Published in final edited form as:

Br J Dermatol. 2014 November ; 171(5): 1156–1163. doi:10.1111/bjd.13119.

Improving acne keloidalis nuchae with targeted ultraviolet B treatment: a prospective, randomized, split-scalp comparison study

G.A. Okoye^{1,*}, B.M. Rainer^{1,*}, S.G. Leung¹, H.S. Suh^{1,2}, J.H. Kim¹, A.M. Nelson¹, L.A. Garza¹, A.L. Chien¹, and S. Kang¹

¹Department of Dermatology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

²Department of Dermatology, University of Ulsan College of Medicine, Ulsan, Korea

Abstract

Background—Acne keloidalis nuchae (AKN) is a chronic scarring folliculitis with fibrotic papules on the occipital scalp. Its treatment is limited and unsatisfactory.

Objectives—To determine if targeted ultraviolet B (tUVB) phototherapy will (1) improve the clinical appearance of AKN and (2) induce extracellular matrix remodeling in affected lesions.

Methods—Eleven patients with AKN were enrolled in a prospective, randomized, split-scalp comparison study. One randomly selected side of the scalp was treated with tUVB up to three times weekly for eight weeks. After week 8, both sides were treated for eight additional weeks. Assessment included lesion counts in two 3×3 cm regions of interest (ROI), one on each side of the scalp (ROI-1: tUVB week 0–16, ROI-2: tUVB week 9–16), patient self-assessment, and analysis of MMP-1, MMP-9, TGF-β1, and Col1a1 mRNA expression by qRT-PCR.

Results—Before treatment, the mean lesion count was similar between tUVB-treated and untreated sides (14.8 vs. 15.0). After eight weeks of tUVB, the mean lesion count decreased significantly to 9.4±1.2 (P=0.03), with no change on the untreated side. With continued treatment, the mean lesion count in ROI-1 decreased further to 7±1.5 (P=0.04) after 16 weeks of tUVB.

Conclusion—Targeted UVB significantly improved clinical appearance of AKN, led to patient satisfaction, and was well tolerated.

Keywords

acne keloidalis nuchae; ethnic skin; targeted ultraviolet B; phototherapy; extracellular matrix remodeling

Corresponding author: Barbara M. Rainer, M.D., Department of Dermatology, Johns Hopkins University School of Medicine, 1550 Orleans Street, Baltimore, MD 21231, USA, phone: 1 (410) 502-7546; fax: 1 (410) 502-2309, bm.rainer@gmail.com.

*These authors contributed equally to this work.

Disclosures: None declared.

A portion of this work was presented at the International Investigative Dermatology meeting in Edinburgh, UK, in May 8–11, 2013. The contents of this manuscript have not been copyrighted or published previously and are not under consideration by any other journal.

Introduction

Acne keloidalis nuchae (AKN) is a chronic scarring folliculitis characterized by fibrotic, keloid-like papules and plaques on the occipital scalp and posterior neck and can significantly affect patients' quality of life. AKN prevalence is highest among men of African descent (up to 10%), and the male to female ratio is at least 20:1.^{1,2} Early AKN lesions manifest as inflammatory papules and pustules, and they often coexist with firm fibrotic follicular papules and hypertrophic scars.³ As the disease progresses the papules tend to coalesce and form hairless keloid-like plaques that may be painful and disfiguring. Histological studies show evidence of follicular and perifollicular inflammation in early lesions, whereas more advanced lesions reveal disrupted hair follicles, a foreign-body reaction with acute and granulomatous inflammation, and subsequent dense dermal fibrosis and scarring.⁴

The pathogenesis of AKN is associated with several factors including chronic mechanical irritation (e.g. close shaving and mechanical shearing of the hairs) stimulating an inflammatory reaction, and low-grade bacterial infection; the exact mechanisms, however, have remained elusive.⁵

Several treatment options including topical and oral antibiotics are available for the early inflammatory stage of AKN. However, many patients present with more pronounced fibrotic lesions for which treatment modalities are limited. The current surgical and conservative treatments of fibrotic papules and plaques including excision, topical and intralesional steroids, and cryotherapy often lead to unsatisfactory results.⁵ To date, there are very few rigorous studies examining novel, noninvasive, efficacious, and cost-effective treatment options with few side effects for the prevention or treatment of the dermal fibrosis seen in AKN.

