SPECIAL ARTICLE

Consensus on the therapeutic management of rosacea – Brazilian Society of Dermatology

Clívia Maria Moraes de Oliveira a,*, Luiz Mauricio Costa Almeida b,c, Renan Rangel Bonamigo d, Carla Wanderley Gayoso de Lima e, Ediléia Bagatin f

a Dermatology Service, Universidade Federal do Pará, Belém, PA, Brazil
b Department of Dermatology, Faculdade de Ciências Médicas de Minas Gerais, Belo Horizonte, MG, Brazil
c Dermatology Service, Santa Casa de Misericórdia de Belo Horizonte, Belo Horizonte, MG, Brazil
d Dermatology Service, Hospital das Clínicas de Porto Alegre, Faculty of Medicine, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil
e Dermatology Service, Universidade Federal da Paraíba, João Pessoa, PB, Brazil
f Department of Dermatology, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, SP, Brazil

Received 26 May 2020; accepted 14 August 2020
Available online 10 October 2020

Abstract

Background: Rosacea is a chronic inflammatory disease of the skin, relatively more frequent in women over 30 with a low phototype and proven genetic predisposition. Although its etiology is unknown and possibly multifactorial, the immunological abnormality, associated with neurovascular dysregulation and triggering factors, are important elements in its pathophysiology, which lead to the main changes of inflammation, vasodilation, and angiogenesis that are responsible for the clinical manifestations. Despite the lack of cure, numerous therapeutic options are available for the different clinical presentations of the disease, with satisfactory responses.

Objective: To reach a consensus, with recommendations from experts, on the therapeutic management of rosacea suitable to the Brazilian setting.

Methods: The study was conducted by five specialized dermatologists from university centers, representatives of the different Brazilian regions, with experience in rosacea, who were appointed by the Brazilian Society of Dermatology. Based on the adapted DELPHI methodology, the experts contributed through an updated bibliographic review of the scientific evidence, combined with personal experiences.

* How to cite this article: Oliveira CMM, Almeida LMC, Bonamigo RR, Lima CWG, Bagatin E. Consensus on the therapeutic management of rosacea – Brazilian Society of Dermatology. An Bras Dermatol. 2020;95(1):53–69.
** Study conducted at the Brazilian Society of Dermatology, Rio de Janeiro, RJ, Brazil.
* Corresponding author.
E-mail: cliviaoliveiracarneiro@gmail.com (C.M. Oliveira).

https://doi.org/10.1016/j.abd.2020.08.001
0365-0596/© 2020 Sociedade Brasileira de Dermatologia. Published by Elsevier España, S.L.U. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).
**Introduction**

**Epidemiology**

Rosacea is a chronic inflammatory skin disease with complex etiopathogenesis, involving immunological changes and neurovascular dysregulation; there are established risk factors and clinical conditions, which can significantly compromise the quality of life of patients. It has a broad worldwide distribution (5% affected, globally), predominantly in populations of low phototypes (I and II in the Fitzpatrick classification), although studies have demonstrated that it can affect different ethnicities.\(^1\)\(^-\)\(^3\) A slight female predominance is observed and, although it also affects children and the elderly, the predominant age group is between 30 and 60 years.\(^1\)\(^-\)\(^6\)\(^-\)\(^8\)

Most epidemiological reports were conducted in Europe and North America, although recent articles describe rosacea as a health problem in different regions of the world.\(^1\)\(^-\)\(^5\)\(^9\) Recent publications certify that the disease appears to be universal and does not just affect Caucasians.\(^2\)\(^-\)\(^4\)\(^6\)\(^-\)\(^8\)\(^9\)

The worldwide distribution of rosacea appears to range from 2% to 22%. Estimates in relation to prevalence in different countries are: Estonia 20%, Germany 12%, Sweden 10%, Russia 5%, United States 5%, Colombia 3%, France 3%. The rates for countries such as China, Brazil, India, and Australia are not reliably recognized.\(^2\)\(^-\)\(^10\)

In Brazil, there are no reports on rosacea that take into account the country’s population heterogeneity. A study conducted in Southern Brazil, including 62 cases and 124 controls, confirmed age between 40 and 50 years and female predominance, in addition to European ancestry, in most cases.\(^10\) However, there are numerous cases of patients with higher phototypes followed-up in dermatology services in different Brazilian regions, which need to be considered.

In this article, the main aspects of rosacea will be presented, in order to synthesize knowledge and indicate the best current therapeutic management.

**Pathophysiology**

Although the pathogenesis of rosacea is not completely understood, it is considered a multifactorial disease.\(^11\) Genetic predisposition, abnormalities of the immune system, and neurovascular dysregulation – associated with triggering factors – are the main elements involved in the pathophysiology of the disease.\(^12\)

The genetic predisposition to carry the polymorphic variant rs3733631 in the TACR3 tachykinin receptor gene, and polymorphism in the glutathione S-transferase (GST) enzyme are related to the disease.\(^13\)\(^-\)\(^15\) Chang et al. identified that genes associated with rs763035 are expressed in rosacea skin samples and identified that three class II alleles of the major histocompatibility complex (MHC), including HLA-DRB1, HLA-DQB1, and HLA-DQA1, are involved.\(^16\)\(^-\)\(^18\)

Dysregulation of the innate immune response increases the secretion of antimicrobial peptides (AMP) and cytokines, via activation of toll-like receptor 2 (TLR-2). The main AMP is cathelicidin, which is cleaved by kallikrein 5 (KLK-5) into the active peptide LL-37. This is the fundamental mediator for activating and controlling numerous processes: release of cytokines and metalloproteinases (MMP) by leukocytes, mast cells, and keratinocytes, regulation of the expression of extracellular matrix components, and increased proliferation of endothelial cells, causing angiogenesis. MMP-2 and MMP-9 are elevated on the skin of patients, exerting inflammatory, angiogenic, and dermal framework disruption functions in addition to helping in the activation of KLK-5, retrofeeding the system. MMP-9 is directly stimulated by the mite *Demodex folliculorum* (Df).\(^17\)\(^-\)\(^19\)\(^-\)\(^22\)

The impairment of the cutaneous barrier in rosacea contributes to the pathophysiology of the disease, since its integrity is essential for the innate immune system. An increase in the loss of transepidermal water and a more alkaline pH is observed, possibly due to the activation of epidermal proteases, especially KLK-5. It is also important that Df can lead to the rupture of the skin barrier, causing micro abrasions on the skin, producing hypersensitivity in rosacea.\(^23\)\(^-\)\(^27\)

In adaptive immunity, there is a predominance of cytokines of the Th1/Th17 pathways. IL-17 appears to induce angiogenesis through VEGF and affect the expression of LL-37 in keratinocytes.\(^28\)\(^-\)\(^29\) Serum vitamin D levels in rosacea patients were higher than in the control group. This steroid hormone probably influences the pathway associated with TLR-2, KLK-5, and LL-37, altering the immune system.\(^17\)\(^-\)\(^23\)\(^,\)\(^24\)

In neurovascular dysregulation, vanillloid and ankyrin receptors – present in neuronal tissues, in the endothelium, and in keratinocytes – can release important neuropeptides in the characteristic flushing of rosacea; they can be triggered by heat, cold, alcohol, spicy foods, and chemicals.\(^2\)\(^,\)\(^7\)\(^,\)\(^8\)\(^,\)\(^11\)\(^,\)\(^17\)\(^,\)\(^30\)\(^-\)\(^32\)

The pathophysiological mechanisms, in particular the inflammatory and vascular mechanisms, which act to potentiate the rosacea triggering and maintenance, induce the
acceleration of proliferation and epidermal differentiation, as well as the dysfunction of the stratum corneum, decreasing the ability to attract and retain water, worsening the inflammatory process, and aggravating the damage to the skin barrier.\textsuperscript{33}

**Triggering factors**

One of the characteristics of rosacea is the possibility that signs and symptoms (especially flushing) are triggered by environmental factors or lifestyle habits. In 2002, the National Rosacea Society (NRS) conducted a study with 1,066 patients with rosacea to identify the main related factors; the most cited were the following: sun exposure (81%), emotional stress (79%), hot weather (75%), wind (57%), intense physical exercise (56%), alcohol consumption (52%), hot baths (51%), cold weather (46%), spicy foods (45%), humidity (44%), certain skin care products (41%), hot drinks (36%), certain cosmetics (27%), medicines (15%), and medical conditions (15%), among others.\textsuperscript{34}

Despite not being mentioned in this research, later studies indicated the mite Df as an important triggering factor.\textsuperscript{35}

In non-scientific surveys, also conducted by NRS, over 90% of the interviewed rosacea patients who identified and avoided their triggering factors presented improvement, in varying degrees.\textsuperscript{36}

**Classification**

In 2002, the NRS developed a classification that was revised in 2004, which provided standardized criteria for conducting research, analyzing results, and comparing data from different sources, serving as a diagnostic reference in clinical practice.\textsuperscript{37,38} It classifies rosacea into four subtypes: (1) erythematotelangiectatic; (2) papulopustular; (3) phymatous; and (4) ocular. Although excellent from an educational standpoint, this classification clearly ignored the differences in the intensity of clinical manifestations, the possibility of progression between different forms, and even the chances of overlapping subtypes.\textsuperscript{35}

The etiopathogenesis of rosacea was then unknown, and there were no histological or serological markers for the disease; therefore, the system was based merely on the characteristic morphology to provide a “framework” that could be updated in the face of new discoveries. Therefore, since its introduction, the NRS classification has been proposed as a provisional system, which should be modified/updated as scientific knowledge and clinical practice experience advance.\textsuperscript{39}

Rosacea findings may encompass several subtypes, progress between different subtypes, demonstrate varying intensities, or even be pathognomonic (e.g., phyma).\textsuperscript{40,41} A system based on phenotypes – observable characteristics that may result from genetic and/or environmental influences – provides the necessary means to evaluate and propose treatments individually, according to the presentation of each patient.\textsuperscript{42}

The Rosacea Consensus (ROSCO) panel – composed of dermatologists and ophthalmologists from Africa, Asia (including India, China, and Singapore), Europe, North America, and South America – was the first to adopt and propose a global approach to address the diagnosis and classification of rosacea. The group aimed to establish an international consensus on diagnosis, severity, and treatment options, in order to improve diagnostic and therapeutic results.\textsuperscript{42,43} Soon thereafter, still in 2017, NRS, through a panel of experts, adopted criteria very similar to those proposed by the ROSCO panel, also recommending assessment by phenotypes.\textsuperscript{39}

**Diagnosis and clinical aspects**

**Diagnostic phenotypic criteria**

Both the new ROSCO classification and the updated NRS consider two manifestations as signs or diagnostic criteria when

| Table 1 Rosacea phenotypes. Diagnostic, major, and secondary characteristics.\textsuperscript{a} |
| --- |
| **Diagnostic**\textsuperscript{b} | **Major criteria**\textsuperscript{c} | **Secondary criteria** |
| Persistent centrofacial erythema associated with periodic intensification due to possible triggering factors | Flushing | Burning sensation on the skin |
| Phymatous changes | Papules and pustules Telangiectasia Ocular manifestations: \* Telangiectasia on the margin of the eyelid \* Blepharitis \* Keratitis/Conjunctivitis/Sclerocerotisit | Ardency on the skin Edema Dryness of the skin Ocular manifestations: \* Accumulation of crusts and a collarette at the base of the eyelashes \* Irregularity of the eyelid margin \* Tears evaporation dysfunction |

\textsuperscript{a} Adapted from Tan et al., 2017\textsuperscript{39} and Gallo et al., 2017.\textsuperscript{42}

\textsuperscript{b} These findings alone are sufficient for the diagnosis of rosacea.

