers has been reported to improve acne.

Objective To evaluate the clinical efficacy of pulsed dye laser therapy in the treatment of acne.

Design, Setting, and Patients Randomized, single-blind, controlled, split-face clinical trial of a volunteer sample of 40 patients aged 13 years or older with facial acne conducted at an academic referral center from August 2002 to September 2003.

Intervention One or 2 nonpurpuric pulsed dye laser treatments to half of the face (fluence of 3 J/cm²), serial blinded clinical assessments (lesion counts), and grading of acne severity using standardized bilateral serial photographs.

Main Outcome Measures Comparison of the changes in lesion counts from baseline to 12 weeks between treated and untreated sides of the face and changes in photographic evidence of acne severity as graded by a panel of dermatologists blinded to treatment assignment.

Results After 12 weeks, using intent-to-treat analysis with last observation carried forward, there were no significant differences between laser-treated and untreated skin for changes in mean papule counts (-4.2 vs -2.2; $P=.08$), mean pustule counts (0 vs -1.0; $P=.12$), or mean comedone counts (2.9 vs 1.6; $P=.63$). Grading of serial photographs confirmed the clinical assessments, showing no significant mean (SE) differences in Leeds scores (range, 1-12) for treated skin (3.98 [0.32] at baseline and 3.94 [0.27] at week 12) compared with untreated skin (3.83 [0.32] at baseline and 3.79 [0.28] at week 12) ($P>.99$).

Conclusions In this study, the nonpurpuric pulsed dye laser therapy did not result in significant improvement of facial acne. More research is needed before this laser therapy may be recommended as an acne treatment.

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tion, clinical improvement in acne has been reported following treatment with both visible and infrared wavelength lasers.¹⁴ Infrared lasers are purported to provide benefits in acne patients by transiently damaging sebaceous glands via thermal effects.¹⁵ More recently, pulsed dye laser therapy was reported to reduce acne lesion counts.¹⁶ The low morbidity of such treatments and the possible additional benefit of simultaneously treating acne scarring make this therapy

attractive. Thus, we evaluated the benefits of pulsed dye laser therapy for acne.

METHODS

This study was approved by the University of Michigan Medical School's institutional review board and written in-

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formed consent was obtained from all study participants. Recruitment for the study was performed with the use of newspaper and online advertising and flyers posted at various sites on the undergraduate and medical campuses at the University of Michigan. Recruitment occurred from August 2002 to June 2003 and the study was completed in September 2003.

Inclusion criteria included age of 13 years or older, general good health, willingness and ability to comply with the requirements of the protocol, and the presence of clinically evident facial acne. Patients presenting with acne so mild (Leeds acne severity scale rating¹⁷ <2 on a 12-point ordinal scale) that a clinical effect of the laser therapy, if present, would be difficult to demonstrate were excluded. Potential participants were also excluded for a history of oral retinoid use within 1 year of study entry, other systemic or topical acne therapies within 1 month, alpha hydroxy acid or glycolic acid use within 1 month, or microdermabrasion to the face within 3 months. Exclusion criteria were age of 12 years or younger and a history of prior dermabrasion or laser resurfacing of the face. In addition, individuals were excluded for the use of nonsteroidal anti-inflammatory medications within 10 days prior to or for 2 weeks following the laser treatments provided in this study.

The study design was a randomized, single-blind, split-face clinical trial. Patients were randomized to 1 of 2 treatment groups using a table of random numbers. In the first group, participants underwent a single pulsed dye laser treatment with the NLite laser (ICN Pharmaceuticals Inc, Costa Mesa, Calif) to half of the face with the opposite, nontreated side of the face serving as a control. In the second group, participants underwent 2 pulsed dye laser treatments at baseline and 2 weeks later, with all treatments to half of the face with the opposite side left untreated and serving as a control. A randomized code was used to determine the side of the face that would receive laser therapy as well as the number of

treatments the patient would receive. The randomization of the side of the face receiving treatment was meant to control for possible uneven environmental effects (ie, more extensive exposure of the left side of the face to sunlight among individuals who drive in the United States) and helped to ensure that evaluators were unaware of the side in which an individual had received the laser treatment, thereby minimizing the potential for evaluator bias. Evaluating physicians were blinded to treatment assignment and regimen. Patients were specifically instructed not to tell the evaluating physician which side of the face was treated.

