American Journal of Clinical Dermatology
https://doi.org/10.1007/s40257-022-00746-4

REVIEW ARTICLE

Truncal Acne and Scarring: A Comprehensive Review of Current Medical and Cosmetic Approaches to Treatment and Patient Management

Stefano G. Daniele[1] · Sa Rang Kim[2] · Ayman Grada[3] · Angela Y. Moore[4,5] · Kathleen C. Suozzi[2] · Christopher G. Bunick[2,6]

Accepted: 27 November 2022

Abstract
Acne vulgaris is one of the most common skin disorders worldwide. It typically affects skin areas with a high density of sebaceous glands such as the face, upper arms, chest, and/or back. Historically, the majority of research efforts have focused on facial acne vulgaris, even though approximately half of patients with facial lesions demonstrate truncal involvement. Truncal acne vulgaris is challenging to treat and poses a significant psychosocial burden on patients. Despite these characteristics, studies specifically examining truncal acne vulgaris are limited, with treatment guidelines largely derived from facial protocols. Therefore, truncal acne remains an understudied clinical problem. Here, we provide a clinically focused review on the epidemiology, evaluation, and available treatment options for truncal acne vulgaris. In doing so, we highlight knowledge gaps with the goal of spurring further investigation into the management of truncal acne vulgaris.

Key Points

The majority of acne literature and treatment guidelines have focused on facial acne, despite nearly 50% of patients with acne exhibiting lesions on the trunk and the negative impact truncal acne has on a patient's quality of life.

We comprehensively review the current clinical knowledge regarding the medical management of truncal acne and the cosmetic interventions that can be utilized to ameliorate its consequences.

New targeted, effective, and safe therapies for truncal acne, along with its scarring sequelae, are needed to enhance the quality of life of patients with acne.

1 Introduction

Acne vulgaris (AV) is one of the most common skin disorders, present in nearly 10% of all individuals worldwide [1]. While AV affects more than 85% of adolescents, it often continues well into the fifth decade of life for both men and women [2, 3]. It is a multifactorial inflammatory condition of the pilosebaceous unit characterized by the appearance of various cutaneous lesions including closed and open comedones, inflammatory papules and pustules, nodules, and cysts. These lesions are typically limited to skin areas with a high density of sebaceous glands such as the face, shoulders, and trunk (chest and/or back) [4].

The majority of AV literature and guidelines have focused on facial acne [5, 6], despite the high percentage of patients exhibiting lesions on both the face and trunk [7–9] and the

✉ Christopher G. Bunick
christopher.bunick@yale.edu

1 Medical Scientist Training Program, Yale School of Medicine, New Haven, CT, USA

2 Department of Dermatology, Yale School of Medicine, New Haven, CT, USA

3 Department of Dermatology, Case Western Reserve University School of Medicine, Cleveland, OH, USA

4 Arlington Research Center, Arlington, TX, USA

5 Baylor University Medical Center, Dallas, TX, USA

6 Program in Translational Biomedicine, Yale School of Medicine, New Haven, CT, USA

Published online: 20 December 2022

negative impact of truncal acne on a patient's quality of life [9–11]. The overall paucity of clinical data and management options dedicated to truncal acne may be due in part to the greater visibility of facial lesions compared with lesions on the trunk. As such, truncal acne is a largely underappreciated clinical problem that requires further attention.

2 Methodology

We performed a literature search of articles published from inception to April 2022 on the topic of truncal acne, querying PubMed for the keywords: "Truncal Acne;" "Trunk" AND "Acne;" "Chest" AND "Acne;" "Back" AND "Acne;" "Acne Conglobata;" "Acne Fulminans;" "Truncal Acne" AND "Scars;" "Truncal acne" AND "Laser;" and "Acne scars" AND "[name of treatment modality]". Treatment modalities were determined based on the availability of treatments in an outpatient setting and the authors' experience with acne scarring. These included: pulsed dye laser, intense pulsed light, ablative fractional laser, non-ablative fractional laser, picosecond laser, microneedling, radiofrequency, intralesional corticosteroid/triamcinolone, 5-fluorouracil (5-FU), poly-L-lactic acid, and polymethylmethacrylate. Queries were also performed with the application of filters for randomized clinical trials, systematic reviews, and reviews. Further searches were conducted to expand the queries for the epidemiology, evaluation, grading scales, differential diagnosis, treatment, and the psychological/quality-of-life burden associated with truncal acne. Article titles and abstracts were screened for review. Only articles written in the English language were considered and subsequently selected based on their relevance to the topics described herein. In cases where data were not available for truncal acne, articles from the facial acne literature were included and facial data were denoted in the text. We additionally searched the references of selected articles for appropriate and related articles. Other articles were also included after the initial search period and initial article submission based on new publications. A systematic review was not performed.