\textsuperscript{c} The presence of two or more findings is considered diagnostic.
present in isolation or associated with other manifestations (Table 1). 39,42

**Persistent centrofacial erythema**

It presents a characteristic pattern that is intensified periodically by triggering factors. In patients with Fitzpatrick skin phototypes I to IV, this is the most frequent presentation of rosacea. Differential diagnosis with lupus erythematosus, seborrheic dermatitis, photodermatoses, and steroid-induced rosacea is important. In patients with phototypes V and VI, skin pigmentation can hinder clinical evaluation; however, irritation symptoms such as burning and stinging can help in the assessment. In these phototypes, papules and pustules may be the first clearly visible signs. 43

**Phymatous changes**

In the newer classifications, this is a pathognomonic finding of rosacea. 39,42 It is more frequent in males and, although it can affect any area of the face, the nasal region is the most common (rhinophyma). 44 It initially presents as a thickening of the skin, with erythema and edema, which is visibly inflammatory. It progresses with the proliferation of fibrous tissue and sebaceous glands, as well as accentuation of follicular orifices with sebum and keratin plugs that drain an unpleasant odorous material, a residual condition with no evident inflammation. 45

**Major phenotypic criteria**

The main phenotypic criteria of rosacea may be observed associated or unassociated with the diagnostic criteria. If they are not associated, at least two major criteria are required for diagnosis. 39,42

**Flushing**

It consists of diffuse erythema, which occurs in outbreaks of varying duration and frequency, intensifying centrofacial redness; long-term outbreaks are common. It often occurs in association with edema of varying degrees and can present with sensations of heat, burning, and/or pain. In individuals with high phototypes, it can be difficult to observe; at times, it is not observed, being only subjective. Its occurrence is linked to neurovascular stimuli triggered by several factors. 46,47

**Papules and pustules**

The papules are erythematous, arranged predominantly in the centrofacial region; some can be larger and deeper, and they may be accompanied by pustules. The association with erythema and edema of varying degrees is common. Come-done, when present, signal concomitance of acne unrelated to rosacea and assist in the differential diagnosis. 47–49

**Telangiectasias**

Telangiectasias have a facial center location; as their presence in the nasal wings is frequent in the general population, they are not considered in the diagnosis. It is important to exclude steroid use and chronic actinic damage as causative factors. In patients with high phototypes, V and VI, dermoscopy can assist in the diagnosis. 39

**Ocular manifestations**

They can be part of the primary or secondary criteria, and will be addressed in a separate topic.

**Secondary phenotypic criteria**

In the ROSCO and NRS classifications, the secondary phenotypic dermatological manifestations are similar and include: burning sensation, stinging sensation, dryness, and edema. The difference between these two classifications lies only in ophthalmological criteria. 39,42

**Ardeny and burning sensations**

Both are more frequent in patients with rosacea. Lonne-Rahm et al. evaluated patients with a burning complaint and demonstrated a higher incidence in this population, especially in the malar region. 52 Pruritus, although it can occur, is not a characteristic symptom.

**Edema**

In rosacea, edema can be linked to vascular changes and inflammation, and its association with erythema and flushing is quite common. Although it is often associated with other manifestations, it can occur in isolation. It can be depressible or firm, self-limited or persistent, with variable duration. Both lymphatic or blood vessels can be implicated, and the dominance is variable. 46,51,52

**Dryness of the skin**

The central region of the face can be rough and scaly, despite the patient reporting having "oily skin." The coexistence of seborrheic dermatitis increases the difficulty of the diagnosis, as rosacea can simulate an eczematous condition.

**Ocular rosacea**

Ocular rosacea is regularly neglected by dermatologists, who tend to address only skin manifestations. Greater knowledge by dermatologists and ophthalmologists can improve the diagnosis and management of these patients. 52 It is important to emphasize that this manifestation can behave independently of skin lesions, and may be present in mild, moderate, and severe degrees, or even in the absence of the main phenotypic criteria. 37,39

The ROSCO panel attributes the following ocular manifestations to an increased possibility of association with rosacea: 52

- Telangiectasias of the margins of the eyelids: Vessels visible around the margins of the eyelids.
- Blepharitis: Inflammation of the eyelid margin, most commonly due to dysfunction of the Meibomian glands.
- Keratitis: Inflammation of the cornea that can lead to defects and, in the most severe cases, loss of vision.
- Conjunctivitis: Inflammation of the mucosa that lines the inner surface of the eyelids and bulbar conjunctiva. It is typically associated with vascular congestion and conjunctival edema.
- Anterior uveitis: Inflammation of the iris and/or ciliary body.
The new NRS classification also includes symptoms that commonly appear in rosacea, but are not specific. They include burning, stinging, photosensitivity, and foreign body sensation.29

In most cases, the diagnosis of ocular rosacea is eminently clinical. The assessment of telangiectasias in the margins of the eyelids and conjunctival interpalpebral erythemas, as well as the inspection of the meibomian glands and chalazion, can be performed without the aid of instruments and by non-specialized professionals. There are, however, conditions in which the aid of an ophthalmologist may be necessary, such as keratitis, scleritis, and infiltrates with corneal vascularization.29

Methods

This consensus was elaborated by five dermatologists, from different Brazilian regions, experienced in rosacea, who were appointed by the Brazilian Society of Dermatology. An updated systematic review on the subject was carried out, based on scientific evidence, combined with personal experiences. Based on the modified DELPHI methodology, the experts contributed by indicating their agreement on a Likert scale, measured by the variables: (1) strongly agree, (2) partially agree, (3) neither agree nor disagree, (4) partial- ally disagree, or (5) totally disagree. Thus, it was possible to identify the different levels of intensity of opinion on the same subject. All meetings were remote, and all members answered all questions. The data obtained were evaluated and the degree of agreement of the panel was greater than 90% for all items in the manuscript.

Treatment

General measures

Rosacea is characterized by sensitive skin on the face, with compromised skin barrier and vascular hyper-reactivity. Many patients complain of exaggerated sensitivity to cleaning agents and cosmetics. Therefore, guidance on triggering and aggravating factors and general measures on skin care are essential in any form and severity for maintaining the integrity of the skin in the long term and for the success of the treatment.

The guidelines should be aimed at identifying and preventing exposure to triggering factors, which cause aggression to the skin barrier and/or vasodilation.51-59

General care must include gentle cleaning, only once or twice a day, with agents without soap, i.e., lotions for sensitive skin such as micellar water or with mild soaps, with pH 5.5; daily use of non-greasy moisturizers, similar in composition to the skin’s natural moisturizing factor, preferably rich in ceramides, hyaluronic acid, glycerin, allantoin, licorice, niacinamide, plant oils (triglycerides, polyphenols, triterpenes, free fatty acids, phospholipids, antioxidants, such as tocopherol, etc.), and without alpha-hydroxy acids.60

As the inflammation compromises the barrier function, increasing the loss of transepidermal water, leaving the skin dry and sensitive, moisturizers with occlusive and humectant function should be applied, preferably at night, when the recovery of the epidermal barrier is slower, and permeability and water loss are higher. Moisturizers for sensitive skin are more suitable, some with green pigment, which are useful to mask erythema.61

Broad spectrum photoprotection should be used daily and continuously, with a protection factor above 30, preferably containing dimethicone, zinc oxide, or titanium dioxide to avoid irritating dermatitis, and be tinted, to act as color correction. Camouflage is very useful for transient or persistent erythema, reducing the impact on quality of life and the stress due to the appearance of the skin.

Even with care in choosing the products to be prescribed, there are always risks of adverse events, given the sensitivity of the skin; this should be informed to patients. The following products should be avoided: waterproof cosmetics, due to the difficulty of removal; tonics and astringents containing alcohol, menthol, camphor, or eucalyptus oil; and products with sodium lauryl sulfate, strong fragrances, fruit acids, and exfoliants.54-59

Topical treatments

They aim to control flares, with therapeutic options that lead to effective control, good tolerability, satisfaction, and a positive impact on quality of life. It is relevant to emphasize that, although there is no cure, total improvement and long periods of remission are possible; in mild to moderate cases, topical treatments have a good level of confirmatory evidence and may be sufficient.

The most cited topical treatments in the literature are: 0.75% metronidazole in gel or cream and 1% in cream; azelaic acid 15% gel or 20% cream; α-1 adrenergic receptor agonists (brimonidine tartrate 0.5% gel and oxymetazoline 1% cream); and ivermectin 1% cream.55-57,59 Although not yet commercialized in Brazil, 4% topical minocycline foam has also been described in the recent literature.59

In the 1990s, metronidazole was reported in studies; its main mechanisms of action are the anti-inflammatory effect and reduced Df density.53,54 In Brazil, it is commercially available at 0.75% gel; other presentations are available in manipulation pharmacies.

Azelaic acid is considered effective for its anti-inflammatory activity established in in vitro studies, through the inhibition of neutrophil functions and the generation of reactive oxygen species (ROS).62,63 A recent study has demonstrated its anti-inflammatory effect in vivo on adult women’s acne, by significantly reducing the expression of TLR-2 which is also involved in the pathophysiology of rosacea.64 In rosacea, its effectiveness compared to the vehicle was demonstrated in a randomized study and confirmed in a systematic review.65,66 In Brazil, azelaic acid is commercially available as 15% gel and 20% cream

The α-1 adrenergic receptor agonists present in dermal vessels, particularly in arterioles, cause vasoconstriction. The use of 0.5% brimonidine gel was approved by the Food and Drug Administration (FDA) in 2014. There was a great expectation as a solution for the transient and persistent rosacea erythema; however, adverse events were reported in around 31% of patients.57 A study published in 2017 observed worsening of erythema, flushing, rebound, contact dermatitis, pruritus, and burning in about 10% to 20% of patients, with interruption of use by 17%. The authors suggested that its use could be helpful only in cases of persistent erythema. In 2017, the FDA approved the use of oxymeta-
zoline 1% cream, once a day in the morning for persistent erythema. Several authors have demonstrated its effectiveness in improving erythema by two degrees according to the scale used.\footnote{58,60} Adverse events such as dermatitis and/or erythema, paraesthesia, pain, dryness, and pruritus were observed in 8.2% of patients, most frequently in the first 90 days of treatment; only 3.2% of patients discontinued use, without worsening of the erythema. Rebound occurred in less than 1% of patients. Evidently, there was no effect on telangiectasias. The present authors consider that, due to the short time of use, it is not possible to ensure its safety, efficacy, and tolerability. In Brazil, only 0.5% brimonidine gel is approved, and already commercially available.

Ivermectin 1% cream was approved by the FDA in 2017, indicated for moderate to severe papulopustular rosacea, with less effectiveness in the milder form, with less lesions.\footnote{70} Recently, its beneficial effects on ocular changes have been described.\footnote{71} Its mechanism of action is based on inhibiting the cathelicidin pathway and reducing the density of DF, which activates toll-like receptor 4 (TLR-4), with the release of inflammatory mediators; it acts as an anti-inflammatory, with decreased expression of TNF-\(\alpha\) and IL-1 beta.\footnote{70} The role of DF in rosacea is still controversial; however, some authors suggest that rosacea-like demodectisosis and rosacea can be considered two phenotypes of the same disease that improve not only by the anti-inflammatory action of ivermectin, but also by its anti-parasitic action.\footnote{72} Side effects were irritation, xerosis, pruritus, and itching.\footnote{73} A systematic review published in 2018 confirmed the efficacy of topical ivermectin compared to other topicals, but no comparative studies with doxycycline and isotretinoin alone or in combination were retrieved.\footnote{74} In Brazil, ivermectin for topical use is only available in handling pharmacies.

Other topical agents for the treatment of rosacea, reported in older publications, include: 10% sodium sulfacetamide, 5% or 10% sulfur lotions, 5% benzoyl peroxide, and retinoids (0.05% retinaldehyde and 0.025% or 0.05% tretinoin). The last two present a high risk of causing irritative dermatitis and would only be justified if rosacea is associated with acne or photoaging.\footnote{53,54}

**Systemic treatments**

More severe or refractory cases require isolated systemic treatment or, more commonly, association with the topical treatment.

The drugs for systemic use are antibiotics, especially from the group of cyclins (tetracycline, doxycycline, and minocycline), metronidazole, and isotretinoin, which will be detailed below, highlighting their adverse events that should be monitored. Although in clinical practice tetracycline is frequently used in Brazil, there is no evidence to support its use in the treatment of rosacea. Among the aforementioned oral medications, doxycycline and minocycline are available in manipulation pharmacies in Brazil, while the others are commercially available.\footnote{53,54,56-59}

\(\beta\)-Adrenergic receptor antagonists, also called beta-blockers, such as carvedilol, atenolol, nadolol, and propranolol – for systemic use – have vasoconstrictive properties in the smooth muscle of dermal arterioles and do not act on capillaries. The use of carvedilol was published in a case report of severe and refractory rosacea, with high efficacy for erythema and few side effects; however, there is an increased risk of hypotension and bradycardia.\footnote{75}

**Phenotype-based treatments**

Global approach in the management of rosacea should be based on knowledge and choice of the various topical and systemic therapeutic options, according to the phenotype and severity of the disease.\footnote{53,54,56-59} At the end of this consensus, the experts’ treatment suggestions will be presented, based on phenotypic manifestations.