Nonpurpuric pulsed dye laser treatments were performed using the following laser parameters: wavelength of 585 nm, pulse duration of 350 μ sec, spot size of 7 mm, and fluence of 3 J/cm². Two identical lasers were used during the course of the study. The proper functioning of both devices was analyzed and confirmed to ensure calibration and output accuracy by a biomedical engineering laser specialist at the University of Michigan prior to the initiation of the study as well as during the course of the study using a Nova laser meter that measures power and energy with a PE50-BB pyroelectric detector head (Ophir Optics, Wilmington, Mass).

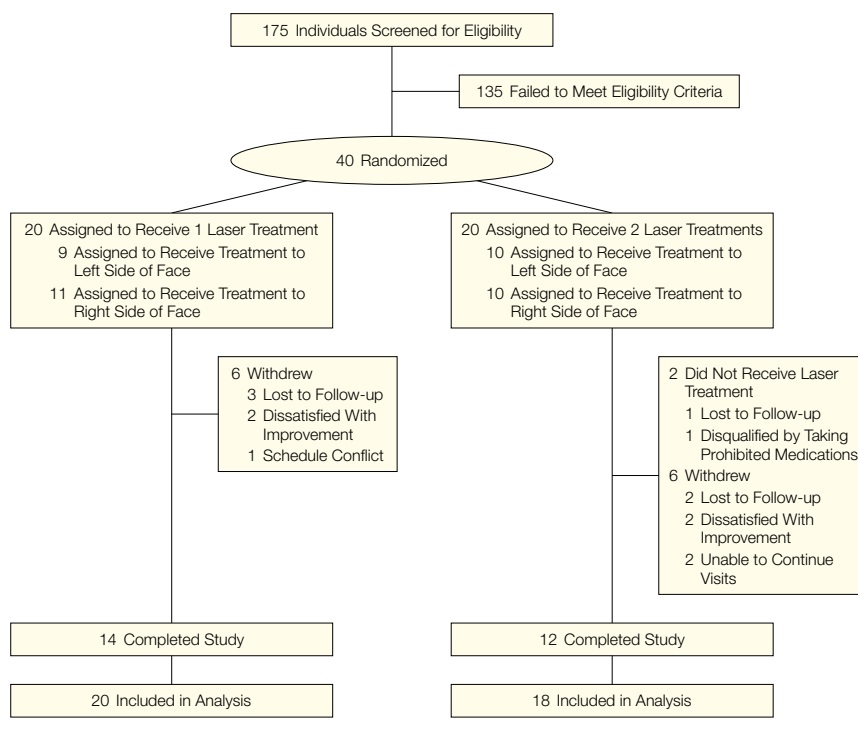
Treatments were performed by a single physician (J.S.O.), who did not participate in the clinical evaluation of patients. Nonoverlapping pulses were delivered in a "painting" motion to cover the entire side of the face to be treated from the hairline to the jawline, excluding the eyelids. At the end of the study, patients were given the option of having the previously nontreated side of the face treated.

Participants were clinically assessed every other week for a total of 12 weeks, including the baseline visit during which the pulsed dye laser treatment was administered. Evaluation visits included lesion counts of papules, pustules, cysts, comedones, and erythematous macules (as representative of resolving previously inflammatory lesions). Because oxygenated hemoglobin is a chromo-

phore for pulsed dye lasers, we hypothesized that absorption of the laser light by inactive, resolving acne lesions (termed *red macules*) might hasten the resolution of these troublesome lesional remnants. All lesion counts were performed at baseline and at weeks 2, 4, 6, 8, 10, and 12. Determination of sebum production via the use of Sebutape (CuDerm Corp, Dallas, Tex) and subsequent image analysis using Image-Pro Plus software (Media Cybernetics, Silver Spring, Md) were performed at baseline and at weeks 4, 8, and 12.¹⁸

