

# Cosmetic Concerns in Melasma, Part 2: Treatment Options and Approaches

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Melasma often is recalcitrant to treatment, making it difficult for patients and physicians; therefore, it is best to approach the treatment of melasma with realistic expectations for improvement. An individualized treatment plan is recommended for each patient, as a single method may not work for every patient. Because of the predilection for melasma to affect darker skin phototypes, physicians should avoid aggressive treatments that may lead to further hyperpigmentation, hypopigmentation, scarring, or keloid formation. Treatment options range from topical bleaching and medicinal agents to surgical techniques such as chemical peels as well as lasers and light sources. We describe a stepwise approach to treatment and long-term maintenance therapy options that account for the recalcitrant nature of the disease. Patient education about the importance of photoprotection and strong adherence to a sun protection regimen are central to treatment. If more aggressive techniques are warranted, such as chemical peels or laser modalities, they should only be performed by physicians with extensive experience in treating darker skin phototypes. *Cosmet Dermatol.* 2011;24:575-582.

**M**elasma is a common hyperpigmentation disorder that can present a range of cosmetic concerns for affected patients. There is no single treatment that works for all melasma patients;

therefore, we recommend a stepwise approach that is carefully individualized to the patient's specific needs. Various nonsurgical and surgical treatments are available. Patients often have tried many over-the-counter or at-home remedies before seeking dermatologic consultation; in these cases, the physician should conduct a thorough review of self-administered treatments to discontinue any agents that may cause further hyperpigmentation or possible allergic/irritant contact dermatitis. It also is important to initially discuss the lengthy treatment times and commitment needed to successfully treat melasma to help manage unrealistic expectations. Combination therapy usually is needed and recommended. Because melasma preferentially affects darker skin phototypes, physicians should always be aware of the potential for further hyperpigmentation or

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hypopigmentation secondary to treatment, as these phototypes may have more labile melanocytes.<sup>1</sup>

### PHOTOPROTECTION

Photoprotection is one of the most effective steps in melasma treatment and should be initiated early and throughout the treatment process. Frequent exposure to UV radiation and visible light causes melanocyte activation and continued melanin deposition, which can influence both the pathogenesis and persistence of melasma; therefore, broad-spectrum sun protection that covers both the UVB and UVA ranges should be utilized. Patients should use photoprotection year round, as daily sun exposure can contribute even in winter months. Because the action spectrum of melanogenesis is considered to be in the longer-wavelength UVA range, UVA protection is paramount.<sup>2</sup> Protection against UV exposure is of particular importance for patients with skin of color and those with darker phototypes who may not routinely use photoprotection or even believe that it is necessary. Hall and Rogers<sup>3</sup> analyzed data from the 1992 National Health Interview Survey and found that only approximately half (53%) of the 1583 black participants responded that they were likely to use sunscreen, wear protective clothing, or stay in the shade.

### NONSURGICAL THERAPY

#### Hydroquinone

Hydroquinone (HQ) is a phenolic compound that is a mainstay in melasma treatment. This skin-lightening medication blocks the conversion of 3,4-dihydroxyphenylalanine (dopa) to melanin through the inhibition of the enzyme tyrosinase, an essential step in melanin synthesis.<sup>4</sup> Hydroquinone causes a gradual reduction of dyschromia through mechanisms such as melanocyte downregulation, prevention of melanosome production, and reduction of melanin transfer to keratinocytes. Hydroquinone most commonly is prescribed in a 4% concentration but is available by prescription at up to a 10% concentration and over-the-counter in a 2% concentration. In mild forms of pigment deposition, the 2% concentration may be effective; however, chronic use of topical HQ, even at a 2% concentration, is associated with a risk for exogenous ochronosis, especially in darker phototypes.<sup>5</sup> This effect is most commonly reported in black individuals in South Africa, with a few reports of exogenous ochronosis in the United States. When used as monotherapy, HQ remains effective for approximately 20 weeks of treatment and the efficacy plateaus after 6 months.<sup>6</sup> Hydroquinone is effective when applied twice daily and should be applied to the entire face because bull's-eye areas of discoloration can develop from localized or spot treatments.<sup>7</sup>

Excessive lightening of unaffected skin, however, has not been documented.