Ultraviolet (UV) irradiation induces the production of several members of the matrix metalloproteinase (MMP) family, which degrade collagen fibrils and other components of the dermal extracellular matrix (ECM). The subfamily of collagenases including MMP-1 (interstitial collagenase) degrades native fibrillar interstitial collagens, whereas gelatinases including MMP-9 (gelatinase B) efficiently digest degraded collagen, thus complementing collagenases in the degradation of fibrillar collagen.⁶⁻⁸ In addition to turnover and degradation of the ECM, MMPs also regulate various inflammatory, repair and immune processes. MMPs are also key players in activating transforming growth factor beta (TGF- β 1), a ubiquitously expressed cytokine with multiple regulatory properties depending on cell type, growth conditions and context-specific cofactors.⁹

Whereas longer wavelengths of UVA were more effective in inducing anti-fibrotic responses in lighter skin¹⁰, our previous work suggests that the more energetic, shorter wavelengths of UVB are more potent in inducing anti-fibrotic responses in darker skin (data unpublished). Thus, we sought to investigate the effects of UVB-based phototherapy on AKN.

We used a targeted UVB (tUVB) phototherapy device (Daavlin Lumera Phototherapy System, Bryan, Ohio, USA). The main benefit of tUVB therapy is focused delivery of radiation directly to lesional skin without affecting uninvolved areas.

Methods

Study design

The study was a single-center, investigator-initiated, prospective, randomized, split-scalp trial to evaluate the efficacy and safety of tUVB radiation in improving the clinical appearance of AKN lesions. The study was approved by the Johns Hopkins Institutional Review Board and registered with ClinicalTrials.gov (NCT01328080). Study procedures were conducted at the Johns Hopkins Department of Dermatology in Baltimore, MD, between April 2011 and August 2012.

Patient population

Eligible patients were 18 years of age and older with Fitzpatrick skin types III to VI and had a clinical diagnosis of AKN with at least three papular keloid-like lesions on each side of the occipital scalp. Study exclusion criteria included a history of photosensitive disorders, use of photosensitizing medications, history of skin cancer, and previous radiation therapy to the scalp. Also those with lidocaine allergy, bleeding disorders, pregnancy, and lactation were excluded. For the duration of the study, patients were not allowed to use any other treatment modality for their AKN, and they were advised to avoid close shaving of the occipital scalp. There was a 4-week washout period for antibiotics (topical/oral), corticosteroids (topical), and a 6-month washout period for oral isotretinoin. Patients were recruited from the dermatology clinics at the Johns Hopkins University Hospitals, Baltimore, Maryland, USA, and through newspaper advertisements. The study was conducted in accordance with the ethical principles originating from the Declaration of Helsinki and in compliance with local regulatory requirements. Written informed consent was obtained from all patients.

This was a pilot study in a poorly studied medical condition, and a convenience sample of 11 patients presenting between April 2011 and May 2012 was enrolled.

Randomization and masking

The side of the scalp to be treated was randomized as 'left' or 'right' using a computer-generated sequence. This was put into a sealed envelope by a research staff member who was not involved in the clinical assessment. The envelope was opened once the patient was consented. The grading investigator was not involved in randomization of patients or skin biopsies.

