Vitiligo Guidelines

Mauro Picardo
San Gallicano Dermatologic Institute, IRCCS
Rome, Italy
Poor outcomes sharing
Poor criteria (diagnosis and effectiveness) sharing
Variable duration treatment
Home-made trial design
Repigmentation and melanocyte reservoir: different vitiligo?

How to define and measure disease?

How to compare effectiveness?
Broadband ultraviolet B vs. psoralen ultraviolet A in the treatment of vitiligo: a randomized controlled trial

M. El Mofty, M. Bosseila, H. M. Mashaly, H. Gawdat and H. Makaly

Phototherapy Unit, Dermatology Department, Cairo University, Cairo, Egypt

doi:10.1111/ced.12099

Journal of Dermatological Treatment. 2013; Early Online: 1–4
© 2013 Informa Healthcare USA on behalf of Informa UK Ltd.
ISSN: 0954-6634 print/1471-1753 online
DOI: 10.3109/09546634.2013.777381

Comparison of efficacy of narrow band UVB therapies with UVB alone, in combination with calcipotriol, and with betamethasone and calcipotriol in vitiligo

Necmettin Akdeniz¹, Ibrahim Halil Yavuz², Serap Gunes Bilgili³, Gokturk Ozaydin Yavuz² & Omer Calka³

Figure 1. (A) The patient before treatment with betamethasone plus calcipotriol plus narrow-band UVB therapies. (B) The patient after treatment with betamethasone plus calcipotriol plus narrow-band UVB therapies.
The Efficacy of Afamelanotide and Narrowband UV-B Phototherapy for Repigmentation of Vitiligo

Pearl E. Grimes, MD; Iltefat Hamzavi, MD; Mark Lebwohl, MD; Jean Paul Ortonne, MD; Henry W. Lim, MD

Courtesy of Vitiligo International
VEFT Authors

Aims

• *What is already known about this topic?* Vitiligo is a disease lacking definitive and completely effective therapies. Phototherapy and combined treatments are the most effective treatments.

• *What is the goal of the treatment in vitiligo?* Therapy should stop the progression of the lesions and provide complete or almost complete repigmentation to be satisfactory for the patient. The results should be maintained over time.

• *What does this study add?* The criteria for treatment have been critically reviewed. Evidence-based recommendations (S1) for the treatment of vitiligo have been made. A proposal for clinical evaluation, treatment and follow-up has been outlined.
IL1β appeared to be expressed more in samples overlapping the border of the lesion and in perilesional and lesional samples than in non-lesional vitiligo skin.
1. Topical corticosteroids

- Limited, extra-facial involvement - potent TCS, once daily for 3 months or 15 days/month for 6 months

- First and safest choice - potent TCS rather than super potent

- If systemic absorption - consider mometasone furoate or methylprednisolone aceponate

- For facial lesions - consider topical calcineurin inhibitors rather than TCS
2. Calcineurin inhibitors

- For new and actively spreading lesions and face/neck areas
- Twice daily, initially for 6 months, for both adults and children
- Safety profile is better concerning risk of skin atrophy
- During the treatment- moderate but daily sun exposure
- If effective consider prolonged treatment (↑12 months)
NB-UVB and targeted phototherapies

- Total body NB UVB for NSV- arrest and repigment vitiligo
- Targeted phototherapies for localized vitiligo, recent onset & childhood vitiligo
- Maximum cycle duration- 1 year for adults and 6 months for children. One year interruption between cycles
- Stop treatment: if no results in 3 months or if ↓ 25% repigmentation in 6 months
- Maintenance treatment-not recommended. Regular follow-ups necessary
PUVA and photochemotherapy

• Oral PUVA-second line therapy in adults
  
  • 12 to 24 months therapy
  
  • Topical PUVA-very low dosage psoralens creams
Topical steroids and phototherapy

For difficult to treat areas such as bony prominences

Highly potent topical steroids once a day (3 weeks out of 4) for the 3 first months of phototherapy
4. Combination treatments (2/3)

Topical calcineurin inhibitors and phototherapy

• Effective and provides better results than the two treatments alone
• Should be used only in controlled or experimental settings due to ? carcinogenicity
• Use of adequate photoprotection due to the lack of data on long term safety (or not) of combination of TCI and UV
4. Combination treatments (3/3)