#### Retinoids

Topical HQ often is combined with a topical retinoid, such as tretinoin 0.1%. Tretinoin and retinol (the precursor to tretinoin) have been shown to be effective in both preventing and reversing photodamage at the molecular level. Callender<sup>8</sup> conducted a clinical trial in darker racial ethnic groups to test the efficacy and safety of tazarotene 0.1% in the treatment of postinflammatory hyperpigmentation (PIH). Tazarotene was more effective in treating PIH than the control; however, retinoid dermatitis was a noticed adverse effect.<sup>8</sup> Some ways to combat retinoid dermatitis are to titrate the dosage, change the dosage to alternate days, and dilute the tretinoin with a moisturizer base. Griffiths et al<sup>9</sup> reported significant improvement of melasma in 68% (13/19) of participants who were treated with tretinoin 0.1% during a 40-week trial ( $P=.0006$ ). The newer, third-generation retinoids adapalene and tazarotene both effectively treat PIH. Tazarotene is a pregnancy category X product.

Pathak et al<sup>10</sup> conducted clinical trials involving 300 Hispanic women with melasma who were treated with various concentrations of HQ formulations. It was concluded that a combined treatment of HQ 2% and retinoic acid 0.05% to 0.1% produced the most favorable results; however, when HQ is combined with a topical retinoid, the risk for irritation is increased and patients should be monitored for adverse effects.<sup>10</sup> If after 3 months the patient does not see improvement from this treatment regimen, a triple therapy that includes a topical corticosteroid can be initiated.<sup>10,11</sup> Kligman and Willis<sup>12</sup> described an early triple-therapy formulation that included HQ 5%, tretinoin 0.1%, and dexamethasone 0.1%, which was highly effective but exhibited inherent problems related to high concentrations of tretinoin and the fluorinated steroid. Kligman and Willis<sup>12</sup> actually noted poor results when each ingredient was used in monotherapy. Triple therapy should be tried once daily for 2 months; after 2 months, treatment should continue with daily use of HQ and retinol for 6 months. After 1 year with no recurrence, maintenance therapy should be initiated with the use of the tretinoin cream at night. If melasma does recur, the patient should resume the original therapy. Patients with severe melasma who are being treated with the triple therapy should be monitored, as steroid-related side effects such as telangiectases and steroid acne have been observed after 8 weeks of therapy.<sup>13</sup>

#### Mequinol

If HQ causes the patient too much irritation, a derivative alternative is mequinol (4-hydroxyanisole), which

has been found to be less irritating. The mechanism of action is thought to involve a competitive inhibition of tyrosinase. Mequinol is available as a 2% concentration and can be formulated with tretinoin 0.01%. Mequinol can effectively treat solar lentigos in a broad range of skin phototypes. One study compared a combination of mequinol 2% and tretinoin 0.01% to HQ 4% and showed that both were equally effective.<sup>14</sup>

### Nonphenolic Compounds

Nonphenolic compounds that are used to treat melasma include, azelaic acid, kojic acid, arbutin, niacinamide, *N*-acetylglucosamine, ascorbic acid, licorice, and soy, as well as the previously discussed retinoids.

