Melasma: update on management
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Abstract
Melasma is a common, acquired, chronic cutaneous pigmentation disorder that is often difficult to treat and has a high recurrence rate. The goal of a melasma treatment regimen is to decrease pigment production and increase elimination. Topical tyrosinase inhibitors block melanin synthesis in melasma and thereby reduce pigment production. Peels and laser- and light-based devices increase melanin elimination. A multimodality treatment approach targeting both pigment production and elimination is necessary to achieve equilibrium and disease remission. Maintenance treatments are often necessary due to the high recurrence rate. Strict photoprotection is critical to prevent melanogenesis and rebound. Targeting the vasculature via pulsed dye laser or tranexamic acid is another approach to treatment.

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elasma is a common, acquired cutaneous pigment disorder frequently involving the sun-exposed areas of the central face. Women of Fitzpatrick skin type (FST) III to IV are most commonly affected.1 Genetics, ultraviolet (UV) light, and hormonal factors contribute to its development.1 Melasma is difficult to treat, is often chronic, and has a high recurrence rate. Treatment involves a multimodality approach with a combination of photoprotection, topicals, chemical peels, and laser- and light-based devices. This article will present highlights from our recent review published in Seminars in Cutaneous Medicine and Surgery2 and will explore new advances in laser and light devices for melasma. Tranexamic acid will also be discussed.

Pathophysiology
In melasma, there is a disrupted pigment equilibrium leading to more pigment production and less elimination (Figure 1).3,4 This results in pigment accumulation in the epidermis, dermis, or both.3 In general, epidermal melasma responds better to treatment than dermal. The goal of a melasma treatment regimen should be to decrease pigment production and increase elimination. Tyrosinase, the rate-limiting enzyme for melanin production, is a key player in melasma pathogenesis.5,6 Topical tyrosinase inhibitors, such as hydroquinone, block melanin synthesis and therefore reduce pigment production in melasma. On the other side of the equation, laser- and light-based devices increase elimination of melanin. A multimodality treatment approach targeting both pigment production and elimination is often necessary to achieve equilibrium and disease remission (Figure 2).

Risk factor reduction
The core of any melasma treatment regimen is reduction of risk factors, especially light exposure. Strict photoprotection is critical to prevent melanogenesis.1,5,6 Daily use of a broad-spectrum sunscreen with UVA and UVB coverage is recommended.7 Research has suggested that visible light may also induce pigment formation.8,10 Iron oxide, an ingredient in many tinted sunscreens, absorbs visible light. Daily use of a broad-spectrum iron oxide-containing tinted sunscreen may enhance the melasma treatment regimen.2,9,11

As discussed above, melasma is a multifactorial disease. Genetics are predetermined, but we can minimize risk factors and exacerbators. Reducing light exposure and minimizing hormonal factors can increase the likelihood of treatment success. If applicable, the authors recommend considering discontinuation of oral contraceptive pills (OCPs) prior to starting a laser treatment regimen for melasma. If discontinuation of OCPs is not feasible, switching to a low-estrogen formulation may be beneficial.2

Increasing pigment elimination: laser- and light-based devices
Topical therapies and risk factor modification are first line for melasma treatment. With topicals alone, improvement is often temporary, and risk of recurrence is high. Therefore, alternative treatments with laser- or light-based devices are frequently added to the regimen.3 Laser- and light-based devices increase pigment elimination but do not influence the melanin production part of the equation. Setting expectations prior to treatment is crucial because these devices help to remove the accumulated pigment but will not “cure” melasma. It is also important to discuss risks of the procedure such as dyspigmentation, rebound, and recurrence prior to starting any laser treatment plan. Regardless of the device(s) used, many patients will have recurrence of their melasma3 and may need maintenance treatments. Multimodality combination therapy with topicals to decrease pigment production and lasers to increase pigment elimination are ideal. Lasers and topical melain inhibitors work synergistically to reestablish a pigment equilibrium. A multimodality approach reduces the risk of dyspigmentation and helps to maintain the clinical improvement.3

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The most commonly used devices for melasma are intense pulsed light (IPL), quality-switched (QS), and nonablative fractionated lasers. Picosecond lasers are emerging as potential pigment eliminators. Vascular lasers can be added to the regimen to target the vascular component of melasma. The goal of laser- and light-based treatments is to reduce pigment. Each device targets a given chromophore(s) (melanin, water, hemoglobin). Choosing the correct device based on melasma type (eg, dermal versus epidermal), FST, and degree of vascularity decreases the risk of side effects and increases the probability of treatment success.

