Oxymetazoline and Energy-Based Therapy in Patients with Rosacea: Evaluation of the Safety and Tolerability in an Open-Label, Interventional Study

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Background and Objectives: The objectives of this study were to evaluate the safety, tolerability, and efficacy of oxymetazoline hydrochloride cream, 1% (oxymetazoline) when used as an adjunctive treatment with energy-based therapy for patients with moderate to severe facial erythema associated with rosacea.

Study Design/Materials and Methods: In this Phase 4, multicenter, interventional, open-label study, eligible patients received one of four energy-based therapies (potassium titanyl phosphate laser; intense pulsed light therapy; pulsed-dye laser Vbeam Perfecta, or pulsed-dye laser Cynergy) on day 1 and day 29 and once-daily application of oxymetazoline on days 3 through 27 and days 31 through 56. Improvement from baseline in Clinician Erythema Assessment (CEA) score, patient satisfaction measures, incidence of treatment-emergent adverse events (TEAEs), and worsening from baseline on dermal tolerability assessments and the Clinician Telangiectasia Assessment (CTA) were assessed. Data were summarized using descriptive statistics.

Results: A total of 46 patients (mean age, 51.1 years; 78.3% female) enrolled in this study. Similar numbers of patients received each of the energy-based therapies in addition to oxymetazoline. All patients demonstrated an improvement from baseline in CEA during the study with 39 of 43 evaluable patients (90.7%) demonstrating an improvement 6 hours posttreatment on day 56. Most patients were satisfied or very satisfied with treatment at the end of the study. All TEAEs were mild or moderate in severity. Some patients experienced worsening in dermal tolerability assessment symptoms (range: 4–21 patients; 8.7–45.7%). Worsening in CEA and CTA were each reported by three patients (6.5%) at any time during the study.

Conclusions: Treatment with oxymetazoline as adjunctive therapy with energy-based therapy was safe, well tolerated, and reduced facial erythema in patients with moderate to severe persistent facial erythema associated with rosacea.

Key words: oxymetazoline; rosacea; potassium titanyl phosphate lasers; intense pulsed light therapy; pulsed dye lasers; erythema; telangiectasias; topical administration

INTRODUCTION

Rosacea is a chronic skin condition estimated to affect more than 5% of adults worldwide [1]. The primary diagnostic criteria for rosacea include transient-to-persistent centrofacial erythema, typically exacerbated by trigger factors...
that may vary by patient, inflammatory papules and/or pustules, and telangiectasia [2,3]. Additional features that may be present can include burning or stinging sensations, erythematos plaques, facial dryness/scaling, edema, ocular manifestations such as blepharitis and conjunctivitis, and, in patients with long-standing disease, phymatous changes [2,3]. When these features are not treated effectively, rosacea can negatively affect patients’ emotional well-being, self-esteem, social life, and work life [4], and greater severity of facial erythema of rosacea may be associated with a greater impact on the patient’s quality of life [5].

The pathophysiology of rosacea is thought to involve dysregulation of the facial neurovasculature and an abnormally heightened immune response, resulting in chronic dilation of facial blood vessels, persistent erythema, and the formation of telangiectasias [6]. Despite this vasodilatation becoming fixed over time, the blood vessels responsible for persistent erythema remain responsive to sympathetic nervous system signaling. Activation of α1- and α2-adrenoceptors on smooth muscle cells in the cutaneous vasculature results in vasconstriction of the vessels and may improve the persistent erythema associated with rosacea [6]. Conversely, telangiectasias do not contain a smooth muscle layer, are not vasoactive [7], and may therefore become more visible when background persistent erythema is reduced [8].

Energy-based therapies such as lasers and intense pulsed light (IPL) have been employed in rosacea in order to selectively target and thermally damage dysregulated blood vessels and can often effectively manage some of the vascular signs of the disease, including telangiectasia and persistent erythema. However, not all patients respond to energy-based therapies, some patients may require more than one treatment—with substantial associated costs—and energy-based therapies may result in adverse side effects including unwanted purpura or erythema [8–10]. Energy-based treatment also has limited efficacy in reducing diffuse erythema associated with acne rosacea due to the small caliber of vessels, which are more difficult to target. A combination approach to treatment including both pharmacological and physical approaches may allow more effective management of the vascular manifestations of rosacea than utilization of any one treatment modality as monotherapy.

