Novel 1726 nm laser demonstrates durable therapeutic outcomes and tolerability for moderate-to-severe acne across skin types

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Background: Traditional acne management with topical therapy, systemic antibiotics, hormonal agents, or oral isotretinoin requires compliance and may produce significant side effects. However, alternative treatments with lasers had failed to demonstrate durable clearance.

Objective: To assess the tolerability and therapeutic outcomes of a novel 1726 nm laser treatment of moderate-to-severe acne across skin types.

Methods: A prospective, open-label, single-arm, Investigational Device Exemption-approved, institutional review board-approved study of 104 subjects with moderate-to-severe facial acne and Fitzpatrick Skin Types ranging from II-to-VI was conducted. Subjects received 3 laser treatments at 3 (-1/+2)-week intervals.

Results: Following final treatment, ≥50% reduction in active acne inflammatory lesions was 32.6% at 4-weeks follow-up, increasing further to 79.8% and 87.3% at 12 and 26-weeks, respectively. The percentage of subjects clear or almost clear increased from 0% at baseline to 9%, 36.0%, and 41.8% at 4-, 12-, and 26-weeks follow-up. No serious adverse events were observed related to device or protocol; treatments were well tolerated, requiring no anesthetic. Therapeutic outcomes and discomfort were similar across all skin types.

Limitations: Lack of control group.

Conclusions: The study findings demonstrate the novel 1726 nm laser is well tolerated with durable progressive posttreatment improvement to at least 26 weeks for moderate-to-severe acne across skin types. (J Am Acad Dermatol 2023;89:703-10.)

Key words: acne; acne guidelines; acne management; acne scarring; acne severity; acne skin types; acne treatment alternatives; acne vulgaris; antibiotic therapy; hormone therapy; isotretinoin; laser; light therapies; sebaceous glands; selective photothermolysis.

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INTRODUCTION

Acne is the most common skin condition nationally and eighth-most common disease worldwide, affecting 85% of teens and 50% of adults.[1,2] Predominantly facially distributed, acne causes poor self-image, anxiety, depression, negative psychosocial impact, and permanent scarring.[3-5] The financial burden of acne treatment is approximately $3 billion in the United States annually.[6]

Traditional acne management follows a well-established treatment algorithm of topical therapy with multiple pharmacologic classes and progressive implementation of oral antibiotics, hormonal agents, or isotretinoin[5] (Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/7cdmrv3pjz). To date, durable outcomes in moderate-to-severe acne treatment have been attained by combining topical therapy with systemic antibiotics, hormonal agents, or oral isotretinoin. While lasers and energy-based devices have been tested, reproducible, durable outcomes in moderate-to-severe acne, has been lacking. The traditional pharmacologic algorithm endures, while lasers remain absent from the American Academy of Dermatology's first- and second-line acne treatment options.

The potential for device-based acne treatment alternatives was portended by early research with aminolevulinic acid red-light photodynamic therapy (PDT).[7] Durable results were reported; however, adverse events (AEs) included periprocedural discomfort, postprocedure pustular eruptions, blistering, and postinflammatory hyperpigmentation in darker skin types.[7,8] Alternative acne PDT protocols with variable success and photosensitivity are employed by some dermatologists, but not considered mainstream.[9-11]

The current pharmacologic treatment algorithm imposes a burden, variable clearance rates, side effects, and complications. Topical treatments are often irritating and require high patient compliance. Oral antibiotics may cause drug allergy, gastrointestinal upset, and bacterial resistance. Hormonal agents, including oral contraceptives and spironolactone are associated with risks of hypercoagulability, and cardiac arrhythmia. Isotretinoin, while curative in approximately 60% of moderate-to-severe acne cases, entails high administrative burden and AEs—namely birth defects and depression.[12] Thus, researchers continued search for targeted and durably effective acne treatment alternatives.

