Treatment of Moderate or Marked Melasma in Darker Skin with a 4% Hydroquinone Skin Care System Plus 0.05% Tretinoin Cream

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Funded by OMP, Inc.
Conflicts of Interest

- Dr Gold - consultant, investigator, and speaker for OMP, Inc.
- Dr Rendon - investigator for OMP, Inc.
- Dr DiBernardo - consultant and investigator for OMP, Inc.
- Dr Bruce - consultant and investigator for OMP, Inc.
- Dr Lucas-Anthony - investigator for OMP, Inc.
- Dr Watson – employee of, and holds stock and stock options in, OMP, Inc.
Purpose

• To evaluate the efficacy and tolerability of treating melasma in darker skin using a 4% hydroquinone skin care system plus 0.05% tretinoin cream

[This regimen treats melasma and provides a complete skin care routine]
Rationale for Study

• A previous study\(^1\) has evaluated the efficacy and safety of treating mild or moderate epidermal melasma in darker skin using a 4% hydroquinone skin care system plus 0.025% tretinoin cream.

• Study presented here has similar protocol except:
  – Evaluates higher concentration of tretinoin (0.05% rather than 0.025%)
  – Evaluates moderate or marked melasma (rather than mild or moderate melasma)

\(^1\) Grimes & Watson, Eposter 4581, AAD March 2012
Inclusion Criteria

- 25- to 65-year old females with:
  - Moderate or marked epidermal melasma (covering 26% to 50% of face), confirmed by Wood’s lamp examination
  - Mild to marked intensity of melasma pigmentation
  - Cutaneous melanosis stable over preceding 3 months
  - Fitzpatrick skin type III-VI
Study Design

• Patients used a 4% hydroquinone skin care system + tretinoin 0.05% cream on their face every day for up to 24 weeks (initial 12 weeks + optional 12-week extension)
## Components of 4% Hydroquinone Skin Care System

<table>
<thead>
<tr>
<th>Component</th>
<th>Key Ingredients</th>
<th>Potential Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foaming gel cleanser</td>
<td>Aloe barbadensis leaf juice</td>
<td>Soothing and anti-inflammatory activity</td>
</tr>
<tr>
<td>Toner</td>
<td>Aloe barbadensis leaf juice + witch hazel</td>
<td>Soothing and anti-inflammatory activity, scavenging activity against active oxygen, suppression of UV-induced erythema</td>
</tr>
<tr>
<td>4% hydroquinone</td>
<td>Hydroquinone</td>
<td>Reduction in pigmentation</td>
</tr>
<tr>
<td>Exfoliation enhancer</td>
<td>Glycolic acid + lactic acid</td>
<td>Exfoliation</td>
</tr>
<tr>
<td>Sunscreen SPF 35</td>
<td>Zinc oxide + octinoxate</td>
<td>Physical + chemical sunscreen</td>
</tr>
</tbody>
</table>
Treatment Regimen

4% hydroquinone skin care system, consisting of 6 proprietary products:

1. Foaming gel cleanser (contains aloe barbadensis leaf juice)  
   Twice daily

2. Toner (contains aloe barbadensis leaf juice and witch hazel)
   Each morning

3. 4% hydroquinone

4. Exfoliation enhancer (contains glycolic acid and lactic acid)

5. Sunscreen SPF 35

6. 4% hydroquinone (different formulation to above)
   Each evening

0.05% tretinoin cream

Plus, as needed:

Moisturizer for dryness

0.5% hydrocortisone for other tolerability issues
Potential Advantages of Treatment Systems

- Convenient
  - Provide medical treatment and overall skin care in one regimen, saving confusion juggling different regimens
- Popular with patients\(^1\)
- May enhance compliance\(^1\)
- May enhance efficacy:
  - Cleansing and exfoliating may help penetration of other ingredients into skin
  - Sunscreen may help maintain efficacy of treatment
- May enhance tolerability:
  - May contain agents with soothing and anti-inflammatory properties (eg, aloe barbadensis leaf juice and witch hazel)

\(^1\) Bowe et al. Semin Cutan Med Surg 2008
Investigator Evaluations

- Melasma severity
- Pigmentation intensity
- Melasma improvement
- Erythema, dryness, peeling
Patient Evaluations

- Improvement in photodamage-related parameters:
  - Skin texture/roughness
  - Skin firmness
  - Brown spots/discoloration
  - Fine lines and wrinkles

- Quality of life:
  - Embarrassment/self-consciousness due to skin
  - Focus by others on skin discoloration
  - Feeling unattractive due to skin
  - Effort put into hiding skin discoloration
  - Social/leisure activities affected by skin

- Effectiveness of treatment compared with other medications
- Satisfaction with effectiveness of treatment
- Ease of use
- Burning/stinging
Results

• 37 females enrolled:
  – 34/37 (92%) completed initial 12-week study
  – 25/27 (93%) completed extension study to 24 weeks

• Mean of 46 years old

• 60% white/Caucasian, 35% black/African American, 5% Asian

• Fitzpatrick skin type:
  – III (27%)
  – IV (51%)
  – V (11%)
  – VI (11%)

• Melasma was:
  – Centrofacial in 65%
  – Malar in 27%
  – Mandibular in 8%
Melasma Severity

Median grade for melasma severity

Scale
None (0)
Minimal/trace (1)
Mild (2 or 3)
Moderate (4 or 5)
Marked (6 or 7)
Severe (8)

Week
0 4 8 12 18 24

None
Minimal/trace
Mild
Moderate
Marked
Severe

*** P≤.001 versus baseline
Pigmentation Intensity

Median grade for pigmentation intensity

Scale
None (0)
Minimal (1)
Mild (2 or 3)
Moderate (4 or 5)
Marked (6 or 7)
Severe (8)