Standardized bilateral facial photographs were obtained at baseline and every 2 weeks throughout the study. Participants were photographed at a fixed distance using a Nikon D1x digital camera (Nikon Corp, Tokyo, Japan). Participants had been positioned at a defined spot in the studio and instructed to look at a fixed target during photography. Lighting was provided by studio strobe lights that were fixed in position and images were exposed at f22. Views included face front and left and right profiles. Images were taken at a reproduction ratio equivalent of 1:6 on 35-mm film. Subsequently, participants' photographs were viewed by a panel of 3 dermatologists who were blinded to treatment side. The severity of acne in the images obtained at baseline, week 4, and week 12 was then graded using the Leeds acne severity scale for both treated and untreated sides of the face.¹⁷ This is an ordinal photonic scale ranging from 1 (least severe) to 12 (most severe).

The primary comparison of interest was that of the treated vs the untreated side of the face. However, because of the variability in lesion counts from one side of the face to the other and the potential for significant baseline differences, we decided that a direct comparison of lesion counts was less likely to reveal a true treatment effect than a comparison of the change (ie, absolute difference) from baseline between the treated and untreated sides of the face. We compared these differences using the paired *t* test. For missing data, we performed last observation carried forward analysis of lesion counts in which each patient's last

Figure 1. Trial Profile

available data were carried forward to the end of the study and analyzed.

The secondary comparisons of interest were the time course trends within treatment groups over the 12-week study. These were evaluated statistically with the repeated measures analysis of variance using the Dunnett test for multiple comparisons. Comparisons were considered significant at $P \leq .05$ and P values were 2-tailed. Summary data are represented as either mean (SE) or mean (95% confidence interval). The data were analyzed using SAS analytic software (version 8.2, SAS Institute Inc, Cary, NC).

Interrater reliability for the panel of dermatologists who evaluated photographs of participants was measured as the average absolute deviation of the mean score for each photograph. This provided information about how closely aligned the raters were for each of the 192 photographs evaluated.

A sample size of 40 patients provides a power level of 0.85 for detecting a difference of 3 (approximately 30%) in the reduction of mean papule

count from baseline between treated and untreated skin, with a type I error rate of .05 for a 2-tailed hypothesis and assuming an SD of difference of 6.

RESULTS

One hundred seventy-five individuals were evaluated for eligibility (FIGURE 1). Of these, 24 males and 16 females with a mean age of 20.7 years (range, 13-31 years) and clinically evident acne vulgaris on the face met inclusion criteria and were enrolled. Of these, 28 described themselves as white, 7 as Asian, 2 as black, and 3 as unknown. Nineteen participants were randomized to receive treatment to the left side of the face and 21 to the right side. Of those receiving laser treatments to the left side of the face, 9 were randomized to receive 1 treatment session and 10 were to receive 2 treatments. Among patients randomized to undergo laser therapy to the right side of the face, 11 were randomized to receive 1 treatment and 10 were to receive 2 treatments. Thus, 20 patients were randomized to receive 1 treatment and 20 to receive 2 treatments.

Among all patients who were randomized to receive only 1 treatment, 14 of 20 completed the study. Of the 20 patients randomized to receive 2 laser treatment sessions, 12 of 20 completed the study. Among the 26 patients who completed the study, 14 elected to have the opposite (previously untreated) side of the face treated with the pulsed dye laser.

Laser therapy was generally well tolerated with 7 (18%) of 38 patients requiring minor reductions in the fluences delivered due to discomfort during the treatments. While most patients were treated at a fluence of 3 J/cm², the energy level was decreased to 2.5 J/cm² in 4 cases and to 2.7 J/cm², 2.0 J/cm², and 1.5 J/cm² in one instance each. The only treatment-related adverse events were a single episode of postinflammatory hyperpigmentation (occurring in a patient with Fitzpatrick type VI skin) and 2 episodes of minimal focal bruising. In all other patients, the immediate clinical response to the laser treatment consisted of transient (approximately <2 seconds) cutaneous cyanosis followed in some cases by minimal to mild erythema that resolved within minutes or a few hours. A treatment lasted approximately 10 to 12 minutes to perform and an average of 385 pulses were delivered per treatment.