3 Background

3.1 Epidemiology

One of the first cohort studies ($n = 696$) evaluating the prevalence of truncal AV in patients aged 14–20 years found that 52.3% of patients with facial acne also had truncal involvement, while only 2.3% of patients presented with truncal acne alone [7]. Of note, 22.4% of patients who presented with a chief complaint of facial acne were found to have truncal lesions only after examination of the chest and/or back [7], underscoring the importance of thoroughly evaluating extra-facial involvement. Importantly, 78.2% of these patients desired treatment for their truncal acne, irrespective of whether truncal lesions were part of their main concern [7]. In a separate cohort of 965 patients with AV, 45% and 61% exhibited acne on the chest and back, respectively [12]. Moreover, approximately 33% of these patients erroneously denied any truncal involvement, emphasizing the necessity of properly examining the chest and back, as patients may not fully recognize the breadth of their AV. In the largest European cohort of 2926 patients, 35.6% of all patients displayed lesions on both the face and trunk, with men exhibiting a greater likelihood of truncal involvement (48.6% vs 30.8% [female]; $p < 0.0001$) and scarring (50.7 vs 44.5 [female]; $p < 0.0042$) [13]. In a smaller cohort of 98 Portuguese medical students, a similar proportion (36.1%) exhibited AV lesions on both the face and back [14]. However, in the STRIDE online survey, a greater proportion of respondents (53%; $n = 694/1309$) had both facial and truncal AV [9], a finding supported by the Wakefield online survey, which revealed that 51% ($n = 1019/2000$) of individuals reported facial and truncal involvement [15]. In the STRIDE study, of the individuals who reported facial and truncal involvement, 54.3% had face and back only; 38.5% had face, chest, and back; and 7.3% had face and chest only [9]. Importantly, analysis of acne severity in these latter two studies also appeared to serve as a prognostic risk factor for truncal involvement [9, 15].

Other studies have focused on male, female, and transgender rates of truncal acne. In a cohort of 2200 18-year-old Brazilian male individuals, Isaacsson et al. report that 76.2% of patients had facial acne, while 31.1% of patients displayed back lesions and 50.1% exhibited chest lesions [16]. In a separate cohort of 374 adult women, 89.8% of patients exhibited facial acne while 48.4% of patients had truncal acne [17]. Considering the close pathogenic relationship between androgens and acne [4], it is important for dermatologists to recognize truncal AV in transgender patients [18]. In a prospective study evaluating acne in 20 transgender men undergoing gender-affirming hormonal therapy, acne on the chest and/or back increased from a baseline of 15% to 88.2% after 6 months of androgen therapy, ultimately decreasing to 50% after 12 months of therapy [19].

Overall, these studies indicate that truncal AV occurs in approximately 50% of patients with facial acne without a clear predilection for either the chest or back based on the limited epidemiological studies available. Further information regarding the epidemiology of truncal acne, including the age-based distribution, has been reviewed previously

[15]. Moving forward, large-scale international studies are needed to accurately quantify the global incidence and prevalence of truncal AV, as well as to assess possible variations in chest and/or back acne—especially as they pertain to unique subgroups such as age, sex, ethnicity, and severity.

3.2 Distinguishing Truncal Acne

When evaluating patients for the presence of truncal AV (Fig. 1), it is important to remain mindful of other skin conditions that may present with similar clinical findings. The primary entities in the differential diagnosis of truncal AV include folliculidities of varying etiologies, such as bacterial folliculitis, Malassezia (Pityrosporum) folliculitis, and immunosuppression-associated eosinophilic folliculitis, along with demodicosis, acneiform drug eruptions, miliaria rubra, and transient acantholytic dermatosis (Fig. 2).