**Azelaic Acid**—Azelaic acid is a dicarboxylic acid (1,7-heptanedicarboxylic acid) that naturally occurs and is isolated from pityriasis versicolor. Azelaic acid inhibits tyrosinase and DNA synthesis in abnormal and hyperactive melanocytes, which may be mediated via the inhibition of mitochondrial oxidoreductase activity. It is formulated as a 15% gel and a 20% cream. Lowe et al<sup>15</sup> tested azelaic acid in patients with Fitzpatrick skin types IV to VI who had facial PIH or melasma and demonstrated that azelaic acid was a safe and effective treatment of both conditions in these darker skin types. Azelaic acid has been studied in Indo-Malay-Hispanic patients in comparison with HQ. In one study, melasma treated with azelaic acid 20% showed more improvement with HQ 2%<sup>16</sup>; however, when compared with HQ 4%, azelaic acid 20% was found to have an equivalent effect in Hispanic patients.<sup>17</sup> Allergic sensitization and phototoxic reactions are rare, and more common side effects include mild erythema, scaling, and burning.<sup>18</sup>

**Kojic Acid**—Kojic acid is another nonphenolic treatment of both melasma and PIH. It is a fungal metabolite of *Acinetobacter*, *Aspergillus*, and *Penicillium*. It inhibits tyrosinase and is available in 1% to 4% concentrations and also can be formulated with other skin-lightening medications such as HQ. Lim<sup>19</sup> studied the use of kojic acid 2% in combination with HQ for the treatment of melasma, with results showing improvement and efficacy; therefore, in patients who do not see results from HQ alone, the addition of kojic acid to the treatment regimen may help. Kojic acid is becoming a frequently added ingredient in over-the-counter cosmeceutical formulations; as a result, it also is becoming an increasing offender in allergic contact dermatitis.

**Arbutin**—Arbutin is a naturally derived compound that is used to treat hyperpigmentation. It is formulated from the dried leaves of the bearberry shrub and the cranberry, pear, or blueberry plants. It is a derivative of HQ but does not have the same melanotoxic effects. It inhibits

tyrosinase activity but also inhibits melanosome maturation. Its effects are dose dependent, but high concentrations of arbutin can cause hyperpigmentation. Synthetic forms also are available and show greater tyrosinase inhibition. One study showed arbutin to be effective in treating solar lentigines in lighter phototypes but was not effective in darker-skinned patients.<sup>20</sup>

**Niacinamide**—Niacinamide is an active derivative of vitamin B<sub>3</sub> (niacin) and has been shown in vitro to decrease melanosome transfer from melanocytes to keratinocytes without inhibiting tyrosinase or cell proliferation. It also is postulated that niacinamide interferes with cell-signaling pathways.<sup>21</sup> The compound is stable in an array of compounds and is not inactivated by light. It is formulated in 2% to 5% preparations, but its efficacy has not been shown in darker phototypes. Niacinamide has been shown to have efficacy in treating melasma and hyperpigmentation in lighter-skinned patients when combined with *N*-acetylglucosamine, which is a precursor to hyaluronic acid. *N*-acetylglucosamine inhibits tyrosinase glycosylation, which is one step in melanin production. In cosmeceuticals, it usually is formulated as a 2% compound combined with niacinamide.<sup>22</sup>

**Ascorbic Acid**—Ascorbic acid, or vitamin C, is an antioxidant found in various fruits and foods that also has been used for the treatment of hyperpigmentation. The mechanism of action for pigment alteration involves interaction with copper ions at the tyrosinase active site as well as the reduction of oxidized dopaquinone, which is a substrate in melanin synthesis. There also are some documented anti-inflammatory and photoprotective properties.<sup>23</sup> Because ascorbic acid is unstable in many topical preparations, esterified derivatives such as L-ascorbic acid 6-palmitate and magnesium ascorbyl phosphate are used in compounds. There are reports of its efficacy in Latino and Asian patients in the treatment of melasma.<sup>24</sup>

**Flavonoids**—Flavonoids from licorice roots, such as glabrene and isoliquiritigenin, are effective tyrosinase inhibitors and therefore can be used to treat hyperpigmentation. The flavonoid liquiritin is available in a 2% cream and causes depigmentation through melanin dispersibility. A study of women with melasma showed efficacy of liquiritin in 80% (16/20) of participants; mild irritation was seen in only 20% (4/20) of patients.<sup>25</sup>