When transient erythema, also known as flushing, prevails, there is no treatment with established confirmatory evidence. General measures and skin care are advised. Soothing masks with chamomile, feverfew, green tea, etc. can be used. Topical alpha-adrenergic agonists and oral beta-blockers are no longer indicated.\footnote{53,54,58,59} The use of botulin in intradermal injections has been successfully suggested in case reports and may represent an alternative therapy that needs further studies.\footnote{76,77}

Alpha-adrenergic agonists, such as 0.5% brimonidine tartrate in gel and 1% oxymetazoline in cream, are recommended for persistent erythema.\footnote{59,67-70} Laser and intense pulsed light (IPL) can be used.

Telangiectasias should be treated with technologies such as IPL, with 550 or 600 nm filters and laser, with widely documented success.\footnote{78} The laser mechanism of action is that of selective photothermolysis and the target chromophore is the hemoglobin pigment present in blood vessels.\footnote{79} It is a safe and effective method, with secondary results, such as reduction of erythema, improvement of skin texture and, sometimes, reduction of papules and pustules. Multiple sessions (up to 15) are required at intervals of 1–3 weeks. The parameters must be adjusted individually, according to the prototype, severity, and tolerance, in order to minimize side effects. There are few reports in the literature about the time of remission of rosacea, but it is believed that it can reach 1 year.\footnote{78,79} Electrocauterization is an alternative.

For inflammatory papulopustular lesions, topical and/or systemic treatments are indicated.\footnote{53-59} For mild to moderate forms, the order of preference includes azelaic acid, ivermectin, topical metronidazole, and doxycycline 40 mg/day; for severe forms, topical ivermectin, doxycycline 40 mg/day, and oral isotretinoin in a low daily dose (25–0.3 mg/kg), in off-label use.\footnote{58} Other options, without confirmatory, are: tetracycline, lymecycline, minocycline, azithromycin, oral metronidazole, topical alpha-agonists, sulfacetamide, calcineurin inhibitors, and topical retinoids.

The anti-inflammatory action of doxycycline was well documented in a review article published in 2007.\footnote{80} The 40 mg/day dose combined with the use of 1% metronidazole gel was effective and safe.\footnote{81} The dose of 40 mg was compared to that of 100 mg/day, with the same efficacy.\footnote{82} Likewise, effectiveness has been demonstrated with the combined use of 1% ivermectin cream.\footnote{83} In Brazil, it is not commercially available, and only manipulation pharmacies offer it. However, it is important to note that it is different from the one available in the United States, which has slow release, a factor that may cause some change in bioavailability and pharmacokinetics and consequently on the efficiency of the drug.
Oral isotretinoin is only approved for moderate to severe acne, providing healing or prolonged remission. Many off-label indications, such as rosacea, have been reported. The perspective of efficacy is related to the breadth of its mechanisms of action, particularly the potent inhibition of sebaceous glands and the anti-inflammatory properties by TLR-2 modulation, with increased expression in the keratinocytes in rosacea. Isotretinoin has a high degree of recommendation for moderate to severe punctate rosacea, or when recurrent or unresponsive to antibiotic therapy. In 1994, a Chilean author reported a series of cases on the use of isotretinoin in severe rosacea, for periods of 3–6 months, with rapid remission of papules and pustules, improvement of ocular manifestations, few side effects, and maintenance of results for an average 14.8 months. In 2010, a German multicenter, double-blinded, randomized study including 573 patients with papulopustular and phymatous rosacea compared different doses of isotretinoin (0.3, 0.5, 1 mg/kg/day) with doxycycline 100 mg/day for 14 days and then 50 mg/day and placebo. It was observed that isotretinoin 0.3 mg/kg/day was more effective than placebo, and was equally or even more efficient than doxycycline, with fewer side effects than in higher doses. To better control relapses, studies have suggested a treatment schedule with isotretinoin 10–20 mg/day for 4–6 months, followed by maintenance with continuous microdoses (0.03–0.17 mg/kg/day – mean: 0.07 mg/kg/day) for up to 33 months, resulting in a better option than multiple cycles of antibiotic therapy. Another study used intermediate doses, i.e., an initial daily dose of 20 mg/day for 4 months, with rapid reduction of erythema and inflammatory lesions and subsequent slow and progressive dose reduction, for 6 months, up to 20 mg/week, with recurrence rate of 45% at the 11-month follow-up. Oral isotretinoin, associated with oral corticosteroids (prednisone, 40–60 mg/day) is considered the treatment of choice for rosacea fulminans, a very severe variant. It is recommended to start with a low daily dose, 0.2–0.5 mg/kg, and then increase to 0.5–1 mg/kg for 3–4 months.

Side effects are well known, dose-dependent, predictable, preventable and controllable with early care. The most common are mucocutaneous, such as: chilblains (present in 100% of patients), xerophthalmia, conjunctivitis, nasal dryness, epistaxis, and irritant dermatitis. Laboratory changes such as elevated liver enzymes, triglyceride, and cholesterol levels, elevated LDL fraction, and decreased HDL fraction may occur. The association with depression, suicidal ideation, or attempted suicide, as well as the onset of inflammatory bowel disease related to the use of oral isotretinoin was not demonstrated in the literature. Clinical and laboratory assessment should be made before and repeated 8 weeks after the start of treatment; new assessments are required only for altered parameters. Special attention should be paid to teratogenicity, since rosacea often affects adult women of childbearing age.

In phymatous rosacea, there is hyperplasia of sebaceous glands, connective tissue, and blood vessels. By suppressing the activity of the sebaceous gland, oral isotretinoin may delay progression when used in the pre-fibrotic or inflammatory phase. Some reports demonstrated a reduction in size, number, and activity of the sebaceous glands; the dose of 1 mg/kg/day, for 18 weeks, reduced the nasal volume from 9% to 23%. Better results are obtained in young patients, but there is recurrence after discontinuation of the drug. A case report demonstrated the efficacy of isotretinoin 20 mg/day, for 6 months, with recurrence after suspension and maintenance of the result with 10 mg/day for a prolonged period. Other alternatives are doxycycline 100 mg/day and intralesional infiltration with corticosteroids. Fibrotic or non-inflammatory phymas are treated with surgery, ablative laser, electro surgery, dermabrasion, and radiofrequency, which will be addressed later.

The treatment of ocular rosacea should include eyelid hygiene, use of artificial tears for eye lubrication, and sunglasses; in mild cases, 0.75% metronidazole; i vermectin, fusidic acid applied to the eyelids, 0.05% cyclopamine in eye drops or emulsion, topical corticosteroids; in severe cases, oral doxycycline. Few studies with isotretinoin were retrieved in the literature, but the tendency is for the drug to improve signs such as blepharitis and conjunctivitis; low daily doses of 10 mg/day are recommended. Topical ivermectin, of recent use, has shown satisfactory results in ocular changes. Other options mentioned in the literature are omega 3, erythromycin, azithromycin, and oral corticosteroids. Topical maintenance treatment and evaluation by an ophthalmologist are recommended.

Granulomatous rosacea is rare; therapeutic options can include isotretinoin, 0.7 mg/kg/day for 6 months, cyclins, dapsone, laser, photodynamic therapy, bromidine, azelaic acid, topical metronidazole, benzoyl peroxide, and topical and systemic corticosteroids.

**Maintenance treatment**

The recommendation is to use topical medication, such as azelaic acid, metronidazole, and ivermectin. In selected cases, isotretinoin in microdoses (20 mg/week) can be used, with strict laboratory and risk-of-pregnancy control.

**Technology and surgery**

Various sources of laser, IPL, and light-emitting devices can be used in the treatment of rosacea. Radiofrequency, ultrasound, electro surgery, and microneedling can also be indicated in certain cases.

The main applications of technological equipments are for the improvement of erythema, telangiectasias, and phymas.

Three principles are fundamental in the handling of lasers and IPL: choosing the appropriate wavelength for the target chromophore, choosing a pulse duration shorter than the thermal relaxation of this chromophore, and applying enough energy to destroy the target within an appropriate time interval. New equipments present robust cooling capacity, high energies in short pulses, and larger tips. These elements represent effectiveness, speed, and security. Overlapping pulses and making multiple passes can also increase effectiveness.

IPL: It is well indicated in the treatment of telangiectasias. It may act on erythema, mainly perilesional, and on papules and pustules, depending on the cutting filter. Inflammatory symptoms, such as pruritus, edema, burning sensation, and pain may be alleviated.
Despite papules are present in red colored lesions, deoxygenated hemoglobin, present in bluish lesions, or methemoglobin. The mechanism of action is based on photothermal or thermal damage to the vessels, which induces intravascular coagulation.114,123,136-140

IPL works by collating vessels, remodeling collagen, and reorganizing connective tissue, actions that provide longevity of the effects induced by this technology.179,181

The lesions are treated with one or two pulses, until the start of vasospasm, associated with mild erythema and/or edema. Vessel rupture is not desired, as it leads to hemosiderin deposition and possible skin hyperpigmentation. Telangiectasias located on the nasal wings are more resistant and prone to relapse.122,130

The use of filters according to the prototype is suggested. If vasconstriction is not noticed, energy should be increased and then, if necessary, the pulse duration should be reduced. In general, reducing the spot requires increased energy (greater fluence) and vice versa. Longer wavelengths are effective for treating deeper vessels, while shorter ones target more superficial vessels. Multiple sessions (at least three) are required, at intervals of 1-3 weeks.110,142

Pulsed dye laser (PDL) (585 nm or 595 nm): well indicated in erythema and telangiectasia. The introduction of longer pulses (between 20-40 ms) reduced the occurrence of purpura and hyperpigmentation, maintaining the effectiveness.110,111,133,137,143-145

Nd: Long pulse YAG (1.064 nm): good efficacy in the treatment of facial telangiectasia. In deeper vessels and in telangiectasias larger than 1 mm, it was superior to IPL. Studies report some effectiveness in the treatment of papules and pustules.106,111,120,133,146-149

KTP – potassium-titanyl-phosphate (532 nm): more effective in small and superficial telangiectasias. Its use in the higher phototypes due to the risk of hyperpigmentation.

Alexandrite laser (755 nm): less frequently used in rosacea, but has potential in subdermal telangiectasias.111,121

Pro-yellow laser: 577 nm laser emitting 100% yellow light energy. A study in Turkey reported the effectiveness of its use in the treatment of erythema and facial telangiectasia in rosacea.156

Light emitting diode (LED): its action comes from low intensity non-thermal irradiation, with modification of cellular activity and anti-inflammatory effect. It has an additional indication in erythema and inflammatory lesions.111,133,157-166

Radio frequency: it is part of the electromagnetic spectrum and provides energy in the form of electricity. Its effectiveness in the treatment of facial erythema, papulopustular lesions, and rhinophyma is variable.113,115,167,168

Ultrasound: the device used in dermatology is similar to that used for imaging, but its energy is highly convergent and has higher frequencies. In rosacea, there are reports of improvement of erythema and telangiectasia.111,169,170

Electrosurgery: it can be used in low configurations to treat telangiectasia, but there is a risk of thermal damage, with punctate or linear scars.171

Microneedling: with or without transdermal delivery of active agents to the skin through microchannels, can improve erythema and telangiectasia in rosacea. The lesion should be mild to moderate. The most frequently mentioned active agents are botulin and tranexamic acid, which acts to restore skin permeability and suppress angiogenesis.125-128,171-174

Photodynamic therapy (PDT): studies with multiple sources of light and laser for activation of topical amnolunin acid in PDT for the treatment of rosacea have resulted in divergent responses, from insignificant to effective.175-178

**Phyma treatment**

Non-inflammatory phyma: they represent a therapeutic challenge and no method is universally adopted as the gold standard.42,106,107,153,153,157,179-188

Techniques that cause less damage to adnexal structures, along with minimal surgery time and costs, are preferred. Each method presents varying degrees of risk, related to low hemostasis, insufficient tissue removal, and scarring. Treatments can be excisional or ablative.182,183

**Excision**

The techniques involve conventional surgery, removing the phyma through shaving, scissors, scalpel blade, and/or electrocoagulation, electrosurgery with wire in loop, radiofrequency, and laser ablation.