We will review the evidence for device treatment in melasma based on target chromophore, as follows: melanin (QS, picosecond), water (nonablative fractionated), hemoglobin (vascular lasers), and multiple chromophores (IPL). Evidence for these devices was discussed in our prior review. Highlights from this review will be given for each device. To provide the reader with an update on melasma management, an emphasis will be placed on new studies not mentioned previously.

Target chromophore: melanin (QS and picosecond lasers)

**QS lasers**

QS lasers can be used to treat pigmented lesions, tattoos, and melasma. High-energy light is delivered at short, nanosecond pulse durations. In the treatment of melasma, QS lasers target melanosomes via selective photothermolysis and photomechanical effects. QS laser wavelengths that target melanin include 694 nm (Ruby), 755 nm ( Alexandrite), 1064 nm (Nd:YAG), and 532 nm (Nd:YAG). QS Nd:YAG 1064 nm is commonly used for melasma because it penetrates deeper into the dermis, selectively targets melanosomes, and is safer in higher FST.

Treating melasma with “traditional” QS fluences increases the risk of rebound and post-inflammatory dyspigmentation likely due to photomechanical effects. To reduce risk of dyspigmentation with QS Nd:YAG 1064 nm, the authors recommend monthly treatment sessions at lower fluences (1.6-2.0 J/cm²), as was published by Kauvar et al. Multiple treatments are required, but dyspigmentation risk is reduced. Subthreshold, low fluences are believed to shatter the melanin within melanosomes while sparing surrounding skin. Collateral damage is less, resulting in a safer, more effective treatment. Laser toning with frequent low-fluence, large-spot-size, multiple-pass treatments can inactivate any remaining melanocytes, thereby reducing the risk of recurrence. Caution is advised because too many treatments at too-frequent (eg, weekly) intervals increases the risk of hypopigmentation. Therefore, monthly treatment sessions are recommended.

Although low-fluence QS Nd:YAG 1064 nm has been shown to effectively reduce the Melasma Area and Severity Index (MASI) score, the high recurrence rate is a concern. Kaminaka et al recently published a more promising split-faced study with lower recurrence rates. The investigators treated 13 melasma patients with low-fluence QS Nd:YAG 1064 nm (6 mm spot size; 2.0-2.5 J/cm² fluence; 5 Hz; 3 passes; 10 sessions; weekly intervals plus 1 month rest after treatment) versus control. Mean melanin index (MI) and erythema index (EI) were significantly reduced. More than 50% clearance was observed in 6 of 13 melasma patients after treatment 10. Recurrence rate was 8.3% and 16.7% at 3- and 6-month follow-ups. Low-fluence QS Nd:YAG targets only the pigment-elimination side of the equation. It is important to combine these low-fluence treatments with a daily, topical melanin production inhibitor (eg, hydroquinone, vitamin C) in an attempt to achieve treatment equilibrium.
also work synergistically with microdermabrasion, microneedling, and other light-based devices.22-25

Higher-efficiency laser toning via photoacoustic twin pulse (PTP)-mode QS Nd:YAG 1064 nm was recently evaluated by Kim et al. Twenty-two females were treated with low-fluence, PTP-mode Nd:YAG 1064 nm (7 mm spot size; 2.5 J/cm² fluence; 5-7 passes; 5 sessions; 2-week intervals). Investigator assessment found 13 patients (59.1%) to be “significantly improved.” After 5 sessions, MASI scores decreased, on average, by 20.4%. MASI scores increased in 4 patients (18%). No dyspigmentation was reported. PTP emits 2 consecutive beams leading to more peak power.26 More studies are needed to determine whether PTP mode is superior to single-pulse QS Nd:YAG.

Picosecond lasers
Like low-fluence QS, picosecond lasers are thought to shatter pigment. Their extremely short pulse duration is thought to efficiently break apart pigment with even less damage to surrounding tissue.27 Since our 2016 review,2 there have been new published studies using picosecond lasers for treatment of melasma.

