Afamelanotide and Narrowband UV-B Phototherapy for the Treatment of Vitiligo
A Randomized Multicenter Trial

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IMPORTANCE Narrowband UV-B (NB–UV-B) phototherapy is used extensively to treat vitiligo. Afamelanotide, an analogue of α–melanocyte-stimulating hormone, is known to induce tanning of the skin.

OBJECTIVE To evaluate the efficacy and safety of combination therapy for generalized vitiligo consisting of afamelanotide implant and NB–UV-B phototherapy.

DESIGN, SETTING, AND PARTICIPANTS This study was performed in 2 academic outpatient dermatology centers and 1 private dermatology practice. We enrolled men and women 18 years or older with Fitzpatrick skin phototypes (SPTs) III to VI and a confirmed diagnosis of nonsegmental vitiligo that involved 15% to 50% of total body surface area. Vitiligo was stable or slowly progressive for 3 months. Patients were randomized to combination therapy (n = 28) vs NB–UV-B monotherapy (n = 27). After 1 month of NB–UV-B phototherapy, 16 mg of afamelanotide was administered subcutaneously to the combination therapy group monthly for 4 months while NB–UV-B phototherapy continued; the other group continued to receive NB–UV-B monotherapy.

INTERVENTIONS Narrowband UV-B monotherapy vs combined NB–UV-B phototherapy and afamelanotide.

MAIN OUTCOMES AND MEASURES Response on the Vitiligo Area Scoring Index and Vitiligo European Task Force scoring system.

RESULTS Response in the combination therapy group was superior to that in the NB–UV-B monotherapy group (P < .05) at day 56. For the face and upper extremities, a significantly higher percentage of patients in the combination therapy group achieved repigmentation, and at earlier times (face, 41.0 vs 61.0 days [P = .001]; upper extremities, 46.0 vs 69.0 days [P = .003]). In the combination therapy group, repigmentation was 48.64% (95% CI, 39.49%-57.80%) at day 168 vs 33.26% (95% CI, 24.18%-42.33%) in the NB–UV-B monotherapy group. Notable adverse events included erythema in both groups and minor infections and nausea in the combination therapy group. Comparison between Fitzpatrick SPTs showed patients with SPTs IV to VI in the combination therapy group had improvement in the Vitiligo Area Scoring Index at days 56 and 84 (P < .05); no significant difference was noted in patients with SPT III.

CONCLUSIONS AND RELEVANCE A combination of afamelanotide implant and NB–UV-B phototherapy resulted in clinically apparent, statistically significant superior and faster repigmentation compared with NB–UV-B monotherapy. The response was more noticeable in patients with SPTs IV to VI.

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Vitiligo is characterized by white patches of skin due to selective loss of epidermal melanocytes. It affects 1% to 2% of the general population, with devastating psychological impact. Autoimmune, genetic, biochemical, oxidative stress, neural, and viral mechanisms have been proposed as etiologic factors. Although topical corticosteroids, calcineurin inhibitors, and narrowband UV-B (NB-UV-B) phototherapy can be effective treatment options, none are universally successful.

The cutaneous melanocortin system consists of bioactive peptides, including α-melanocyte-stimulating hormone (α-MSH), corticotropin, β-endorphin, and other peptides derived from the precursor peptide proopiomelanocortin. The peptide α-MSH is a pivotal regulatory protein that stimulates melanogenesis and melanocyte proliferation.

Afamelanotide is a potent synthetic linear analogue of the naturally occurring α-MSH in a controlled-release formulation. Subcutaneous injections result in increased skin pigmentation owing to increased expression of eumelanin. Pilot studies have shown afamelanotide to be beneficial in the treatment of erythropoietic protoporphyria and solar urticaria. Studies have demonstrated defects in the melanocortin system in patients with vitiligo. Thus, restoring the system by use of exogenous melanocortin peptides theoretically should benefit these patients.

A recent pilot study of afamelanotide and NB-UV-B phototherapy for repigmentation of nonsegmental vitiligo described repigmentation in 4 patients. The present investigation reports the results of a multicenter randomized clinical trial comparing the efficacy and safety of afamelanotide implants and NB-UV-B phototherapy (combination therapy) with NB-UV-B monotherapy for the treatment of nonsegmental vitiligo in 55 patients.

Methods

Study Oversight

The study was designed jointly by the investigators and the sponsor, Clinuvel Pharmaceuticals, Melbourne, Australia. The protocol was approved by the institutional review boards of Henry Ford Hospital and Mount Sinai Hospital and a central institutional review board.