Surgical excision is the basis of treatment for rhinophyma. It can be divided into four main stages: dermalization/decorticartion of the excess phymatous tissue, refinement of the nasal contour, hemostasis, and post-operative care.42,106,182-185

There are numerous reports of the use of dermabrasion to refine the removal of phymatous tissue. The main risks are intraoperative bleeding, unsightly scars, and excessive tissue removal.42,106,182,183,189-192

**Ablatives**

CO2 laser (10,640 nm): used in conventional ablative mode, or fractionated in milder phymas, with more sessions for satisfactory results.42,106,133,182 Despite the risk of permanent depigmentation, texture changes, and scarring, cosmetic results are usually good.42,111,114,143,182,193-195

Er-Yag (erbium: yttrium-aluminum-garnet) laser (2,940 nm): similar to the CO2 laser, induces high temperatures in the target, resulting in vaporization and ablative phyma correction.42,114

Dermabrasion: isolated or in association with other methods, promotes excellent response.196-202

Trichloroacetic acid (30%, 50%, 70%, or 90%): isolated or in association, usually with dermabrasion and/or tangential exeresis, provides favorable results.179,183,189,203,204

Cryosurgery with liquid nitrogen: acts through direct freezing action and by formation of vascular thrombi.202

**Botulin toxin**

It has recently been used in the treatment of erythema, flushing, and inflammatory lesions of rosacea, especially when other therapies are ineffective. Its application is intradermal to prevent muscle dysfunction. It should be used in larger dilutions and, to date, its mechanism of action is still controversial.76,112,133,171,205-212

It is postulated that it inhibits the release of neuropeptides associated with vasodilation and inflammation, such
as acetylcholine and vasoactive intestinal peptide, or that the toxin prevents the release of neuropeptides involved in sebaceous activity, vascular homeostasis, and inflammation, such as substance P, calcitonin, and glutamate.\textsuperscript{120,178}

The therapeutic benefits may result from the blocking effects of acetylcholine on the erector muscles of the hair and on the muscarinic receptors of the sebaceous glands. The improvement reported in erythema, flushing, and inflammation results from the interruption of the release of acetylcholine in the peripheral autonomic nerves of the cutaneous vasodilator system, together with the inhibition of the release of inflammatory mediators.\textsuperscript{120,213}

In 2004, in a case report, after PDL failure for persistent erythema, a group applied botulinum type A (BTX-A) to the centrofacial region, diluting 100 U in 5 mL of 0.9% saline solution in a proportion of 2 U per 0.1 mL, in 1 cm intervals, adding 10 U (0.5 mL) in each hemiface. The outcome was improvement in symptoms.\textsuperscript{209}

In 2012, Dayan et al. performed a study injecting onabotulinum toxin in 13 patients with rosacea, diluting 100 U in 7 mL of 0.9% saline solution, resulting in 1.4 U for each 0.1 mL. At each injection site, 0.05 mL of the product was applied, spaced 0.5 cm apart, adding 8–12 U per hemiface. After 1 week, a reduction in transient erythema, persistent erythema, and inflammation were observed; the results persisted for 3 months.\textsuperscript{112,211}

Another report termed the combination of BTX-A microinjection and associated IPL in the treatment of rosacea as mesobotox, with good response. The vial was reconstituted with 10 mL of 0.9% saline solution. Each hemiface received eight applications of 0.1 mL of BTX-A (1 U of BTX-A per application point, for a total dose of 8 U) 2 cm apart. The forehead was also inoculated with five applications of 0.1 mL.\textsuperscript{214}

Abobotulinum toxin A and incobotulinum toxin A have demonstrated good results in studies of rosacea treatment.\textsuperscript{205,206,215,216}

In Brazil, in 2018, a study demonstrated improvement of transient and persistent erythema for approximately 6 months with BTX-A in a dilution of 100 U to 5 mL of 0.9% saline solution, 0.2–0.5 U per application point. In that study, intradermal injections were applied to the malar regions, with an interval of 0.5 cm per point of application, totaling a volume that varied from 6 to 15 U per affected malar region (12–30 total units, equivalent to 0.6 to 1.5 mL of the dilution).\textsuperscript{213} This dilution and application method is recommended by the authors of this consensus.

Similar efficacy was observed in another Brazilian study that used onabotulinum toxin A in rosacea patients with erythema and inflammatory lesions, with good response.\textsuperscript{217}

Other authors failed to reproduce the benefits of BTX-A in facial erythema. These divergent results may simply be a reflection of different pathophysiological mechanisms and various rosacea subtypes.\textsuperscript{207,218}

Quality of life

As rosacea affects visibly apparent areas of the skin, it usually has a strong impact on patients’ quality of life, which is often underestimated by dermatologists. Studies demonstrate that the disease can lead to depression, anxiety, shame, low self-esteem, and social phobia.\textsuperscript{219–221}

Stress can be a triggering factor, and is related to vascular dysregulation and skin immunity resulting from the release of neuropeptides after excessive nerve stimulation. Therefore, failure to control symptoms can aggravate stress, resulting in a vicious cycle.\textsuperscript{219–221}

RosaQol is a specific quality of life assessment instrument for rosacea, consisting of a questionnaire with 21 questions. Some studies suggest that RosaQol presents high reliability and validity, in addition to high consistency with the internationally accepted DLQI; however, other authors do not corroborate this statement.\textsuperscript{52,223} RosaQol has already been translated and validated for Brazilian Portuguese, and should be considered as a measure of effectiveness in future clinical studies.\textsuperscript{223}

Comorbidities

Once considered a limited skin disorder, rosacea has been described in association with systemic diseases.\textsuperscript{224–226}

In 2015, Hua et al. published an important study, describing rosacea as a “systemic inflammatory disease,” showing similarities with psoriasis in relation to the risk of cardiovascular (CV) disease, possibly because both diseases have altered innate immunity, increased cathelicidin and C-reactive protein, in addition to decreased paraoxonase activity, which are predictors of CV events. They concluded that patients with rosacea should be alerted to possible CV events, especially in relation to arterial hypertension, dyslipidemia, and coronary artery disease.\textsuperscript{226}

More recently, in addition to CV diseases, other disorders have been described as associated with rosacea: neurodegenerative diseases (Parkinson’s disease, multiple sclerosis, Alzheimer), neurological disorders (migraine, glioma), psychiatric disorders (depression, anxiety, obsessive-compulsive disorder, social phobia, stress), intestinal disease (Crohn’s disease, ulcerative colitis, celiac disease, dysbiosis, \textit{H. pylori} infection, small intestinal bacterial overgrowth), oncological diseases (thyroid, breast and liver cancer, non-melanoma skin tumors), and autoimmune diseases (diabetes mellitus, rheumatoid arthritis, multiple sclerosis, frontal fibrosing alopecia), among others.\textsuperscript{224,224–242}

In an attempt to explain the coexistence of these systemic diseases with rosacea, studies have been designed to search for similar elements, such as the sharing of genetic and environmental factors, or of immunological and cellular characteristics. However, further research is needed to consolidate these associations.\textsuperscript{224,225,229,243,244}

Physicians should be aware of the possibility of comorbidities, and should be alert and vigilant, since there is a possibility that rosacea is only the tip of the iceberg of the patient’s systemic impairment.

Final considerations

Because it is a chronic inflammatory disease, with different clinical manifestations and with no possibility of cure at the present moment, the therapeutic management of rosacea is highly challenging.

This Brazilian consensus, prepared by five specialists from the Brazilian Society of Dermatology, aims to guide the dermatologist in the therapeutic approach of rosacea, also
**Table 2** Recommendations of Brazilian experts on therapeutic options for rosacea, according to clinical manifestations.

|                      | Erythema | Inflammatory lesions | Telangiectasias | Phymas | Ocular rosacea | Granulomatous rosacea |
|----------------------|----------|----------------------|-----------------|--------|----------------|-----------------------|
| **Transient**        |          |                      |                 |        |                |                       |
| Soothing masks with  |          |                      |                 |        |                |                       |
| chamomile, feverfew, |          |                      |                 |        |                |                       |
| green tea etc.       |          |                      |                 |        |                |                       |
| **Persistent**       |          |                      |                 |        |                |                       |
| Topical alpha-adrenergic agonists (brimonidine) | | | | | | |
| Technologies (pulsed |          |                      |                 |        |                |                       |
| light or laser)      | Topical |                      |                 |        |                |                       |
|                       | azelaic  |                      |                 |        |                |                       |
|                       | acid     |                      |                 |        |                |                       |
|                       | topical  |                      |                 |        |                |                       |
|                       | ivermectin |                  |                 |        |                |                       |
|                       | metronidazole |             |                 |        |                |                       |
|                       |          |                      |                 |        |                |                       |
| Doxycycline 40 mg/day |          |                      |                 |        |                |                       |
| **Intradermal botulinum toxin in large dilutions (as cited in the text)** | | | | | | |
| Intradermal botulin  |          |                      |                 |        |                |                       |
| in large dilutions   |          |                      |                 |        |                |                       |
| (as cited in the text) |          |                      |                 |        |                |                       |
| Other options:       |          |                      |                 |        |                |                       |
| tetracycline, azithromycin, limecycline, minocycline, topical alpha-agonists, sulfacetamide, calcineurin inhibitors, topical retinoids | | | | | | |
| **General measures:** |          |                      |                 |        |                |                       |
| Avoid triggering factors; clean skin with soap-free agents or mild soaps with pH 5.5, photoprotection; use non-greasy moisturizers, with a composition similar to the skin's natural moisturizing factor; use cosmeceuticals (chamomile, green tea, niacinamide, feverfew, licorice). | | | | | | |
providing updated information on its epidemiology, pathophysiology, clinical manifestations, diagnostic methods, and comorbidities. These data converge in the quest to improve patients’ quality of life.

Several consensuses, as well as a Cochrane Library systematic review, published in 2015 and updated in 2019, were retrieved in the recent literature on rosacea treatment. The systematic review published in 2015 included 106 controlled and randomized studies with 13,631 patients, and the 2019 update included 46 more studies, totaling 152, and 20,944 patients. The conclusions regarding the levels of evidence were: (1) high for brimonidine and moderate for oxytetracycline for temporary reduction of persistent erythema; (2) low to moderate for laser and IPL for erythema and telangiectasias; (3) high for azelaic acid andivermectin, moderate to high for doxycycline 40 mg and isotretinoin, moderate for topical metronidazole, topical and oral minocycline (same as doxycycline 40 mg), and low for tetracycline and minocycline in low doses for papules and pustules; (4) moderate for oral omega-3 and low for ophthalmic cyclosporine in emulsion and doxycycline for ocular rosacea; (5) association of topical and systemic treatments is useful; and (6) maintenance treatment is recommended.245-248

Based on personal experiences, associated with literature reviews, the authors of this consensus prepared a table on the recommendations of treatment options to be used in each clinical manifestation of rosacea. These recommendations are summarized in Table 2.

## Financial support
None declared.

## Authors’ contributions
Clívia Maria Moraes de Oliveira: Statistical analysis; approval of the final version of the manuscript; design and planning of the study; drafting and editing of the manuscript; collection, analysis, and interpretation of data; effective participation in research orientation; critical review of the literature; critical review of the manuscript.

Luiz Maurício Costa Almeida: Approval of the final version of the manuscript; drafting and editing of the manuscript; critical review of the literature; critical review of the manuscript.

Renan Rangel Bonamigo: Approval of the final version of the manuscript; drafting and editing of the manuscript; critical review of the literature; critical review of the manuscript.

Carla Wanderley Gayoso de Lima: Approval of the final version of the manuscript; drafting and editing of the manuscript; critical review of the literature; critical review of the manuscript.

Ediléia Bagatin: Approval of the final version of the manuscript; design and planning of the study; drafting and editing of the manuscript; critical review of the literature; critical review of the manuscript.

## Conflicts of interest
The members of this consensus declare that they participated in scientific meetings, lectures and/or received support for events from the following pharmaceutical laboratories: Clívia Maria Moraes de Oliveira Carneiro (Janssen, Novartis, Sanofi), Luiz Maurício C Almeida (Galdarfer, Leo Pharma), Ediléia Bagatin (Leo Pharma, USK, Natura, Galderma, Pierre-Fabre Dermo Cosmétique, Gelita, Douglas Pharmaceuticals). Renan Rangel Bonamigo and Carla Wanderley Gayoso de Lima declare no conflicts of interest.