Bacterial folliculitis (Fig. 2a) can mimic and co-exist with truncal AV. It is most commonly caused by *Staphylococcus* and Gram-negative bacteria [20]. Bacterial folliculitis can be distinguished from AV by the lack of comedones associated with monomorphic pustules. The type of bacterial folliculitis that most readily mimics the corporeal distribution of truncal AV is *Pseudomonas* folliculitis, which is associated with the use of spas, hot tubs, or swimming pools—colloquially known as "hot-tub folliculitis" [21]. A patient history detailing such activities 24–48 hours before presentation raises clinical suspicion for Pseudomonal etiology. In these patients, pustule cultures reveal the presence of *Pseudomonas*, and lesions usually resolve without treatment after several days. Gram-negative folliculitis can also result from antibiotic use, particularly in the setting of AV treatment. Long-term use of broad-spectrum antibiotics can disrupt the normal cutaneous flora, leading to the replacement of Gram-positive microbes with the overgrowth of Gram-negative bacteria, including *Pseudomonas* [22]. Therefore, Gram-negative folliculitis should be considered in patients with a history of prolonged oral antibiotic use, especially in patients with recalcitrant AV. Other features of Gram-negative folliculitis include male predominance, Gram-negative isolation from nares, and hyperseborrhea. Gram-negative folliculitis secondary to *Pseudomonas* tends to self-resolve within a week with good skin hygiene; however, oral ciprofloxacin 250–750 mg twice daily can be utilized in patients with widespread skin involvement [23]. For non-Pseudomonal Gram-negative culprits, ampicillin 250–500 mg four times daily or trimethoprim-sulfamethoxazole 160/800 mg (double strength) twice daily for 2 weeks typically suffices. For recalcitrant Gram-negative folliculitis, patients can be treated with isotretinoin 0.5–1.0 mg/kg daily for 4–5 months, which is the preferred treatment [22].