Patients

Eligible patients included men and women 18 years or older with a confirmed diagnosis of nonsegmental vitiligo involving 15% to 50% of total body surface area, stable or slowly progressive vitiligo during a 3-month period, and Fitzpatrick skin phototypes (SPT) III to VI. Exclusion criteria consisted of SPT I or II, vitiligo involving the hands and feet only, extensive leukotrichia, previous treatment with NB-UV-B phototherapy within 6 months, lack of response to previous NB-UV-B phototherapy, allergy to afamelanotide or the polymer contained in the implant, allergy to lidocaine hydrochloride or any other local anesthetic to be used during the administration of the implant, current or previous treatment with topical immunomodulators within 4 weeks of the screening visit, history of photosensitivity disorders or photosensitive lupus, history of clausrophobia, history of any active and/or unstable autoimmune disease judged to be clinically significant by the investigator, history of melanoma or lentigo maligna, history of dysplastic nevus syndrome, the presence of any malignant skin lesions, any skin disease that may interfere with the study evaluation, childbearing potential (for female patients), and use of any current or prior therapy that may interfere with the objective of the study (including drugs that cause photosensitivity or skin pigmentation) within 60 days before the screening visit. All patients provided written informed consent.

Study Protocol

The study consisted of 8 visits during a period of 7 months, including a screening period no longer than 28 days before study initiation, the visit at the onset of the study (visit 1), and monthly visits for the 6-month study period (Figure 1). The treatment was assigned according to a computer-generated randomization list for each study site. Patients were randomized...
in equal numbers to 1 of 2 treatment groups (combination therapy and NB-UV-B monotherapy). Both groups received NB-UV-B phototherapy 2 to 3 times weekly for 6 months, for a maximum of 72 treatments; all subjects were required to have a minimum of 10 treatments per month. The combination therapy group received 4 monthly subcutaneous afamelanotide implants (on days 28, 56, 84, and 112) (Figure 1). During the 6-month active treatment phase, participants underwent weekly evaluation for onset of repigmentation. At the end of the 6-month active treatment phase, a total of 3 follow-up visits were scheduled and participants underwent evaluation during a planned period of 6 months. We are reporting results to the end of the 6-month active treatment phase.

**Time to Onset of Repigmentation**

Time to onset of repigmentation is defined as the number of days for the first sign of repigmentation to be identified visually. Repigmentation was assessed every 7 (±3) days from day 0 until occurrence at several anatomical sites.

**Scoring of Disease Activity and Involvement**

We used 2 validated scoring systems. The Vitiligo Area Scoring Index (VASI) is a validated quantitative assessment scale for vitiligo. Briefly, the body is divided into the following 6 separate and mutually exclusive sites: head/neck, hands, upper extremities (excluding hands), trunk, lower extremities (excluding feet), and feet. The percentage of vitiligo involvement was estimated in hand units by the same investigator during the entire course of the study to eliminate variations in hand size. The degree of depigmentation for each body site was determined and estimated to the nearest of the following percentages: 0, 10%, 25%, 50%, 75%, 90%, or 100%. Any new depigmented lesions that developed during the study were also estimated and included in the VASI calculation. The VASI was then calculated using the following formula:

\[
\text{VASI} = \sum \text{All Values From All Body Sites [in Hand Units]} \times \text{[Residual Depigmentation]}
\]

The other validated scoring system, the Vitiligo European Task Force (VETF) score, assesses 3 dimensions of the disease (extent, staging, and spreading/progression). The body is divided into the following 5 separate and mutually exclusive sites: head/neck, trunk, and extremities (excluding hands and feet). Each study visit, the extent of vitiligo involvement was estimated at the same investigator during the entire course of the study to eliminate variations in hand size. Stage of vitiligo was estimated as 0 (normal pigmentation), 1 (incomplete depigmentation), 2 (complete depigmentation), 3 (partial hair whitening (<30%), and 4 (complete hair whitening). Spreading of vitiligo was estimated as 0 (stable disease), −1 (observed ongoing subclinical repigmentation), and +1 (additional patches in a given area or observed ongoing subclinical depigmentation). The VETF score for each dimension of the disease (extent, staging, and spreading) was then calculated as follows:

\[
\text{VETF Extent or Staging or Spreading} = \sum \text{All Values From All Body Sites [% of Area or Staging or Spreading]}
\]

**Ophthalmoscopic Examination**

A basic ophthalmoscopic examination was performed by a qualified ophthalmologist. Any lesions, vascular malformations, anomalies, or retinopathies were recorded and discussed with the principal investigator.