## References
1. Gether L, Overgaard LK, Egeberg A, Thyssen JP. Incidence and prevalence of rosacea: a systematic review and meta-analysis. Br J Dermatol. 2018;179:282-9.
2. Buddentkote J, Steinhoff M. Recent advances in understanding and managing rosacea. F1000Research. 2018;7(F1000 Faculty Rev):1885.
3. Rueda LJ, Motta A, Pabón JG, Barona MI, Meléndez E, Orozco B, et al. Epidemiology of rosacea in Colombia. Int J Dermatol. 2017;56:510-3.
4. Lee JB, Moon J, Moon KR, Yang JH, Kye YC, Kim KJ, et al. Epidemiological and clinical features of rosacea in Korea: a multicenter cross-sectional study. J Dermatol. 2018;45:546-53.
5. Alexis AF, Callender YD, Baldwin HE, Desai SR, Rendon MI, Taylor SC. Global epidemiology and clinical spectrum of rosacea, highlighting skin of color: review and clinical practice experience. J Am Acad Dermatol. 2019;80:1722-9.
6. Bonamigo RR, Bakos L, Cartell A, Edelweiss ML. Factors associated with rosacea in population samples of Southern Brazil: analysis of case-control studies. An Bras Dermatol. 2008;83:419-24.
7. Rainer BM, Kang S, Chien AL. Rosacea: epidemiology, pathogenesis, and treatment. Dermaendoecrinol. 2017:9:e1361574.
8. Mikkelsen CS, Holmgren HR, Kjellman P, Heidenheim M, Kappinnen A, Bjerring P, et al. Rosacea: a clinical review. Dermatology Reports. 2016;6:6387.
9. Tan J, Schöfer H, Aravissiaka E, Audilbert F, Kerrouche N, Berg M. Prevalence of rosacea in the general population of Germany and Russia – The RISE study. J Eur Acad Dermatol Venereol. 2016;30:428-34.
10. Berg M, Lidén S. An epidemiological study of rosacea. Acta Derm Venereol. 1989;69:419-23.
11. Vera N, Patel NU, Seminario-Vidal L. Rosacea Comorbidities. Dermatol Clin. 2018;36:115-22.
12. Two AM, Wu W, Gallo RL, Hata TR. Rosacea: part I. Introduction, categorization, histology, pathogenesis, and risk factors. J Am Acad Dermatol. 2015;72:749-60.
13. Karpouzis A, Aygeridis P, Tripsiani G, Gatzidou E, Kouroumi N, Velzeta S. Assessment of Tachykinin receptor 3′ gene polymorphism rs3733631 in Rosacea. Int Sch Res Notices. 2015;2015:469402.
14. Yazici AC, Tamer L, Ikizoglu G, Kaya TI, Api H, Yıldırım H, et al. GSTM1 and GSTT1 null genotypes as possible heritable factors of rosacea. Photodermatol Photoimmunol Photomed. 2006;22:208-10.
15. Aldrich H, Gerstenblith M, Fu P, Tuttle MS, Varma P, Gotow E, et al. Genetic vs environmental factors that correlate with rosacea: a cohort-based survey of twins. JAMA Dermatol. 2015;151:1213-9.
16. Chang ALS, Raber I, Xu J, Li R, Spitale R, Chen J, et al. Assessment of the genetic basis of rosacea by genome-wide association study. J Invest Dermatol. 2015;135:1548–55.

17. Bonamigo RR, Bentolila W. Rosacea. In: Bonamigo RR, Donnellis ST, editors. Dermatology in public health environments. Cham: Springer Nature; 2018. p. 465–79.

18. Van Steensel MA, Badeloe S, Winneppeninkx V, Vreeburg M, Steijlen PM, van Geel M. Granulomatous rosacea and Crohn’s disease in a patient homozygous for the Crohn-associated NOD2/CARD15 polymorphism R702W. Exp Dermatol. 2008;17:1057–8.

19. Two AM, Del Rosso JQ, Kallikrein 5-mediated inflammation in rosacea: clinically relevant correlations with acute and chronic manifestations in rosacea and how individual treatments may provide therapeutic benefit. J Clin Aesthet Dermatol. 2014;7:20–5.

20. Kim JY, Kim YJ, Lim BJ, Sohn HJ, Shin D, Oh SH. Increased expression of cathelicidin by direct activation of protease-activated receptor 2: possible implications on the pathogenesis of rosacea. Yonsei Med J. 2014;55:1648–55.

21. Kim JY, Chang ALS. Increased expression of cathelicidin by direct activation of protease-activated receptor 2: possible implications on the pathogenesis of rosacea. J Invest Dermatol. 2015;135:1548–55.

22. Bonamigo RR, Bakos L, Edelweiss M, Cartell A. Could matrix metalloproteinase-9 be a link between Demodex folliculorum and rosacea? J Eur Acad Dermatol Venereol. 2005;19:646–7.

23. Dirschka T, Tronnier H, Fölsler-Holst R. Epithelial barrier function and atopic diathesis in rosacea and perioral dermatitis. Br J Dermatol. 2004;150:1136–41.

24. Ni Raghallagh S, Powell FC. Epidermal hydration levels in patients with rosacea improve after minocycline therapy. Br J Dermatol. 2014;171:259–66.

25. Forton FM. Papulopustular rosacea, skin immunity and Demodex: pityriasis follicullorum as a missing link. J Eur Acad Dermatol Venereol. 2012;26:19–28.

26. Gerber PA, Buhren BA, Steinhoff M, Homey B. Rosacea: the cytokine and chemokine network. J Invest Dermatol Symp Proc. 2011;15:40–7.

27. Buhl T, Sulik M, Nowak P, Bunkenkotte J, McDonald I, Aubert J, et al. Molecular and morphological characterization of inflammatory infiltrate in rosacea reveals activation of Th1/Th17 pathways. J Invest Dermatol. 2015;135:2198–208.

28. Ekiz O, Balta I, Sen BB, Dikiliças M, Ozuğuz P, Rifaioğlu EN. Vitamin D status in patients with rosacea. Cutan Ocul Toxicol. 2014;33:60–2.

29. Morizane S, Yamasaki K, Kabigting FD, Gallo RL. Kallikrein expression and cathelicidin processing are independently controlled in keratinocytes by calcium, vitamin D3, and retinoic acid. J Invest Dermatol. 2010;130:1297–306.

30. Kim M, Kim KE, Jung HY, Jo H, Jeong SW, Lee J, et al. Recombinant erythroid differentiation regulator 1 inhibits both inflammation and angiogenesis in a mouse model of rosacea. Exp Dermatol. 2015;24:680–5.

31. Seeliger S, Bunkenkotte J, Schmidt-Choudhury A, Rosignoli C, Shapovitch V, von Arnim U, et al. Pituitary adenylate cyclase activating polypeptide: an important vascular regulator in human skin in vivo. Am J Pathol. 2010;177:2563–75.

32. Gneo EW, Mantey P, Vercellotti GM, Moldow CF. Functional neurokinin 1 receptors for substance P are expressed by human vascular endothelium. J Exp Med. 1993;177:1269–76.

33. Addor FAS. Skin barrier in rosacea. An Bras Dermatol. 2016;91:59–63.

34. rosacea.org [Internet]. New survey pinpoints leading factors that trigger symptoms. [cited 05.15.20]. Available from: http://www.rosacea.org/rr/2002/summer/article3.php

35. Holmes AD, Steinhoff M. Integrative concepts of rosacea pathophysiology, clinical presentation and new therapeutic agents. Exp Dermatol. 2017;26:659–67.

36. rosacea.org [Internet]. Survey shows lifestyle changes help control rosacea flare-ups. [cited 05.14.20]. Available from: http://www.rosacea.org/rr/1998/winter/article3.php

37. Wilkin J, Dahl M, Detmar M, Drake L, Feinstein A, Odom R, et al. Standard classification of rosacea: report of the National Rosacea Society Expert Committee on the Classification and Staging of Rosacea. J Am Acad Dermatol. 2002;46:584–7.

38. Wilkin J. Standard grading system for rosacea: report of the National Rosacea Society Expert Committee on the classification and staging of rosacea. J Am Acad Dermatol. 2004;50:907–12.

39. Gallo RL, Granstein RD, Kang S, Mannis M, Steinhoff M, Tan J, et al. Standard classification and pathophysiology of rosacea: the 2017 update by the National Rosacea Society Expert Committee. J Am Acad Dermatol. 2018;78:148–55.

40. Weinkle AP, Doktor V, Emer J. Update on the management of rosacea. Clin Cosmet Investig Dermatol. 2015;8:159–77.

41. Tan J, Blume-Peytavi U, Ortonne JP, Wilhelm K, Marticou L, Baltas E, et al. An observational cross-sectional survey of rosacea: clinical associations and progression between subtypes. Br J Dermatol. 2013;169:555–62.

42. Tan J, Almeida L, Bewley A, Cribier B, Dlova NC, Gallo R, et al. Updating the diagnosis, classification and assessment of rosacea: recommendations from the global ROSacea Consensus (ROSCO) panel. Br J Dermatol. 2017;176:431–8.

43. Alexis FA, Callender BD, Baldwin HE, Desai SR, Rendon MI, Taylor SC. Global epidemiology and clinical spectrum of rosacea, highlighting skin of color: review and clinical practice experience. J Am Acad Dermatol. 2019;80:1722–9.

44. Barco D, Alomar A. Rosácea. Actas Dermosifiliogr. 2008;99:244–56.

45. Troielli P, González FM, Rios JM, Vásquez OT, Pabón JG, Ibarra M, et al. Actualización y recomendaciones para el diagnóstico y tratamiento de la rosácea en Latinoamérica. Med Cutan Iber Lat Am. 2016;44:7–26.

46. Schwab VD, Sulik M, Seeliger S, Nowak P, Aubert J, Mess C, et al. Neurovascular and neuroimmune aspects in the pathophysiology of rosacea. J Invest Dermatol Symp Proc. 2011;15:53–62.

47. Steinhoff M, Bunkenkotte J, Aubert J, Sulik M, Novak P, Schwab VD, et al. Clinical, cellular, and molecular aspects in the pathophysiology of rosacea. J Invest Dermatol Symp Proc. 2011;15:2–11.

48. Trivedi NR, Gilliland KL, Zhao W, Liu W, Thiboutot DM. Gene array expression profiling in acne lesions reveals marked upregulation of genes involved in inflammation and matrix remodeling. J Invest Dermatol. 2006;126:1071–9.

49. Buhl T, Sulik M, Nowak P, Bunkenkotte J, McDonald I, Aubert J, et al. Molecular and morphological characterization of inflammatory infiltrate in rosacea reveals activation of Th1/Th17 pathways. J Invest Dermatol. 2015;135:2198–208.

50. Lonne-Rahm S-B, Fischer T, Berg M. Stinging and rosacea. Acta Derm Venereol. 1999;79:460–1.

51. Steinhoff M, von Muentzer B, Geppetti P, Pothoulakis C, Bunnett NW. Tachykinins and their receptors: contributions to physiologic control and the mechanisms of disease. Physiol Rev. 2014;94:265–301.

52. Schaller M, Almeida L, Bewley A, Cribier B, Del Rosso J, Dlova N, et al. Recommendations for rosacea diagnosis, classification and management: update from the global ROSacea Consensus 2019 panel. Br J Dermatol. 2020;182:1269–76.