Lee et al published a case report of picosecond Alexandrite 755-nm laser treatment for 2 melasma patients (6-mm spot size; 0.57 J/cm²; 6 and 14 sessions, respectively; 2-week intervals). The patient who received more treatment sessions had more improvement (good versus fair).28 Choi et al published a multicenter, randomized, split-face study (n = 39) evaluating picosecond 1064-/595-nm laser (1064 nm; 7 to 10 mm spot size; 0.2-1.5 J/cm² fluence; 5 or 10 Hz; 2-4 passes—followed by 595 nm; 5 mm spot size; 0.1-0.55 J/cm²; 2 or 5 Hz; 1-2 passes; 750-ps pulse duration; 5 sessions; weekly intervals) plus hydroquinone versus hydroquinone alone. One week after the final treatment, colorimetry showed improved lightening by at least 51% in 76.92% of laser-treated patients compared with 2.56% of control sides. Erythema was also decreased per the investigators. Recurrence was observed in 76.92% of laser and 69.23% of control sides during follow-up.29 A split-faced study (n = 30) published by Chalermchai evaluated fractional picosecond 1064 nm (resolve fractional mode; 100 dots per 6 × 6 mm; 1.3-1.5 mJ/microbeam fluence; 450-ps pulse duration; 4 Hz; 4% coverage; 2-3 passes; 3 sessions; 4-week intervals) plus hydroquinone 4% versus hydroquinone alone for treatment of melasma. The laser side had significantly reduced modified MASI (mMASI) scores at 12 weeks.29 Picosecond lasers appear promising for treatment of melasma. However, more research is needed to determine the optimum wavelengths and treatment settings to increase pigment elimination and decrease risk of recurrence.

Fractional modes for pigment-specific lasers
Fractional modes for melanin-specific lasers are gaining popularity. As will be discussed in the next section of this review, “traditional” nonablative fractional lasers (eg, 1550-nm Erbium-doped laser) do not preferentially target melanin and therefore may not be as effective for pigment elimination as melanin-specific lasers. The downside to melanin-specific lasers (eg, QS) is that they carry risks of recurrence and dyspigmentation. The fractional mode creates
columns (microscopic treatment zones [MTZs]) in treated skin areas (the same way traditional fractional lasers do) that can deliver high energy while minimizing collateral damage. The use of a fractional mode for melanin-specific lasers may increase efficacy while decreasing adverse effects.

The split-faced study by Chalermchai et al discussed above showed reduced mMASI scores after fractional picosecond 1064 nm. A retrospective analysis (n = 48) by Lee et al found fractional, long-pulsed Alexandrite laser (15-mm spot size; 60-80 J/cm² fluence; 0.5- to 1-ns pulse width; no dynamic cooling; 2-4 sessions; 2- to 3-week intervals) to significantly decrease mean MASI score on 2-month follow-up. Epidermal melasma responded better than dermal. This was likely attributed to the long pulse duration that targets epidermal melanosomes and fractional technology that decreases depth of penetration. Post-inflammatory hyperpigmentation (PIH) was reported in 1 patient, which improved on follow-up. Yue et al treated 27 Chinese patients with fractional Pixel QS 1427 nm (5.5-mm spot size containing 25 dots; 125-μm dot diameter; 42.4% area coverage; 2.6-3.6 J/cm² fluence; 2 Hz; 8 sessions; 2- to 3-week intervals). Mean MASI and MI scores decreased after treatment. At 3 months, 40% of patients had partial recurrence. Tong et al treated 53 Chinese melasma patients with 2 courses of fractional QS Ruby laser (7.1-mm spot size; 14 × 14 fractional dot; 300-μm dot diameter; 200-μm distance between dots; 2.5-3.5 J/cm² fluence; 40-ns pulse duration; 3 consecutive sessions; 2-week intervals) followed by IPL (590- to 640-nm filter; 14-16 J/cm² fluence; 4.0-ns pulse width; 40-ns delay; triple pulse mode; one treatment after the 3 QS Ruby laser sessions). There was a reduction in MI, EI, and mean MASI scores, which was maintained at 3 months. No PIH was reported.

Fractional mode for melanin-specific lasers holds promise for melasma because higher energy can be delivered with lower risk of dyspigmentation. The fractional mode can decrease penetration depth, which is an important consideration when treating dermal melasma. Combining fractional melanin-specific lasers with other light-based devices may increase pigment elimination and treatment response. More research is needed to determine the optimum treatment parameters as well as the safety and efficacy of these devices.