Oxymetazoline hydrochloride cream, 1% (oxymetazoline; RHÔFADE®, EPI Health, Charleston, SC) is an α1A-adrenoceptor agonist approved by the U.S. Food and Drug Administration for the topical treatment of persistent facial erythema associated with rosacea in adults [11]. Oxymetazoline applied once daily has been shown to be well tolerated and safe, and was effective in the treatment of moderate to severe persistent facial erythema of rosacea in Phase 3 clinical trials (REVEAL studies) that evaluated short-term treatment (29 days) [12,13] and 1 year of treatment [3]. The current study was designed to evaluate the safety and tolerability of oxymetazoline when used as an adjunctive treatment with energy-based therapy for patients with moderate to severe facial erythema associated with rosacea; efficacy assessments were exploratory.

METHODS

Study Design and Treatment

This was a Phase 4, multicenter, interventional, open-label study to evaluate the safety and tolerability of once-daily oxymetazoline when used as an adjunctive treatment with energy-based therapies. Eligible patients with moderate to severe facial erythema associated with rosacea received one of four energy-based therapies on day 1 and day 29 (Fig. 1). Energy-based therapies included the Excel® V (Candela, Malirno, CA) potassium titanyl phosphate (KTP) laser; Palomar Icon™ (Cynosure, Westford, MA) IPL therapy; the pulsed-dye laser Vbeam Perfecta® (Syneron-Candela, Mississauga, Ontario, Canada; PDL-Vbeam); or the pulsed-dye laser Cynergy™ (Cynosure, PDL-Cynergy). Each study center was assigned a specific device to utilize during the study based on the current expertise and devices present at each center. The protocol followed for each laser treatment was based on the investigator’s current standard of practice.

Once-daily application of oxymetazoline was initiated on day 3 and continued through day 27; on day 28, patients underwent a washout of oxymetazoline before energy-based therapy on day 29 (Fig. 1). Patients were instructed by the study staff and an instructional video to apply an approximately pea-sized amount of oxymetazoline topically to the face at approximately the same time daily, avoiding application to the eyes, eyelids, scalp, neck, ears, and any mucous membranes or open wounds. On study visit days, patients applied oxymetazoline at the study site after completing predose study assessments and procedures. Daily application of oxymetazoline was re-initiated on day 31 and continued until study end on day 56. Patients who discontinued the

![Fig. 1. Study design. *Baseline assessments were conducted predose on day 1.](image-url)
study early were asked to return for the last study visit (day 56 exit visit) for end-of-study data collection.

No stratification or randomization was used; patients were assigned to an energy-based therapy based on their study site. The study was conducted from December 5, 2017 to May 30, 2018 at four centers in the United States in compliance with International Council on Harmonization Good Clinical Practice guidelines and the Declaration of Helsinki. The study protocol was reviewed and approved by the independent ethics committee/institutional review board for each study center. All participants provided their written informed consents before entering the study. The study was registered on ClinicalTrials.gov (identifier NCT03380390).

**Study Participants**

Eligible patients were adults with moderate to severe persistent facial erythema associated with rosacea (grade ≥3 on the Clinician Erythema Assessment [CEA] scale with photonumeric guide). Patients were excluded if they had any uncontrolled systemic disease; had more than three inflammatory facial lesions; had any condition or facial characteristics that could interfere with erythema assessments; had abused drugs or alcohol within 12 months; were being treated with monoamine oxidase inhibitors, or with niacin ≥500 mg/day; were being treated with or had a prior dermal adverse reaction to brimonidine topical gel, 0.33%; had received any of the following products or treatments within 14 days: oxytetracycline (e.g., eye drops and nasal sprays), topical glucocorticoids applied to the face, systemic or nasal corticosteroids, or any acne treatment; or had taken isotretinoin within 180 days.

**Study Endpoints**

Study efficacy endpoints included the number and percentage of patients with at least a one-grade improvement in CEA score from baseline over a 6-hour period (measured at hours 1, 3, and 6) posttreatment; the proportion of patients indicating that they were “satisfied” or “very satisfied” with treatment on the Satisfaction Assessment for Rosacea Facial Redness (SAT-RFR); and the proportion indicating they were “somewhat satisfied” or “very satisfied” with treatment on the FACE-Q™ Satisfaction with Skin scale. The CEA is a 5-point scale that reliably evaluates the average overall severity of persistent facial erythema associated with rosacea [14]. Ratings range from 0 (clear skin) to 4 (severe erythema). The SAT-RFR is a 5-point, patient-reported outcomes scale evaluating patient satisfaction with their facial redness caused by rosacea. Answers on the SAT-RFR range from 0 (very dissatisfied) to 4 (very satisfied). The FACE-Q Satisfaction with Skin scale is a 12-question patient-reported outcomes measure designed to evaluate patient satisfaction with various aspects of their facial skin. Answers on the 4-point scale range from 0 (very dissatisfied) to 3 (very satisfied).