Intervention

All patients were randomly assigned to receive tUVB phototherapy three times a week for 16 weeks to either the right or the left side of the scalp. The untreated side served as an internal control for the first eight weeks, after which both sides of the scalp were treated. Only clinically affected areas of the scalp were treated. The Lumera Phototherapy System uses an enhanced metal halide arc lamp. The energy emitted is in the UVB band (290 to 320

nm) with peaks at 303 nm and 313 nm. The device's flexible fiber hand piece (light output profile of 1.7×1.7 cm) allows for localized treatment of skin lesions. As there are currently no data to guide the initial UVB radiation dose, nor the subsequent incremental dose escalations, we decided that the individual's minimal erythema dose (MED) (0.23–0.48 J/cm²) was appropriate for the initial treatment dose. The dose was increased by 20% with each treatment as tolerated. If erythema and discomfort developed during treatment, planned incremental increases in UVB dose were postponed or treatments were skipped until the erythema and local symptoms resolved. At week 9, investigators started treatment to both sides of the scalp. Maintenance therapy using the last UVB dose given at week 8 was given for up to eight additional weeks on the initially treated side of the scalp. The UVB dose on the previously untreated side was started at the patient's MED and increased by 20% per session as described above. After 16 weeks, treatment to both sides was stopped.

Clinical assessment

To standardize AKN lesion counts, two 3×3 cm regions of interest (ROI) were selected within the affected area of the occipital scalp, one on each side of the scalp prior to randomization. ROI-1 was determined to receive tUVB treatment from baseline to week 16, while ROI-2 received tUVB from weeks 9 to 16 (Fig. 1). The total number of palpable AKN lesions in each ROI was recorded at baseline and at the end of weeks 8 and 16. Lesions were classified according to size as small (<2 mm), medium (2–4 mm) and large (>4 mm) by a dermatologist.

At baseline, patients completed a self-administered questionnaire that collected basic demographic information and their AKN history. At the end of weeks 8 and 16, patients evaluated the efficacy of treatment according to the following global improvement scale: (–1) worse; (0) no improvement; (1) mild-to-moderate improvement; (2) marked improvement; (3) clear.

Primary outcomes were reduction in AKN lesion count after 16 weeks of tUVB treatment and patient's self-assessed improvement.

Quantitative analysis of MMP, TGF-β, and collagen expression by real-time PCR

Clinically similar fibrotic AKN lesions outside the ROIs were pre-selected at baseline. Skin specimens were obtained by 3-mm punch biopsies from lesional treated (ROI-1), lesional untreated (ROI-2), and non-lesional unexposed scalp (post auricular) at the end of week 8 and from lesional treated (ROI-1) scalp at the end of week 16. The specimens were placed in RNeasy Lysis Buffer (Qiagen, St. Louis, MO, USA) and stored at –80°C. Samples were homogenized and RNA extracted with the RNeasy Fibrous Tissue kit (Qiagen, Valencia, CA, USA) and transcribed to cDNA (High Capacity RNA to cDNA; Applied Biosystems, Carlsbad, CA, USA) according to manufacturer's instructions. qRT-PCR was performed on samples (50 ng cDNA) for MMP-1, MMP-9, TGF-β1, Col1a1 (collagen, type I, alpha I), and the housekeeping gene acidic ribosomal phosphoprotein P0 (36B4) using inventoried TaqMan gene expression assays from Applied Biosystems. Differences in gene expression were assessed by comparative CT values with fold-change calculations.

Statistical analyses

Data are expressed as mean and standard error of the mean (SEM). Data distributions were tested for normality with the Shapiro-Wilk test. Statistical analyses were performed by two-tailed Student's *t*-test and by two-way analysis of variance (ANOVA) followed by Bonferroni post hoc test using SPSS statistical software (version 21.0; SPSS Inc., Chicago, IL, USA). $P < 0.05$ was accepted as significant.

Results

Participant flow

Patients were recruited between April 2011 and May 2012, with the final treatment/assessment completed by August 2012. Eleven patients were enrolled; their progression throughout the study is presented in Fig. 2. One patient withdrew before the start of treatment, and one no longer met the inclusion criteria (usage of oral antibiotics/photosensitizing drugs). Two patients failed to attend after week 1 and week 7, respectively, and were not included in the weeks 8 and 16 assessments. Seven patients completed eight weeks of tUVB phototherapy to the randomized side of the scalp and started treatment to both sides. Six patients completed the entire 16-week trial.