Vitamin D analogues and phototherapy
• Not recommended

Phototherapy and other treatment
• Phototherapy+oral antioxidants-possibly beneficial

Phototherapy after surgery
• NB-UVB or PUVA should be used for 3-4 weeks after skin surgery
Oral Mini Pulse

- Stable vitiligo-not useful
- Fast spreading vitiligo- weekend OMP (2.5 mg/day) of dexamethasone before phototherapy (based on author’s experience)
- Optimal duration of OMP to stop vitiligo progression is 3-6 months
5. Other immunosuppressants and biologics

- Cyclophosphamide, Cyclosporine & Anti-TNF-α
  Not recommended due to lack of data and for the possible side effects
6. Other systemic interventions: antioxidants

- Vitamin E, vitamin C, ubiquinone, lipoic acid, Polypodium Leucotomos, Ginko biloba etc.

- Antioxidant supplementation could be useful during UV therapy and reactivation phases
7. Surgery

- For NSV- patients with stable disease and negative Koebner phenomenon

- Risk of relapse

- For SV and other localized forms-after failure of medical interventions
Camouflage

Self-tanners
• Lasts 3-5 days, stain free, waterproof
• Sea water makes them fade away quickly

Highly pigmented cover creams
• Easy to apply, fragrance free, waterproof
• Fixing spray
• Applied and removed daily with caution to avoid Koebner's phenomenon

Dermal pigmentation, cosmetic tattoos
• For lips, nipples especially in black people
• In other areas to be used with caution
8. Other interventions (2/3)

for extensive disfiguring vitiligo & after exploring other therapies

Depigmentation with:
• Monobenzone
• Q-switched ruby laser alone or in combination with methoxyphenol,
• Cryotherapy
Psychological interventions

• Subjective assessment- DLQI, QoL questionnaire or Patient-defined outcome questionnaire for vitiligo

• Psychological support and community interventions may be needed

• Adolescents and dark skinned individuals- often stigmatised
Algorithm for NSV

1. Diagnosis
2. Avoidance triggering factors
   - NB-UVB (3 months) ± systemic/topical therapies
3. Stabilization/repigmentation
4. Progression
   - CS minipulse (3-4 months)
   - Other immunosuppressants
5. No repigmentation
   - KP +
   - Depigmenting agents
6. Stabilization without repigmentation
   - KP -
   - Surgery
Algorithm for SV
Genomewide association analysis indicate 10 independent SNP: in MHC loci (6p21.3), in seven regions related to autoimmune diseases, and in 11q14.3 (TYR)

Variant thermosensitive, aberrantly glycosilated, retained in ER
Th17 and Dendritic Cells

Wang, 2001

- KC
- LC
- DR+NALP1+
- CD11c
- epidermis
- dermis
- IL23
- IL1β
- Th17

LC in half lower epidermis
SASP factors

- IGFBP3
- IGFBP7
- Cox-2
- MMP3

mRNA fold increase

- NHM
- VHM

- pg/ml/μg proteins

- NHM
- VHM
How we link oxidative stress and inflammation?
Clinical type of VTG lesions

(a) Inflammatory lesion with raised borders.
(b) Trichrome vitiligo.
(c) Hypomelanotic lesion with poorly defined borders.
(d) Amelanotic lesion with sharply demarcated borders.
Table 4 The relationship between the clinical aspect and activity of vitiligo lesions

<table>
<thead>
<tr>
<th>Clinical aspect</th>
<th>Activity of the lesion</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Actively spreading</td>
<td>Stable</td>
</tr>
<tr>
<td>Hypomelanotic lesion with poorly defined borders H.P.D.B</td>
<td>Yes, n = 26</td>
<td>92.85%</td>
</tr>
<tr>
<td></td>
<td>No, n = 2</td>
<td>7.15%</td>
</tr>
<tr>
<td>Amelanotic lesion with sharply demarcated borders A.S.D.B</td>
<td>Yes, n = 3</td>
<td>15%</td>
</tr>
<tr>
<td></td>
<td>No, n = 17</td>
<td>85%</td>
</tr>
</tbody>
</table>