*** P ≤ .001 versus baseline
Improvement in Melasma

At least 1-grade improvement in melasma severity
- Week 4: 72%
- Week 8: 82%
- Week 12: 91%
- Week 18: 93%
- Week 24: 96%

At least 1-grade improvement in melasma pigmentation intensity
- Week 4: 86%
- Week 8: 97%
- Week 12: 100%
- Week 18: 96%
- Week 24: 100%

Marked (≥ 51%) improvement in melasma
- Week 4: 31%
- Week 8: 50%
- Week 12: 71%
- Week 18: 78%
- Week 24: 84%
Patient-Reported Improvements in Photodamage-Related Parameters at Week 24

Patients with rating of good, very good, or excellent improvements (%)

- Skin texture/roughness: 100% (Excellent), 80% (Very good), 0% (Good)
- Skin firmness: 100% (Excellent), 80% (Very good), 0% (Good)
- Brown spots/discholoration: 96% (Excellent), 84% (Very good), 0% (Good)
- Fine lines and wrinkles: 92% (Excellent), 88% (Very good), 0% (Good)
Improvement in Quality of Life Parameters

- **Embarrassed/self-conscious due to skin:**
  - Baseline: 78%
  - Week 4: 19%
  - Week 12: 12%
  - Week 24: 4%

- **Feeling unattractive due to skin:**
  - Baseline: 61%
  - Week 4: 22%
  - Week 12: 15%
  - Week 24: 16%

- **Effort put into hiding skin discoloration:**
  - Baseline: 67%
  - Week 4: 25%
  - Week 12: 18%
  - Week 24: 13%

- **Focus on skin discoloration by others:**
  - Baseline: 50%
  - Week 4: 17%
  - Week 12: 12%
  - Week 24: 8%

- **Social/leisure activities affected:**
  - Baseline: 44%
  - Week 4: 8%
  - Week 12: 15%
  - Week 24: 4%
Patient Ratings at Week 24

100% of patients found the study treatment more effective than other medications.

100% of patients were satisfied with the overall effectiveness of the treatment.

100% of patients found the study treatment easy to apply.
Improvements in Melasma
Improvement in Melasma
Improvements in Melasma

Baseline  Week 8  Week 12  Week 24
Improvements in Melasma

Baseline

Week 4

Week 12

Week 24
Efficacy Summary

• Treating melasma with the 4% hydroquinone skin care system + 0.05% tretinoin was associated with:
  – Significant improvements in melasma
    • Less severe melasma (P ≤ 0.001 from week 4 onward)
    • Less intense pigmentation (P ≤ 0.001 from week 4 onward)
  – High levels of patient satisfaction
  – Considerable improvements in quality of life
    • Less embarrassment/self-consciousness
    • Less feeling of being unattractive
    • Less effort hiding skin discoloration
    • Less focus from other people on the melasma
    • Less effect on social and leisure activities
  – Good improvements in photodamage-related parameters:
    • Skin texture
    • Skin firmness
    • Brown spots/dисcoloration
    • Fine lines and wrinkles
Adverse Events

- 4 patients had adverse events at least probably related to treatment:
  - Erythema
  - Erythema/vesicles
  - Dryness/tightness/soreness
  - Acne

} moderate

} mild
**Erythema**

- **Median score**
  - 0 (Trace)
  - 1 (Mild)
  - 2 (Moderate)
  - 3 (Marked)
  - 4 (Severe)

- **Week**
  - 0
  - 4
  - 8
  - 12

*** P≤.001 versus baseline
Dryness

**Median score**

- **0**: None
- **1**: Slight
- **2**: Moderate
- **3**: Marked
- **4**: Severe
- **5**: None

*** P ≤ .001 versus baseline
Peeling

Median score

Week

0 4 8 12

Severe
Marked
Moderate
Mild
Trace
None

*** P≤.001 versus baseline
Burning/Stinging

Week

Median score

0 4 8 12

Severe
Marked
Moderate
Mild
Trace
None

*** P≤.001 versus baseline
Tolerability

• Erythema, dryness, peeling, and burning/stinging (evaluated up to week 12 only):
  – All increased transiently and then reverted to baseline levels by week 12
  – Mean and median grades were no more than “trace/slight” at any timepoint

• 26/37 (70%) patients used the study moisturizer:
  – 17 (46%) as preventive measure

• 16/37 (43%) used hydrocortisone:
  – 7 (19%) as preventive measure
Conclusion (1)

• Using the 4% hydroquinone skin care system + 0.05% tretinoin cream to treat epidermal melasma can achieve significant reductions in:
  – Melasma severity
  – Melasma pigmentation intensity
• Importantly, treatment is also associated with considerable improvements in:
  – Quality of life
  – Signs of photodamage (eg, skin roughness, fine lines/wrinkles)
• Treatment is generally well tolerated and associated with a high level of patient satisfaction
Conclusion (2)

• Comparing with results from earlier study,\(^1\) which used 0.025% tretinoin instead of 0.05% tretinoin, shows that the 0.05% tretinoin regimen used in the study presented here is associated with:
  – Greater efficacy (eg, melasma severity and pigmentation intensity)
  – Faster improvement in efficacy and quality of life parameters
  – Greater likelihood of a transient increase in erythema, dryness, peeling, or burning/stinging

• The choice of regimen could be:
  – Selected based on whether individuals prefer to optimize efficacy over tolerability or vice versa
  – Titrated up during treatment
    • Initially optimizing tolerability during the period of retinization
    • Subsequently optimizing efficacy

\(^1\) Grimes & Watson, Eposter 4581, AAD March 2012