When comparing patients randomized to receive either 1 or 2 laser treatment sessions, no statistically significant differences in efficacy at any time point or for any subtype of acne lesion were demonstrated. Thus, the data from these groups were combined to provide summary statistics of patient responses to laser therapy (provided as either 1 or 2 treatment sessions) compared with no treatment and without reference to a dose response.

The changes in lesion counts for treated compared with untreated sides of the face showed no statistically significant differences from baseline to week 12 (TABLE 1 and TABLE 2). There was a tendency for bilateral lesion counts to ebb and flow with insignificant minor improvements or periods of slight worsening occurring on both sides of the face (FIGURE 2).

A separate analysis of the time course within each treatment group by analysis of variance revealed that papule count was the only clinical end point to show a significant reduction in number of lesions compared with baseline levels on the treated side of the face. However, the untreated side of the face also showed a decrease in number of papules over the course of the study, although not to the same degree. Thus, the comparison of changes in lesion counts from baseline over time between treated and untreated skin failed to demonstrate any statistically significant differences.

Bilateral facial photographs obtained at baseline, week 4, and week 12 were graded by a panel of 3 dermatologists using the Leeds acne severity scale.¹⁷ These evaluators did not perform the laser treatments or the clinical lesion counts and were blinded to which images included treated compared with untreated skin. Baseline mean (SE) Leeds scores were similar: 3.98 (0.32) for the treated side and 3.83 (0.32) for the untreated side of the face. At week 4, there were statistically nonsignificant mean (SE) increases in Leeds severity scores of 0.07 (0.12) for the treated side and 0.01 (0.10) for the untreated side of the face ($P = .56$). Similarly, at week 12 the mean (SE) severity scores changed from baseline only by 0.04 (0.15) for the treated and 0.04 (0.09) for the untreated side of the face ($P > .99$). As a measure of interrater reliability, the average absolute deviation of the mean (SD) score was 0.55 (0.35) on the 12-point Leeds scale, suggesting that on average the raters stayed within about a half unit on the Leeds scale for a given photograph among all images that were rated.

Sebutape measurements were obtained at baseline and weeks 4, 8, and 12. Image analysis provided a quantitative measurement of sebum production on the forehead and cheek on both treated and untreated sides of the face. No statistically significant differences in sebum production were found when treated and untreated skin was compared at these time points (data not shown).

COMMENT

Acne vulgaris is a common disorder that has the potential to negatively affect the lives of millions of individuals.¹⁻³ In addition to the sometimes more short-term consequences of physical and emotional discomfort associated with this condition, acne also carries the risk of scarring that may serve as a permanent reminder of the disorder and thus prolong its psychological impact.¹⁹ Therefore, the development of safer, more convenient, and more effective treatments for acne is highly desirable.

Pulsed dye lasers generally emit light at 585 nm or 595 nm. These wavelengths are strongly absorbed by oxygenated hemoglobin. On this basis, pulsed dye lasers have been clinically used to treat numerous types of erythematous (vascular) lesions, including inflammatory conditions such as psoriasis. The specific device used in this study emits light at a wavelength of 585 nm, has a relatively brief pulse duration of 350 μ sec, and is designed to target the superficial cutaneous microvasculature. With the use of treat-

Table 1. Analyses of All Patients Using Last Observation Carried Forward Method (n = 38)

