STUDY

Randomized Double-blind Trial of Treatment of Vitiligo

Efficacy of Psoralen–UV-A Therapy vs Narrowband–UV-B Therapy

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Objective: To compare the efficacy of oral psoralen–UV-A (PUVA) with that of narrowband–UV-B (NB-UVB) phototherapy in patients with nonsegmental vitiligo.

Design: Double-blind randomized study.

Setting: Phototherapy unit in a university hospital.

Patients: Fifty-six patients with nonsegmental vitiligo.

Interventions: Twice-weekly therapy with PUVA or NB-UVB.

Main Outcome Measures: The change in body surface area affected by vitiligo and the color match of repigmented skin compared with unaffected skin were assessed after 48 sessions of therapy, at the end of the therapy course, and 12 months after the end of therapy.

Results: The results in the 25 patients each in the PUVA and NB-UVB groups who began therapy were analyzed. The median number of treatments was 47 in the PUVA-treated group and 97 in the NB-UVB–treated group ($P=.03$); we suspect this difference was because of the differences in efficacy and adverse effects between the 2 modalities, such that patients in the NB-UVB group wanted a longer course of treatment. At the end of therapy, 16 (64%) of 25 patients in the NB-UVB group showed greater than 50% improvement in body surface area affected compared with 9 (36%) of 25 patients in the PUVA group. The color match of the repigmented skin was excellent in all patients in the NB-UVB group but in only 11 (44%) of those in the PUVA group ($P<.001$). In patients who completed 48 sessions, the improvement in body surface area affected by vitiligo was greater with NB-UVB therapy than with PUVA therapy ($P=.007$). Twelve months after the cessation of therapy, the superiority of NB-UVB tended to be maintained.

Conclusion: In the treatment of nonsegmental vitiligo, NB-UVB therapy is superior to oral PUVA therapy.

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THE PSYCHOSOCIAL EFFECT OF vitiligo should not be underestimated.[1] Several treatments have been advocated, including topical therapy with potent topical corticosteroids, calcipotriol, or tacrolimus; pseudocatalase therapy; melanocyte transplantation; skin grafting; cosmetic camouflage or self-tanning preparations; and psychological therapy, but these are often unsatisfactory.[2] The combination of treatment with psoralen followed by irradiation with UV-A (PUVA) is a well-established treatment for nonsegmental vitiligo, but it has many disadvantages. In the past decade, there have been reports of good efficacy using narrowband UV-B therapy (NB-UVB; 311-313 nm, TL-01 lamp, Koninklijke Philips Electronics NV, Amsterdam, the Netherlands) to treat the condition.[3-18] To our knowledge, we report the first double-blind randomized trial of PUVA therapy using oral psoralen vs NB-UVB therapy for vitiligo.

For editorial comment see page 643

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METHODS

PATIENTS

The trial was approved by the local research ethics committee, and all participants gave informed consent. Sample size calculations suggested that for 80% power to detect a difference of at least 20 percentage points in the improvement in surface area affected (measured as percentage of the pretreatment surface area affected), using nonparametric analysis at the 5% significance level, 44 patients with vitiligo were needed. Therefore, to allow for

dropouts, 56 patients with vitiligo were recruited through the phototherapy clinic of St John's Institute of Dermatology, London, United Kingdom, between April 1, 2002, and January 31, 2004; the study was terminated in September 30, 2005.

The inclusion criterion was nonsegmental vitiligo affecting 2% to 70% of the body surface area. Exclusion criteria included age younger than 18 years or older than 70 years, previous skin malignancy, previous failure of intolerance to photochemotherapy, more than 100 sessions of photochemotherapy in the patient's lifetime, treatment for vitiligo within the last 3 months (phototherapy, systemic therapy, or topical therapy with corticosteroid agents, vitamin D analogues, or tacrolimus), pregnancy, lactation, renal or hepatic disease, lupus erythematosus, a history of photosensitivity, or administration of a drug known frequently to cause photosensitization.

ADMINISTRATION OF ORAL PSORALEN OR PLACEBO

After enrollment in the study, patients were randomly allocated to receive either PUVA or NB-UVB therapy by means of a sequentially numbered list held in the pharmacy. The dermatologist conducting the assessments (S.S.Y.) was blinded to the treatment allocations; nursing and pharmacy staff conducting the treatment were necessarily aware of them. To ensure full patient blinding, the phototherapy cabinet labels were concealed, and 2 hours before treatment, all patients ingested identical-appearing tablets: placebo in the NB-UVB group and 8-methoxypsoralen (8-MOP; 10-mg Puvasoralen tablets; Crawford Pharmaceuticals Ltd, Milton Keynes, United Kingdom) in the PUVA group. The dose of 8-MOP was determined according to patient body surface area, namely, 25 mg/m^2, and ranged from 30 to 60 mg. All patients were advised that nausea from the medication was a possibility. During the course of the study, patients intolerant of 8-MOP because of nausea instead were given identical-appearing 5-methoxypsoralen (5-MOP) tablets (20-mg Pentaderm tablets; Crawford Pharmaceuticals Ltd) at a dose of 50 mg/m^2 (range, 60-80 mg) 3 hours before phototherapy.

UV SOURCES

Therapy with PUVA was administered in a Waldmann 6002 cabin (Herbert Waldmann GmbH, Villingen-Schwenningen, Germany) containing 40 Waldmann 100-W UV-A fluorescent tubes. The UV-A irradiance at the surface of the patient's skin was approximately 17.4 mW/cm^2. The NB-UVB treatments were administered in a Waldmann UV5000 cabinet containing 24 Philips 100-W NB-UVB fluorescent tubes emitting predominantly in the wavelength range of 311 to 313 nm. The UV-B irradiance in the cabin at the surface of the patient's skin was typically between 7 and 8 mW/cm^2. The exact irradiance of both sources was checked monthly.