**Soy Proteins**—Soy proteins are naturally occurring compounds. Soybean trypsin inhibitor and Bowman-Birk inhibitor act by inhibiting the activation of protease-activated receptor 2 cell receptors on keratinocytes. These keratinocyte receptors mediate the transfer of melanosomes from melanocytes to keratinocytes, and thus this inhibition mitigates hyperpigmentation. Soy is formulated alone or in combination with retinol and other

products in cosmeceuticals, not only for the treatment of hyperpigmentation but also for photodamage.<sup>26</sup>

### SURGICAL THERAPY

Surgical treatment options exist for more severe or refractory melasma, which includes the use of chemical peels. It is important for the physician to record a detailed medical history, including prior medications, prior herpes simplex infection, prior reactions to cosmetic procedures, and other dermatologic conditions. Although chemical peels can ameliorate dyspigmentation, they also can induce new areas of hyperpigmentation as well as keloid formation and hypertrophic scarring in susceptible patients; therefore, chemical peeling in darker phototypes (Fitzpatrick skin types IV–VI) should be performed with caution. The mechanism of action involves the removal of melanin, unlike previously discussed treatments that inhibit the melanocytes or the process of melanogenesis. The risk for complications from chemical peels increases with the depth of the insult created. Therefore, superficial peels impart the lowest risk for complications; however, resultant hyperpigmentation can still develop. Glycolic acid (GA) peels are most commonly used but others include salicylic acid, trichloroacetic acid (TCA), lactic acid, tretinoin, and resorcinol peels.

#### Glycolic Acid

Glycolic acid is an  $\alpha$ -hydroxy acid that acts via epidermolysis as well as through the dispersal of basal layer melanin. The available concentrations range from 20% to 70%, and it often is used as an ingredient in skin-lightening creams in a 10% concentration. It requires neutralization with water or sodium bicarbonate. Glycolic acid peels are effective in the treatment of melasma and have been safely used in Fitzpatrick skin types IV to VI.<sup>27,28</sup> Burns et al<sup>29</sup> showed that GA peels in combination with topical treatment in patients with Fitzpatrick skin types IV to VI led to a more rapid and greater improvement compared to controls and topical treatment alone.

#### Salicylic Acid

Salicylic acid is another superficial peeling agent. It is a  $\beta$ -hydroxy acid that is derived from willow tree bark and induces keratolysis by breaking intercellular lipid linkages. Superficial salicylic acid peels range from concentrations of 20% to 30% and are considered self-neutralizing peels, which can be seen as a frost once the peel neutralizes. Grimes<sup>30</sup> reported the effects of a series of 5 salicylic acid peels ranging from 20% to 30% in 25 patients with pigmentary disorders. The results showed that the peels were well-tolerated in Fitzpatrick skin types V and VI and that 84% (21/25) of participants experienced no side

effects. Of those patients who were treated for melasma, 66% (4/6) showed improvement after treatment with a combination of the salicylic acid peels and HQ 4%.<sup>30</sup> Salicylic acid peels are preferred for patients with oily skin, whereas GA peels are preferred in patients with dry skin.

#### Trichloroacetic Acid

Superficial TCA and lactic acid peels also can be utilized. Lactic acid is another mild  $\alpha$ -hydroxy acid. All peels should be titrated slowly, and patients should be continually monitored posttreatment. Adverse effects include erythema; burning; PIH; and reactivation of herpes simplex virus, superficial desquamation, and vesiculation. Patients should be started at the lowest strength 4 weeks after topical therapy is initiated, and the potency should be increased on a monthly basis as tolerated. These superficial peels can accelerate improvement, both as adjuvant and maintenance therapies. An experienced physician can perform a medium-depth peel, as described by Rossi and Perez,<sup>31</sup> for treatment of severe melasma by using GA 70% for 3 to 4 minutes, followed by a TCA 35% peel; however, this combination should not be done as an initial peel because medium-depth peels can induce postpeel pigmentary alteration. After the skin recovers, the patient should resume topical therapy with HQ 4%/retinol twice daily for 6 weeks.<sup>31</sup> These medium-depth combination peels can be used on select patients with Fitzpatrick skin types IV and V but should never be used on patients with Fitzpatrick skin type VI. When treating darker skin types with chemical peels, the physician must anticipate hyperpigmentation and initiate skin-lightening therapy before hyperpigmentation develops. An individualized approach should always be utilized, as every patient will not react the same way to chemical peels.