N, number of patients; n = number of lesions studied.
<table>
<thead>
<tr>
<th>Staining</th>
<th>Biopsy 1</th>
<th>Biopsy 2</th>
<th>Biopsy 3</th>
<th>Biopsy 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>H &amp; E</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
</tr>
<tr>
<td>Melan A</td>
<td><img src="image5.png" alt="Image" /></td>
<td><img src="image6.png" alt="Image" /></td>
<td><img src="image7.png" alt="Image" /></td>
<td><img src="image8.png" alt="Image" /></td>
</tr>
<tr>
<td>Melanin</td>
<td><img src="image9.png" alt="Image" /></td>
<td><img src="image10.png" alt="Image" /></td>
<td><img src="image11.png" alt="Image" /></td>
<td><img src="image12.png" alt="Image" /></td>
</tr>
<tr>
<td>CD4</td>
<td><img src="image13.png" alt="Image" /></td>
<td><img src="image14.png" alt="Image" /></td>
<td><img src="image15.png" alt="Image" /></td>
<td><img src="image16.png" alt="Image" /></td>
</tr>
<tr>
<td>CD8</td>
<td><img src="image17.png" alt="Image" /></td>
<td><img src="image18.png" alt="Image" /></td>
<td><img src="image19.png" alt="Image" /></td>
<td><img src="image20.png" alt="Image" /></td>
</tr>
<tr>
<td>CD1a</td>
<td><img src="image21.png" alt="Image" /></td>
<td><img src="image22.png" alt="Image" /></td>
<td><img src="image23.png" alt="Image" /></td>
<td><img src="image24.png" alt="Image" /></td>
</tr>
</tbody>
</table>

**SV and inflammation**

- **Reduced Treg (FOXP3)**
  - In lesional vs non lesional

- **High melanocyte specific T**

- **Halo nevi occurrence** as basis for the Ag exposure and immune damage

(Histology relevance)

Van Geel, 2010
Irradiance, but not fluence, plays a crucial role in UVB-induced immature pigment cell development: new insights for efficient UVB phototherapy.

Lan CC, Yu HS, Lu JH, Wu CS, Lai HC.

Department of Dermatology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan; Department of Dermatology, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan; Department of Dermatology, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan.

Abstract

Light exposure modulates development of living organisms. In the field of medicine, light has frequently been used for regenerative purposes. Excimer light (308 nm) has demonstrated superior efficacy in treating vitiligo, a condition requiring development of melanoblasts and a model for studying nerve cell regeneration, as compared to narrow-band ultraviolet B (NBUVB; 311 nm). Using mouse-derived melanoblast cells to examine the pro-differentiation effects of these two light sources, we demonstrated that at equivalent fluence, excimer light induces melanoblast differentiation, while NBUVB failed to so. Mechanistically, activation of aryl hydrocarbon receptor pathway and nuclear translocation of epidermal growth factor receptor are involved in pro-differentiation effects of excimer light. Reduction in irradiance by filter abrogated the effects of excimer light in melanoblasts, even when equivalent fluence was delivered by the same light source. As ultraviolet B (UVB) irradiation is closely associated pigment cell development, future therapy employing UVB for pigmentation purposes should incorporate irradiance as a crucial specification.

© 2013 John Wiley & Sons A/S.
Comparison between eximer laser and light
Leucotrichia repigmentation with noncultured cellular grafting

, E.Y. Gan et al. 2011
Microenvironment alteration contributes to melanocyte dysfunction in vitiligo

The melanocyte-stimulating cytokines SCF and ET-1 show a lower expression in vitiligo skin

Moretti et al., 2009
Laser plus NB UVB

Co2

Erbium
He-neon

Growth factors release
Signal transduction induction
ATP production
KER/FIBRO proliferation
MEL migration
Melanin production

migration

3hrs  6hrs  9hrs  18hrs  24hrs

distance (um)

FAK expression

0  0.5  1  1.5  2  2.5  3

relative intensity

He-Ne  0 J/cm²  1 J/cm²

Lan, 06
Afamelanotide plus NB-UVB

14 days of treatment

Persistence of repigmentation after not implant for 5 months

Types and Therapies

- Arrest of the progression
- Induction of proliferation and migration of differentiated melanocytes
- Improve of melanocyte survival
International consensus on core outcomes set for vitiligo research

Dr Viktoria Eleftheriadou MD PhD
Centre of Evidence Based Dermatology
University of Nottingham
28/02/2013
4 to 7 Sep 2014
Singapore
www.ipcc2014.org

Bringing Colours to Life
Advances in Pigment Cell Research and Translation into Clinical Practice
www.ipcc2014.org