TREATMENT

Patients were treated twice weekly, initially with an irradiation dose of 0.1 J/cm^2 (NB-UVB group) or 0.5 J/cm^2 (PUVA group), followed by 20% increments (NB-UVB group) or 0.25 J/cm^2 (PUVA group) at each visit, if tolerated. Doses were adjusted according to the maximum erythema occurring since the previous session, determined by patient self-report and by physical examination. Grade 1 erythema (just perceptible) resulted in repetition of the same dose. In patients with grade 2 erythema (easily perceptible but causing no symptoms or only mild discomfort), treatment was discontinued until resolution of symptoms and emollients were applied frequently; subsequently, the previous dose (not resulting in erythema) was used. After an episode of erythema, NB-UVB increments were reduced by moving 1 point down a scale, from 20% to 10% to 5% to 0%. Corresponding figures for PUVA were 0.25 J/cm^2 to 0.1 J/cm^2 to 0.05 J/cm^2 to 0 J/cm^2. After reduction to an increment of zero, if patients remained free of erythema for several sessions, a small increment was reintroduced. Episodes of erythema localized to small areas, such as the face, were not included and were managed by shielding with clothing or a broad-spectrum sunscreen during exposure until resolution of symptoms and then for part of subsequent exposures. There were no erythemal episodes of severity greater than grade 2. No further increments were applied once a dose of 2 J/cm^2 (NB-UVB) or 5 J/cm^2 (PUVA) was reached.

All patients were requested to apply aqueous cream (30% emulsifying ointment, 1% phenoxyethanol) twice daily and to use daily a moisturizing bath additive of an active emollient containing 13% isopropyl myristate and 37.8% light liquid paraffin (Hydromol; Ferndale Pharmaceuticals Ltd, Thorp Arc Estate, United Kingdom) throughout therapy and follow-up to standardize patient washing regimens and minimize any tendency for vitiligo progression as a result of the Koebner phenomenon. For 12 hours after treatment, all patients wore eye protection because of oral PUVA therapy. During treatment sessions, unaffected skin was covered insofar as practically possible with clothing and male patients wore genital protection.

ASSESSMENTS OF THERAPY

All patients were assessed immediately before the commencement of treatment and subsequently after every 16 sessions, and photographs were taken on each occasion. All assessments were made by 1 blinded investigator (S.S.Y.) and consisted of estimation of the percentage of body surface area with vitiligo (BSA-V) in a darkened room using a Wood's lamp. The first assessment was made using the rule of nines or, for small areas, by tracing affected areas and comparing the tracings with diagrams of size corresponding to known percentages (planimetry). At subsequent assessments, comparison was made with the baseline photograph to determine the percentage improvement in BSA-V.

In addition, at each visit, patients completed the Dermatology Life Quality Index (DLQI)[19] and a visual analog scale (VAS). The VAS was a visual scale of numbers from 0 to 10 prefaced with the question, "At the moment, how would you grade or rate your vitiligo on a scale of 0 to 10? Please circle as appropriate between 0 (no vitiligo) and 10 (the worst vitiligo you have ever had)."

At the end of the study, the nature of repigmented areas was examined using photographs, as follows. The color of repigmented areas was compared with that of the patient's unaffected skin and the matching was classified as either excellent or not excellent. The presence of follicular, peripheral, and/or diffuse repigmentation was recorded.

TERMINATION OF THERAPY AND FOLLOW-UP

Treatment was terminated in the event of any of the following: complete or almost complete resolution of vitiligo, absence of improvement after 32 treatments or very slow progress or deterioration thereafter, intolerance of therapy necessitating termination, completion of 200 treatments in a patient's lifetime, or request by the patient for termination because of logistical reasons unrelated to the efficacy of treatment or adverse effects. After termination of treatment because of any of these reasons, patients were assessed every 3 months for 1 year.

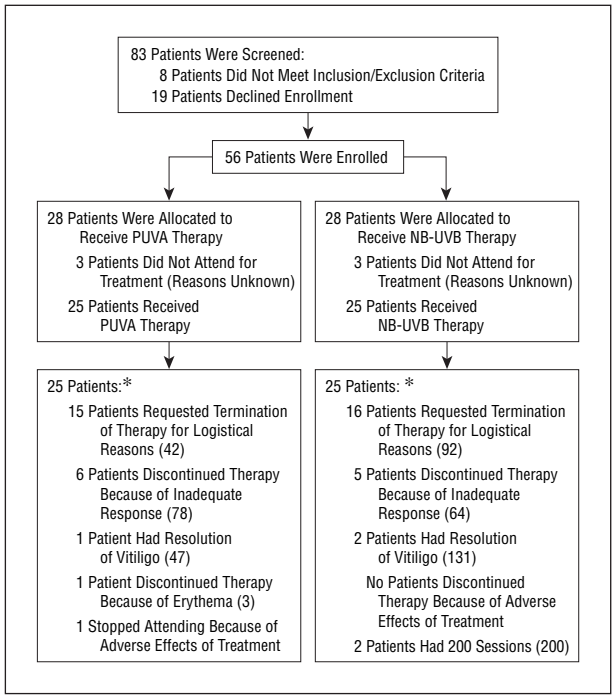

Figure 1. Progression of patients through the study. NB-UVB indicates narrowband UV-B; PUVA, oral psoralen followed by irradiation with UV-A. *The median number of treatments in each category is given in parentheses.

Table 1. Characteristics of Patients Who Commenced Treatment

Characteristic	Treatment Group	
	PUVA (n = 25)	NB-UVB (n = 25)
Male patients, %	48	68
Age, median (range), y	36 (18-70)	38 (18-64)
Duration of vitiligo, median (range), y	6 (1-36)	10 (1-47)
Skin type, %*		
I-II	40	40
III-IV	24	36
V-VI	36	24
BSA-V before therapy, median (range), %	8.4 (3-64)	6.9 (2-55)
Site of vitiligo, % of patients		
Face	84	92
Trunk	80	76
Arms	80	88
Hands	80	76
Legs	80	80
Feet	76	56

Abbreviations: BSA-V, body surface area with vitiligo; NB-UVB, narrowband–UV-B therapy; PUVA, oral psoralen followed by irradiation with UV-A.