CAPSULE SUMMARY

- Traditional acne therapies require compliance and may cause side effects; though prior to this article, lasers had failed to prevail as an alternative treatment option.
- A novel 1726-nm laser results in durable long-term acne clearance across skin types providing a potential alternative to traditional acne therapies including isotretinoin.

As presaged by PDT, light may target sebaceous glands by selective photothermolysis, the principle of matching a wavelength and pulse duration to a specified skin target. While wavelengths 532, 585-595, and 1450 nm have been applied to acne, they were not preferentially absorbed by sebaceous glands over water, hemoglobin, or melanin. Selective sebaceous gland destruction was demonstrated using a free electron laser tuned from 1600 to 1800 nm.[13] The absorption spectra of sebum and water measured in near-infrared 800-2400 nm region demonstrated a narrow band (approximately 40 nm) of selective absorption in sebum over water peaking at 1726 nm[14,15] (Supplementary Fig 1, available via Mendeley at https://data.mendeley.com/datasets/7cdmrv3pjz).

The laser with a tight bandwidth of the specific absorption ratio peak of 1726 nm achieves spectral selectivity for sebaceous glands. In this study, a novel 1726 nm laser was developed, optimized and applied to determine tolerability, therapeutic outcomes, and durability of the responses in moderate-to-severe acne across skin types II-VI.

METHODS

Subjects

One hundred four subjects, 59 women, 45 men, ages 16-40, with Fitzpatrick Skin Types ranging from II to VI, were enrolled in this prospective, open-label, single-arm, Investigational Device Exemption-approved, institutional review board-approved study conducted at 7 sites (Supplementary Table II, available via Mendeley at https://data.mendeley.com/datasets/7cdmrv3pjz). None of the subjects were previously treated with isotretinoin.

Study design

Following a 30-day washout from all acne medications, baseline standardized digital photographs were taken. Three independent expert dermatologist graders assessed and scored acne severity per subject using the Investigator's Global

Abbreviations used:

AE: adverse event
IGA: Independent Global Assessments
PDT: photodynamic therapy
RR: responder rate

Assessment (IGA) scale (Supplementary Table III, available via Mendeley at https://data.mendeley.com/datasets/7cdmrv3pjz).

Three laser treatments were administered at 3 (−1/+2) week intervals. Follow-up visits were at 4, 12, and 26 weeks after the third treatment. All enrolled subjects comprised the intent to treat cohort and those completing 3 treatments and 12-week or 26-week follow-up without major protocol deviations comprised the per protocol cohort.

Standardized digital photographs were taken from frontal, 45-and 90-degree angles at baseline, pretreatment and follow-up using consistent camera settings (Canon EOS Rebel T7 Manual capture mode), and lighting conditions (camera brightness [ISO] ranges 100-6400 based on skin type, shutter speed 20 [1/20th of second] and aperture size f/20). Subjects completed a Subject Satisfaction Questionnaire to self-assess their acne and satisfaction with treatment outcome.

Laser treatment

Immediately pretreatment, skin was cleansed and degreased using acetone with gauze wipe. No topical anesthetic was administered. During treatment, the handpiece was applied ensuring complete skin contact. The laser spot size used was 3.1 mm scanned over 7 adjacent locations to form a hexagonal pattern. Following precooling 1-second delay, 1726 nm energy was delivered as single or double pulse with average fluence of 20.5 J/cm^2 and 22.8 J/cm^2, respectively. The maximum pulse duration is 50 ms and a maximum fluence of 30 J/cm^2. After postcooling 2-second delay with full contact, the handpiece was then moved to the next adjacent treatment area. Process was repeated until entire face treated in single pass with no overlap. The average treatment time ranged between 30 and 40 minutes.