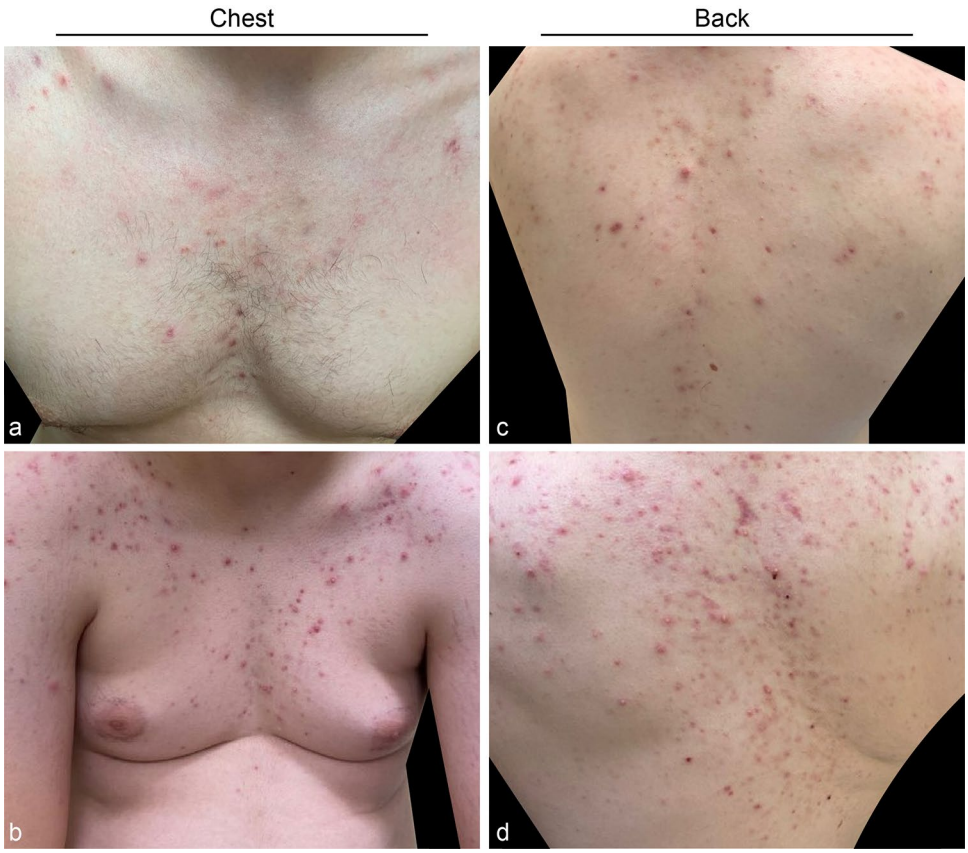

Fig. 1 Truncal acne vulgaris. Clinical images of acne vulgaris affecting the chest (**a**, **b**) and back (**c**, **d**). Erythematous inflammatory papules and pustules can be seen on the chest and back (**a–d**), along with nodular lesions on the back (**c**, **d**). General chest- and back-specific distribution patterns can also be observed in patients. Specifically, chest acne frequently drapes across the clavicles towards the sternum with a concentration often seen centrally over the sternum. On the back, acne often presents broadly across the upper back and tapers centrally over the spine