Due to protocol violations of exclusion criteria in two patients that were discovered after the database was locked, the efficacy assessments were evaluated in a post hoc analysis of the evaluable population. The evaluable population included patients treated with energy-based treatment and at least one dose of oxymetazoline who had at least one baseline efficacy assessment and at least one posttreatment efficacy assessment between days 3 and 56, excluding the two patients with protocol violations.

Study safety endpoints included the incidence of treatment-emergent adverse events (TEAEs; defined as AEs first occurring post-baseline or reported at a greater severity post-baseline than the maximal severity reported during screening or at baseline) and serious adverse events; the number and percentage of patients with one-grade or greater worsening from baseline on the dermal tolerability assessments; and the number and percentage of patients with one-grade or greater worsening from baseline in the Clinician Telangiectasia Assessment (CTA). The CTA is a 5-point scale evaluating the average overall severity of facial telangiectasia. Answers range from 0 (clear) to 4 (severe). Dermal tolerability assessments included investigator assessments of dryness and scaling as well as patient assessments of stinging/burning and pruritus of the treatment area. Answers on a 4-point scale ranged from 0 (none) to 3 (severe).

Safety endpoints were evaluated in the safety population, which included all patients who received an energy-based therapy and at least one dose of oxymetazoline.

**Statistical Analyses**

Data were summarized using descriptive statistics.

**RESULTS**

**Study Population**

A total of 46 patients enrolled in this study and completed at least one treatment session (Fig. 2). Similar numbers of patients received each of the energy-based therapies in addition to oxymetazoline treatment (KTP laser, n = 12; IPL, n = 12; PDL-Vbeam, n = 11; PDL-Cynergy, n = 11). Three participants who received PDL-Vbeam and oxymetazoline discontinued the study due to AEs prior to days 29 (n = 2) and 31 (n = 1) study visits; 43 patients completed the study. Baseline disease characteristics were similar in all treatment groups (Table 1).

**Efficacy**

**Improvement in erythema.** Patients demonstrating one-grade or greater improvements in CEA by energy-based treatment type, visit, and time point are shown in Figure 3. Among all 44 evaluable patients on day 1, 6 (13.6%) showed at least one-grade improvement in CEA 1 hour after energy-based therapy. On day 3, one-grade or greater improvement was observed in 20 (45.5%) patients before application of oxymetazoline, and by 35 (79.5%) patients at 6 hours posttreatment. On day 31, of 43 evaluable patients, one-grade or greater improvement was observed in 26 (60.5%) patients before application of oxymetazoline, and by 38 (88.4%) patients at 6 hours posttreatment. On day 56, improvements were observed in 30 (68.2%) patients pretreatment and in 39 (90.7%) patients at 6 hours posttreatment. The facial erythema of
a representative patient at baseline and improvements in erythema at 1, 3, and 6 hours posttreatment on days 3, 31, and 56 are shown in Figure 4.

Overall CEA grade distributions improved over time; grade 0 CEA assessments were attained by 6 (13.6%), 7 (16.3%), and 9 (20.9%) patients 6 hours after oxymetazoline application on days 3, 31, and 56, respectively (Fig. 5). Three (6.8%) patients experienced one-grade or greater worsening from baseline in CEA at any time during the study.

**Patient satisfaction.** The proportions of patients who indicated satisfaction with treatment based on their appearance and amount of facial erythema increased throughout the study (Fig. 6A). Overall, 28 (65.1%) patients were satisfied or very satisfied with treatment based on the appearance of their skin 6 hours posttreatment on day 56. Similar results were observed on the FACE-Q Satisfaction with Skin assessment (Fig. 6B).