Clinical assessments

Lesion count reduction assessment. Clinical outcomes were assessed by a trained, blinded expert panel of 3 lesion count evaluators using a validated photography-based lesion count technique. Due to COVID-19 restrictions and regulatory agencies' concerns regarding blinding and bias of live assessments for single-arm studies, live in-person lesion counts were not performed. Photography-based lesion count methodology was designed, validated, and deployed for this study by blinding the evaluator(s) through randomization and label-masking of images taken at disparate study time points and remote assessments independent of other evaluators. Past criticisms of photographic assessments included difficulties visualizing small lesions, standardizing photographs, maintaining constant lighting and positioning, inconsistent photo-development procedure, and lack of palpation.[16-18] As a result, photographic advancements and standardization methods have since improved clarity, sharpness, depth visualization,[17] and qualitative and quantitative consistency across sessions and raters.[19]

Photographs at baseline, 4-week and 12-week follow-up were randomized, label-masked, and presented to each expert evaluator for independent assessment. Each evaluator assessed, quantified, and recorded all active inflammatory lesions (papules, pustules, and nodules) and noninflammatory (comedones) lesions within the defined facial treatment area with the jawline as the inferior boundary. The median of 3 counts per subject visit was utilized when summarizing the data. At 26-week follow-up, evaluators were presented with 45° angle photographs to assess improvement.

For lesion assessments, the following definitions and reference measurement scale were used to ensure consistency and minimize bias. Papules were defined as erythematous, raised lesions less than 5 mm in diameter. Pustules were defined as erythematous, raised lesions containing white exudate or pus, less than 5 mm in diameter. Nodules were defined as deep-seated, erythematous lesions greater than or equal to 5 mm in diameter.

Investigator acne severity assessments. The digital photographs, without randomization or label-masking, were reviewed and scored by the expert panel of 3 investigator dermatology graders to rate each subject's acne severity.

Endpoint reporting/statistical analysis

Primary. *Inflammatory lesion count assessment.* The primary study objective was to evaluate therapeutic outcomes, durability, and tolerability of laser treatment. The primary endpoint was percent reduction in active inflammatory lesions from baseline to 12 weeks after the third and final laser treatment. Subjects with a ≥50% reduction in active inflammatory lesions at follow-up compared to baseline were defined as responders. The responder rate (RR) was the percentage of the responder population in the study.

Table I. Primary and secondary endpoints of clinical results for 1729 nm laser treatment of acne

Responder rate per protocol	4-week FU	12-week FU	26-week FU
Responder	29 (32.6%)	71 (79.8%)	69 (87.3%)
Nonresponder	60 (67.4%)	18 (20.2%)	10 (12.7%)
95% confidence interval	(0.23, 0.43)	(0.70, 0.88)	(0.78, 0.94)

Responder rate subgroup per protocol	4-week FU	12-week FU	26-week FU
Female	25.6	80.9	88.4
Male	40.5	78.6	86.1
Skin type			
II	25	83.3	100
III	29.6	74.1	81.8
IV	38.2	82.4	81.3
V	33.3	75	100
VI	25	100	100
Age group			
16-19	37.8	81.1	96.8
20-22	35	85	79
23-25	21.4	71.4	76.9
26+	27.8	77.8	87.5
Baseline IGA			
Moderate	33.3	81.2	90.5
Severe	0.316	79	75

IGA per protocol cohort

Category	Baseline	4-week FU	12-week FU	26-week FU
Individual IGA				
Clear skin	0 (0.0%)	1 (1.1%)	2 (2.2%)	9 (11.4%)
Almost clear	0 (0.0%)	7 (7.9%)	30 (33.7%)	24 (30.4%)
Mild	1 (1.1%)	39 (43.8%)	38 (42.7%)	33 (41.8%)
Moderate	69 (77.5%)	38 (42.7%)	17 (19.1%)	13 (16.5%)
Severe	19 (21.3%)	4 (4.5%)	1 (1.1%)	0 (0.0%)
IGA Subgroup				
Clear skin or almost clear	0 (0.0%)	8 (9.0%)	32 (36.0%)	33 (41.8%)
Mild, moderate, or severe	89 (100.0%)	81 (91.0%)	56 (62.9%)	46 (58.2%)
95% confidence interval		(3.96, 16.95)	(26.37, 47.31)	(30.77, 53.41)