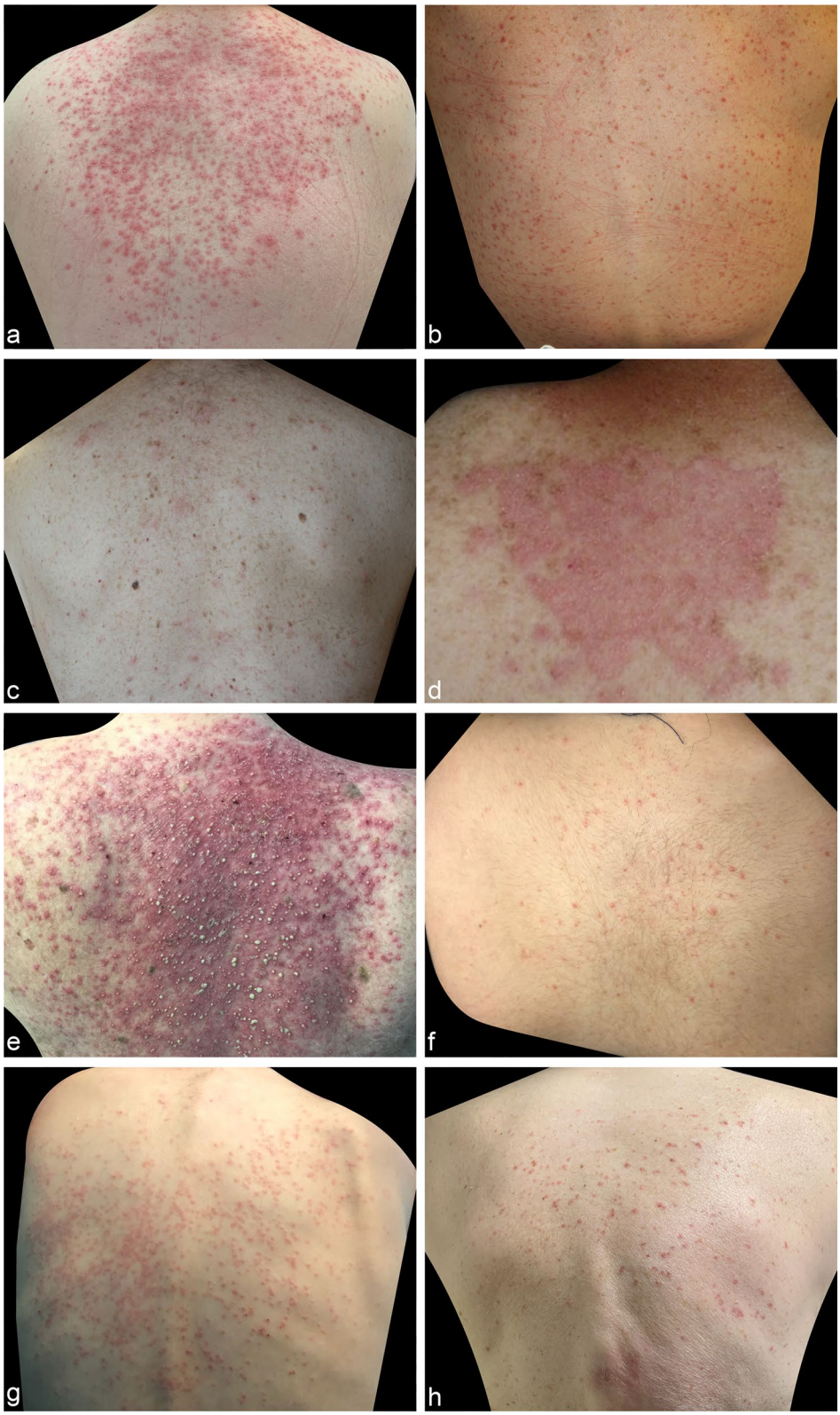

Fig. 2 Differential diagnosis for truncal acne illustrated through disease on the back. Clinical images of bacterial folliculitis (**a**), *Malassezia* folliculitis (**b**), eosinophilic folliculitis (**c**), *Demodex* folliculitis (**d**), acneiform drug eruption following epidermal growth factor receptor inhibitor (**e**), acneiform drug eruption following corticosteroid use (**f**), miliaria rubra (**g**), and transient acantholytic dermatosis (**h**). The image in (**d**) courtesy of T.J. Orlowski, MD; H.H. Reynolds, MD; and L.V. Graham, MD, PhD. from [60]

Malassezia (*Pityrosporum*) folliculitis (Fig. 2b) is an inflammatory skin disorder that mainly affects the trunk and is caused by the overgrowth of the lipophilic yeast, *Malassezia furfur* [24]. It can be distinguished from truncal AV by a microscopic assessment of follicular pustule content using a potassium hydroxide preparation, which

characteristically shows clusters of round spores and hyphal elements [25]. *Malassezia* can also be detected on a skin biopsy with periodic acid-Schiff staining, demonstrating yeast clusters and inflammatory cells within dilated follicles [26]. Other features more consistent with *Malassezia* include increased lesional pruritus [27], the absence of cysts or comedones [28], and, importantly, swift resolution with antifungal agents and exacerbation with antibiotics [25]. Of note, both AV and *Malassezia* can co-exist in patients [13, 29], making patient-tailored treatment plans essential for optimal management. Treatment options for *Malassezia* include systemic antifungal agents such as oral fluconazole 100–200 mg daily up to 4 weeks [30], or topical agents including ketoconazole and selenium sulfide shampoos [25].

Another folliculitis often misdiagnosed as truncal AV is immunosuppression-associated eosinophilic folliculitis (EF; Fig. 2c), which is characterized by relapsing waves of sterile pruritic follicular papules and pustules commonly affecting the trunk of HIV-positive men [31]. In women with HIV-associated EF, facial involvement may be the primary site in contrast to the trunk [32]. Patients with hematologic malignancies have also been reported to present with EF [33, 34]. This form is distinct from classical eosinophilic pustular folliculitis, also known as Ofuji disease, owing to the absence of typical arcuate or annular plaques with central-clearing and pink pustule-studded borders [35]. The invariant feature of immunosuppression-associated EF is intense pruritus, which is infrequently reported in truncal AV. Histopathological analysis of skin biopsies demonstrates characteristic eosinophilic spongiosis in the epithelial layer of the follicular infundibulum with eosinophilic infiltrate of the follicle. In HIV-associated cases, patients typically have CD4+ counts below 200 cells/mm^3, although it can occur with higher CD4 counts [32]. Patients with HIV infection who present with EF should be started on anti-retroviral therapy and topical corticosteroids to affected areas; antipruritic medicines such as antihistamines may help treat EF-associated pruritus [36].