**Target chromophore: water ("traditional" fractionated lasers)**

**Nonablative fractionated lasers**

As described above, “traditional” nonablative fractionated lasers do not preferentially target melanin and instead favor water. MTZs are created in treated skin, which leads to coagulation and eventual transepidermal elimination of melanin while favoring the surrounding skin. Recovery time is fast, and the risks for scarring and pigment changes are reduced. The nonablative fractionated laser wavelengths include 1440 nm, 1535 nm, 1540 nm, 1550 nm, and 1927 nm. The nonablative fractional 1550-nm laser is commonly used for treating photoaging. It has been studied for the treatment of melasma, but overall recurrence rate is high. In general, the 1550-nm laser does not result in significant melasma improvement compared with other, more cost-effective measures such as photo-protection and triple combination cream (TCC). The 1927 nm wavelength has more affinity for water and less for melanin, thereby allowing both depth of penetration and risk of dyspigmentation to be reduced. The 1927 nm wavelength can be used to treat melasma. The 1927 nm thulium laser has been shown to reduce pigment in melasma with less risk of dyspigmentation. Another 1927 nm device that is gaining popularity for treatment of melasma is the 1927 nm low-powered diode. A recently published randomized study by Vanaman Wilson et al treated 38 subjects with facial hyperpigmentation with nonablative 1927 nm fractional diode laser (5 mJ; 140-μm spot size; 170-μm depth; 5% coverage; 8 passes; 4 sessions; 2-week intervals) with versus without topical hydroquinone. At 4 and 12 weeks post treatment, both groups had improvement in hyperpigmentation (as assessed by blinded investigator) and in the Mottled Pigmentation Area and Severity Index. There was no significant difference between the 2 groups. The laser treatments did not induce worsening of hyperpigmentation or melasma in any subjects. More melanin-specific studies are needed to evaluate the efficacy and risk of long-term recurrence after 1927 nm fractional laser treatment. In the authors’ experience, the 1927 nm low-powered diode has a better safety profile than the 1927 nm fractional thulium laser, especially in darker skin types. Currently, the 1927 nm wavelength (in general) appears to have less recurrence than its 1550-nm counterpart, but, again, more studies are needed. Additional studies are also needed to assess whether both epidermal and dermal melasma can be treated with this device given the limited depth of penetration of the 1927 nm wavelength. Combining this laser treatment with tyrosinase inhibitors to decrease pigment production and other pigment-elimination lasers (such as QS Nd:YAG) may increase treatment efficacy. In the vascular section, we will discuss a study by Geddes et al that evaluated pulsed dye laser (PDL) plus 1927 nm fractional low-powered diode for melasma.

**Target chromophore: hemoglobin (vascular lasers)**

Targeting the vascular component of melasma to reduce stimulation of melanocytes is another approach that may work synergistically with other modalities already discussed. Vascular endothelial growth factor (VEGF) receptors are expressed by melanocytes. Vascularity and VEGF may play a role in melasma (Figure 3). The picosecond 1064/595 nm split-face study by Choi et al already has been discussed. Our focus in this section will be on the millisecond PDL. PDL is commonly used for the treatment of erythromelanocytic rosacea and vascular lesions. It may be effective for melasma when combined with pigment-production reducers (eg, TCC, hydroquinone) or pigment-elimination lasers, especially in patients with telangiectatic erythema underlying lesions of melasma (Table). A randomized split-face study of 17 patients evaluating PDL plus TCC versus TCC alone found both to significantly reduce MASI score. In FST II-III, the combination side maintained MASI score reduction after one summer, whereas the TCC did not. PIH was noted in half of the FST IV patients. Each session had 2 passes of PDL treatment. The first targeted melanin; the second targeted the vasculature. The investigators attributed the high PIH rate to the first pass targeting melanin and recommended that these settings not be used. A few recent studies combining PDL with other laser- and light-
based devices have been published. In 2018, Hassan et al published a split-face study (n = 28) evaluating 595-nm PDL (right face) versus IPL (left face). Both lasers reduced mMASI score (no significant difference between groups), and both significantly reduced VEGF. However, PDL was less effective compared with IPL for vascularity secondary to melasma and for treatment of epidermal melasma.46 Kong et al published a split-face study evaluating the efficacy of using PDL to target oxyhemoglobin and QS Nd:YAG to target melanin. Seventeen melasma patients were treated with low-fluence QS Nd:YAG 1064 nm. At 3 time points, half of the face also received PDL (nonpurpuric settings) immediately after. A reduction in MASI score was noted on both sides, with no significant difference between sides. Subset analysis of 7 patients with wide capillaries on dermoscopy at baseline showed significantly more percent change in MASI score on the combination compared with the QS Nd:YAG monotherapy side.25 Geddes et al published a 2-year retrospective analysis of 11 melasma patients with subtle telangectasias on spectrocolorimetry. Each patient was treated with PDL followed by 1927-nm fractional low-powered diode laser. More than 50% improvement in melasma was noted in 6 of 11 patients (54.5%; Figure 4). In general, erythema and melasma improved together. No rebound or PIH was noted. Ten of the 11 patients (91%) were satisfied with the procedure.44,47