Nodule and noninflammatory lesion counts per protocol cohort

Nodule lesion count	Baseline	4-week FU	12-week FU	26-week FU
Mean (SD)	0.55 (1.08)	0.30 (0.87)	0.17 (0.53)	0.04 (0.19)
Range (min, max)	0, 6	0, 6	0, 3	0, 1
Comedonal lesion count				
Median	41	32	28	23
Range (min, max)	6, 132	5, 98	6, 102	5, 88

Adverse events per protocol cohort

Category	All	Device related mild	Device related moderate	Protocol related
Subjects ≥1 adverse event	104 (100.0%)	103 (99.0%)	1 (1.0%)	1 (1.0%)
Acneiform flare-up	46 (44.2%)	44 (42.3%)	1 (1.0%)	1 (1.0%)
Dryness	19 (18.3%)	19 (18.3%)	0 (0.0%)	0 (0.0%)
Edema	102 (98.1%)	102 (98.1%)	0 (0.0%)	0 (0.0%)
Erythema	104 (100.0%)	104 (100.0%)	0 (0.0%)	0 (0.0%)
Itchiness	2 (1.9%)	2 (1.9%)	0 (0.0%)	0 (0.0%)
Oiliness	1 (1.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)

Continued

Table I. Cont'd

Adverse events per protocol cohort				
Category	**All**	**Device related mild**	**Device related moderate**	**Protocol related**
Prolonged erythema	1 (1.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
Skin sensitivity	2 (1.9%)	2 (1.9%)	0 (0.0%)	0 (0.0%)

Subject assessment per protocol			
My skin looks better	**4-week FU**	**12-week FU**	**26-week FU**
Agree	70 (78.7%)	78 (87.6%)	63 (79.7%)
Disagree	19 (21.3%)	11 (12.4%)	16 (20.3%)
My skin is smoother			
Agree	70 (78.7%)	76 (85.4%)	65 (82.3%)
Disagree	19 (21.3%)	13 (14.6%)	14 (17.7%)

Primary endpoints include responder rates (overall and by subgroup), summary of adverse events by relationship and severity. Secondary endpoints include Investigator's Global Assessment (IGA) and nodule and noninflammatory (comedonal) lesion counts, and subject satisfaction assessment at baseline and follow-up visits.
FU, Follow-up; IGA, Investigator's Global Assessment.

AEs assessment. The tolerability of the laser treatment was assessed by review of all AEs reported by each subject immediately posttreatment and at follow-up visits.

Secondary. Secondary endpoints evaluated at 4, 12 and 26 weeks following final treatment included the percentage of subjects with IGA scores of 0 or 1 (Clear/Almost Clear), and subject satisfaction assessment from the Subject Satisfaction Questionnaire.

Other assessments

Nodule and noninflammatory lesion analysis. The percentage reduction in nodules and noninflammatory (comedonal) lesion count compared to the baseline was reported for the 4-, 12-, and 26-week follow-ups.

Periprocedural discomfort. Immediately following each treatment, subjects were asked to rate the pain associated with the laser treatment by indicating a number that best represents the highest average pain level experienced during treatment using the 0-10 Visual Analog Mosby Pain Rating Scale (VAS).

Subgroup analysis. Several subgroup analyses of the RRs and periprocedural discomfort were conducted to further summarize the scalability of the procedure. The subgroups of interest were gender, age, Fitzpatrick skin type, and baseline acne severity.

Statistical analysis

All statistical analyses were performed using a two-sided hypothesis test at the overall 5% level of significance. Continuous data were summarized using descriptive statistics: mean, standard deviation, median, minimum, and maximum, unless otherwise noted. In addition, Exact Binomial Confidence Intervals were presented for selected percentages.