Demodex folliculitis (Fig. 2d), also known as demodicosis, is a skin disease caused by over-colonization of the pilosebaceous unit by the saprophytic mites, *Demodex folliculorum* or *Demodex brevis*. *Demodex* folliculitis shares many cutaneous features with AV, and can lead to misdiagnosis [37]. Patients with *Demodex* folliculitis display cutaneous lesions of varying severity and morphology including follicular papules, pustules, or nodules [38]. Similar to *Malassezia*, one of the cardinal features is lesional pruritus, which is usually absent in AV. Diagnosis is made with an increased mite density (> 5 organisms/cm^2) as assessed by a standard skin surface biopsy [39], or superficial needle scraping of pustular lesions followed by mineral oil preparation and visualization with light microscopy [40]. Further studies have shown an increased rate of demodicosis in patients with AV, indicating that *Demodex* infestation should be considered in patients with treatment-resistant AV [41]. Treatments include oral therapies such as metronidazole and ivermectin, as well as topical treatments including permethrin, crotamiton, and benzoyl benzoate [42–44].

Drug-induced acne is another cutaneous process that mimics AV. While there are no firm criteria to define drug-induced AV, the temporal relationship between the start of a medication and the appearance of monomorphic comedone-free inflammatory lesions provides support for a drug-induced reaction. Furthermore, acneiform drug eruptions improve after discontinuation of the culprit medication and recur with rechallenge. Multiple drugs have been reported to cause acneiform eruptions, including epidermal growth factor receptor inhibitors (Fig. 2e) [45], topical and systemic corticosteroids (Fig. 2f) [46], anti-epileptic drugs [47], lithium [48], Janus kinase inhibitors [49], and many others [50, 51]. Treatment often depends on the severity of the eruption. Tetracycline-based antibiotics and topical tazarotene are often utilized to mitigate severe reactions [51, 52]; however, although rare, discontinuation of the drug may be required.

Last, miliaria rubra (Fig. 2g) and transient acantholytic dermatosis (Fig. 2h) are processes that present clinically like truncal AV. Miliaria rubra is caused by obstruction of eccrine sweat glands, leading to the retention of sweat within the epidermis and dermis [53]. Typically affecting the trunk, miliaria is characterized by pink non-follicular macules and papules, which may also contain a central vesicle. It can be distinguished from truncal AV via its minimal follicular involvement, along with intense pruritic or stinging sensations that are usually precipitated by circumstances that promote sweating. Furthermore, skin occlusion, such as from tight non-breathable clothing [54] or bandages/patches [55] can also cause miliaria. Because hot and humid environments are the most significant factors contributing to the development of miliaria, its treatment mainly centers on reducing the patient's exposure to heat and humidity, or removal of occlusive materials. Transient acantholytic dermatosis, also called Grover's disease, presents with monomorphic red, scaly papules, and papulovesicles usually distributed along the trunk. Like miliaria, the condition is associated with excess heat and sweating [56], and has been described in patients with prolonged bedrest [57]; other causes include ionizing radiation and various medications [58, 59]. Lesions are typically pruritic, which may promote excoriations. Treatment usually consists of avoiding heat and sweating, application of emollients, and the use of topical corticosteroids [56, 59].

3.3 On the AV Spectrum: Acne Conglobata, Follicular Occlusion Tetrad, and Acne Fulminans

Acne conglobata (AC) is a severe and rare form of inflammatory AV that typically affects the chest and/or back. While AC is on the spectrum of AV, its severity and high rates of scarring necessitate specific management, differentiating it from typical truncal AV. Major clinical features distinguishing AC from AV include the presence of polyporous comedones, cysts, abscesses, and sinus tracts that often drain purulent malodorous fluid; scar formation along with disfigurement is a prominent and common consequence [61–63]. History should be obtained from the patient in regard to performance-enhancing supplements as AC has been associated with the use of anabolic steroids and is common in bodybuilders [64]. It has also been observed after administration of high-dose testosterone therapy for the treatment of hereditary tall stature [65]. While AC can occur alone, when it coincides with hidradenitis suppurativa, dissecting cellulitis of the scalp, and pilonidal disease [63], it becomes part of a rare syndrome known as the "follicular occlusion tetrad" [66–68]. These four conditions share common pathogenic processes consisting of follicular occlusion and rupture, suppurative inflammation, bacterial overgrowth, and sinus tract formation. Treatment for AC can be challenging as it is often resistant to therapy, but includes isotretinoin 0.5–1 mg/kg daily for multiple months [6, 69] with the possible combination of oral prednisone 1 mg/kg daily for several weeks should patients exhibit systemic symptoms such as fever, malaise, and weight loss [61, 67]. Oral antibiotics such as minocycline in combination with azelaic acid may also be utilized when patients do not tolerate isotretinoin [6, 70]. Simultaneous use of systemic retinoids and tetracycline class antibiotics should be avoided to prevent the development of drug-induced intracranial hypertension (also known as pseudotumor cerebri) [71]. While large-scale trials have not yet been conducted, beneficial effects of adalimumab [62, 72] and infliximab [73] have been described in individual case reports and warrant further investigation.