### LASER AND LIGHT THERAPY

Lasers and light sources have become increasingly utilized treatment modalities for melasma. Melanin, the target chromophore, has a wide absorption spectrum ranging from 250 to 1200 nm. The choice of the laser's wavelength determines the depth of penetration, with longer wavelengths penetrating deeper into dermal skin. In the 400- to 600-nm wavelength, there is strong competition for absorption by oxyhemoglobin, another chromophore in skin. It will compete with melanin in this wavelength range and therefore vascular damage will occur more than melanin destruction. At longer wavelengths greater than 600 nm, absorption by oxyhemoglobin is substantially reduced and absorption by melanin over blood pigment is favored, with resultant destruction of the melanin-containing structures.

For the treatment of melasma the intense pulsed light (IPL) system, 1064-nm Nd:YAG laser, 1550-nm mid-infrared erbium-doped laser (Fraxel SR, Solta Medical Inc; Mosaic, Lutronic Inc), and 2790-nm erbium:yttrium-scandium-gallium-garnet (Er:YSGG) laser (Pearl, Cutera, Inc) are discussed.

### Intense Pulsed Light

The IPL system has been employed to treat melasma and hyperpigmentation in a variety of skin types, particularly Fitzpatrick skin types IV and V. Wang et al<sup>32</sup> documented improvement in patients with refractory melasma with Fitzpatrick skin types III and IV when treated with 4 sessions of the IPL system as well as HQ. On average, there was 40% improvement on the relative melanin index compared with controls. The majority of patients experienced posttreatment microcrust formation 2 to 3 days after.<sup>32</sup> Longer wavelengths that are greater than 600 nm should be utilized because of decreased competition from oxyhemoglobin with less vascular damage. Intense pulsed light has been reported to exacerbate subclinical melasma when aggressive fluences are used. Negishi et al<sup>33</sup> reported that lower IPL parameters should be used in patients who have subclinical melasma detected by UV photography. As a guide, the IPL-induced erythema should last only a few minutes, not hours; the longer the erythema lasts, the greater the risk for melasma-like posttreatment hyperpigmentation.<sup>33</sup>

### Nonablative Lasers

Nonablative lasers also are useful in treating melasma, especially in patients with Fitzpatrick skin types IV to VI. The nonablative 1064-nm Nd:YAG laser often is utilized for treatment of melasma and hyperpigmentation. The laser's longer wavelength and longer pulse duration are able to target dermal melanin deep in the dermis, which often is a component of both disorders. This wavelength also protects the epidermis from incident damage that can exacerbate both conditions. The Q-switched Nd:YAG laser at 1064 nm is useful for all skin types. Treatments should be performed approximately 1 to 2 months apart, and a total of 4 to 8 sessions may be needed to achieve a clinical response. Chan et al<sup>34</sup> reported that the Q-switched Nd:YAG laser was more effective than the Q-switched alexandrite laser after 3 treatment sessions for Ito and Ota nevi. Of note, Chan et al<sup>35</sup> also reported a case series of facial depigmentation after treatment with a low-fluence 1064-nm Q-switched Nd:YAG laser for skin rejuvenation and melasma treatment in Asian patients. Polnikorn<sup>36</sup> reported 2 cases of refractory dermal melasma that were treated with 10 weekly sessions with 1064-nm Q-switched Nd:YAG laser therapy at subthreshold