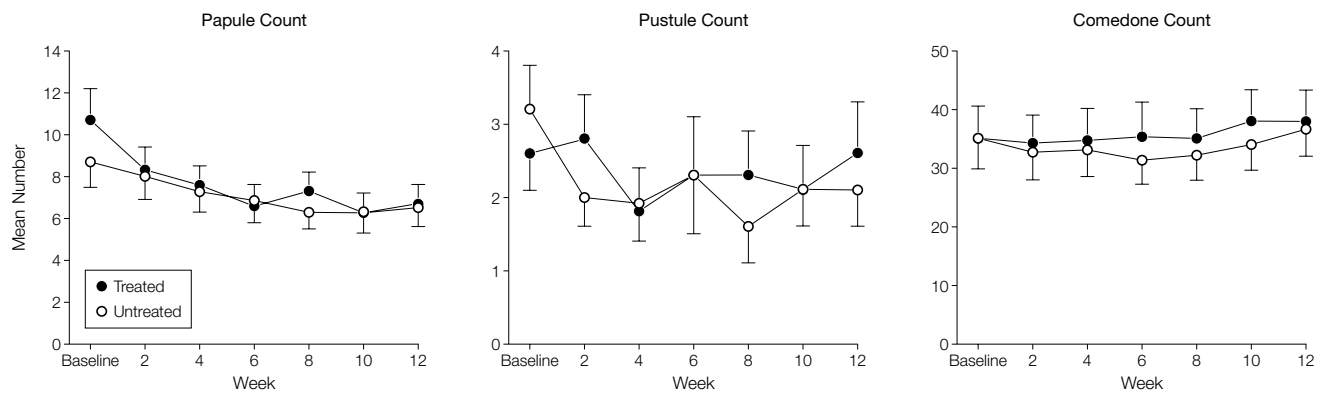
	Baseline Score (95% CI)	Week 12 Score (95% CI)	Change in Score at Week 12 (95% CI)	P Value
Papules				
Treated	10.7 (7.6 to 13.9)	6.6 (4.5 to 8.6)	-4.2 (-7.7 to -0.6)	.08
Untreated	8.7 (6.3 to 11.1)	6.5 (4.7 to 8.3)	-2.2 (-5.3 to 0.9)	
Pustules				
Treated	2.6 (1.5 to 3.7)	2.6 (1.1 to 4.1)	0 (-1.4 to 1.4)	.12
Untreated	3.2 (1.9 to 4.4)	2.1 (1.1 to 3.2)	-1 (-2 to -0.01)	
Comedones				
Treated	35 (25 to 45)	38 (27 to 49)	2.9 (-4.0 to 9.7)	.63
Untreated	35 (24 to 46)	37 (27 to 46)	1.6 (-5.2 to 8.4)	
Cysts				
Treated	1.1 (-0.2 to 2.4)	1.1 (0.1 to 2.2)	0 (-0.5 to 0.5)	>.99
Untreated	1.1 (-0.1 to 2.3)	1.1 (0.1 to 2.1)	0 (-0.6 to 0.6)	
Red macules				
Treated	27 (21 to 34)	33 (26 to 40)	5.1 (-1 to 11.2)	.51
Untreated	25 (19 to 30)	31 (25 to 38)	6.6 (1.8 to 11.5)	
Leeds summary score				
Treated	4 (3.3 to 4.6)	3.9 (3.4 to 4.5)	-0.04 (-0.4 to 0.3)	>.99
Untreated	3.8 (3.2 to 4.5)	3.8 (3.2 to 4.4)	-0.04 (-0.4 to 0.3)	

Abbreviation: CI, confidence interval.

Table 2. Analyses Restricted to Patients Completing the Study (n = 26)

	Baseline Score (95% CI)	Week 12 Score (95% CI)	Change in Score at Week 12 (95% CI)	P Value
Papules				
Treated	10.9 (7.4 to 14.4)	7.0 (4.4 to 9.5)	-3.9 (-8.5 to 0.7)	.13
Untreated	8.3 (6.1 to 10.5)	6.7 (4.3 to 9.1)	-1.5 (-5.2 to 2.1)	
Pustules				
Treated	2.1 (0.9 to 3.3)	2.7 (0.8 to 4.7)	0.7 (-1.2 to 2.5)	.29
Untreated	2.1 (1 to 3.3)	1.9 (0.7 to 3.1)	-0.2 (-1.2 to 0.7)	
Comedones				
Treated	33 (22 to 44)	35 (24 to 46)	1.3 (-7.3 to 9.8)	.95
Untreated	34 (22 to 47)	36 (24 to 47)	1.1 (-8.0 to 10.1)	
Cysts				
Treated	1.5 (-0.4 to 3.4)	1.4 (-0.1 to 2.9)	-0.04 (-0.7 to 0.6)	.47
Untreated	1.2 (-0.5 to 3)	1.5 (-0.03 to 3)	0.2 (-0.6 to 1.0)	
Red macules				
Treated	30 (20 to 40)	35 (25 to 45)	5.0 (-4.0 to 14.0)	.86
Untreated	26 (18 to 33)	30 (21 to 39)	4.4 (-1.7 to 10.6)	
Leeds summary score				
Treated	4.4 (3.4 to 5.3)	4.4 (3.6 to 5.1)	0.01 (-0.4 to 0.5)	.92
Untreated	4.2 (3.2 to 5.1)	4.2 (3.4 to 5.0)	0 (-0.5 to 0.5)	