### TABLE 1. Patient Demographics and Baseline Disease Characteristics

|                     | KTP laser (n = 12) | IPL (n = 12) | PDL-Vbeam (n = 11) | PDL-Cynergy (n = 11) | All patients (N = 46) |
|---------------------|--------------------|--------------|--------------------|----------------------|-----------------------|
| Age, mean, years (SD) | 54.8 (11.7)        | 52.5 (10.6)  | 48.5 (14.6)        | 48.1 (12.9)         | 51.1 (12.4)           |
| Sex, female, n (%)  | 12 (100)           | 6 (50.0)     | 9 (81.8)           | 9 (81.8)            | 36 (78.3)             |
| Race, white, n (%)  | 12 (100)           | 12 (100)     | 11 (100)           | 11 (100)            | 46 (100)              |
| Fitzpatrick skin phenotype, n (%) |                  |              |                    |                     |                       |
| I                   | 0                  | 0            | 1 (9.1)            | 0                    | 1 (2.2)               |
| II                  | 11 (91.7)          | 4 (33.3)     | 9 (81.8)           | 2 (18.2)            | 26 (56.5)             |
| III                 | 1 (8.3)            | 7 (58.3)     | 0                  | 9 (81.8)            | 17 (37.0)             |
| IV                  | 0                  | 0            | 1 (9.1)            | 0                    | 1 (2.2)               |
| V                   | 0                  | 1 (8.3)      | 0                  | 0                    | 1 (2.2)               |
| CEA grade, n (%)    |                    |              |                    |                     |                       |
| 3 (moderate)        | 9 (75.0)           | 9 (75.0)     | 8 (72.7)           | 11 (100)            | 37 (80.4)             |
| 4 (severe)          | 3 (25.0)           | 3 (25.0)     | 3 (27.3)           | 0                    | 9 (19.6)              |

CEA, Clinician Erythema Assessment; IPL, intense pulsed light; KTP, potassium titanyl phosphate; PDL, pulsed dye laser; SD, standard deviation.
Safety Endpoints

**Adverse events.** Of the 46 patients who received at least one dose of study treatment, 5 (10.9%) patients experienced one or more TEAEs (KTP, n = 1; PDL-Vbeam, n = 4) and 4 (8.7%) patients experienced one or more treatment-related TEAEs (PDL-Vbeam, n = 4). All TEAEs were mild or moderate in severity. Three (6.5%) patients experienced TEAEs related to oxymetazoline (Table 2); all led to study discontinuation. No serious, severe, or fatal TEAEs were reported.

**Dermal tolerability.** Overall, 25 (54.3%), 14 (30.4%), 14 (30.4%), and 7 (15.2%) patients experienced stinging/burning, dryness, pruritus, and scaling, respectively, at any time point post-baseline. No patients experienced severe dryness, scaling, pruritus, or stinging/burning in any of the treatment arms at any time during the study (Fig. 7). Patients demonstrating one-grade or greater worsening in dermal tolerability assessments at any time during the study are shown in Table 2.

**CTA grade distributions in each treatment group are shown in Figure 8.** Overall, no patients demonstrated grade 0 assessments and 6 (13.0%) demonstrated grade 4 assessments at baseline, whereas 12 (26.1%) patients demonstrated grade 0 assessments and none demonstrated grade 4 assessments pretreatment on day 56. Three (6.5%) patients experienced one-grade or greater worsening from baseline in CTA at any time during the study.

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**Fig. 3.** Proportion of patients with one-grade or greater improvement in Clinician Erythema Assessment in the evaluable population (days 1–3, n = 44; days 29–56, n = 43) receiving adjunctive treatment with oxymetazoline and energy-based therapy with (A) potassium titanyl phosphate (KTP) laser, (B) intense pulsed light (IPL) therapy, (C) pulsed dye laser (PDL-Vbeam), or (D) PDL-Cynergy. *Days 1–3, n = 9; days 29–56, n = 8.

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Fig. 4. Representative images of a study patient who received adjunctive treatment with oxymetazoline and energy-based therapy (Vbeam pulsed-dye laser).

Fig. 5. Distribution of Clinician Erythema Assessment grades in the evaluable population (baseline [BL] through day 3, \( n = 44 \); days 29-56, \( n = 43 \)). \( ^{1} \)Hour 0, assessment before oxymetazoline dosing.
**DISCUSSION**

This unique study demonstrated that adjunctive treatment with oxymetazoline and an energy-based therapy was safe, well tolerated, and effective for reducing moderate to severe persistent facial erythema associated with rosacea. All patients demonstrated improvements from baseline in CEA during the study, and most patients indicated that they were satisfied or very satisfied with treatment at the end of the study.
the study. All adverse events reported in the study were mild or moderate, none of the symptoms recorded during dermal tolerability assessments were severe, and only three (6.5%) patients experienced any worsening from baseline in CTA during the study.