*Skin type I indicates burns in the sun, never tans; II, usually burns, sometimes tans; III, usually tans, sometimes burns; IV, always tans, rarely burns; V, Asian skin; and VI, Afrocaribbean skin.

STATISTICAL ANALYSIS

Patients who enrolled in the study but withdrew before starting treatment were excluded from statistical analysis, whereas all those who commenced therapy were included regardless of withdrawal for any reason thereafter (on-treatment analysis). Analysis was performed using Statistical Package for Social Sciences software (version 11.5; SPSS Inc, Chicago, Ill).

Comparisons of the 2 treatment groups were made using the exact χ^2 test for nominal data and the exact Mann-Whitney test for ordinal data. Pretreatment vs posttreatment BSA-V, DLQI, and VAS scores were compared using the exact Wilcoxon signed rank test. Correlations were assessed with the Spearman rank correlation (ρ) coefficient. All tests of significance were 2-sided, and statistical significance was assumed at $P<.05$.

RESULTS

Fifty-six patients were enrolled; their progression through the study is shown in **Figure 1**. Six patients withdrew before commencement of treatment and were not considered further. Fifty patients commenced therapy and all were included in the results; their characteristics are shown in **Table 1**. There were no statistically significant differences in baseline variables between the 2 groups. The median number of treatments in the PUVA group was 47 compared with 97 in the NB-UVB group ($z=2.1$; $P=.03$). Only 1 patient in the PUVA group reached the maximum dose (5 J/cm^2) compared with 8 patients in the NB-UVB group (2 J/cm^2). Three patients had been previously treated with PUVA; in this study, 2 of these patients were treated with NB-UVB.

EFFICACY

Both PUVA and NB-UVB therapy produced a significant improvement in BSA-V (PUVA, $z=3.5$, $P<.001$; NB-UVB, $z=3.9$, $P<.001$; **Figure 2**). Considering the BSA-V at the end of treatment in all 50 patients, the improvement in BSA-V with NB-UVB tended to be greater than with PUVA, but this was not quite statistically significant ($P=.06$; **Table 2**). We also considered the percentage improvement in BSA-V at the end of 48 treatments only in the patients who completed at least 48 sessions (13 in the PUVA group and 21 in the NB-UVB group); NB-UVB showed greater efficacy ($z=2.7$; $P=.007$; Table 2). The improvement in BSA-V was not associated with sex or correlated with age, skin type, or disease duration. Four patients with disease duration longer than 30 years showed improvement greater than 70%.

In the NB-UVB group, 16 patients (64%) had peripheral repigmentation compared with 9 patients (36%) in the PUVA group ($\chi^2_1=3.9$, $P=.09$). Corresponding figures for follicular repigmentation were 22 patients (88%) in the NB-UVB group and 23 patients (92%) in the PUVA group. Diffuse repigmentation was not observed in any patients. All 25 patients in the NB-UVB group and 23 (92%) of 25 patients in the PUVA group had areas of repigmentation, and the assessment of the color match in comparison with the patient's unaffected skin at the end of treatment was excellent for all patients in the NB-UVB group but for only 11 patients (44%) in the PUVA group ($\chi^2_1=19$, $P<.001$). In the remaining 12 patients in the PUVA group, the repigmented areas were noticeably darker than the patients' unaffected skin (**Figure 3**).

At baseline, BSA-V scores were not correlated with the DLQI scores (r_s=–0.01, P=.94). The DLQI scores were significantly lower after both forms of photochemotherapy than before therapy (**Figure 4**A; z=4.3, P<.001), with a median of 9 before and 4 afterward, reflecting an improvement in quality of life. These improvements in DLQI were correlated with the percentage improvement in BSA-V (r_s=0.60, P<.001). Patients rated their vitiligo as less severe after therapy, with the median VAS score before therapy of 9 compared with 5 afterward (Figure 4B; z=4.6, P<.001). These reductions in DLQI and VAS scores did not differ significantly between the NB-UVB and PUVA groups (reduction in DLQI, z=0.2, P=.8; reduction in VAS, z=0.8, P=.5).

ADVERSE EFFECTS

Twenty-four patients (96%) in the PUVA group but only 17 patients (68%) in the NB-UVB group developed erythema at some stage during their treatment, a statistically significant difference (χ^2_1=6.6, P=.02). The median number of erythemal episodes per patient was 9 in the PUVA group and 2 in the NB-UVB group (z=3.7, P<.001), of which 8 were grade 2. Seven episodes were in patients being treated with PUVA (χ^2_1=3.0, P=.2). For all 50 patients, the median number of sessions until the first episode of erythema was 5 in patients in the PUVA group and 21 in patients in the NB-UVB group (z=5.1, P<.001). One patient in the PUVA group and no patients in the NB-UVB group terminated treatment because of adverse effects. There was no association between the number of erythemal episodes and sex, age, or skin type. Eight patients switched from 8-MOP to 5-MOP during the study because of nausea.

FOLLOW-UP

Thirteen patients in the PUVA group and 21 in the NB-UVB group were followed up at 3-month intervals for 12 months; an additional 6 patients in the PUVA group and 4 in the NB-UVB group were followed up for 3 to 9 months before declining further follow-up. Six patients in the PUVA group and none in the NB-UVB group declined all follow-up after the inter-

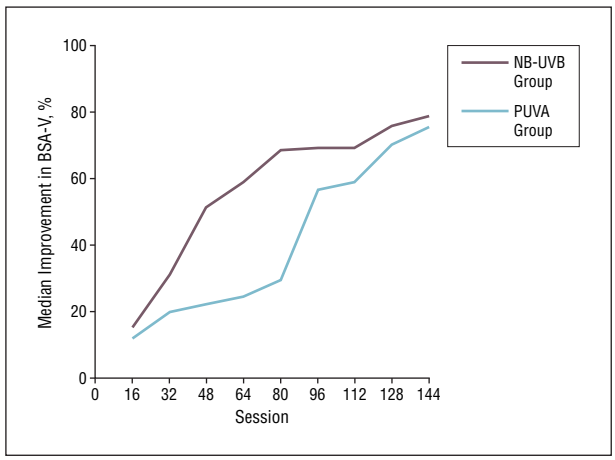

Figure 2. Improvement in body surface area affected by vitiligo (BSA-V). The data at each time point refer only to patients who received at least that number of sessions. NB-UVB indicates narrowband UV-B; PUVA, oral psoralen followed by irradiation with UV-A.