Combination treatment using a pigment-elimination laser (eg, QS Nd:YAG or 1927-nm fractional diode) plus PDL (to eliminate vessels) may be efficacious in vascular-predominate melasma. To reduce risk of PIH and melasma recurrence, the authors recommend using long-pulsed, nonpurpuric PDL settings as was suggested by Passeron et al, Kong et al, and Geddes et al.25,44,45 The use of tranexamic acid to reduce vascularity and pigment in melasma will be discussed later in this review.

**Target: multiple chromophores (IPL)**

IPL emits noncoherent light with wavelengths ranging from approximately 500 to 1200 nm. Like the other devices discussed, IPL has its pros and cons. Utilizing a spectrum of wavelengths allows IPL to target multiple chromophores and penetrate to different depths. In addition, the larger spot size of the device can treat more surface area in a shorter time. IPL is a favorite among providers looking for one device with multiple uses and quick treatment times. IPL is thought to treat melasma and other pigmented lesions via extrusion of epidermal melanosomes, formation of microcrusts, and pigment shedding.2,49,50 One of the downsides to IPL is that it is not specific for melanosomes or melanocytes and therefore treats pigment indiscriminately. There is a risk of PIH when using this device in higher-FST patients. Filters can be used to better target a given chromophore (eg, melanin). However, these filters are not as specific as monochromatic, coherent laser beams. Unlike some of the other devices discussed (eg, low-fluence QS Nd:YAG) that inactivate left-behind melanocytes, some residual melanocytes are still present and active after IPL,49 increasing the risk of rebound and PIH.5 IPL may be efficacious for epidermal melasma,51 but caution is advised when treating dermal or mixed types.32 The longer (millisecond) pulse duration cannot effectively target melanosomes in the dermis,5 and diffusion of heat is higher. The greater diffusion of heat plus left-behind active melanocytes can increase the risk of PIH and melasma exacerbation.2 The use of a tyrosinase inhibitor (eg, hydroquinone or TCC) may decrease melanin production in left-behind active melanocytes, thereby increasing the efficacy of treatment and reducing risk of recurrence. In 2011, Goldman et al showed that combination treatment with IPL plus TCC is superior to IPL monotherapy.53 Recently, Shakeeb et al (n = 96) evaluated TCC (n = 32) versus IPL (n = 32; 560-nm filter; 14-18 J/cm2; double pulses 3-3.5 ms; delay time 20 for FST II/III and 30 for FST IV/V; 4 sessions; 2-week intervals) versus TCC plus IPL (n = 32; same settings). The combination group had a greater reduction in MASI score (93.8%) compared with the other groups (68.8% in TCC group; 62.5% in IPL group).54

Like melanin-specific lasers, fractional or pulse-in-pulse modes are gaining popularity for IPL. Fractional IPL has been shown to decrease MASI score55,56 and may have a lower risk of rebound than conventional IPL.56 Fractional IPL may be a promising future option for melasma. However, given the paucity of published studies, more research is needed to determine the effectiveness of, and optimum treatment parameters for, these devices.
Melasma: update on management

Decreasing pigment production: tranexamic acid
Is tranexamic acid the solution to establishing equilibrium in melasma? This plasmin inhibitor is Food and Drug Administration approved for menorrhagia. There have been a number of recent dermatologic publications on its off-label for melasma. Tranexamic acid is thought to treat melasma by inhibiting melanin synthesis and reducing vascularity.

Lee et al published a retrospective analysis of 561 Asian melasma patients treated with tranexamic acid (mean dose: 250 mg twice daily; median treatment duration: 4 months). Improvement was seen in 89.7% of patients. Most improvement was within the first 2 months. Relapse rate was 27.2% at a median follow-up of 7 months. Oral tranexamic acid was an adjuvant treatment in 98.2% of subjects who used various topical products, including tretinoin, hydroquinone, TCC, and others. One case of deep vein thrombosis occurred that was attributed to an undiagnosed protein S deficiency. The study emphasized the importance of screening for thromboembolic risk factors prior to starting treatment.