Abbreviation: CI, confidence interval.

Figure 2. Papule, Pustule, and Comedone Counts in Treated or Untreated Skin With Pulsed Dye Laser Treatment

Values are means (SEs). There was no statistically significant difference when comparing the changes from baseline in treated vs untreated skin at any time point.

ment parameters featuring low fluences, nonpurpuric treatments may be provided. In addition, low fluence treatments with this laser have been reported to result in increased collagen production and clinical improvements in fine wrinkles and atrophic acne scarring.^{20,21} For all of these reasons, we postulated that such therapy might be of particular benefit for patients with inflammatory acne.

In this study, we were not able to demonstrate significant efficacy for nonpurpuric pulsed dye laser therapy in this setting. We believe that our use of a split-face protocol design was vital with respect to assessing changes in the patients' acne based on the natural course of the disorder. That is, acne is a clinically dynamic condition in which both spontaneous improvements and flares are known to occur. With the use of other study designs, a significant risk exists that changes in disease severity not based on treatment might be misinterpreted as successful therapy or that other sources of bias may inadvertently impact results.

In our study, there were patients whose acne severity decreased over the 12-week follow-up period, but this improvement was bilateral, making it unlikely that the change was due to the laser treatment. Conversely, several patients' acne worsened bilaterally during the assessment phase of the study, but this increased severity was not likely due to the unilaterally applied laser

therapy. Pulsed dye laser energy has been demonstrated to act locally in the skin and there is no reason to believe that the positive or negative effects would have extended to the opposite side of the face. One theory regarding how pulsed dye lasers may improve acne relates to decreased levels of *P. acnes*. However, if this is true, there is no evidence that migration or transfer of bacteria from untreated skin into the treated areas would account for the lack of efficacy using a split-face model. By analogy, prior split-face acne research using unilaterally applied topical antibiotics demonstrated efficacy in treated skin and no evidence of bacterial migration or transfer (James Leyden, MD, written communication, May 2004). A split-face study design might not be practical for more invasive laser treatments. However, with nonablative laser therapy, using the patients' own skin as a control is often feasible and likely provides the most meaningful control possible.

Although lesion counts were performed by an experienced clinical investigator (S.C.), the fluctuation in the counts reported herein could potentially be based not on the natural course of the disease, but rather on the inherent difficulties associated with reproducibly performing such counts. However, subsequent grading of patient photographs by dermatologists not involved in the counting of lesions corroborate the clinical findings.

Because individuals with mild acne (Leeds acne severity scale ratings of <2) were excluded from this study, we cannot comment on the potential impact of pulsed dye laser therapy for such patients. In addition, this study was meant to assess the value of subpurpuric dosing of pulsed dye laser energy because delivering treatments that cause bruising would negate many of the potential advantages of the therapy. Given this, we cannot speculate whether the use of higher fluences might result in clinical benefits.

During the course of our study, an article by Seaton et al¹⁶ was published reporting marked clinical improvements following a single pulsed dye laser treatment and using the same type of laser and similar treatment parameters that we used. Seaton et al provided treatments at fluences of 1.5 J/cm² to half of the face and 3 J/cm² to the opposite side on 31 patients randomized to receive laser therapy to evaluate efficacy and include a dose-response assessment. Ten participants received sham therapy only to the entire face. The authors reported that there were no clinical differences between the results achieved with these 2 different fluences. Therefore, their primary outcome measure was a comparison of the results of laser-treated patients' whole faces with sham-treated patients' whole faces. Thus, Seaton et al did not include a split-face design nor a split-face control protocol.