Table 2. Outcome of Treatment

Outcome	Treatment Group	
	PUVA (n = 25)	NB-UVB (n = 25)
Final dose, median (range), J/cm^2	2 (0.7 to 5)	1.3 (0.18 to 2)
No. of treatments, median (range)	49 (3 to 196)	97 (16 to 200)
Cumulative dose, median (range), J/cm^2	62 (3 to 406)	69 (2 to 240)
Median improvement in BSA-V (range), %	23 (–9 to 96)	61 (–175 to 92)
Patients showing improvement in BSA-V at the end of the course, % (No.)		
<0% (ie, deterioration in vitiligo)	16 (4)	4 (1)
0%-25%	36 (9)	20 (5)
>25%-50%	12 (3)	12 (3)
>50%-75%	16 (4)	32 (8)
>75%	20 (5)	32 (8)
Patients showing improvement in BSA-V at the end of follow-up compared with before therapy, % (No.)		
<0% (ie, deterioration of vitiligo)	28 (7)	12 (3)
0%-25%	24 (6)	8 (2)
>25%-50%	12 (3)	24 (6)
>50%-75%	12 (3)	20 (5)
>75%	24 (6)	36 (9)
No. of patients who completed ≥48 treatments	13	21
Patients with improvement in BSA-V after 48 treatments, % (No.)		
<0% (ie, deterioration in vitiligo)	8 (1)	0
0%-25%	54 (7)	14 (3)
>25%-50%	15 (2)	33 (7)
>50%-75%	23 (3)	48 (10)
>75%	0	5 (1)

Abbreviations: BSA-V, body surface area with vitiligo; NB-UVB, narrowband–UV-B therapy; PUVA, oral psoralen followed by irradiation with UV-A.

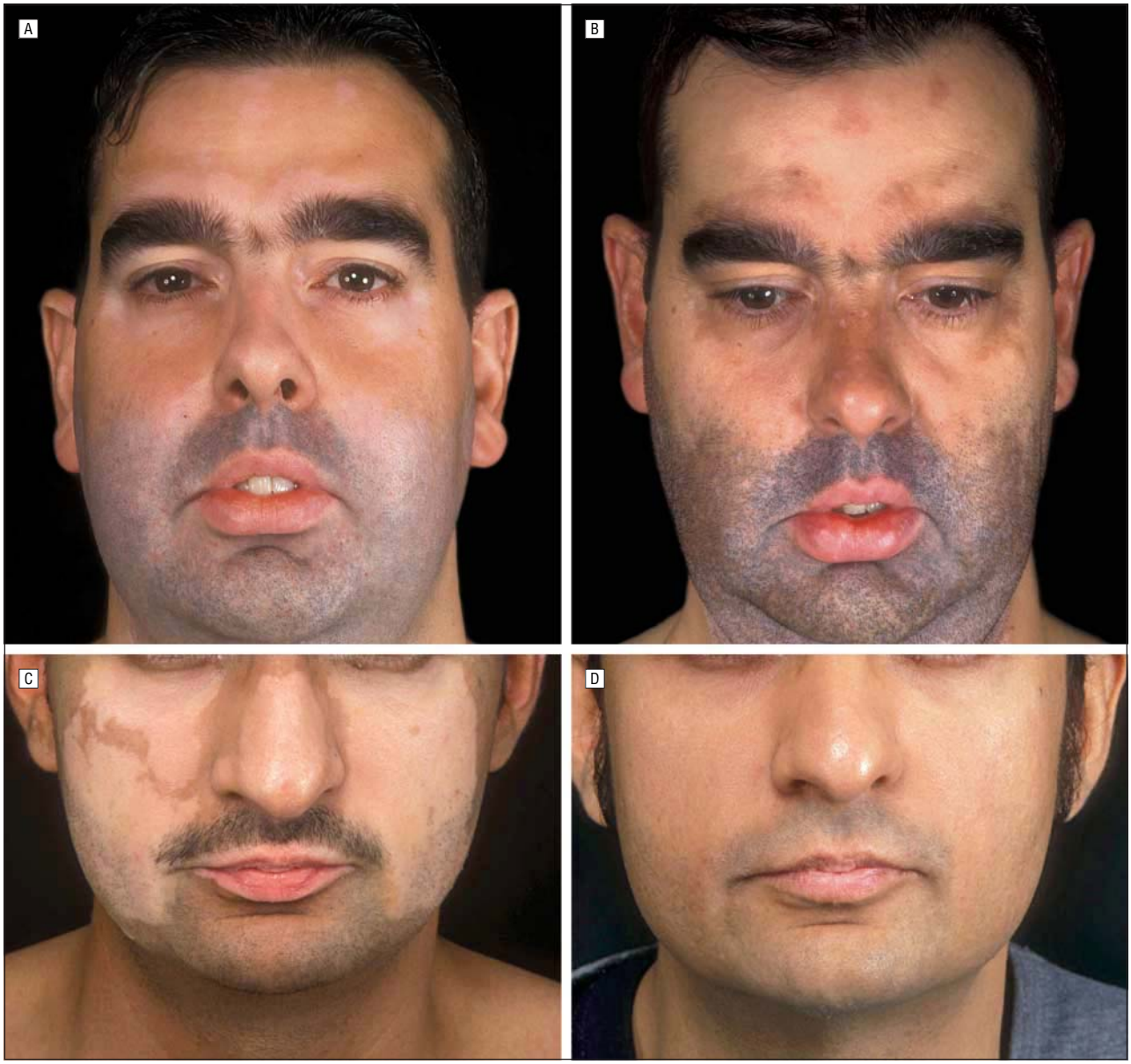

Figure 3. Improvement in vitiligo in patients treated with oral psoralen followed by irradiation with UV-A (PUVA) and narrowband UV-B (NB-UVB).
A, A patient before therapy. B, Same patient as in A after 48 sessions of PUVA therapy. The repigmented skin is noticeably darker than the patient's unaffected skin.
C, A patient before therapy. D, Same patient as in C after 48 sessions of NB-UVB therapy. The repigmented skin is the same color as the patient's unaffected skin.