Patients

Demographic data, AKN history (age range at onset, previous treatment, family history) and MED/UVB start dose for all enrolled patients is presented in Table 1. The mean age was 36.6 years (range 25–45) and all patients were male with skin types V and VI. Eight patients (72.7%) developed AKN before the age of 25 and three patients (27.3%) after the age of 25.

Treatment characteristics

Treatment characteristics for each patient are presented in Table 2. The initial mean dose administered was 0.3 (0.23–0.48) J/cm² at the start of tUVB treatment. At the end of weeks 8 and 16, the mean cumulative UVB doses administered to the initially randomized side were 29.7 (15.4–40.8) J/cm² and 82.2 (32.8–118.3) J/cm², with a median number of 17 (13–21) and 33 (26–39) treatments, respectively.

At the start of tUVB treatment to the contralateral side of the scalp (week 9), the mean dose administered was 0.3 (0.23–0.48) J/cm². At the end of week 16, the mean cumulative UVB dose administered to the contralateral side was 13.2 (5.0–19.2) J/cm² with a median number of 15 (10–16) treatments.

Clinical efficacy assessment

Lesion counts—Detailed information on the AKN lesion counts and percentage reduction from baseline is presented in Table 3. All patients had reductions in AKN lesion counts after tUVB phototherapy. Before treatment, the mean total lesion counts for ROI-1 and ROI-2 were 14.8 ± 4.2 and 15.0 ± 6.2 ($P = 0.94$), respectively. After eight weeks of tUVB treatment, the mean total lesion count decreased significantly in ROI-1 to 9.4 ± 1.2 ($P = 0.03$). There was a significant difference between treated and untreated sides with mean lesion count reduction of $34 \pm 5.3\%$ and $1.3 \pm 5.2\%$ in ROI-1 and ROI-2, respectively ($P = 0.009$).

After 16 weeks of treatment, the mean lesion count in ROI-1 decreased further to 7 ± 1.5 (mean 49% reduction; $P=0.04$). After initiation of treatment to both sides of the scalp at week 9, the mean total lesion count in ROI-2 decreased to 10.8 ± 3.4 (mean 33% reduction; $P=0.07$) by week 16 (Fig. 3). Categorized by size, significant lesion count reductions of medium-sized (2–4 mm) lesions from baseline were obtained after 16 weeks of treatment (Fig. 4) and showed up to a 75% reduction ($P=0.02$).

Patient self-assessments—Six patients completed a simple self-administered questionnaire relating to the outcome of treatment. Of the six patients, all were responders (at least mild-to-moderate improvement). Five patients (83.3%) had “marked improvement” and one (16.7%) had “mild-to-moderate improvement”. All patients tolerated the tUVB exposure well. The clinical improvement is shown in a representative photograph in Fig. 5.

MMP-1, MMP-9, TGF- β 1, and Col1a1 expression

MMP-1, MMP-9, TGF- β 1, and Col1a1 mRNA expression was significantly higher in untreated AKN lesions compared to clinically uninvolved skin ($P<0.05$). After 16 weeks of tUVB, expression levels further increased compared to untreated lesions, however, due to the limited number of samples the results did not reach statistical significance (Fig. 6).

Side effects

None of the study patients experienced any serious side effects from the tUVB therapy. A mild transient burning sensation and erythema was reported by two patients; treatment was held until erythema and symptoms resolved and restarted at the previous lower dose. Neither patient required cessation of treatment. UV induced pigmentation was visible in the treatment area.