**Administration of Afamelanotide Implant**

The afamelanotide implant is a sterile biodegradable and biocompatible poly(D,L-lactide-co-glycolide) polymer implant core (Sigma-Aldrich Corp) containing 16 mg of afamelanotide. The drug is a subcutaneous dissolving implant approximately the size of a grain of rice. Implants were placed subcutaneously above the suprailiac crest, using a sterile technique with a 14-gauge catheter after injection of 1% lidocaine hydrochloride as anesthesia.

**Outcome Measures**

The primary efficacy outcome is the change from day 0 to day 168 in the pigmentation of the full body, face, trunk, and extremities between the 2 treatment groups, assessed using the VASI and the VETF scoring system. A Wood’s lamp was used to assess subclinical repigmentation and determine the VASI and VETF score. Furthermore, we analyzed a secondary efficacy outcome measure, time to onset of repigmentation. Because hands and feet are sites known to be recalcitrant to treatment, these sites were not included in this part of the analysis.

**Safety End Points**

Safety end points included treatment-emergent adverse events, defined as clinically significant changes in laboratory values summarized by the Medical Dictionary for Regulatory Activities. Treatment-emergent adverse events were further summarized by intensity, seriousness, outcome, and relationship to the study drug.

**Statistical Analysis**

We compared treatment groups by means of the nonparametric Mann-Whitney test for continuous variables and the χ² test or Fisher exact test (if >20% of the cells in a contingency table had expected counts of <5) for categorical variables. Unless otherwise stated, hypothesis testing was performed at the α = .05 level (2-sided) when comparing treatments. For all inferential analyses, the P value was rounded to 3 decimal places. Unless otherwise stated, a rounded P value of less than or equal to .05 indicated statistical significance. Comparison within treatment groups was also performed using the Wilcoxon signed rank test. The comparison between treatment groups in the time to onset of repigmentation of the full body, face, trunk, and extremities was performed by means of the log-rank test.

**Results**

**Patients**

The demographic and baseline characteristics of all patients are shown in Table 1. A total of 28 patients (8 from Detroit, 10...
Table 1. Demographic Characteristics of Study Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Study Groupa</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Combination Therapy (n = 28)</td>
</tr>
<tr>
<td></td>
<td>NB-UV-B Monotherapy (n = 27)</td>
</tr>
<tr>
<td>Sex, No. male:female</td>
<td>11:17</td>
</tr>
<tr>
<td>Age, mean (SD) [range], y</td>
<td>46.5 (16.3) [18-79]</td>
</tr>
<tr>
<td>Fitzpatrick SPT</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>9 (32)</td>
</tr>
<tr>
<td>IV</td>
<td>5 (18)</td>
</tr>
<tr>
<td>V</td>
<td>8 (29)</td>
</tr>
<tr>
<td>VI</td>
<td>6 (21)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>7 (25)</td>
</tr>
<tr>
<td>African</td>
<td>9 (32)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>6 (21)</td>
</tr>
<tr>
<td>Asian</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Native American/Alaska native</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (11)</td>
</tr>
<tr>
<td>Disease duration, mean (SD) [range], y</td>
<td>5.4 (5.5) [1-26]</td>
</tr>
<tr>
<td>Disease activity in last 3 mo</td>
<td></td>
</tr>
<tr>
<td>Slowly progressive</td>
<td>24 (86)</td>
</tr>
<tr>
<td>Nonprogressive</td>
<td>4 (14)</td>
</tr>
<tr>
<td>Previous episodes of repigmentation</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>18 (64)</td>
</tr>
<tr>
<td>Spontaneous</td>
<td>3 (11)</td>
</tr>
<tr>
<td>After treatment</td>
<td>7 (25)</td>
</tr>
<tr>
<td>After sun exposure</td>
<td>0</td>
</tr>
<tr>
<td>Depigmentation on scars</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>10 (36)</td>
</tr>
<tr>
<td>No</td>
<td>18 (64)</td>
</tr>
<tr>
<td>Stress as a causative/precipitating factor</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>14 (50)</td>
</tr>
<tr>
<td>No</td>
<td>14 (50)</td>
</tr>
<tr>
<td>Pruritus before development of lesions</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3 (11)</td>
</tr>
<tr>
<td>No</td>
<td>25 (89)</td>
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<tr>
<td>Vitiligo on genitals</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>21 (75)</td>
</tr>
<tr>
<td>No</td>
<td>7 (25)</td>
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<tr>
<td>Associated autoimmune disease</td>
<td></td>
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<td>Yes</td>
<td>6 (21)</td>
</tr>
<tr>
<td>No</td>
<td>22 (79)</td>
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<tr>
<td>Family history of premature graying of hair (&gt;50% gray by age 40 y)</td>
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<td>Yes</td>
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<tr>
<td>No</td>
<td>25 (89)</td>
</tr>
<tr>
<td>Family history of vitiligo</td>
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</tr>
<tr>
<td>Yes</td>
<td>10 (36)</td>
</tr>
<tr>
<td>No</td>
<td>18 (64)</td>
</tr>
<tr>
<td>Occupational vitiligo</td>
<td></td>
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<tr>
<td>Yes</td>
<td>1 (4)</td>
</tr>
<tr>
<td>No</td>
<td>27 (96)</td>
</tr>
</tbody>
</table>