53. Aksoy B, Altaykan-Hapa A, Egemen D, Karagöz F, Atakan N. The impact of rosacea on quality of life: effects of demographic
and clinical characteristics and various treatment modalities. Br J Dermatol. 2010;163:719–25.
54. Gupta AK, Chaudhry MM. Rosacea and its management: an overview. J Eur Acad Dermatol Venereol. 2005;19:273–85.
55. van Zuuren EJ, Gupta AK, Gover MD, Graber M, Hollis S. Systematic review of rosacea treatments. J Am Acad Dermatol. 2007;56:107–15.
56. van Zuuren EJ, Fedorowicz Z. Interventions for rosacea. J Am Acad Dermatol. 2015;71:2403–4.
57. van Zuuren EJ, Fedorowicz Z, Carter B, van der Linden MM, Charland L. Interventions for rosacea. Cochrane Database Syst Rev. 2015. 2015:CD003262.
58. van Zuuren EJ, Rosso DM, Reichelt EJ, Eleni J, Rosso RH, Jirgensons DM. Topical treatments. J Eur Acad Dermatol Venereol. 2018;32:1011–24.
59. Lin TK, Zhong L, Santiago JL. Anti-Inflammatory and sebaceous barrier repair effects of topical application of some plant oils. Int J Mol Sci. 2018;19:70.
60. Saino T, Teshieda S. A novel night moisturizer enhances cutaneous barrier function in dry skin and improves dermatological outcomes in rosacea-prone skin. J Clin Aesth Dermatol. 2018;11:11–7.
61. Jones DA. Rosacea, reactive oxygen species, and azelaic acid. J Clin Aesthet Dermatol. 2009;2:26–30.
62. Sieber MA, Hegel JK. Azelaic acid: properties and mode of action. Skin Pharmacol. 2014;27:9–17.
63. Rocha MAD, Guadanhim LRS, Sanudo A, Bagatin E. Modulation of Toll Like Receptor-2 on sebaceous gland by the treatment of adult female acne. Dermatoendocrinol. 2017;9:e1361570.
64. Thiboutot D, Thieroff-Ekerdt R, Graupe K. Efficacy and safety of azelaic acid (15%) gel as a new treatment for papulopustular rosacea: results from two vehicle-controlled, randomized phase III studies. J Am Acad Dermatol. 2003;48:836–45.
65. Liu RH, Smith MK, Basta SA, Farmer ER. Azelaic acid in the treatment of papulopustular rosacea: a systematic review of randomized controlled trials. Arch Dermatol. 2006;142:1047–52.
66. Del Rosso JQ. Management of facial erythema of rosacea: what is the role of topical α-adrenergic receptor agonist therapy? J Am Acad Dermatol. 2013;69:44–56.
67. Del Rosso JQ. Topical a-agonist therapy for persistent facial erythema of rosacea and the addition of oxymetazoline to the treatment armamentarium: where are we now? J Clin Aesthet Dermatol. 2017;10:28–32.
68. Draelos ZD, Gold MH, Weiss RA, Baumann L, Grekin SK, Robinson DM, et al. Efficacy and safety of oxymetazoline cream 1.0% for treatment of persistent facial erythema associated with rosacea: findings from the 52-week open label REVEAL trial. J Am Acad Dermatol. 2018;78:1156–63.
69. Del Rosso JQ. Topical ivemectin: data supporting dual modes of action in rosacea. J Clin Aesthet Dermatol. 2017;10:39–42.
70. Sobolewska B, Doycheva D, Deuter CM, Schaller M, Zierhut M. Efficacy of topical ivemectin for the treatment of cutaneous and ocular rosacea. Ocul Immunol Inflamm. 2020;7:1–5.
71. Forton FMN, De Maertelear V. Papulopustular rosacea and rosacea-like demodiosis: two phenotypes of the same disease? J Am Acad Dermatol Venereol. 2018;32:1011–6.
72. Taieb A, Ortonne JP, Ruzicka T, Roszkiewicz J, Berth-Jones J, Peirone MH, et al. Superiority of ivemectin 1% cream over metronidazole 0.75% cream in treating inflammatory lesions of rosacea: a randomized, investigator-blinded trial. Br J Dermatol. 2015;172:1103–10.
73. Ebbelaa CF, Venema AW, Van Dijk MR. Topical ivemectin in the treatment of papulopustular rosacea: a systematic review of evidence and clinical guideline recommendation. Dermatol Ther. 2018;8:379–87.
74. Hsu CC, Lee YJ. Carvedilol for the treatment of refractory facial flushing and persistent erythema of rosacea. Arch Dermatol. 2011;147:1253–60.
75. Park KY, Hyun MY, Jeong SY, Kim BJ, Kim MN, Hong CK. Botulinum toxin for the treatment of refractory erythema and flushing of rosacea. Dermatol. 2015;230:299–301.
76. Silva LC, Ferreira ILD, Silveira ML, Steiner D. Prospective study for the treatment of rosacea flushing with botulinum toxin type A Estudo prospectivo para tratamento do rubor da rosácea com toxina botulinica tipo A. Surg Cosmet Dermatol. 2018;10:121–6.
77. Kassir R, Kolluru A, Kassir M. Intense pulsed light for the treatment of rosacea and telangiectasias. J Cosmet Laser Ther. 2011;13:216–22.
78. Pelle MT, Crawford GH, James WD, Rosacea: II. Therapy. J Am Acad Dermatol. 2004;51:499–512.
79. Fowler Jr. JR. Anti-inflammatory dose doxycycline for the treatment of rosacea. Expert Rev Dermatol. 2007;6:523–31.
80. Fowler Jr. JR. Combined effect of anti-inflammatory dose doxycycline (40-mg doxycycline, us monohydrate-controlled-release capsules) and metronidazole topical gel 1% in the treatment of rosacea. J Drugs Dermatol. 2007;6:641–64.
81. Del Rosso JQ, Schlessinger J, Werschler P. Comparison of anti-inflammatory dose doxycycline versus doxycycline 100 mg in the treatment of rosacea. J Drugs Dermatol. 2008;7:573–6.
82. Steinhoff M, Vaccaroni M, Voegel JJ, Hacini-Rachinel F, Schäfer G. Topical Ivermectin 10 mg/g and Oral Doxycycline 40 mg modified-release: current evidence on the complementary use of anti-inflammatory rosacea treatments. Adv Ther. 2016;33:1481–501.
83. Nickle BS, Peterson N, Peterson M. Updated physician’s guide to the off-label uses of oral isotretinoin. J Clin Aesthet Dermatol. 2014;7:22–34.
84. Yamasaki K, Kanada K, Macleod DT, Borkowski AW, Morizane S, Nakatsui T, et al. TLR2 expression is increased in rosacea and stimulates enhanced serine protease production by keratinocytes. J Invest Dermatol. 2011;131:688–9.
85. Gajardo J. Severe rosacea treated with oral isotretinoin. Rev Med Chil. 1994;122:177–9.
86. Gollnick H, Blume-Peytavi U, Szabó EL, Meyer KG, Hauptmann P, Popp G, et al. Systemic isotretinoin in the treatment of rosacea· doxycycline· and placebo-controlled, randomized clinical study. J Dtsch Dermatol Ges. 2010;8:505–15.
87. Hofer T. Continuous “microdose” isotretinoin in adult recalcitrant rosacea. Clin Exp Dermatol. 2004;29:204–5.
88. Uslu M, Savk E, Karaman G, Sendur N. Rosacea treatment with intermediate-dose isotretinoin: follow-up with erythema and sebum measurements. Acta Derm Venereol. 2012;92:73–7.
89. Walsh RK, Endicott AA, Shinkai K. Diagnosis and treatment of rosacea fulminans: a comprehensive review. Am J Clin Dermatol. 2018;19:79–86.
90. Hodgkiss-Harlow CJ, Eichenfield LF, Dohil MA. Effective monitoring of isotretinoin safety in a pediatric dermatology population: a novel “patient symptom survey” approach. J Am Acad Dermatol. 2011;65:517–24.
91. De Marchi MA, Maranhão RC, Brandizzi LL, Souza DR. Effects of isotretinoin on the metabolism of triglyceride-rich lipoproteins and on the lipid profile in patients with acne. Arch Dermatol Res. 2006;297:403–8.
92. Shibian E, Vicaut É, Chidilack H, Anselin E, Cribier B, Dréno B, et al. A randomized-controlled trial of oral low-dose isotretinoin for difficult-to-treat papulopustular rosacea. J Invest Dermatol. 2016;136:1124–9.
93. Marcouillier AL, Zane LT. Depression and suicidal behavior in acne patients treated with isotretinoin: a systematic review. Semin Cutan Med Surg. 2007;26:210–20.
95. Li C, Chen J, Wang W, Ai M, Zhang Q, Kuang L. Use of isotretinoin and risk of depression in patients with acne: a systematic review and meta-analysis. BMJ Open. 2019;9:e021549.

96. Bernstein CN, Nugent Z, Longobard T, Blanchard JF. Isotretinoin is not associated with inflammatory bowel disease: a population-based case-control study. Am J Gastroenterol. 2009;104:2774–8.

97. Crockett SD, Porter CQ, Martin CF, Sandler RS, Kappelian MD. Isotretinoin use and the risk of inflammatory bowel disease: a case-control study. Am J Gastroenterol. 2010;105:1986–93.

98. Altman RS, Altman L, Altman JS. A proposed set of new guidelines for routine blood tests during isotretinoin therapy for acne vulgaris. Dermatology. 2002;204:232–5.

99. Brzezinski P, Borowska K, Chiriac A, Smigielis J. Systemic isotretinoin treatment and pregnancy: a comparative study of two groups of women: a retrospective analysis of 569 women. Our Dermatol Online. 2017;9:e2.

100. Khalil S, Gharekhani A, Entezari-Maleki T. Isotretinoin: a review on the utilization pattern in pregnancy. Adv Pharm Bull. 2018;8:377–82.

101. Korting HC, Schöllmann C. Current topical and systemic approaches to treatment of rosacea. J Eur Acad Dermatol Venereol. 2009;23:876–82.

102. Wee JS, Tan KB. Phymatous rosacea presenting with leonine facies and clinical response to isotretinoin. Australas J Derma- tol. 2017;58:72–3.

103. Webster G, Schaller M. Occular rosacea: a dermatologic perspective. J Am Acad Dermatol. 2013;69:42–3.

104. Lee GL, Zirwas MJ. Granulomatous rosacea and periorificial dermatitis: controversies and review of management and treatment. Dermatol Clin. 2015;33:447–55.

105. Steinhoff SM, Schaub J. Facial erythema of rosacea – aetiology, different pathophysiology and treatment options. Acta Derm Venerol. 2016;96:579–86.

106. Tanghetti E, Del Rosso QJ, Thiboutot D, Gallo R, Webster G, Eichenfield LF, et al. Consensus recommendations from the American Acne & Rosacea Society on the management of rosacea, part 4: a status report on physical modalities and devices. Cutis. 2014;93:71–6.

107. Tsunoda K, Akasaka T, Akasaka H. Successful treatment of erythematotelangiectatic rosacea with intense pulsed light: report of 13 cases Kanako. J Dermatol. 2018;45:1113–6.

108. Elewski BE, Draelos Z, Dréno B, Jansen T, Layton A, Picard M. Rosacea – global diversity and optimized outcome: proposed international consensus from the Rosacea International Expert Group. J Eur Acad Dermatol Venereol. 2011;25:188–200.

109. Del Rosso QJ, Thiboutot D, Gallo R, Webster G, Tanghetti E, Eichenfield LF, et al. Consensus recommendations from the American Acne & Rosacea society on the management of rosacea, part 5: a guide on the management of rosacea. Cutis. 2014;93:134–8.

110. Neuhaus IM, Zane LT, Tope WD. Comparative efficacy of nonpurpuragenic pulsed dye laser and intense pulsed light for erythematotelangiectatic rosacea. Dermatol Surg. 2009;35:920–7.

111. Karal C, Campos VB. Manual Prático do Laser e Outras Fontes de Energia Eletromagnética na Dermatologia. Rio de Janeiro: Elsevier Editora Ltda; 2017.

112. Dayan SH, Pritzker RH, Arkins JP. A new treatment regimen for rosacea: onabotulinumtoxin A. J Drugs Dermatol. 2012;11:e76–9.

113. Taub AF, Devita EC. Successful treatment of erythematotelangiectatic rosacea with pulsed light and radiofrequency. J Clin Aesthet Dermatol. 2008;1:37–40.

114. Weinkle A, Doctor V, Emer J. Update on the management of rosacea. Clinical, Cosmetic and Investigational Dermatology. 2015;8:159–77.

115. Del Rosso QJ, Tanghetti E, Webster G, Gold LS, Thiboutot D, Gallo RI. Update on the Management of Rosacea from the American Acne & Rosacea Society (AARS). J Clin Aesthetic Derma- tol. 2019;12:17–24.

116. Kennedy Carney C, Cantrell W, Elewski BE. Rosacea: a review of current topical, systemic and light-based therapies. G Ital Dermatol Venereol. 2009;144:673–88.

117. Baldwin HE. Diagnosis and treatment of rosacea: state of the art. J Drugs Dermatol. 2012;11:725–30.

118. Clark SM, Lanigan SW, Marks R. Laser treatment of erythema and telangiectasia associated with rosacea. Lasers Med Sci. 2002;17:26–33.

119. Mark KA, Sparacio RM, Voigt A, Marenus K, Samnoff DS. Objective and quantitative improvement of rosacea-associated erythema after intense pulsed light treatment. Dermatol Surg. 2003;29:600–4.

120. Lee JH, Kim M, Jm B, Cho Bk, Park HJ. Efficacy of the long-pulsed 1064-nm neodymium: yttrium-aluminum-garnet laser (LPND) (rejuvenation mode) in the treatment of papulopustular rosacea (PPR): a pilot study of clinical outcomes and patient satisfaction in 30 cases. J Am Acad Dermatol. 2015;73:333–6.

121. Dahan S. Prise em charge par laser et lampes pulsées de la couperose et de la rosacée laser and intense pulsed light managemenr of couperose and rosacea. Ann Dermatol Venereol. 2011;138:219–22.

122. Kalil CLPV, Reinehr CPH, Milman LM. Luz intensa pul- sada: revisão das indicações clínicas. Surg Cosmet Dermatol. 2017;9:9–17.

123. Bernstein EF. The pulse-dyed laser for the treatment of cutane- ous conditions. G Ital Dermatol Venereol. 2009;144:557–72.

124. Anderson RR, Parrish JA. Selective photothermolysis: precise microsurgery by selective absorption of radiation. Science. 1983;220:524–7.