photothermolytic fluences (<5 J/cm<sup>2</sup>), resulting in a reduction of epidermal and dermal pigmentation with no recurrences at 6 months and 1 year of follow-up. Wattanakrai et al<sup>37</sup> reported data demonstrating that 5 weekly treatments with a low-fluence 1064-nm Q-switched Nd:YAG laser is an effective treatment of dermal and mixed melasma. Zhou et al<sup>38</sup> recently published a study of the efficacy and safety of the 1064-nm Q-switched Nd:YAG laser for the treatment of melasma. They treated 50 participants with 9 laser treatments, each administered 1 week apart. The laser parameters included a 6-mm spot size and a fluence range of 2.5 to 3.4 J/cm<sup>2</sup>, with a frequency of 10 Hz. They reported a decrease in mean melanin index of 35.8% (*P*<.001) as well as a decrease in mean melasma and severity index score of 61.3% (*P*<.001). A recurrence rate of 64% was seen at 3 months. Participants also were evaluated with a confocal laser scanning microscope and it was found that there were substantially fewer melanin particles after treatment, which also were smaller and darker as observed in the stratum spinosum. The oval or circular melanocytes that were interspersed at the basal layer before treatment also were shown to be gone after treatment.<sup>38</sup>

Fractional photothermolysis is a nonablative laser technique that has been utilized in the treatment of melasma and PIH in a range of skin phototypes. This process creates microscopic treatment zones (MTZ) of thermal injury that have a depth to width ratio of 5 to 1 without causing extensive cutaneous damage. Manstein et al<sup>39</sup> published guidelines regarding the use of fractional photothermolysis in the treatment of melasma. They used a 1550-nm mid-infrared erbium-doped laser. For Fitzpatrick skin types I and II, they recommended an energy/MTZ parameter of 6 mJ, a density of 250 MTZ/cm<sup>2</sup>, and 12 passes for a total treatment density of 3000 MTZ/cm<sup>2</sup>. For Fitzpatrick skin types III to VI, they recommended the same parameters but decreased the number of passes to 8 for a total treatment density of 2000 MTZ/cm<sup>2</sup>.<sup>39</sup>

### Ablative Lasers

Ablative lasers remove the epidermis through the process of ablation and also stimulate contraction and remodeling of the dermis through the process of coagulation with water acting as the main target chromophore. Ablative lasers are not recommended for use in patients with Fitzpatrick skin types V and VI because of the risk for scarring and pigmentary alteration. The main ablative lasers are the 10,600-nm CO<sub>2</sub> laser, the 2940-nm erbium:YAG laser, and the newer 2790-nm Er:YSGG laser. The wavelength of the 2790-nm Er:YSGG laser is slightly less than the erbium:YAG laser whose 2940-nm wavelength is close to the absorption peak of water and



yields an absorption coefficient 16 times that of the CO<sub>2</sub> laser. The 2790-nm Er:YSGG laser has a slightly shorter wavelength and is thought to ablate the top 10 to 30 μm of the epidermis, under which the epidermis is coagulated. The residual thermal damage also is thought to stimulate new dermal collagen synthesis.

In fractional ablation, a laser is used to produce microscopic thermal wounds in the skin, while the intact undamaged skin around each wound acts as a reservoir, allowing relatively rapid reepithelialization of the treatment zone with consequently little risk for infection or scarring. Fractional ablative CO<sub>2</sub> lasers have been shown to reduce downtime and result in more rapid wound healing.<sup>40</sup>