Abbreviations: NB-UV-B, narrowband UV-B; SPT, skin phototype.

*Unless otherwise indicated, data are expressed as number (percentage) of patients. Percentages have been rounded and might not total 100. Study groups are described in the Study Protocol subsection of the Methods section. For all between-group comparisons, P > .05.
from Los Angeles, and 10 from New York) were enrolled in the combination therapy group (afamelanotide and NB–UV-B) and 27 were enrolled in the NB–UV-B monotherapy group (8 from Detroit, 10 from Los Angeles, and 9 from New York). The intent-to-treat population consisted of all participants who received at least 1 treatment and underwent an efficacy evaluation at 28 days. One patient from each group failed to fulfill these criteria, resulting in the intent-to-treat populations of 27 and 26, respectively. We found no statistically significant differences in age, body weight, height, body mass index, race, or Fitzpatrick SPT among patients in both groups. On day 0, the VASI and VETF score of both groups were similar.

Response to Treatment Evaluated by the VASI
Response in the intent-to-treat population in the combination therapy group compared with the NB–UV-B monotherapy group is shown in Figure 2. In both groups, the degree of repigmentation improved (P < .001), as reflected by the decreased VASI observed from day 56 until the end of the observation period (day 168). Repigmentation in both groups was noted to be peripheral and follicular. The between-groups comparison showed that response in the combination therapy group was superior to that in the NB–UV-B monotherapy group (P < .05), starting at day 56; the improvement in the combination therapy group compared with the NB–UV-B monotherapy group was more marked at day 168 than day 56. Similar findings were observed by analyzing data from patients who completed the treatment (n = 17 in the combination therapy group and n = 24 in the NB–UV-B monotherapy group). We found a statistically significant response in both groups (P < .001), starting from day 56; the between-groups comparison showed a superior response in the combination therapy group with repigmentation (represented by a relative reduction in the VASI) of 48.64% (95% CI, 39.49%-57.80%) at day 168 vs 33.26% (95% CI, 24.18%-42.33%) in the NB–UV-B monotherapy group.

Response to Treatment Evaluated by VETF Scores
Data from the intent-to-treat population were analyzed using disease extent, reflecting the body surface involvement. Although both groups achieved statistically significant improvement, the combination therapy group achieved it at day 56, whereas the NB–UV-B monotherapy group achieved it at day 84 (Figure 2D). Between-groups analysis showed a superior response in the combination therapy group on days 140 and 168 (P < .04).

Analysis of disease staging, which assesses severity of vitiligo, in the intent-to-treat population failed to detect differences between the 2 groups. Analysis of disease spreading, a reflection of progression, in the intent-to-treat population showed a statistically significant (P < .001) improvement of pigmentation in both groups starting on day 56. Between-groups analysis showed a statistically significant superior response (P ≤ .03) in the combination therapy group, starting from day 56.

Time to Onset of Repigmentation
Compared with the NB–UV-B monotherapy group, a statistically significantly higher percentage of patients in the combination therapy group achieved repigmentation on the face and upper extremities, and they did so at earlier times (face, 41.0 vs 61.0 days [P = .001]; upper extremities, 46.0 vs 69.0 days [P = .003]). Although a similar trend was observed for the trunk and lower extremities, the differences did not reach statistical significance (P > .05).