vention period. A slight but gradual loss of repigmentation induced by the photochemotherapy was noted: 7 patients (28%) in the PUVA group and 3 patients (12%) in the NB-UVB group had more severe vitiligo than before they began treatment; nevertheless, 6 patients (24%) in the PUVA group and 9 patients (36%) in the NB-UVB group maintained greater than 75% improvement in BSA-V (Table 2). For improvement in BSA-V seen from the start of therapy until the last follow-up in the 44 patients, the difference between the 2 modalities was not significant ($z=0.8$, $P=.4$).

At the end of follow-up, the color match in repigmented areas in all patients in the NB-UVB group remained excellent. In patients in the PUVA group, color matching improved slightly since the end of therapy, but was excellent in only 14 (61%) of 23 patients (NB-UVB vs PUVA: $\chi^2_1=12$, $P<.001$).

COMMENT

To our knowledge, this is the first double-blind randomized trial of oral PUVA therapy vs NB-UVB therapy in the treatment of vitiligo. Both methods produced a reduction in BSA-V. At the end of therapy, 16 patients (64%) in the NB-UVB group showed greater than 50% improvement compared with 9 patients (36%) in the PUVA group. The color match of the repigmented skin was excellent in all patients in the NB-UVB group but in only 11 patients (44%) in the PUVA group ($P<.001$). In patients who completed 48 sessions, the improvement in BSA-V was greater with NB-UVB therapy than with PUVA therapy ($P=.007$). It was previously found in a study of PUVA therapy for vitiligo that relapse usually occurs within a year of treatment.[20] Therefore, we observed patients for

up to 12 months after ceasing therapy; at this time, the previous differences between the 2 modalities tended still to be present but were not statistically significant. There were also fewer adverse effects with NB-UVB therapy. We were unable to detect a difference between the modalities insofar as the improvement seen in quality of life (DLQI scores) and patient-assessed disease severity (VAS scores). We did not detect any association between success of treatment and duration of vitiligo.

Perhaps the most dramatic finding was the difference in the nature of repigmentation, which was often markedly darker than the unaffected skin in patients treated with PUVA (Figure 3). This hyperpigmentation has been reported previously,[18,20] but, to our knowledge, this is the first time this difference between PUVA and NB-UVB therapy has been confirmed in a double-blind study. At 12 months after treatment, the darker color tended to persist and was cosmetically unsatisfactory. The predominance of follicular repigmentation, with some patients also showing peripheral repigmentation, and an absence of diffuse repigmentation in patients exposed to both treatments is consistent with previous reports.[21]

There was a higher incidence of erythema in the PUVA group. This difference may have resulted because of a difference in protocols in the 2 groups, namely, an increment of 0.25 J/cm^2 with PUVA vs a 20% increment with NB-UVB. The starting dose of PUVA was 0.5 J/cm^2, so the initial increment with PUVA was quite high, 50%. However, only 1 patient in the PUVA group withdrew from treatment because of erythema, and it is sometimes claimed that erythema is a prerequisite for maximal PUVA efficacy.[22] Eight (32%) of 25 patients switched from 8-MOP to 5-MOP because of severe nausea. It is possible that these patients may have become aware of their treatment allocation, but all patients were told beforehand that nausea was a possibility, and, overall, we believe most patients remained blinded to their treatment throughout the study.

Patients receiving PUVA had significantly fewer sessions than patients who received NB-UVB (median, 47 vs 97 sessions, respectively), although the usual stated reason for any early termination of therapy was related to commuting problems. However, we suspect that within the PUVA group a relative lack of repigmentation, a poor color match within repigmenting areas, and a high incidence of erythema may have combined to dissuade patients from continuing therapy.

The results of previous studies of NB-UVB therapy for vitiligo are shown in the eTable (available at http://www.archdermatol.com). These studies included patients with various characteristics and reported outcomes in various ways, making comparison between them difficult. However, overall they showed that approximately 50% of patients who continued with treatment for 6 to 12 months had 75% repigmentation or better. Our results suggest somewhat less efficacy than this. Of note, the starting doses of NB-UVB in the reported studies varied considerably, ranging from 75 mJ/cm^2,[3] to 740 mJ/cm,[2,17] although these differences may reflect variations in calibration.[23] Other studies used starting doses based on the minimum erythema dose.[11,16]

Three previous studies have compared NB-UVB therapy with PUVA therapy. The first, an observer-blinded study, suggested that NB-UVB might produce greater repigmentation than gel PUVA.[3] Recently, a left-right comparison study of 15 patients treated with NB-UVB vs oral PUVA showed similar outcomes between the 2 modalities[17] and a retrospective study suggested greater efficacy for NB-UVB compared with oral PUVA.[18]