Discussion

Our study resulted in three key findings. First, tUVB treatment significantly improved the clinical appearance of AKN, as reflected in the lesion count reduction and patient self-assessment. Second, no instance of unusual photosensitivity was noted, and all patients tolerated the treatment well. Third, MMP-1, MMP-9, TGF- β 1, and Col1a1 expression is high in AKN lesions, and 16 weeks of tUVB treatment tended to further increase their expression, suggesting that matrix turnover is additionally enhanced by this treatment.

Due to the well-known anti-inflammatory, immunosuppressive and anti-fibrotic effects of UV radiation, phototherapy is widely used in the treatment of psoriasis, atopic dermatitis, sclerosing skin conditions (e.g. morphea, scleroderma), vitiligo, and mycosis fungoides. To our knowledge, however, the effects of phototherapy on AKN were not previously investigated or published.

Based on the above-mentioned effects of phototherapy, we hypothesized that tUVB may improve the clinical appearance of AKN lesions and induce matrix remodeling in affected lesions.

For this pilot study, we used a split-scalp design, with patients serving as their own control until the end of week 8. During the first eight weeks of treatment, there was a significant clinical improvement of the AKN lesions that received tUVB phototherapy up to three times weekly, compared with those that did not receive tUVB treatment. After 16 weeks (end of treatment), a significant reduction in the total lesion count (up to 61%; $P=0.04$) was observed compared to baseline. ROI-1 (weeks 0–8) and ROI-2 (weeks 9–16) showed comparable lesion count reductions after eight weeks of tUVB treatment [34% (21–52) and 33% (20–53), respectively]. While the decrease in lesion count was significant for ROI-1, it was not significant (but trended at $P=0.07$) for ROI-2. Fewer treatments (median of 17 and 15 sessions for ROI-1 and ROI-2, respectively), and thus lower mean cumulative UVB dose administered to ROI-2 (29.7 J/cm² and 13.2 J/cm² for ROI-1 and ROI-2, respectively), may have affected the statistical significance. Particularly, as we used an incremental dose-escalation regimen, and failure to participate in treatment sessions prevented the dose-escalation. Importantly, despite the lower UVB dose administered to ROI-2, the lesion count reduction showed a strong statistical trend ($P=0.07$) suggesting that a lower dose may still be effective.

When fibrotic AKN lesions were categorized by their size, small (<2mm) lesions showed a mean reduction from baseline of 36% ($P=0.11$) after eight and 27% ($P=0.17$) after 16 weeks. Medium-sized (2–4 mm) lesions demonstrated a mean reduction from baseline of 23% ($P=0.3$) after eight and 68% ($P=0.02$) after 16 weeks. The relatively higher reduction in medium-sized lesions compared to small-sized lesions after 16 weeks of treatment may be the result of UVB-induced collagen breakdown, hence shrinking of lesions. In support of this notion, larger lesions became smaller in the course of tUVB treatment and small lesions seemed to clinically disappear (Fig. 4).

In addition to the clinical appearance, we also assessed the expression levels of MMP-1, MMP-9, TGF- β 1, and Colla1, which play important roles in ECM remodeling. mRNA expression of all of these markers was significantly increased in untreated AKN lesions compared to clinically healthy skin. Hence, even in clinically quiescent AKN lesions, substantial matrix turnover likely takes place. After 16 weeks of tUVB, MMP-1, MMP-9, TGF- β 1, and Colla1 mRNA expression levels further increased compared to untreated lesions suggesting that extracellular matrix turnover is additionally enhanced by tUVB. However, due to the relatively small number of patients in our pilot study and the variance typically observed in patients, the results did not reach statistical significance. Nonetheless, these data provide a hint to a potential mechanism on how tUVB treatment clinically improves AKN. Future studies, which are adequately powered to address the molecular changes in a clinical patient collective, are needed to unequivocally demonstrate the effects of tUVB in this respect.

Inflammatory and fibrotic lesions often coexist in AKN³, and the anti-inflammatory and anti-fibrotic effects of UV radiation may act in concert to improve the overall clinical appearance. Thus, starting treatment with tUVB at an early disease stage may not only prevent the development of new inflammatory lesions, but may also prevent the progression from inflammatory to fibrotic lesions, such as keloidal papules and plaques.