Responses of Patients With Different Fitzpatrick SPTs
Data from the intent-to-treat population were analyzed using the VASI system based on observed Fitzpatrick SPTs, which
were categorized into groups of SPT III and SPTs IV to VI. Between-groups comparison showed that patients with SPTs IV to VI receiving combination treatment had a more rapid response compared with those receiving NB–UV-B monotherapy at days 56 and 84 (P < .05). No noticeable differences were found between the treatment groups for patients with SPT III. Similar analysis using the VETF scores (extent, stage, and spread) failed to detect any differences in response between the combination therapy and NB–UV-B monotherapy groups in patients with SPT III and those with SPTs IV to VI.

Safety and Adverse Events

The most common adverse events reported were cutaneous (Table 2), including erythema noted in 19 patients in the combination therapy group (68%) and 22 in the NB–UV-B monotherapy group (82%). Other cutaneous events include hyperpigmentation of unaffected skin (2 patients [7%] in the combination therapy group and none in the NB–UV-B monotherapy group) and pruritus (2 patients [7%] in both groups). Hyperpigmentation was subjectively experienced by all participants in the combination therapy group but only included as an adverse event if the patient complained of hyperpigmentation or if the hyperpigmentation had an effect on the patient. The 2 patients who complained of hyperpigmentation withdrew from the study for this reason. Nausea was reported in 18% of the combination therapy group. No gastrointestinal adverse events were noted in the NB–UV-B monotherapy group. These findings are consistent with previous studies of afamelanotide in the treatment of solar urticaria and erythropoietic protoporphyria, which demonstrated nausea, headache, and increased pigmentation in existing nevi.14,15

The only serious adverse event noted was hypertension in the combination group. Two patients were noted to have hypertension during the routine examination, which qualified as severe in only 1 patient. In this case, the patient had a known history of hypertension and did not take a prescribed antihypertensive on that day; thus the hypertension was not believed to be related to the study drug.

Discussion

To our knowledge, this multicenter, randomized study involving a total intent-to-treat population of 55 matched individuals with the clinical response evaluated by 2 validated scoring systems is one of the largest such studies to date. The results show an overall clinically apparent and statistically significant superior repigmentation response in the combination therapy group, compared with the NB–UV-B monotherapy group (Figure 2 and Figure 3). For the face and upper extremities, which are clinically the most apparent sites in the daily lives of the patients, the median time to onset of repigmentation in the combination therapy group was 20 days sooner than in the NB–UV-B monotherapy group. Analysis of the database SPTs showed a trend toward more rapid response in those with SPTs IV to VI who underwent combination treatment; this trend was detected using the VASI but not the VETF score. The small sample size in each of the subgroups probably was not sufficiently powered to detect consistent differences.

Two vitiligo treatment outcome scoring systems are used in this study. Significant differences were detected when data were analyzed based on the VASI. Using the VETF score, significant differences were detected in disease spreading and extent, but not in staging. A possible explanation could be that the VASI has an uneven scaling system that allows it to pick up small changes at either end of the spectrum and larger changes in between. The VASI differs from the VETF system, which has a consistent system of staging with the same differences between each stage. Because smaller differences tend to occur at the extremes, the VASI may be more effective at detecting small changes in staging but lacks the ability to measure stability. In addition, most patients had stage I or II disease, which may explain a lack of significant findings in the VETF staging score.

Overall, afamelanotide was well tolerated without any serious adverse effect. As expected, erythema and pruritus were noted in both groups and hyperpigmentation in the combination therapy group. The higher frequency of nausea and abdominal pain, although not serious, is most likely related to afamelanotide administration.

This study has several limitations. The dose of afamelanotide (16 mg) and the frequency of the injection were chosen based on experience with previous studies in erythropoietic

### Table 2. Adverse Events in Safety Populationa

<table>
<thead>
<tr>
<th>Event</th>
<th>Study Group, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Combination Therapy (n = 28)</td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Any adverse eventsb</td>
<td>23 (82)</td>
</tr>
<tr>
<td>Gastrointestinal tract disorders: nausea</td>
<td>5 (18)</td>
</tr>
<tr>
<td>General disorders and administration site conditions: fatigue</td>
<td>3 (11)</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td></td>
</tr>
<tr>
<td>Folliculitis</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Abnormalities on routine investigations</td>
<td></td>
</tr>
<tr>
<td>Hematuria</td>
<td>0</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>0</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>0</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
</tr>
<tr>
<td>Erythema</td>
<td>19 (68)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Skin burning sensation</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Vascular disorders: hypertension</td>
<td>2 (7)</td>
</tr>
</tbody>
</table>