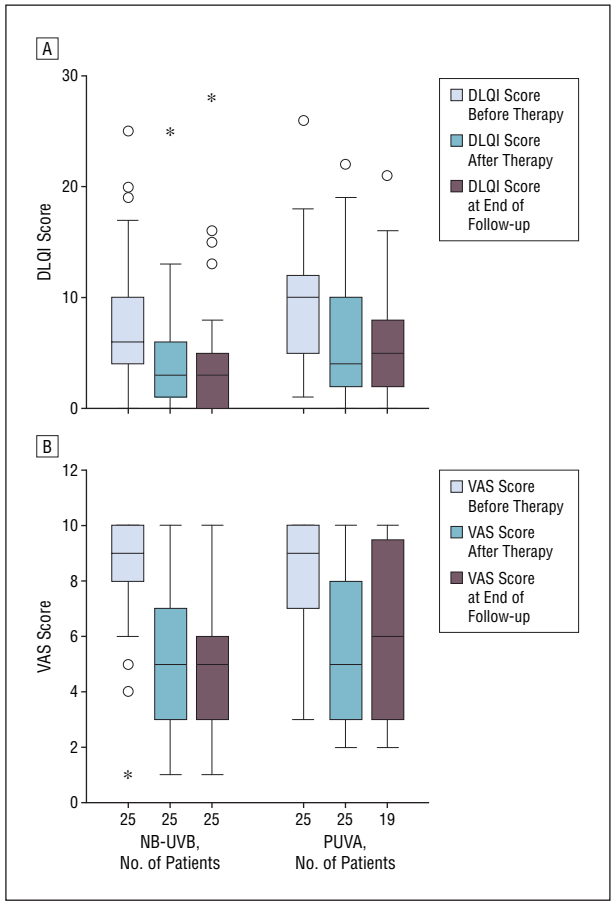

Figure 4. A, Dermatology Life Quality Index (DLQI) scores before therapy, at the end of therapy, and at the end of follow-up. B, Visual Analog Scale (VAS) scores before therapy, at the end of therapy, and at the end of follow-up. The asterisks indicate extremes; circles, outliers, and the lines (from the bottom upward) minimum value, lower interquartile value, median, upper quartile value, and maximum value. NB-UVB indicates narrowband–UV-B therapy; PUVA, oral psoralen followed by irradiation with UV-A.

It is unknown whether NB-UVB therapy is more effective if given 3 times vs twice per week. We administered PUVA twice a week rather than more frequently because PUVA-related erythema peaks at approximately 96 hours[24]; therefore, to enable effective masking of group allocation, we also administered NB-UVB twice per week. With PUVA, there is no convincing evidence to suggest a difference in efficacy between 8-MOP and 5-MOP, so we used 8-MOP because this is standard practice.

Before phototherapy, we could not detect any correlation between DLQI score and BSA-V. However, after the treatment course, the improvement in quality of life was correlated with the percentage improvement in BSA-V, suggesting that, at least in the context of photochemotherapy, quality of life in patients with vitiligo may be related more to recent disease changes than to overall severity of the disease.

In addition to its efficacy and favorable adverse effect profile, NB-UVB therapy offers other advantages over oral

PUVA therapy that make it preferable for most patients. In particular, PUVA therapy requires the use of eye protection after treatment sessions, cannot be used in pregnancy, is contraindicated in patients with hepatic impairment or who are taking warfarin or phenytoin, and requires the somewhat inconvenient prior administration of psoralen. Of greatest concern, however, is the potential of PUVA to cause nonmelanoma and perhaps melanoma skin cancer, although in vitiligo this seems to be rare, perhaps because of the tendency to use much lower doses than for treatment of conditions such as psoriasis. Nevertheless, it is important that NB-UVB seems to be considerably safer than PUVA in comparable numbers of treatment sessions,[25,26] and for this reason too, at least in part, NB-UVB is far preferable for use in children. Until further data become available, however, we prefer to limit the number of NB-UVB treatments to a lifetime cumulative total of 200 sessions.[26]

The mechanism of action of all phototherapy in the treatment of vitiligo may very probably involve diminution of the immunological process followed by the stimulation of residual melanocytes, particularly those residing in hair follicles. Our results firmly suggest that, in most patients, the NB-UVB form of this therapy is preferable to PUVA for the treatment of vitiligo.

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Author Contributions: Dr Yones had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Yones, Garibaldinos, and Hawk. *Acquisition of data:* Yones and Hawk. *Analysis and interpretation of data:* Yones, Palmer, and Hawk. *Drafting of the manuscript:* Yones and Palmer. *Critical revision of the manuscript for important intellectual content*: Yones, Palmer, Garibaldinos, and Hawk. *Statistical analysis:* Yones and Palmer. *Administrative, technical, and material support:* Yones, Garibaldinos, and Hawk. *Study supervision:* Hawk.
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Additional Information: The eTable is available at http://www.archdermatol.com.
Previous Presentations: This study was presented in part at the 14th Annual Meeting of the European Academy of Dermatology & Venerology; October 14, 2005; London, England; at the 15th Annual Meeting of the Photomedicine Society, March 2, 2006; San Francisco, Calif; and at the Second Congress of the Libyan Society of Dermalology & Venerology; September 16, 1006; Al-beida, Libya.
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REFERENCES