Despite the high prevalence of AKN in men of African descent, there have only been very few interventional studies examining the effects of non-surgical, minimally invasive treatments. One recent study assessed the efficacy of Nd-YAG laser assisted hair removal in AKN and concluded that the destruction of hair follicles after five treatments over four months had potential in improving both papules and plaques of AKN.¹¹ The rationale for laser hair removal for AKN is that destruction of the hair follicle removes the nidus of inflammation and may prevent subsequent fibrosis. However, the Nd-YAG laser device is rather costly and hence broad availability is limited; thus, a lower cost device such as the targeted UVB phototherapy system may offer a good alternative.

In conclusion, we used a hypothesis-driven approach to investigate the effects of tUVB phototherapy for AKN. Most treated AKN lesions responded to tUVB, and no new lesions were noticed during the treatment period. Our pilot study provides strong evidence for the efficacy and safety of tUVB in the treatment of AKN for the dose and duration of treatment administered. With additional clinical experience and treatment optimization, tUVB may become a new and effective treatment for AKN.

Limitations

This study was a pilot study and limited by the small number of patients. However, to the best of our knowledge, this is the first report that tUVB phototherapy improves AKN. Larger controlled trials with long-term follow-up are needed to validate our findings, to assess durable effects and long-term hazards of tUVB phototherapy in AKN, and more thoroughly address the molecular changes underlying its clinical effects. Due to tanning/occasional erythema responses and symptom reporting (burning, itching) to tUVB, complete blinding of the treatment side was not possible. Lastly, the time commitment required for this treatment (in-office visit, up to three times weekly) may affect patient compliance in clinical practice.

Acknowledgments

Funding

Grant support was received from the Skin of Color Society. The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. This study was also supported in part from the Provost Young Investigator Fund of the Johns Hopkins Department of Dermatology. LAG was supported in part by the National Institutes of Health (R01AR064297).

Abbreviations

AKN	acne keloidalis nuchae
UV	ultraviolet
TGF-β1	transforming growth factor beta 1
MMP	matrix metalloproteinase
Col1a1	collagen, type I, alpha I
tUVB	targeted ultraviolet B

ROI	region of interest
qRT-PCR	quantitative real-time polymerase chain reaction
ECM	extracellular matrix
MED	minimal erythema dose
cDNA	complementary deoxyribonucleic acid
SEM	standard error of the mean
OTC	over the counter

References

1. Salami T, Omeife H, Samuel S. Prevalence of acne keloidalis nuchae in nigerians. *Int J Dermatol*. 2007; 46(5):482–484. [PubMed: 17472675]
2. Khumalo NP, Jessop S, Gumedze F, Ehrlich R. Hairdressing and the prevalence of scalp disease in african adults. *Br J Dermatol*. 2007; 157(5):981–988. [PubMed: 17725667]
3. Coley MK, Alexis AF. Managing common dermatoses in skin of color. *Semin Cutan Med Surg*. 2009; 28(2):63–70. [PubMed: 19608055]
4. Sperling LC, Homoky C, Pratt L, Sau P. Acne keloidalis is a form of primary scarring alopecia. *Arch Dermatol*. 2000; 136(4):479–484. [PubMed: 10768646]
5. Kelly AP. Pseudofolliculitis barbae and acne keloidalis nuchae. *Dermatol Clin*. 2003; 21(4):645–653. [PubMed: 14717405]
6. Fisher GJ, Wang ZQ, Datta SC, Varani J, Kang S, Voorhees JJ. Pathophysiology of premature skin aging induced by ultraviolet light. *N Engl J Med*. 1997; 337(20):1419–1428. [PubMed: 9358139]
7. Brennan M, Bhatti H, Nerusu KC, et al. Matrix metalloproteinase-1 is the major collagenolytic enzyme responsible for collagen damage in UV-irradiated human skin. *Photochem Photobiol*. 2003; 78(1):43–48. [PubMed: 12929747]
8. Do TT, Bailey EC, Wang F, et al. Targeted broadband ultraviolet B phototherapy improves disorders characterized by increased dermal matrix. *Br J Dermatol*. 2009; 161(6):1405–1407. [PubMed: 19754865]
9. Parks WC, Wilson CL, López-Boado YS. Matrix metalloproteinases as modulators of inflammation and innate immunity. *Nat Rev Immunol*. 2004 Aug; 4(8):617–29. [PubMed: 15286728]
10. Wang F, Garza LA, Cho S, et al. Effect of increased pigmentation on the antifibrotic response of human skin to UV-A1 phototherapy. *Arch Dermatol*. 2008; 144(7):851–858. [PubMed: 18645136]
11. Esmat SM, Abdel Hay RM, Abu Zeid OM, Hosni HN. The efficacy of laser-assisted hair removal in the treatment of acne keloidalis nuchae; a pilot study. *Eur J Dermatol*. 2012; 22(5):645–650. [PubMed: 23018044]