RESULTS

One hundred four subjects (59 Females/45 Males) were enrolled with a mean age of 22.2 (±5.5) years. Almost all Fitzpatrick skin types were represented in the study population, with 67% Caucasian, 20% Asian, and 13% Darker skin types IV, V, and VI (African American, Hawaiian, Others) (Supplementary Table II). Eighty-nine of the 104 subjects completed 3 treatments and the 4- and 12-week follow-ups.

Primary endpoints

Inflammatory lesion count assessment. Quantitative analysis of blinded assessments of inflammatory acne lesion counts demonstrated that the RR, as percentage of subjects with ≥50% reduction from baseline, increased following final treatment. The RR increased from 32.6% at 4-week follow-up to 79.8% at 12-weeks to 87.3% at 26-weeks following final treatment (Table I).

AEs assessments. During the study, 277 transients, mild AEs were observed; 104 transient erythema and 102 transient edema. Erythema resolved in 87% and 97% of subjects within 1 and 3 days, respectively; in 3%, within a week. Edema resolved in 81% and 96% of subjects within 1 and 3 days, respectively; in 4% within a week. Forty-seven AEs consisted of a transient self-limited acneiform flare-up 2 days to 3 weeks postlaser treatment. No incidence of vesiculation, blistering, scarring, or hyperpigmentation was observed across skin phototypes (Table I).

Secondary endpoints

Investigator acne severity assessments. *Baseline IGA.* Each grader scored IGA per subject, and medians of the 3 scores were used to summarize the data. Baseline IGA scores showed 99% of the pretreatment population presented moderate-to-severe acne (Supplementary Table IV, available via Mendeley at https://data.mendeley.com/datasets/7cdmrv3pjz).

Clear or almost clear subjects. Acne IGA severity following treatment demonstrated the percentage of subjects clear or almost clear increased from 0% at baseline to 9%, 36.0%, and 41.8% of subjects at 4-, 12-, and 26-week follow-up intervals, respectively (Table I).

Mild, moderate, or severe subjects. The percentage of subjects rated as mild, moderate, or severe acne decreased from 100% at baseline to 91%, 62.9%, and 58.2% at 4-, 12-, and 26-week follow-up, respectively (Table I).

2-point + IGA improvement. The percentage of subjects showing at least a 2-point improvement in their IGA scores improved progressively from 10.1% to 46% and 51.9% at the 4-week, 12-week, and 26-week follow-up intervals, respectively(Table I).

Subject satisfaction assessments. Subject satisfaction was high, with percentage of subjects reporting their skin looked better at 78.7%, 87.6%, and 79.7% at 4-week, 12-week, and 26-week follow-up intervals, respectively. The percentage of subjects reporting their skin looked smoother was 78.7%, 85.4% at and 82.3% at the 4-, 12-, and 26-week follow-up visits (Table I).

Other assessments

Nodule and noninflammatory lesion assessments. *Nodule count reduction.* The mean nodule count reduction compared to baseline increased progressively from 45% at 4-weeks to 69% at 12-weeks and 93% at 26-weeks following final treatment (Table I). Nodule counts reduced further by at least 35% in successive follow-up visits.

Noninflammatory lesion count reduction. The median noninflammatory (comedonal) lesion count reduction compared to baseline increased from 22% at 4-week follow-up to 31.7% at 12-weeks and 43.9% at 26-weeks following final treatment (Table I).

Periprocedural discomfort. All subjects tolerated all treatments well. Topical or local anesthetics were not used. No sessions ended prematurely due to excessive discomfort. The mean and median Visual Analog Scale scores reported by subjects at each treatment visit are summarized (Table I).