In this study, administration of oxymetazoline was deferred until after application of the energy-based therapy to ensure that the cream was not present on the skin during the energy-based therapy or immediate recovery period. The sequential timing of treatments was implemented in order to address theoretical concerns regarding the safety of combining these treatments. On the basis of the vasoconstrictive mechanism of action of α-adrenergic receptor agonists, their use with energy-based therapies is expected to be efficacious for the treatment of rosacea. Preclinical data suggest that α-adrenergic receptor agonists may be able to attenuate the increased expression of vascular endothelial growth factor induced by the ischemia and oxidative stress caused by energy-based therapies [15], which may account for the additive effects of α-adrenergic receptor agonists and energy-based therapies on rosacea symptoms.

The current study was not designed to evaluate the timing of energy-based treatments relative to oxymetazoline therapy or any potential synergistic effects of combined treatment. However, retrospective and preclinical studies have investigated the efficacy of combining oxymetazoline treatment with PDL therapy. A retrospective study analyzed pretreatment and posttreatment images from 31 patients with rosacea treated with oxymetazoline and PDL at two dermatologic surgery practices [16]. After an average of 4 months of daily oxymetazoline treatment and two PDL treatments, 55% (17/31) of patients demonstrated at least a one-grade improvement in CEA, and 41% of patients (12/29) demonstrated 50–75% clearance of telangiectasias among patients with telangiectasias at baseline. In a preclinical study evaluating the vascular effects of oxymetazoline as an adjunctive treatment to PDL therapy in mice, the combined treatment of oxymetazoline applied 5 minutes before PDL and daily thereafter had a more robust effect on vascular architecture than either of the therapies alone, and resulted in enhanced cutaneous vascular shutdown [17]. These studies demonstrate the potential benefits of combining oxymetazoline and energy-based therapies for the treatment of rosacea.

Several other combinations of topical and energy-based therapies have also shown potential in reducing symptoms associated with rosacea. In an open-label study, the treatment effects of a skin care regimen consisting of a 3-in-1 facial cream and SPF 50 mineral sunscreen powder in combination with IPL were investigated [18]. Patients with rosacea applied the skin care regimen daily for 18 weeks and received a single IPL treatment at week 12. After 12 and 18 weeks of treatment, statistically significant improvements in investigator-assessed mean facial redness were observed, and 95% of patients agreed or strongly agreed that the treatment regimen improved their skin redness after 18 weeks.

Clinical studies have also evaluated use of topical brimonidine gel in combination with energy-based therapies. A randomized, single-blinded study reported that use of brimonidine immediately following IPL therapy was found to consistently and significantly reduce IPL-induced erythema in patients with rosacea more than aircooling alone, while maintaining IPL treatment efficacy and patient satisfaction [19]. Additionally, a case report

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**TABLE 2. Patients With TEAEs Related to Treatment or One-Grade or Greater Worsening in Dermal Tolerability Assessments**

|                                | KTP laser (n=12) | IPL (n=12) | PDL-Vbeam (n=11) | PDL-Cynergy (n=11) | All patients (n=46) |
|--------------------------------|------------------|------------|------------------|--------------------|-------------------|
| One or more TEAEs related to treatment, n (%) |                  |            |                  |                    |                   |
| Energy-based therapy\(^a\)  | 1 (8.3)          | 0          | 0                | 0                  | 1 (2.2)           |
| Oxymetazoline\(^b\)          | 0                | 0          | 3 (27.3)         | 0                  | 3 (6.5)           |
| Hypertension                  | 0                | 0          | 1 (9.1)          | 0                  | 1 (2.2)           |
| Contact dermatitis            | 0                | 0          | 2 (18.2)         | 0                  | 2 (4.3)           |
| Pustular rash                 | 0                | 0          | 2 (18.2)         | 0                  | 2 (4.3)           |
| Papular rash                  | 0                | 0          | 1 (9.1)          | 0                  | 1 (2.2)           |
| Facial edema                  | 1 (8.3)          | 0          | 0                | 0                  | 1 (2.2)           |
| Tachycardia                   | 0                | 0          | 1 (9.1)          | 0                  | 1 (2.2)           |