What's already known about this subject?

- Acne keloidalis nuchae (AKN) is a chronic scarring peri-folliculitis with limited treatment options.
- Ultraviolet (UV) radiation has anti-inflammatory, immunosuppressive, and anti-fibrotic effects.

What does this study add?

- Targeted UVB significantly improves clinical appearance of AKN and is well tolerated.
- Targeted UVB increases MMP-1, MMP-9, TGF- β 1, and Colla1 expression in AKN lesions, suggesting active matrix remodeling.

Fig. 1. Treatment area (affected scalp) and region of interest (ROI, 3×3cm). *ROI-1: tUVB week 0–16, ROI-2: tUVB week 9–16.*

Fig. 2.
Flow chart of participation (CONSORT Flow Diagram)

Fig. 3. Therapeutic response of AKN patients treated with tUVB. **(a)** Mean number of total AKN lesions at baseline, week 8 and 16 in ROI-1 vs. ROI-2. **(b)** Mean percent reduction in lesion counts at week 8 and week 16 in ROI-1 vs. ROI-2, compared to baseline. Results are Mean $\pm$ SEM. * $P < 0.05$. ROI-1: tUVB week 0–16, ROI-2 tUVB: week 9–16.

Fig. 4. Mean number of small (<2mm), medium (2–4 mm), large (> 4 mm) AKN lesions at baseline, week 8 and 16 in ROI-1 (tUVB week 0–16). Results are Mean $\pm$ SEM. * $P < 0.05$.

Fig. 5.

(a) Affected scalp before treatment. **(b)** Reduction in AKN lesions at week 16 (right, ROI-1 tUVB: week 0–16; left, ROI-2: tUVB week 9–16).

Fig. 6.

Upregulation of MMP-1, MMP-9, TGF-β1, and Col1a1 mRNA in 16 weeks treated compared to untreated and uninvolved skin. Total RNA was extracted from full-thickness (3-mm) skin biopsies and (a) MMP-1, (b) MMP-9, (c) TGF-β1, and (d) Col1a1 mRNA levels were determined by qRT-PCR. Results are mean fold-expression changes ± SEM of the target gene normalized to 36B4 (internal control) mRNA. N=4–6, *P<0.05.

Table 1

Patient characteristics at baseline.