1. Papadopoulos L, Bor R, Hawk JLM. *Psychology in Relation to Dermatology*. London, England: British Psychological Society; 1999:1-363.
2. Whitton ME, Ashcroft DM, Barrett CW, Gonzalez U. Interventions for vitiligo. *Cochrane Database Syst Rev*. 2006;1:CD003263.
3. Westerhof W, Nieuweboer-Krobotova L. Treatment of vitiligo with UV-B radiation vs topical psoralen plus UV-A. *Arch Dermatol*. 1997;133:1525-1528.
4. Njoo MD, Bos JD, Westerhof W. Treatment of generalized vitiligo in children with narrowband (TL-01) UVB radiation therapy. *J Am Acad Dermatol*. . 2000;42(2 pt 1):245-253.
5. Scherschun L, Kim JJ, Lim HW. Narrow-band ultraviolet B is a useful and well-tolerated treatment for vitiligo. *J Am Acad Dermatol*. 2001;44:999-1003.
6. Patel DC, Evans AV, Hawk JL. Topical pseudocatalase mousse and narrowband UVB phototherapy is not effective for vitiligo: an open, single-centre study. *Clin Exp Dermatol*. 2002;27:641-644.
7. Tjioe M, Gerritsen MJ, Juhlin L, van de Kerkhof PC. Treatment of vitiligo vulgaris with narrow band UVB (311 nm) for one year and the effect of addition of folic acid and vitamin B_{12}. *Acta Derm Venereol*. 2002;82:369-372.
8. Natta R, Somsak T, Wisuttida T, Laor L. Narrowband ultraviolet B radiation therapy for recalcitrant vitiligo in Asians. *J Am Acad Dermatol*. 2003;49:473-476.
9. Samson Yashar S, Gielczyk R, Scherschun L, Lim HW. Narrow-band ultraviolet B treatment for vitiligo, pruritus, and inflammatory dermatoses. *Photodermatol Photoimmunol Photomed*. 2003;19:164-168.
10. Kullavanijaya P, Lim HW. Topical calcipotriene and narrowband ultraviolet B in the treatment of vitiligo. *Photodermatol Photoimmunol Photomed*. 2004;20:248-251.
11. Hamzavi I, Jain H, McLean D, Shapiro J, Zeng H, Lui H. Parametric modeling of narrowband UV-B phototherapy for vitiligo using a novel quantitative tool: the Vitiligo Area Scoring Index. *Arch Dermatol*. 2004;140:677-683.
12. Kanwar AJ, Dogra S. Narrow-band UVB for the treatment of generalized vitiligo in children. *Clin Exp Dermatol*. 2005;30:332-336.
13. Brazzelli V, Prestinari F, Castello M, et al. Useful treatment of vitiligo in 10 children with UV-B narrowband (311 nm). *Pediatr Dermatol*. 2005;22:257-261.
14. Chen GY, Hsu MM, Tai HK, et al. Narrow-band UVB treatment of vitiligo in Chinese. *J Dermatol*. 2005;32:793-800.
15. Ada S, Sahin S, Boztepe G, Karaduman A, Kolemen F. No additional effect of topical calcipotriol on narrow-band UVB phototherapy in patients with generalized vitiligo. *Photodermatol Photoimmunol Photomed*. 2005;21:79-83.
16. Leone G, Pacifico A, Iacovelli P, Paro VA, Picardo M. Tacalcitol and narrow-band phototherapy in patients with vitiligo. *Clin Exp Dermatol*. 2006;31:200-205.
17. El Mofty M, Mostafa W, Esmat S, et al. Narrow band Ultraviolet B 311 nm in the treatment of vitiligo: two right-left comparison studies. *Photodermatol Photoimmunol Photomed*. 2006;22:6-11.
18. Parsad D, Kanwar AJ, Kumar B. Psoralen-ultraviolet A vs. narrow-band ultraviolet B phototherapy for the treatment of vitiligo. *J Eur Acad Dermatol Venereol*. 2006;20:175-177.
19. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI): a simple practical measure for routine clinical use. *Clin Exp Dermatol*. 1994;19:210-216.
20. Kwok YK, Anstey AV, Hawk JL. Psoralen photochemotherapy (PUVA) is only moderately effective in widespread vitiligo: a 10-year retrospective study. *Clin Exp Dermatol*. 2002;27:104-110.
21. Parsad D, Pandhi R, Dogra S, Kumar B. Clinical study of repigmentation patterns with different treatment modalities and their correlation with speed and stability of repigmentation in 352 vitiliginous patches. *J Am Acad Dermatol*. 2004; 50:63-67.
22. Grimes PE. Psoralen photochemotherapy for vitiligo. *Clin Dermatol*. 1997;15:921-926.
23. Ibbotson SH, Bilsland D, Cox NH, et al; British Association of Dermatologists. An update and guidance on narrowband ultraviolet B phototherapy: a British Photodermatology Group Workshop Report. *Br J Dermatol*. 2004;151:283-297.
24. Man I, Dawe RS, Ferguson J, Ibbotson SH. An intraindividual study of the characteristics of erythema induced by bath and oral methoxsalen photochemotherapy and narrowband ultraviolet B. *Photochem Photobiol*. 2003;78:55-60.
25. British Photodermatology Group. British Photodermatology Group guidelines for PUVA. *Br J Dermatol*. 1994;130:246-255.
26. Diffey BL. Factors affecting the choice of a ceiling on the number of exposures with TL01 ultraviolet B phototherapy. *Br J Dermatol*. 2003;149:428-430.

eTable. Previous Studies of Treatment of Vitiligo With Narrowband UV-B

Source	Design	No. of Subjects	Results and Conclusions
Westerhof and Nieuweboer-Krobotoval,[3] 1997 (study in 2 parts)	Observer blinded: NB-UVB treatment vs gel PUVA treatment	Study 1: 106	After 33 sessions, some repigmentation in 46% (13 patients) of the PUVA group vs 67% (52 patients) of the NB-UVB group (statistical evaluation not performed); fewer adverse-effects with NB-UVB treatment
	NB-UVB treatment for 12 mo	Study 2: 51*	After 100 sessions, 63% (32 patients) had repigmentation over 75% of the affected BSA-V
Njoo et al,[4] 2000	Open	51 Children	After a mean of 78 sessions, 53% (27 children) had repigmentation over 75% of the affected BSA-V
Scherschun et al,[5] 2001	Retrospective	7	After a mean of 27 sessions, 71% (5 patients) had repigmentation over 75% of the affected BSA-V
Patel et al,[6] 2002†	Open	26	After 48 sessions, subjects' conditions were "generally unchanged"
Tjioe et al,[7] 2002†	Open	27	After maximum of about 140 sessions, 92% (25 patients) had some repigmentation
Natta et al,[8] 2003	Retrospective	60	After 36-175 sessions, 33% (20 patients) had repigmentation over 75% of the affected BSA-V
Samson Yashar et al,[9] 2003	Retrospective	77	After 15-123 sessions, 39% (30 patients) had 66%-100% repigmentation; 82% (63 patients) had some improvement of their condition
Kullavanijaya and Lim,[10] 2004†	Open	17	After 67-180 sessions, 47% (8 patients) had over 66% repigmentation of the affected BSA-V
Hamzavi et al, [11] 2004	Left-right comparison: NB-UVB treatment vs no treatment	22	After up to 60 sessions, a mean of 43% (10 patients) had repigmentation
Kanwar and Dogra,[12] 2005	Open	20 Children	After 1 y of treatment 75% (15 children) had repigmentation over 75% of the affected BSA-V
	Open	13 Children	After 1 y of treatment, approximately 73% (10 children) had repigmentation over 75% of the affected BSA-V
Brazelli et al,[13] 2005	Retrospective	10 Children	After a mean of approximately 50 sessions, 50% (5 children) had repigmentation over 75% of the affected BSA-V
Chen et al,[14] 2005	Retrospective	72	After treatment for up to 1 y, 13% (9 patients) had repigmentation of >75%
Ada et al,[15] 2005†	Prospective	20	At 96 treatments, 55% (11 patients) had >50% repigmentation
Leone et al,[16] 2006†	Prospective	32	After 6 mo of treatment, 34% (11 patients) had >50% repigmentation
El Mofty et al,[17] 2006	Left-right comparison: NB-UVB treatment vs oral PUVA treatment	15	At 60 sessions, 57% (9 patients) had repigmentation over 75% of the affected BSA-V with both NB-UVB and PUVA treatments; incidence of adverse effects was also similar
Parsad et al,[18] 2006	Retrospective: NB-UVB treatment vs oral PUVA treatment	69	41.9% of 13 NB-UVB-treated patients showed "marked to complete" repigmentation compared with 23.6% (9 patients) of the PUVA-treated group (No. of sessions not stated); better color match with NB-UVB treatment