In comparing the study by Seaton et al¹⁶ with our study, there are some minor differences in participant demographics. These include a difference in the mean age of those receiving treatments (approximately 26 years in the earlier study and 21 years in our study) and the proportions of patient sex (35% male and 65% female in the study by Seaton et al and 60% male and 40% female in our study). As acne appears to be the same clinical entity among patients of both sexes and over both age ranges, such factors are not likely to have caused the differing results.

There were also differences in dropout rates: 27 of 31 treated patients completed the Seaton et al study and 26 of 40 patients completed our study. This may reflect the relatively better results achieved by Seaton et al. While the early withdrawal rate for our study was substantial, we believe that this was likely a reflection of dissatisfaction with the treatment. The effect that the reduced sample size had on the power of our study was likely mixed. Typically, a reduction in sample size translates to a commensurate reduction in power, which is reflected in less statistically significant results (*P* values) and an increase in the type II error rate. In this case, we believe that attrition selection bias may have offset this at least somewhat. The subgroup of 26 patients who completed the study presumably represented the best clinical responders. To address this issue, a comparison of the results using our primary analysis for all patients using last observation carried forward was performed and a secondary analysis including only the subgroup of 26 patients who completed the study was performed. The *P* values for the carried forward analysis are somewhat smaller, but still nonsignificant. The results from several end points actually favor the untreated group.

Laser and light-based acne therapy is a potentially attractive treatment option. With many such devices, complications are rare and treatments are relatively brief. The treatments do not require significant ongoing patient compli-

ance, which is a major advantage over chronic topical and oral therapies. Disadvantages include the possibility of patient discomfort during treatment. Discomfort is more frequent with the use of some infrared lasers meant to thermally damage sebaceous structures. Other disadvantages include lack of data on long-term effects and lack of insurance coverage for some therapies. However, the high prevalence of acne, its significant morbidity, and the current lack of a treatment that combines convenience, low risk, and more uniform efficacy underscore the potential importance of developing laser therapy for this indication.

Despite much interest, rigorous prospective, randomized, controlled trials in this area are limited. The fact that our study does not substantiate the positive results recently reported is not an indictment of laser therapy for acne in general, and does not necessarily rule out the possible role of this particular pulsed dye laser. However, it does suggest that additional well-designed studies are needed before the use of the pulsed dye laser becomes a part of acne therapy.

Author Contributions: Drs Orringer and Kang had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Both authors contributed equally to this article.

Study concept and design: Orringer, Kang, Cho, Fisher, Johnson, Voorhees.

Acquisition of data: Orringer, Kang, Schumacher, Cho, Hammerberg, Fisher, Johnson.

Analysis and interpretation of data: Orringer, Kang, Hamilton, Fisher, Karimipour, Johnson, Voorhees.

Drafting of the manuscript: Orringer, Hamilton, Hammerberg, Fisher, Johnson.

Critical revision of the manuscript for important intellectual content: Orringer, Kang, Schumacher, Cho, Fisher, Karimipour, Johnson, Voorhees.

Statistical expertise: Hamilton.

Obtained funding: Voorhees.

Administrative, technical, or material support: Orringer, Kang, Schumacher, Hammerberg, Fisher, Karimipour, Johnson, Voorhees.

Study supervision: Orringer, Kang, Hammerberg, Johnson, Voorhees.

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Role of the Sponsor: ICN Pharmaceuticals Inc donated the NLite lasers. During the course of this study, ICN Pharmaceuticals divested itself of its Photonics subsidiary, which was responsible for the NLite device. However, we were permitted to retain the lasers to complete our study. At the time of this divestiture, ICN Pharmaceuticals had no knowledge of the outcomes

of this study. As a condition of acceptance of the research grant from ICN Pharmaceuticals, the study was designed to be performed, analyzed, and reported solely by the faculty and staff of the Department of Dermatology at the University of Michigan.

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