Subgroup analysis. RRs and periprocedural discomfort were analyzed per skin type, gender, age group, and baseline acne severity. Age groups were subdivided into 4 groups: 16-19, 20-22, 23-25, and 26+ years. Since no patient with mild acne at baseline was enrolled, acne severity subgroup included moderate, and severe acne subjects. Since no Fitzpatrick skin type I subjects were enrolled, the skin type subgroup included results for Type II-VI.

Responder rates. The RR was similar across all the subgroups analyzed, including skin phototypes, acne severity, gender, and age ranges (Table I).

Periprocedural discomfort. Discomfort scores were similar across all the subgroups analyzed, including skin phototypes, acne severity, gender, and age ranges (Table I).

Clinical outcomes

Before and after clinical photographs of severe acne in skin types II and VI are shown (Figs 1 and 2, Supplementary Figs 2 and 3, available via Mendeley at https://data.mendeley.com/datasets/7cdmrv3pjz). For each subject, baseline(pretreatment) and follow-up 4, 12, and 26-weeks postfinal treatment demonstrate progressive and durable reduction in acne lesions and posttreatment cosmesis through successive posttreatment follow-up intervals in each representative skin type (Figs 1 and 2, Supplementary Figs 2 and 3).

DISCUSSION

Based on the principles of selective photothermolysis, the 1726 nm wavelength is most preferentially absorbed by sebaceous glands making it an ideal choice for targeting acne lesions. Tuning the laser source and combining an efficient contact cooling system allows for a safe and efficacious treatment with durable outcomes without the need for pain mitigation.

In this study, we demonstrate a significant, durable reduction of moderate-to-severe acne across a broad range of skin types. Following 3 well-tolerated 1726 nm laser treatments, 79.8% of subjects demonstrated ≥50% improvement in inflammatory acne 3 months after the third treatment. Six months post-treatment, this rose to 87.3% of subjects, indicating that the sebaceous gland effect produced durable, progressive improvement. These findings of continued improvement over time without further treatment suggest a sebaceous gland modulating, mechanistic effect impacting the natural history of the disease (Supplementary Table V, available via Mendeley at https://data.mendeley.com/datasets/7cdmrv3pjz).

Ninety-nine of 104 subjects remained enrolled at the 12-week follow-up visit, with 5 dropping out due to nontreatment-related issues. Treatment was remarkably well-tolerated, with an average pain

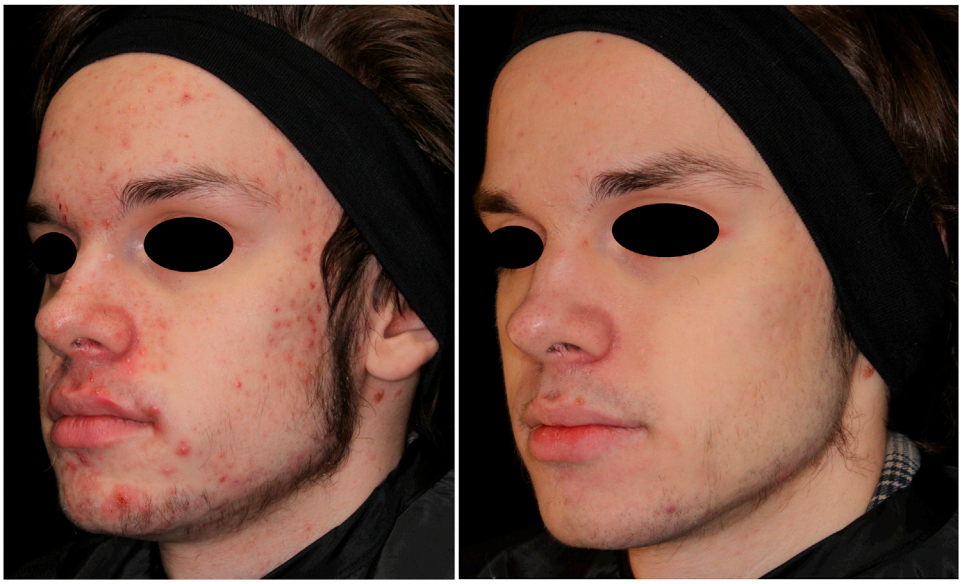

Fig 1. Clinical photos of a male patient (skin type II) taken at baseline pretreatment (left) and at 26 weeks follow-up postfinal treatment (right).