125. Bageorgou F, Vasalou V, Tzanetakou V, Kontochristopoulos G. The new therapeutic choice of tranexamic acid solution in treatment of erythematotelangiectatic rosacea. J Cosmet Derma- tol. 2019;18:563–7.

126. Lima EVA, Lima MA, Takano D. Microneedling experimental study and classification of the resulting injury. Surg Cosmet Dermatol. 2013;5:110–4.

127. Kalil CLPV, Campos VB, Chaves CRP, Pitassi LHU, Cig- nachi S. Comparative, randomized, double-blind study of microneedling associated with drug delivery for rejuvenating the skin of the anterior thorax region. Surg Cosmet Dermatol. 2015;7:211–6.

128. Kwon HJ, Suh JH, Ko EJ, Kim BJ. Combination treatment of propranolol, minocyline, and tranexamic acid for effective control of rosacea. Dermatol Ther. 2017;30:10.

129. Tanghetti E, Sherr EA, Sierra R, Mirkov M. The effects of pulse dye laser double-pass treatment intervals on depth of vessel coagulation. Lasers Surg Med. 2006;38:16–21.

130. Bencini PL, Toulaki A, De Giorgi V, Galimberti M. Laser use for cutaneous vascular alterations of cosmetic interest. Dermatol Ther. 2012;25:340–51.

131. Schroeter CA, Haaf-van Below S, Neuman HA. Effective treatment of rosacea using intense pulsed light systems. Dermatol Surg. 2005;31:1285–9.

132. Tanghetti EA. Split-face randomized treatment of facial telangiectasia comparing pulsed dye laser and an intense pulsed light handpiece. Lasers Surg Med. 2011;44:97–102.

133. Abokwidir M, Feldman SR. Rosacea Management. Skin Appendice Disorder. 2016;2:26–34.

134. Liu J, Liu J, Ren Y, Li B, Lu S. Eficácia comparativa de luz intensa pulsada para diferentes eritemas associados com rosácea. J Cosmet Laser Ther. 2014;25:1–18.

135. Wat H, Wu DC, Rao J, Goldman MP. Application of intense pulsed light in the treatment of dermatologic disease: a system-atic review. Dermatol Surg. 2014;40:359–77.
Consensus on the therapeutic management of rosacea

136. Lim HS, Lee SC, Won YH, Lee JB. The Efficacy of Intense Pulsed Light for Treating Erythematotelangiectatic Rosacea Is Related to Severity and Age. Ann Dermatol. 2014;26:491–5.

137. Juliard J, Wang X, Liu Z, Zhang J, Xu Y, Yuan C. Global rosacea treatment guidelines and expert consensus points: the differences. J Cosmet Dermatol. 2019;18:960–9.

138. Lane JE, Khachemoune A. Use of intense pulsed light to treat refractory granulomatous rosacea. Dermatologic Surgery. 2010;36:571–3.

139. Papageorgiou P, Clayton W, Norwood S, Chopra S, Rustin M. Treatment of rosacea with intense pulsed light: significant improvement and long-lasting results. Br J Dermatol. 2008;159:628–32.

140. Bitter P. Non-invasive photorejuvenation of photodamaged skin using serial, full face intense pulsed light treatments. Dermatol Surg. 2000;26:835–43.

141. Zelickson B, Kist D. Effect of pulsed dye laser and intense pulsed light source on the dermal extracellular matrix remodeling. Lasers Surg Med. 2000;12 Suppl:17.

142. Mansouri Y, Goldenberg G. Devices and topical agents for rosacea management. Cutis. 2014;94:21–5.

143. Baldwin HE. Diagnosis and treatment of rosacea: state of the art. J Drugs Dermatol. 2012;11:725–30.

144. Bernstein EF. The pulse-dyed laser for the treatment of cutaneous conditions. G Ital Dermatol Venerol. 2009;144:557–72.

145. Alam M, Dover JS, Arndt KA. Treatment of facial telangiectasia with variable-pulse high-fluence pulsed-dye laser: comparison of efficacy with fluences immediately above and below the purpura threshold. Dermatol Surg. 2003;29:681–4.

146. Tanghetti EA. Multiplex 595 nm, 1064 nm laser treatment for blebbled port wine birthmarks and telangiectasia. Lasers Surg Med. 2006;38:65.

147. Sarradet DM, Hussain M, Goldberg DJ. Millisecond 1064-nm neodymium:YAG laser treatment of facial telangiectases. Dermatol Surg. 2003;29:56–8.

148. Say EM, Gokhan O, Gokdemir G. Treatment outcomes of long-pulsed nd: yag laser for two different subtypes of rosacea. J Clin Aesthet Dermatol. 2015;8:16–20.

149. See HM, Kim Ji, Kim HS, Choi YJ, Kim WS. Prospective comparison of dual wavelength long-pulsed 755-nm Alexandrite/1,064-nm neodymium: yttrium-aluminum-garnet laser versus 585-nm pulsed dye laser treatment for rosacea. Ann Dermatol. 2016;28:607–14.

150. Hofmann MA, Kokolakis G. A case report of combination treatment with potassium-titanyl phosphate laser and brimondinotopical gel in erythematotelangiectatic rosacea. J Cosmet Laser Ther. 2017;19:222–4.

151. Tanghetti EA, Adrian RM. Long pulsed 532-nm laser treatment of facial telangiectasia. Lasers Surg Med. 1998;10:45.

152. West TB, Alster TS. Comparison of the long-pulse dye (590–595 nm) and KTP (532 nm) lasers in the treatment of facial and leg telangiectasia. Dermatol Surg. 1998;24:221–6.

153. Pelle MT, Crawford GH, James WD. Rosacea: II. Therapy. J Am Acad Dermatol. 2004;51:499–512.

154. Bassichis BA, Swamy R, Dayan SH. Use of the KTP laser in the treatment of rosacea and solar lentigines. Facial Plast Surg. 2004;20:77–83.

155. Uebelhoer NS, Bogle MA, Stewart B, Arndt KA, Dover JS. A split-face comparison study of pulsed 532-nm KTP laser and 595-nm pulsed dye laser in the treatment of facial telangiectasia and diffuse telangiectatic facial erythema. Dermatol Surg. 2007;33:441–8.

156. Kapicoglou Y, Sarac G, Cenik H. Treatment of erythematotelangiectatic rosacea, facial erythema, and facial telangiectasia with a 577-nm pro-yellow laser: a case series. Lasers Med Sci. 2019;34:93–8.

157. Lee JB, Bae SH, Moon KR, Na EY, Yun SJ, Lee SC. Light-emitting diodes downregulate cathelicidin, kallikrein and toll-like receptor 2 expressions in keratinocytes and rosacea-like mouse skin. Exp Dermatol. 2016;25:956–61.

158. Ablon G. Photothermolysis with light emitting diodes: treating a broad range of medical and aesthetic conditions in dermatology. J Clin Aesthet Dermatol. 2018;11:21–7.

159. Goldscheider RG. The photobiological basics behind light-emitting diode (LED) phototherapy. Laser Ther. 2007;16:97–108.

160. Ashkenazi H, Maliz K, Harth Y, Nitzan Y. Eradication of Propionibacterium acnes by its endogenous porphyrins after illumination with high intensity blue light. FEMS Immunol Med Microbiol. 2003;35:17–24.

161. Morton CA, Scholefield RD, Whitehurst C, Birch J. An open study to determine the efficacy of blue light in the treatment of mild to moderate acne. J Dermatol Treat. 2005;16:219–23.

162. Tremblay JF, Sire DJ, Lowe NJ, Moy RL. Light-emitting diode 415 nm in the treatment of inflammatory acne: an open-label, multicentric, pilot investigation. J Cosmet Laser Ther. 2006;8:31–3.

163. Papageorgiou P, Katsambas A, Chu A. Phototherapy with blue (415 nm) and red (660 nm) light in the treatment of acne vulgaris. Br J Dermatol. 2000;142:973–87.

164. Goldberg DJ, Russell BA. Combination blue (415nm) and red (633 nm) LED phototherapy in the treatment of mild to severe acne vulgaris. J Cosmet Laser Ther. 2006;8:71–5.

165. Lee SYC. Shedding light on acne: from myth to science (laser and light therapy for acne). In: Roth DE, editor. Dermatology research focus on acne. Hauppauge, NY: Nova Science Publishers, Inc; 2009.

166. Lee SY, You CE, Park MY. Blue and red light combination LED phototherapy for acne vulgaris in patients with skin phenotype IV. Lasers Surg Med. 2007;39:180–8.

167. Kim SJ, Lee Y, Seo YJ, Lee JH, Im M. Comparative Efficacy of Radiofrequency and Pulsed Dye Laser in the Treatment of Rosacea. Dermatol Surg. 2017;43:204–9.

168. Tambe SÁ, Nayak CS, Gala P, Zambare U, Nagargoje A. Management of rhinophyma with radio frequency: case series of three patients. J Cutan Aesthet Surg. 2019;12:136–40.

169. Schlessinger J, Lupin M, McDaniel D, George R. Safety and effectiveness of microfocused ultrasound for treating erythematotelangiectatic rosacea. J Drugs Dermatol. 2019;18:522.

170. Park JY, Ahn MK, Cho EB, Park EJ, Kim KH. Dual-Frequency ultrasound as a new treatment modality for refractory rosacea: a retrospective study. Dermatol Surg. 2018;44:1209–15.

171. Friedman O, Koren A, Niv R, Mehrabi JN, Artzi O. The toxic edge – a novel treatment for refractory erythema and flushing of rosacea. Lasers Surg Med. 2019;51:325–31.

172. Gratieri T, Alberti I, Lapteva M, Kalia YN. Next generation intra- and transdermal therapeutic systems: using non- and minimally-invasive technologies to increase drug delivery into and across the skin. Eur J Pharm Sci. 2013;50:609–22.

173. Sklar LR, Burnett CT, Walbel JS, Moy RL, Ozog DM. Laser assisted drug delivery: a review of an evolving technology. Lasers Surg Med. 2014;42:49–62.

174. Alster TS, Graham PM. Microneedling: a review and practical guide. Dermatologic Surgery. 2018;44:397–404.

175. Issa MCA, Barcau C, Mesquita AC, Franco de Sá FR, Azulay MA. Intense pulsed light alone versus intense pulsed light and aminolevulinic acid in the treatment of photodamaged skin: importance of long term follow-up. Surg Cosmet Dermatol. 2009;1:125–9.

176. Friedmann DP, Goldman MP, Fabi SG, Guilha I. Multiple sequential light and laser sources to activate aminolevulinic acid for rosacea. J Cosmetic Dermatol. 2016;15:407–12.

177. Bryd LE, Jemec GB. Photodynamic therapy in a series of rosacea patients. J Eur Acad Dermatol Venereol. 2007;21:1199–202.
187. Nybaek H, Jemec BG. Photodynamic therapy in the treatment of rosacea. Dermatolog. 2005;211:135–8.

188. Gaspar NK, Gaspar APA, Aidé MK. Rhinophyma: practical and safe treatment with trichloracetic acid. Surg Cosmet Dermatol. 2014;6:368–72.

189. Rohrich RJ, Griffin JR, Adams WP. Rhinophyma: review and update. Plast Reconstr Surg. 2002;110:860–9.

190. Lutz ME, Otlec CC. Rhinophyma and coexisting occult skin cancers. Dermatol. Surg. 2001;27:201–2.

191. Little SC, Stucker FJ, Compton A, Park SS. Nuances in the management of rhinophyma. Facial Plastic Surgery. 2012;28:231–7.

192. Greaney L, Singh NP, Roberts DN. Surgical management of rhinophyma. Clin Otolaryngol. 2010;35:158–9.

193. Rohrich RJ, Griffin JR, Adams WP Jr. Rhinophyma: review and update. Plast Reconstr Surg. 2002;110:860–9.

194. Sadick H, Goepel B, Borsche C, Goessler U, Hoermann K, Riedel F. Rhinophyma: diagnosis and treatment options for a disfiguring tumor of the nose. Ann Plast Surg. 2008;61:114–21.

195. Husein-ElAhmed H, Armitio-Lozano R. Management of severe rhinophyma with sculpting surgical decortication. Aesthetic Plast Surg. 2013;37:572–5.

196. Lazzera D, Larcher L, Huemer GM, Riml S, Grassetti L, Pantaloni M, et al. Surgical correction of rhinophyma: comparison of two methods in a 15-year-long experience. J Craniomaxillofac Surg. 2013;41:429–36.

197. Prado R, Funke A, Bingham J, Brown M, Ramsey Mellette J. Treatment of severe rhinophyma using scalpel excision and wire loop tip electrosurgery. Dermatol Surg. 2013;39:1556 [Erratum for: Dermatol Surg. 2013;39:807-10].