Abbreviation: NB–UV-B, narrowband UV-B.

a Study groups are described in the Study Protocol subsection of the Methods section. All serious adverse events and all adverse events with n ≥ 2 are reported.
b P = .42.
Figure 3. Clinical Response of Patients’ Study Treatments

A, ResponsetocombinationtreatmentwithafamelanotideandnarrowbandUV-B(NB–UV-B)phototherapycomparedwithNB–UV-Bmonotherapyonthetrunk.

B, Responses to combination therapy and NB–UV-B monotherapy on the upper extremities. D indicates day; D0, baseline. Arrowheads indicate areas of repigmentation noted at day 68 in the combination therapy group.
protoporphyrina and solar urticaria; we did not perform a
dose-response study in vitiligo, and we do not know whether a
monthly injection is the most optimal treatment regimen.
The active treatment phase of 6 months was selected because
we knew it would give more than adequate time to evaluate
the response to NB–UV-B phototherapy properly; however,
we do not know if this duration is optimal to evaluate fully
the response to afamelanotide.

To ensure an adequate number of patients for analysis, we
did not include an afamelanotide-only group. In addition, pre-
vious studies have shown that α-MSH acts on the melanocor-
tin-1 receptor, which is not expressed on nascent melano-
blasts. Combined use of NB–UV-B phototherapy and afamelanotide allowed for further differentiation of melano-
blasts and upregulation of melanocortin-1 receptor. This study
design was developed to maximize the potential therapeutic
effect of afamelanotide. Future areas of investigation include
evaluating any possible effect of afamelanotide as mono-
therapy in the treatment of vitiligo.

Patients with dark skin types (SPTs III–VI) were chosen be-
cause of our collective clinical impression that dark-skinned
patients in general tend to be more responsive to all types of
treatments; therefore, this study was not designed to address
response in fair-skinned patients (ie, those with SPTs I and II).
However, our data suggest that individuals with darker skin
(SPTs IV–VI) responded more rapidly to combined treatment
with afamelanotide and NB–UV-B phototherapy compared with
NB–UV-B monotherapy. Because this group of patients has the
most apparent visual appearance and hence psychological ef-
effect of the disease, rapidity of response for these patients
would be most welcome. In the future, quality-of-life assessments
may be helpful in gauging the impact of treatment.

Conclusions

Even with these limitations, the results of this multicenter, ran-
domized study strongly indicate that administration of
afamelanotide to patients receiving NB–UV-B phototherapy
should be considered as an option that could significantly en-
hance the rate and the total surface area of repigmentation.
Fur-
thermore, our data suggest that patients with lesions on the
face and upper extremities, and potentially those with darker
skin, would have a more rapid response to the combination
treatment. The results of this study offer hope to patients with
vitiligo in the treatment of this disfiguring disease.

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ORIGINAL INVESTIGATION

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During the burning pain for 20 minutes. 3

1 Child, a teenage boy, required hospitalization in a burn unit after en-

The typical result is a well-demarcated reddish brown plaque with

disturb the board snapped when he was halfway across, submerging him in murky water. Soaking wet, embar-
rassed, and tearful, he had to call his mother from the principal’s office to ask for a change of clothes. So starts a story told by one of this ar-
ticle’s authors (E.M.M.).

Another challenge may be riskier. The “salt-and-ice challenge” is rap-

difying the nation’s youth (id: M.D.M.).

When my father was in second grade, a fellow student dared him to walk

Dares on social media have become quickly popular and highly shared, a process known as “trending.” These challenges raise con-
cern for factitial dermatoses and self-inflicted injuries that physicians may encounter, and their recognition by dermatologists is one way to stay on trend.

Figure. “Salt-and-Ice Challenge” Participant

The forearm of an adolescent boy with several well-demarcated reddish brown plaques after attempting the salt-and-ice challenge.

Evidently, the obvious potential to cause serious burns is unrecog-
nized, ignored, or denied in the baffling pursuit of Internet fame. Dares on social media have become quickly popular and highly shared, a process known as “trending.” These challenges raise concern for factitial dermatoses and self-inflicted injuries that physicians may encounter, and their recognition by dermatologists is one way to stay on trend.

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