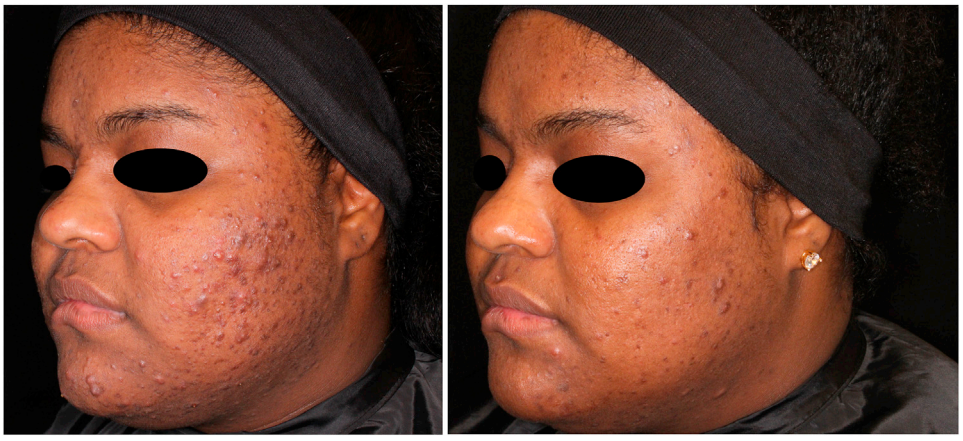

Fig 2. Clinical photos of a female patient (skin type VI) taken at baseline pretreatment (left) and at 26 weeks follow-up postfinal treatment (right).

score of 5.2 out of 10 despite no pain management. There was temporary perilesional erythema, but no residual erythema, edema, blistering, crusting hypo, or hyperpigmentation. An initial transient eruption between 2 days and 3 weeks posttreatment was observed prior to clearing, which resembles our observations postisotretinoin treatment. Subjects experiencing transient worsening were advised to increase topical administration of study physician-approved moisturizer to alleviate itchiness and/or dryness. Importantly, this is the first laser shown to be effective and with a favorable tolerability profile in all skin types II through VI.

The 1726 nm laser mechanism of action involves selective photothermolysis targeting of sebaceous glands. Histological assessments of skin samples excised 5 days posttreatment around the ear, ventrally between the fossa and tragus, demonstrated complete or almost complete sebaceous gland destruction (Supplementary Fig 4, available via Mendeley at https://data.mendeley.com/datasets/7cdmrv3pjz). These findings are consistent with the report by Sakamoto et al of a 1720 nm laser with contact cooling producing selective photothermolysis of sebaceous glands.[13] Furthermore, our findings provide an explanation for the durable, sustained, and progressive acne improvement observed for months following the final treatment. Thus, the 1726 nm laser may be the first treatment since isotretinoin that substantially reduces

sebaceous gland activity in a durable manner but with a far more acceptable AE profile.

The 1726 nm laser was well tolerated in the broad range of skin types studied here, yet controlled trials are needed with larger subject numbers and longer follow-up periods to reproduce treatment outcomes and response duration. The laser described here resulted in clinically meaningful progressive post-treatment improvement to at least 26-week follow-up and may alter the natural history of the disease, inducing a durable amelioration in moderate to severe acne across skin phototypes.

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Conflicts of interest

Dr Macrene Alexiades has no financial disclosures associated with this manuscript. Amogh Kothare is an employee of Cutera Inc. and serves as the Vice President of Clinical and Regulatory Affairs. Dr Jeffrey Dover is on the Medical Advisory Board of Cutera, Inc. Dr David Goldberg is a Clinical Investigator for Cutera, Inc.