A smaller, prospective randomized study comparing the use of the same dose of oral tranexamic acid (250 mg twice daily; treatment duration: 3 months) to placebo was recently published by Del Rosario et al. Thirty-nine melasma patients completed the study. After 3 months of treatment, the nMASI score decreased by 49% in the tranexamic acid and 18% in the placebo group. At 3 months post treatment,

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Abbreviations: DCD, dynamic cooling device; FST, Fitzpatrick skin type; IPL, intense pulsed light; Nd:YAG, Neodymium-doped Yttrium Aluminum Garnet; PDL, pulsed dye laser; QS, quality-switched; RCT, randomized controlled trial; TCC, triple combination cream.
mMASI score was decreased 26% from baseline in the tranexamic acid group and 19% in the placebo, and those with moderate melasma had sustained benefit whereas those with severe melasma lost their improvement. No thromboembolic events were reported.61

Oral tranexamic acid is an encouraging treatment option for refractory melasma (Figure 5). If improvement occurs, it will likely be early. The authors of this review agree with Lee et al that treatment discontinuation should be considered if no improvement is seen by 3 months.60 As with any melasma regimen, strict photoprotection should be emphasized. In accordance with the literature and from the authors’ personal experience, tranexamic acid is well tolerated in the majority of patients. Thorough screening for any thromboembolic risk factors should be performed prior to starting treatment. Tranexamic acid has been shown to be an effective adjunct to laser- and light-based treatments62,63 as well as to topicals such as hydroquinone.64 Based on the available literature, it is unclear whether tranexamic acid works synergistically with other melasma treatments (eg, lasers, topicals, etc.) or whether it is effective as monotherapy.

What about local tranexamic acid? Studies have suggested that both topical and intradermal tranexamic acid are as effective as hydroquinone.65,66 Combination treatment with oral plus topical tranexamic acid has also been shown to be effective for melasma.67 But is oral better than topical or intradermal tranexamic acid? Sharma et al concluded that both oral and intradermal tranexamic acid were equally effective in reducing MASI score.68 Like oral tranexamic acid, topical administration may augment other laser- and light-based treatments. Topical tranexamic acid plus IPL was shown to be superior to IPL alone in a study by Chung et al.69 Further studies are needed to identify the optimal duration of therapy, synergy with laser- or light-based devices, and recurrence rates.

**Conclusion**

A multimodality approach targeting both pigment production and elimination is necessary to achieve and maintain melasma improvement. Photoprotection plus daily use of a topical pigment-production inhibitor (eg, hydroquinone, TCC) should be added to any laser- or light-based treatment.
light-based regimen to prevent recurrence and increase treatment efficacy. Overall, combination therapy works best. To eliminate pigmentation, there are multiple laser- and light-based devices available; each has its pros and cons. Combination treatment with different devices tailored to patient characteristics (FST, vascularity, melasma depth, etc.) may increase treatment response. Low-fluence QS Nd:YAG 1064 nm can be effective, but multiple treatments are required, and recurrence rate is high. Picosecond lasers appear promising, but evidence is limited at this time due to the paucity of studies. Nonablative fractional 1550-nm laser may not be superior compared with other, more cost-effective pigment-production-targeting measures (eg, photoprotection, TCC). Recurrence rate is also high. Based on the available literature, the rate of recurrence appears to be lower with nonablative fractional 1927 nm. IPL may be limited to treatment of epidermal melasma. Fractional modes for IPL and melanin-selective lasers are gaining popularity because higher energy can be delivered with less dyspigmentation risk, but research is currently sparse. For vascular-predominant melasma, combination treatment with a pigment-elimination laser (eg, QS Nd:YAG or 1927-nm fractional diode) plus PDL may be a practical alternative. Tranexamic acid is an encouraging treatment option for refractory melasma and may be an effective adjuvant to laser- and light-based devices. A recent review by Bala et al recommends considering oral tranexamic acid when melasma is refractory to 12 weeks of topical combination treatment and hydroquinone. More research is needed to determine the optimum treatment parameters, safety, and efficacy of these modalities to achieve clinical improvement while reducing recurrence risk and adverse effects.

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