198. Fishman JM, Kundu S, Draper M. "A close shave" – use of a disposable razor blade in the management of rhinophyma. Ann R Coll Surg Engl. 2009;91:167.

199. Teimourian B, Duda G, Nickodem AM. Application of the argon beam coagulator in plastic surgery. Perspect Plast Surg. 1991;5:91–8.

200. Vural E, Royer MC, Kokosha MS. Sculpting resection of rhinophyma using the Shaw scalpel. Arch Facial Plast Surg. 2009;11:263–6.

201. Orenstein A, Haik J, Tamir J, Winkler E, Frad J, Zitinsky I, et al. Treatment of rhinophyma with Er:YAG laser. Lasers Surg Med. 2001;29:230–5.

202. Salem SA, Abdel Fattah NS, Tantawy SM, El-Badawy NM, Abd El-Aziz YA. Department of Dermatology and Venereology, Faculty of Medicine, Ain Shams University, Cairo, Egypt. J Cosmet Dermatol. 2013;12:187–94.

203. Meesters AA, Van der Linden M, De Rie MA, Walkerstorfer A. Fractionated carbon dioxide laser therapy as treatment of mild rhinophyma: report of three cases. Dermatologic Therapy. 2015;28:147–50.

204. Goon PK, Dalal M, Peart FC. The gold standard for decorcification of rhinophyma: combined erbium-YAG/CO2 laser. Aesthetic Plast Surg. 2004;28:456–60.

205. El-Domyati M, Hosam W, Abdel-Azim E, Hossam Abdel-Wahab H, Mohamed E. Micromdermabrasion: a clinical, histometric, and histopathologic study. J Cosmet Dermatol. 2016;15: 503–13.

206. Cemal F, Serkan E, Ahmet HA. An alternative microscopic method for decreasing bleeding and recurrence in the treatment of rhinophyma. Eur Rev Med Pharmacol Sci. 2012;16:418–21.

207. Spencer JM. Microdermabrasion. Am J Clin Dermatol. 2005;6:89–92.

208. Bhalla M, Thami GP. Microdermabrasion: reappraisal and brief review of literature. Dermatol Surg. 2006;32:809–14.

209. El-Domyati M, Medhat W. Minimally invasive facial rejuvena-
tion. Expert Rev Dermatol. 2013;8:565–80.

210. Badawi A, Soliman M, Sobhi R, Fawzy S. Microdermabrasion in cosmetic dermatology: a clinical study. J Cosmet Dermatol. 2006;19:191–8.

211. Cumeau V, Goodman M, Kober MM, Buckley C. Fractionated carbon dioxide laser resurfacing as an ideal treatment option for severe rhinophyma: a case report and discussion. J Clin Aesthetic Dermatol. 2019;12:24–7.

212. Vasconcellos BN, Vasconcellos JB, Fonseca JCM, Fonseca CR. Dermquimioabrasao: um tratamento eficaz e seguro para o rinofima. Surg Cosmet Dermatol. 2016;8:28–31.

213. Zide MF. Surgical removal of rhinophyma. J Oral Maxillofac Surg. 2008;66:2168–77.

214. Dayan SH, Ashourian N, Cho K. A pilot, double-blind, placebo-controlled study to assess the efficacy and safety of Incobotulinumtoxin A injections in the treatment of rosacea. J Drugs Dermatol. 2017;16:549–54.

215. Bloom BS, Payongayong L, Mourin A, Goldberg DJ. Impact of intradermal AbobotulinumtoxinA on facial erythema of rosacea. Dermatol Surg. 2015;41 Suppl 1:59–16.

216. Alexandroff AB, Sinclair SA, Langtry JA. Successful use of botulinum toxin A for the treatment of neck and anterior chest wall flushing. Dermatol Surg. 2006;32:1536.

217. Steroidinas A, Nicolaou M, Paes TR. Successful use of Botulinum toxin-A for the treatment of neck and anterior chest wall flushing. Clin Exp Dermatol. 2003;28:592–4.

218. Yuraitis M, Jacob CI. Botulinum toxin for the treatment of facial flushing. Dermatol Surg. 2004;30:102–4.

219. Campanati A, Martina E, Giuliolodi K, Consales V, Bobyr I, Offiani A. Botulinum toxin off-label use in dermatology: a review. Skin Appendage Disord. 2017;3:39–56.

220. Hsu TS, Dover JS, Arndt KA. Effect of volume and concentration on the diffusion of botulinum exotoxin A. Arch Dermatol. 2004;140:1351–4.

221. Kim MJ, Kim JH, Cheon HI, Hur MS, Han SH, Lee YW, et al. Assessment of skin physiology change and safety after intradermal injections with botulinum toxin: a randomized, double-blind, placebo-controlled, split-face pilot study in rosacea patients with facial erythema. Dermatol Surg. 2019;45:1155–62.

222. Silva LC, Ferreira ILO, Silveira ML, Steiner D. Prospective study for the treatment of rosacea flushing with botulinum toxin type A. Surg Cosmet Dermatol. 2018;10:121–6.

223. Bedewi AEI. The effect of Mesobotox together with intense pulsed light on facial wrinkles and erythema. JCDSA. 2012;2:16–9.

224. Clift SH, Judodihardjo H, Eltringham E. Different formulations of botulinum toxin type A have different migration characteristics: a double-blind, randomized study. J Cosmet Dermatol. 2008;7:50–4.

225. Trindade de Almeida AR, Marques E, de Almeida J, Cunha T, Boraso R. Pilot study comparing the diffusion of two formulations of botulinum toxin type A in patients with forehead hyperhidrosis. Dermatol Surg. 2007;33:37–43.

226. Antonio CR, Tridico LA, Antonio JR. Tratamento de rosácea com toxina botulinica. Surg Cosmet Dermatol. 2018;10:36–9.

227. Kranendonk SK, Ferris LK, Obagi S. Re: botulinum toxin for the treatment of facial flushing. Dermatol Surg. 2005;31:491.

228. Li J, Li M, Chen Q, Fu J, Zhang M, Hao F. Quality of life among patients with rosacea: an investigation of patients in China using two structured questionnaires. J Eur Acad Dermatol Venereol. 2016;30:98–9.

229. Deng Y, Peng Q, Yang S, Jian D, Wang B, Huang Y, et al. The Rosacea-specific Quality-of-Life instrument (RosQol): revision and validation among Chinese patients. PLoS One. 2018;13:e0192487.
Consensus on the therapeutic management of rosacea

221. Ousseddik E, Bourcier M, Tan J. Psychosocial Burden and Other Impacts of Rosacea on Patients’ Quality of Life. Dermatol Clin. 2018;36:103–13.

222. Nicholson K, Abramova L, Chen MM, Yeung J, Chon SY, Chen SC. A pilot quality-of-life instrument for acne rosacea. J Am Acad Dermatol. 2007;57:213–21.

223. Tannus F, Piccoso FR, Soares JLM, Bagatini E. Rosacea-specific Quality of Life Questionnaire (RosaQol): translation, cultural adaptation and validation into Brazilian-Portuguese language. An Bras Dermatol. 2018;93:836–42.

224. Vera N, Patel NU, Serninario-Vidal L. Rosacea Comorbidities. Dermatol Clin. 2018;36:115–22.

225. Aksoy B, Ekiz Ö, Unal E, Ozaydin YG, Gonul M, Kulcu CS, et al. Systemic comorbidities associated with rosacea: a multicentric retrospective observational study. Int J Dermatol. 2019;58:722–8.

226. Hua TC, Chung PI, Chen YJ, Wu LC, Chen YD, Hwang CY, et al. Cardiovascular comorbidities in patients with rosacea: a nationwide case-control study from Taiwan. J Am Acad Dermatol. 2015;73:249–54.

227. Egeberg A, Hansen PR, Gislason GH, Thyssen JP. Patients with rosacea have increased risk of dementia. Ann. Neurol. 2016;79:921–8.

228. Egeberg A, Hansen PR, Gislason GH, Thyssen JP. Exploring the association between rosacea and Parkinson disease: a Danish nationwide cohort study. JAMA Neurol. 2016;73:529–34.

229. Haber R, El Gemayel M. Comorbidities in rosacea: a systematic review and update. J Am Acad Dermatol. 2018;78:786–92.

230. Egeberg A, Ashina M, Gaist D, Gislason GH, Thyssen JP. Prevalence and risk of migraine in patients with rosacea: a population-based cohort study. J Am Acad Dermatol. 2017;76:454–8.

231. Egeberg A, Hansen PR, Gislason GH, Thyssen JP. Association of rosacea with risk for glioma in a Danish nationwide cohort study. JAMA Dermatol. 2016;152:541–5.

232. Bagchi S. Link between rosacea and glioma in nationwide cohort. Lancet Oncol. 2016;17:e94.

233. Gallo RL, Granstein RD, Kang S, Mannis M, Steinhoff M, Tan J, et al. Rosacea comorbidities and future research: the 2017 update by the National Rosacea Society Expert Committee. J Am Acad Dermatol. 2018;78:167–70.

234. Hung CT, Chiang CP, Chung CH, Tsao CH, Chien WC, Wang WM. Risk of psychiatric disorders in rosacea: a nationwide, population-based, cohort study in Taiwan. J Dermatol. 2019;46:110–6.

235. Spoendlin J, Karatas G, Furlano RI, Jick SS, Meier CR. Rosacea in patients with ulcerative colitis and Crohn’s disease: a population-based case-control study. Inflamm. Bowel Dis. 2016;22:680–7.

236. Wu CY, Chang YT, Juan CK, Shieh JJ, Lin YR, Liu HN, et al. Risk of inflammatory bowel disease in patients with rosacea: results from a nationwide cohort study in Taiwan. J Am Acad Dermatol. 2017;76:911–7.

237. Lim HG, Fischer A, Rueda MJ, Kendall J, Kang S, Chien AL. Prevalence of gastrointestinal comorbidities in rosacea: comparison of subantimicrobial, modified release doxycycline versus conventional release doxycycline. J Am Acad Dermatol. 2018;78:417–9.

238. Egeberg A, Fowler JF Jr, Gislason GH, Thyssen JP. Rosacea and risk of cancer in Denmark. Cancer Epidemiol. 2017;47:76–80.

239. Li WQ, Zhang M, Danby FW, Han J, Qureshi AA. Personal history of rosacea and risk of incident cancer among women in the US. Br J Cancer. 2015;113:520–3.

240. Tjahjono LA, Cline A, Huang WW, Fleischer AB Jr, Feldman SR. Rosacea: relative risk versus absolute risk of malignant comorbidities. J Am Acad Dermatol. 2019;81:623–4.

241. Pindado-Ortega C, Saceda-Corralo D, Buendía-Castaño D, Fernández-González P, Moreno-Arrones OM, Fonda-Pascual P, et al. Frontal fibrosing alopecia and cutaneous comorbidities: a potential relationship with rosacea. J Am Acad Dermatol. 2018;78:596–7.

242. Egeberg A, Hansen PR, Gislason GH, Thyssen JP. Clustering of autoimmune diseases in patients with rosacea. J Am Acad Dermatol. 2016;74:667–72.

243. Holmes AD, Spoendlin J, Chien AL, Baldwin H, Chang ALS. Evidence-based update on rosacea comorbidities and their common physiologic pathways. J Am Acad Dermatol. 2018;75:156–66.

244. Nam JH, Yang J, Park J, Seo JH, Chiang Y, Ryu S, et al. Association between rosacea severity and relative muscle mass: a cross-sectional study. J Dermatol. 2019;46:11–7.

245. Kaminsky A, Florez WM, Piquero MJ, Herane M, Dietz MJC, Raimondo N, et al. Informe de Consenso Ibero-Latinoamericano 2016 sobre la clasificación clínica y terapéutica de la rosácea. Med Cutan Iber Lat Am. 2016;44:6–10.

246. Asai Y, Tan J, Baibergenova A, Barankin B, Cochrane CL, Humphrey S, et al. Canadian Clinical Practice Guidelines for Rosacea. J Cutan Med Surg. 2016;20:432–45.

247. Schaller M, Almeida LMC, Bewley A, Cribier B, Divo NC, Kautz G, et al. Rosacea treatment update: recommendations from the global ROSacea Consensus (ROSCO) panel. Br J Dermatol. 2017;176:465–71.

248. Del Rosso JQ, Tanghetti E, Webster G, Gold LS, Thiboutot D, Gallo RL, et al. Update on the Management of Rosacea from the American Acne & Rosacea Society (AARS). J Clin Aesthet Dermatol. 2019;12:17–24.