Acne fulminans is another severe variant of inflammatory acne. It is characterized by an abrupt and dramatic flare of inflammatory lesions with erosions, ulcerations, and hemorrhagic nodules. Acne fulminans can present with or without systemic symptoms (i.e., fever, malaise, arthralgias) [74]. Isotretinoin therapy, specifically when initiated at high doses, may precipitate acne fulminans in patients with severe AV [74, 75]. Treatment consists of immediate use of systemic corticosteroids (0.5–1.0 mg/kg daily) for 2–4 weeks depending on the presence of systemic symptoms and until lesions have healed [74]. Afterwards, low-dose isotretinoin can be started (0.1 mg/kg daily) in conjunction with systemic corticosteroids for at least 4 weeks followed by a gradual steroid taper and concurrent increase in isotretinoin dosing [74].

3.4 Psychosocial Burden of Truncal Acne

Truncal acne significantly impacts a patient's quality of life. An international cross-sectional survey ($n = 1309$) aimed at evaluating the relationship between acne site and quality of life found that individuals with both facial and truncal acne experienced a greater negative impact on their lives as compared with individuals with facial acne alone [9]. Specifically, individuals with truncal acne felt embarrassed to wear clothing that revealed their lesions or attend the beach or pool. Site-specific influences also exhibited differential effects on men and women: while facial acne was associated with greater self-consciousness in women, back acne significantly affected sexual and body self-consciousness in both men and women [11]. The substantial psychological effect that truncal acne exerts on a patient's life is corroborated by the unanimous consensus ($n = 13/13$) of the Experts Panel that truncal acne has a "specific impact on patients that is distinct from that of facial acne" [76]. Indeed, the psychological impact of adult acne can be as severe as other chronic conditions such as asthma, epilepsy, and arthritis [77].

4 Evaluating Truncal Acne

Grading systems are an important clinical tool to help determine disease severity, guide patient care, and measure treatment progress. There is an increasing number of evaluation tools available to clinicians, with no universally agreed upon standard. Unique scales exist for multiple facets of AV: severity [78, 79], number of lesions [80], and anatomical sites affected [81]. There are also scales for scarring [82–84] and the psychological factors associated with acne [77, 85, 86]. In total, more than 25 grading systems exist and have been reviewed previously [87–89]. More recently, two additional scales have been developed. The first aims to create a global grading system that accounts for primary lesions (i.e., types of lesions) and secondary changes (i.e., scarring and post-inflammatory changes) [90]. The second is a grading tool specifically designed to evaluate the global impact of truncal AV, incorporating the patient's disease and family history, disease severity, and quality of life into one holistic score [91]. This latter system joins five other scoring tools described in the English literature that have been utilized for truncal acne [7, 76, 79, 81, 89] (Table 1). As more research trials begin to evaluate the efficacy of novel therapies for treating truncal AV specifically, it will be essential for the AV field to reach a consensus on a global grading standard against which rigorous comparative analyses can be

Table 1 Comparison of grading systems that have been utilized for truncal acne. Only assessment tools from the English literature were included