REFERENCES

1. Bickers DR, Lim HW, Margolis D, et al. The burden of skin diseases: 2004 a joint project of the American Academy of Dermatology Association and the Society for Investigative Dermatology. *J Am Acad Dermatol*. 2006;55(3):490-500.
2. Bhate K, Williams HC. Epidemiology of acne vulgaris. *Br J Dermatol*. 2013;168(3):474-485.
3. Koo J. The psychosocial impact of acne: patients' perceptions. *J Am Acad Dermatol*. 1995;32(5 Pt 3):S26-S30.
4. Smithard A, Glazebrook C, Williams H. Acne prevalence, knowledge about acne and psychological morbidity in mid-adolescence: a community-based study. *Br J Dermatol*. 2001;145(2):274-279.
5. Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2016;74(5):945-973.e33.
6. Layton AM, Thiboutot D, Tan J. Reviewing the global burden of acne: how could we improve care to reduce the burden? *Br J Dermatol*. 2021;184(2):219-225.
7. Hongcharu W, Taylor CR, Chang Y, Aghassi D, Suthamjariya K, Anderson RR. Topical ALA-photodynamic therapy for the treatment of acne vulgaris. *J Invest Dermatol*. 2000;115(2):183-192.
8. Sakamoto FH, Lopes JD, Anderson RR. Photodynamic therapy for acne vulgaris: a critical review from basics to clinical practice: part I. Acne vulgaris: when and why consider photodynamic therapy? *J Am Acad Dermatol*. 2010;63(2):183-193. quiz 193-4.
9. Alexiades-Armenakas MR. Laser-mediated photodynamic therapy. *Clin Dermatol*. 2006;24(1):16-25.
10. Alexiades-Armenakas MR. Aminolevulinic acid photodynamic therapy for actinic keratoses/actinic cheilitis/acne: vascular lasers. *Dermatology Clinics*. 2007;25:25-33.
11. Boen M, Brownell J, Patel P, Tsoukas MM. The role of photodynamic therapy in acne: an evidence-based review. *Am J Clin Dermatol*. 2017;18(3):311-321.
12. Shah N, Smith E, Czermak J, Ferris M, Kirkorian AY. The administrative burden of prescribing and treating with isotretinoin. *J Am Acad Dermatol*. 2022;86(5):1165-1167.
13. Sakamoto FH, Doukas AG, Farinelli WA, et al. Selective photothermolysis to target sebaceous glands: theoretical estimation of parameters and preliminary results using a free electron laser. *Lasers Surg Med*. 2012;44(2):175-183.
14. Ezerskaia A, Pereira SF, Urbach HP, Varghese B. Depth resolved quantitative profiling of stratum corneum lipids and water content using short-wave infrared spectroscopy. In: *Photonics in dermatology and plastic surgery 2018*. International Society for Optics and Photonics; 2018.
15. Ezerskaia A, Pereira SF, Urbach HP, Verhagen R, Varghese B. Quantitative and simultaneous non-invasive measurement of skin hydration and sebum levels. *Biomed Opt Express*. 2016;7(6):2311-2320.
16. Burke BM, Cunliffe WJ. The assessment of acne vulgaris--the Leeds technique. *Br J Dermatol*. 1984;111(1):83-92.
17. Witkowski JA, Parish LC. The assessment of acne: an evaluation of grading and lesion counting in the measurement of acne. *Clin Dermatol*. 2004;22(5):394-397.
18. Chiang A, Hafeez F, Maibach HI. Skin lesion metrics: role of photography in acne. *J Dermatolog Treat*. 2014;25(2):100-105.
19. Chiang A, Hafeez F, Maibach HI. Photography in acne: skin metrics. In: Humbert P, Agache P, eds. *Measuring the skin*. Springer International Publishing; 2015:1-13.