One study reported 9 melasma patients (Fitzpatrick skin types II–V) treated with combination therapy that included IPL (LimeLight, Cutera, Inc) and the 2790-nm Er:YSGG laser.<sup>41,42</sup> Each participant was treated with 1 pass of the IPL set at the following parameters: mode C (wavelength >800 nm), 16 J, and 1 Hz. Subsequently, the epidermis was cooled with cold compresses. Immediately afterward, the skin was prepared with acetone and treated with the 2790-nm Er:YSGG laser, which was utilized at the following parameters: 3.5 J/cm<sup>2</sup>, 0.4-millisecond pulse duration, and 20% overlap with the largest grid pattern. Posttreatment acetic acid soaks were initiated multiple times per day. By 1 week after the procedure, melasma patches were completely resolved and were no longer visible. Maintenance therapy consisting of sun protection, HQ 4%, and tazarotene was subsequently prescribed. All of the participants went into remission for 3 to 6 months, with some participants experiencing recurrence of their

melasma, usually to a lesser degree than the initial incidence. All participants received 6 maintenance treatments with the 1064-nm Nd:YAG laser (GenesisPlus, Cutera, Inc) set at the following parameters: 5-mm spot size, 0.3-millisecond pulse duration, and a total of 2000 pulses delivered to each cosmetic unit (forehead, cheeks, and chin). Currently, all 9 participants have been clear or almost clear for at least 6 months, with some participants experiencing lasting clearance for up to 1 year (Figures 1 and 2).<sup>41,42</sup>

When utilizing laser and light sources for the treatment of melasma, we recommend that clinicians always perform at least one test spot, obtain informed consent and counsel the patient regarding the potential for posttreatment hyperpigmentation, prime the treatment area with HQ for approximately 1 month prior to the procedure, and prescribe antiviral medication for prophylaxis.

**COMMENT**

Melasma is a chronic acquired pigmentation disorder that can be particularly disfiguring and psychologically distressing to patients. Melasma negatively impacts the patient's quality of life. Because melasma can be difficult to treat, resulting in frustration in patients as well as physicians, a stepwise approach to treatment has been proposed.

**Step 1**

Utilize broad-spectrum sun protection, which is paramount to the successful treatment of melasma and is the cornerstone of any therapeutic regimen. Because frequent exposure to UV radiation causes melanocyte activation



**Figure 1.** A melasma patient before (A) and 1 year after combined treatment with intense pulsed light and the 2790-nm erbium:yttrium-scandium-gallium-garnet laser (Pearl, Cutera, Inc) followed by 6 treatments with the 1064-nm Nd:YAG laser (GenesisPlus, Cutera, Inc)(B). Reprinted from Rossi and Perez,<sup>41</sup> © 2011, with permission from Elsevier.



**Figure 2.** A melasma patient before (A), 24 hours after treatment with a 2790-nm erbium:yttrium-scandium-gallium-garnet laser (Pearl, Cutera, Inc) in combination with a 1064-nm Nd:YAG laser (GenesisPlus, Cutera, Inc)(B), and 6 months posttreatment (C). Published in Perez M, Luke J, Rossi A. Melasma in Latin Americans. *J Drugs Dermatol.* 2011;10:517-523.<sup>42</sup>

and continued melanin deposition, judicious use of both UVA and UVB protection with at least sun protection factor 30 is recommended.

### Step 2

Inhibit melanin synthesis and transportation of melanosomes to keratinocytes or promote melanosome degradation, which includes the use of phenolic, nonphenolic, and combination topical therapies. Triple-combination cream is considered a first-line therapy, but if it is unavailable, dual-combination therapy or monotherapy with HQ are advocated. In patients who cannot tolerate phenolic compounds, other agents such as azelaic acid, retinoids, and other adjunctive skin lighteners (eg, kojic acid) are recommended.

### Step 3

Implement adjunctive procedural therapies when appropriate, which includes the use of chemical peels, lasers,

and light sources. When utilizing these methods in patients with refractory melasma, particularly in darker phototypes (eg, Fitzpatrick skin types III and IV), physicians should provide patients with pretreatment counseling to discuss potential side effects (ie, PIH); institute preprocedure priming treatments with HQ and topical retinoids for 2 to 4 weeks (stopping 1 week prior to procedure); institute antiviral prophylaxis; utilize conservative parameters; and provide necessary follow-up to avoid complications. It also is our recommendation that physicians anticipate and be able to manage potential complications as well as recurrences of melasma symptoms.

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