Abbreviations: BSA-V, body surface area with vitiligo; N3-UVB, narrowband UV-B therapy; PUVA, oral psoralen followed by irradiation with UV-A.

*One hundred twenty-four additional patients were treated for a shorter period.

†The following studies included treatment with other therapies: Patel et al,[6] pseudocatalase; Tjioe et al,[7] folic acid and vitamin B_{12}; Kullavanijaya and Lim,[10] calcipotriol; Ada et al,[15] calcipotriol, and Leone et al,[16] tacalcitol; the results presented in the Table are after the effects of these additional treatments have been excluded.

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REFERENCES

1. Greaves MW, Weinstein GD. Treatment of psoriasis. *N Engl J Med*. 1995;332(9):581-588.
2. Krueger JG, Bowcock A. Psoriasis pathophysiology: current concepts of pathogenesis. *Ann Rheum Dis*. 2005;64(suppl 2):ii30-ii36.
3. Gottlieb AB, Krueger JG, Wittkowski K, Dedrick R, Walicke PA, Garovoy M. Psoriasis as a model for T-cell–mediated disease: immunobiologic and clinical effects of treatment with multiple doses of efalizumab, an anti-CD11a antibody. *Arch Dermatol*. 2002;138(5):591-600.
4. Lebwohl M, Tyring SK, Hamilton TK, Toth D, Glazer S, Tawfik NH. A novel targeted T-cell modulator, efalizumab, for plaque psoriasis. *N Engl J Med*. 2003;349(21):2004-2013.
5. Gordon KB, Papp KA, Hamilton TK, et al; Efalizumab Study Group. Efalizumab for patients with moderate to severe plaque psoriasis: a randomized controlled trial. *JAMA*. 2003;290(23):3073-3080.
6. Menter A, Gordon K, Carey W, et al. Efficacy and safety observed during 24 weeks of efalizumab therapy in patients with moderate to severe plaque psoriasis. *Arch Dermatol*. 2005;141(1):31-38.
7. Menter A, Leonardi CL, Sterry W, Bos JD, Papp KA. Long-term management of plaque psoriasis with continuous efalizumab therapy. *J Am Acad Dermatol*. 2006;54(4)(suppl 1):S182-S188.
8. Carey W, Glazer S, Gottlieb AB, et al. Relapse, rebound, and psoriasis adverse events: an advisory group report. *J Am Acad Dermatol*. 2006;54(4)(suppl 1):S171-S181.
9. Hamilton TK. Clinical considerations of efalizumab therapy in patients with psoriasis. *Semin Cutan Med Surg*. 2005;24(1):19-27.
10. Simon D, Vassina E, Yousefi S, Kozlowski E, Braathen LR, Simon HU. Reduced dermal infiltration of cytokine-expressing inflammatory cells in atopic dermatitis after short-term topical tacrolimus treatment. *J Allergy Clin Immunol*. 2004;114(4):887-895.
11. Tan B, Foley P. Guttate psoriasis following Ecstasy ingestion. *Australas J Dermatol*. 2004;45(3):167-169.
12. Tsankov N, Kazandjieva J, Drenovska K. Drugs in exacerbation and provocation of psoriasis. *Clin Dermatol*. 1998;16(3):333-351.
13. Gaspari AA. Innate and adaptive immunity in the pathophysiology of psoriasis. *J Am Acad Dermatol*. 2006;54(3)(suppl 2):S67-S80.
14. Raptiva (efalizumab) [package insert]. South San Francisco, CA: Genentech Inc; 2003.

Correction

Incorrect Dose. In the Study titled "Randomized Double-blind Trial of Treatment of Vitiligo: Efficacy of Psoralen–UV-A Therapy vs Narrowband–UV-B Therapy" by Yones et al, published in the May issue of the *Archives* (2007;143[5]:578-584), the dose for 5-methoxypsoralen was incorrectly reported. On page 579, left-hand column, "Administration of Oral Psoralen or Placebo" subsection of the "Methods" section, the last sentence should have read as follows: "During the course of the study, patients intolerant of 8-MOP because of nausea instead were given identical-appearing 5-methoxypsoralen (5-MOP) tablets (20-mg Pentaderm tablets; Crawford Pharmaceuticals Ltd) at a dose of 50 mg/m^2 (range, 60-80 mg) 3 hours before phototherapy." This article was corrected online prior to publication of the correction in print.