Patient No./Sex/Age	Skin Type	Age at Onset, y	Previous Treatments	Family History of AKN	MED, J/cm ²	Comment
1/M/39*	V	20–25	none	unknown	0.225	dropped out at week 7
2/M/25	V	15–20	Topical corticosteroids, topical and oral antibiotics	no	0.3	
3/M/41*	VI	10–15	Topical and intralesional corticosteroids, topical and oral antibiotics, laser treatment	no	N/A	withdrew consent
4/M/45	V	>25	Topical steroids, oral antibiotics	unknown	0.3	
5/M/32*	V	10–15	none	no	0.25	ineligible for study
6/M/35	V	>25	natural home remedy	no	0.225	
7/M/40	V	20–25	OTC products	yes	0.225	
8/M/32	VI	20–25	Topical and intralesional corticosteroids, topical and oral antibiotics	unknown	0.475	dropped out at week 11
9/M/39	V	20–25	OTC products and topical antibiotics	no	0.3	
10/M/51	V	>25	Oral antibiotics	unknown	0.3	
11/M/35*	V	10–15	OTC products	no	0.3	dropped out at week 1

MED, minimal erythema dose; OTC, over the counter;

* excluded from final analysis.

Table 2

Treatment characteristics of the randomized side of the scalp at week 8 and 16 and efficacy assessment by patient at week 16.

Patient No.	Number of treatments received (week 8/16)	Cumulative tUVB dose, J/cm ² (week 8/16)	Efficacy assessment by patient (week 16)
2	20/39	15.4/62.3	marked improvement
4	17/30	32/96.5	mild/moderate improvement
6	21/34	40.5/118.3	marked improvement
7	20/36	40.8/115.8	marked improvement
8	13/drop out at week 11	22.3/-	-
9	16/26	19/32.8	marked improvement
10	16/31	24.2/67.7	marked improvement

tUVB, targeted ultraviolet B

Table 3

Mean AKN lesion count and percentage reduction from baseline. ROI-1: tUVB week 0–16, ROI-2: tUVB week 9–16. Results are Mean $\pm$ SEM (range).

	ROI-1	ROI-2
Total count of AKN lesions		
Baseline	14.8 $\pm$ 2.6 (8–23)	15.0 $\pm$ 3.9 (5–28)
Week 8	9.4 $\pm$ 1.2 (6–12)	14.8 $\pm$ 4.3 (5–30)
Week 16	7 $\pm$ 1.5 (4–10)	10.8 $\pm$ 3.4 (4–18)
% Reduction from baseline at week 8	34% (21%–52%)	1.3% (–20%–23%)
% Reduction from baseline at week 16	49% (29%–61%)	33% (20%–53%)
Small lesions (<2 mm)		
Baseline	8.6 $\pm$ 1.9 (4–14)	9.4 $\pm$ 2.4 (3–17)
Week 8	4.8 $\pm$ 0.9 (3–7)	9.2 $\pm$ 2.4 (3–18)
Week 16	5.3 $\pm$ 1.0 (3–7)	8.3 $\pm$ 2.6 (3–14)
% Reduction from baseline at week 8	36% (–17%–71%)	0.6% (–33%–25%)
% Reduction from baseline at week 16	27% (–17%–58%)	18% (0–44%)
Medium lesions (2–4 mm)		
Baseline	5.6 $\pm$ 1.1 (3–8)	4.8 $\pm$ 1.4 (1–9)
Week 8	4.6 $\pm$ 0.7 (3–7)	5.0 $\pm$ 2.0 (1–11)
Week 16	1.8 $\pm$ 0.5 (1–3)	2.3 $\pm$ 0.8 (1–4)
% Reduction from baseline at week 8	23% (0–50%)	6% (–22%–67%)
% Reduction from baseline at week 16	68% (62.5%–75%)	44% (0%–67%)
Large lesions (>4 mm)		
Baseline	0.6 $\pm$ 0.5 (0–1)	0.8 $\pm$ 0.4 (0–2)
Week 8	0	0.6 $\pm$ 0.2 (0–1)
Week 16	0	0.3 $\pm$ 0.3 (0–1)
% Reduction from baseline at week 8	75% (0%–100%)	10% (0–50%)
% Reduction from baseline at week 16	75% (0%–100%)	62.5% (0%–100%)

AKN, acne keloidalis nuchae; ROI, region of interest; tUVB, targeted ultraviolet B; SEM, standard error of the mean.