One-grade or greater worsening in dermal tolerability assessments, n (%)

|                                | KTP laser (n=12) | IPL (n=12) | PDL-Vbeam (n=11) | PDL-Cynergy (n=11) | All patients (n=46) |
|--------------------------------|------------------|------------|------------------|--------------------|-------------------|
| Patient-rated pruritus         | 4 (33.3)         | 4 (33.3)  | 6 (54.5)         | 0                  | 14 (30.4)         |
| Patient-rated stinging/burning| 6 (50.0)         | 9 (75.0)  | 6 (54.5)         | 0                  | 21 (45.7)         |
| Clinician-rated dryness        | 5 (41.7)         | 0          | 2 (18.2)         | 1 (9.1)            | 8 (17.4)          |
| Clinician-rated scaling        | 4 (33.3)         | 0          | 0                | 0                  | 4 (8.7)           |

IPL, intense pulsed light; KTP, potassium titanyl phosphate; PDL, pulsed-dye laser; TEAEs, treatment-emergent adverse events.

\(^a\)Facial edema was reported in one patient. It resolved, and the patient continued in the study.

\(^b\)Included contact dermatitis (n=1); pustular rash and papular rash (n=1); and pustular rash and contact dermatitis (n=1). All of these patients discontinued oxymetazoline because of these TEAEs.
investigating the application of brimonidine immediately after KTP laser therapy for the treatment of erythema associated with rosacea reported a substantial reduction in the patient's erythema and a good safety profile [9]. These studies indicate that combined topical and energy-based treatments can result in additive efficacy.

The present study was the first to prospectively analyze the clinical safety and efficacy of oxymetazoline as an adjunctive treatment with energy-based therapy for the treatment of moderate to severe facial erythema associated with rosacea. Although this study was not specifically designed to evaluate any synergistic effects, the results reveal potential additive benefits from combining these therapeutic modalities. The percentage of patients with one-grade or greater improvement in CEA following the first dose of oxymetazoline, 2 days after the first energy-based therapy treatment, was higher in this study (maximum, 93%) than in a pooled analysis of data from the Phase 3 REVEAL trials (maximum, 82%) [20]. There was a transient decrease in CEA improvements at day 29 after the oxymetazoline washout period, but improvements were once again demonstrated when oxymetazoline treatment was restarted. Importantly, the proportion of patients with CEA improvement increased over time, which may reflect the durability of adjunctive treatment with oxymetazoline and energy-based therapy. This observation is similar to the trend seen with oxymetazoline monotherapy in a long-term Phase 3 study [3]. CTA grade distributions also improved over time in each treatment group and among all patients. As α-adrenergic receptor agonists are not expected to improve telangiectasia associated with rosacea based on their mechanism of action, the improvements in CTA grade reported in the current study may reflect the effectiveness of energy-based therapy for the treatment of telangiectasia. Altogether, these results indicate that use of energy-based therapy with adjunctive oxymetazoline at different time points after treatment warrants further investigation.

In this study, more patients experienced one-grade or greater worsening in the dermal tolerability assessment symptom of stinging/burning (46%) than would be expected based on oxymetazoline monotherapy studies [21]. The proportions of patients who experienced one-grade or greater worsening in stinging/burning in the oxymetazoline and vehicle treatment groups were similar in the pooled data analysis from the Phase 3 REVEAL trials (18% and
20%, respectively), so this increase is most likely not due to oxymetazoline treatment. Stinging/burning were most likely caused by temporary exacerbation of the disease from energy-based device treatment, or may have been caused by the disease itself [2] or other factors (ie, location, season). This study had some limitations. The oxymetazoline washout period limited observation of synergy between the oxymetazoline treatment and energy-based therapy; therefore, the scope of this study is limited. Additionally, some patients did not have post-baseline assessments of the symptoms measured in the dermal tolerability assessment, so worsening could not be measured for those patients at some of the later time points. Finally, the study utilized several different types of energy-based devices operated by different evaluators, which could have potentially introduced some variability in results.

CONCLUSIONS

Adjunctive treatment with oxymetazoline hydrochloride cream, 1% and KTP laser, IPL, PDL-Vbeam, or PDL-Cynergy energy-based therapy was safe and well tolerated and effectively reduced moderate to severe persistent facial erythema in patients with rosacea. The efficacy of oxymetazoline hydrochloride cream, 1% was demonstrated by improvements in both clinician (CEA grade) and patient (patient satisfaction scales) assessments. No new safety concerns were identified. Further studies are warranted to more thoroughly evaluate the optimal timing and efficacy of this adjunctive treatment. Additionally, prospective clinical studies assessing the long-term safety and efficacy of combined treatment with oxymetazoline and energy-based therapies are needed.
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