Grading system	GAGS [89]	LRAG [79]	CASS [81]	Del Rosso et al. [7]	PGA [76]	TRASS [91]
Grading methods and notes	Considers 6 locations on the face, chest, and upper back. Each location is graded separately on a 0–4 scale based on the presence of primary lesions (0: no lesion; 1: ≥ one comedone; 2: ≥ one papule; 3: ≥ one pustule; 4: ≥ one nodule). Local scores are multiplied by site-specific factors (1, 2, 3) and then summed to give a global severity score	Revision of the original Leeds Grading System [92]. Numeric grading for the face, chest, and back based on photographic templates for each anatomical site. This system comprises 12 grades for the face and 8 grades for the chest and back. For the chest and back, grades 1–3: mild; grades 4–5: moderate; grades 6–8: severe	6-point severity grading scale adapted from the IGA for assessing acne burden on the face. Repurposed for the chest and back. Grade 0: clear; 1: almost clear; 2: mild; 3: moderate; 4: severe; 5: very severe. Each grade is associated with a text description	Severity score based on the numeric range of lesions for each primary lesion type on either the back or chest	Historically used to assess the severity of facial acne, but applied to the trunk in a recent clinical trial. The system consists of a 5-point severity scale. Grade 0: clear; 1: almost clear; 2: mild; 3: moderate; 4: severe. Each grade is associated with a text description	Total severity score (0–19) based on the summation of 3 sub-scores. Sub-score 1 assesses severity based on disease and family history. Sub-score 2 assesses severity based on anatomical distribution, presence of nodules, and presence of secondary changes. Sub-score 3 assesses severity based on impact on quality of life
Considers psychosocial effects of lesions?	No	No	No	No	No	Yes
Considers secondary changes?	No	No	No	No	No	Yes
Considers primary lesion type and/or count?	Yes	No[a]	Yes	Yes	Yes	Yes
Based on photographic material?	No	Yes	No	No	No	No
Based on textual description?	No	No	Yes	No	Yes	No
Reported sensitivity to change?	No	No	Yes	No	Yes	No
Reported intra-rater reliability?	No	No[b]	No	No	No	No
Reported inter-rater reliability?	No	No[b]	No	No	No	No

CASS Comprehensive Acne Severity Scale, *GAGS* Global Acne Grading System, *IGA* Investigator's Global Assessment, *LRAG* Leeds Revised Acne Grading, *PGA* Physician's Global Assessment, *TRASS* Truncal Acne Severity Scale

[a]A separate 3-point grading scale is described to assess non-inflammatory lesions.

[b]LRAG is based on the original Leeds Grading System [92], which reported both intra- and inter-rater reliability; however, LRAG did not report these metrics

conducted to determine the relative efficacies of each treatment for different anatomical sites.

5 Management of Truncal AV

Despite its well-established prevalence, psychological effects, and potential for physical disfigurement, therapy guidelines specifically tailored for truncal AV remain an unmet clinical need [93, 94]. For the limited number of trials examining topical and oral therapies for truncal AV (Table 2), the protocols have been largely derived from facial AV studies. As such, trunk-specific protocols and guidelines are necessary to optimize care for truncal patients with AV. Currently, both topical and systemic treatments are utilized in the management of truncal AV; the clinical efficacy, advantages, and limitations for each treatment are discussed below. Other forms of clinical management, including preventative measures, adequate skin care, and extensive counseling are not reviewed, but have been described elsewhere [8, 94].

5.1 Topical Therapies

Topical formulations are commonly utilized for mild truncal AV. Currently, common regimens include benzoyl peroxide (BPO), topical antibiotics, and first- or second-generation retinoids, either as single agents or in combination. Recently, several topical agents have been evaluated for truncal AV, including trifarotene [76], tazarotene [95], azelaic acid [96], and dapsone [97].

5.1.1 BPO

One of the major advantages of BPO, a bactericidal agent, is that it has been shown to help reduce antibiotic-resistant strains of *Cutibacterium acnes* [98–100]. It is made in wash, bar, foam, gel, and cream formulations, with some studies reporting a potential advantage of foams when applying to the large and often hairy surface areas of the trunk [101]. Specific formulations have also been designed for leave-on or wash-off applications. Benzoyl peroxide reduced *C. acnes* colony density on participants' backs using both the 5.3% foam leave-on formulation [102], or the 9.8% wash-off formulation with a 2-minute contact time [103]. However, no placebo-controlled trials have examined the efficacy of BPO in treating truncal AV. Despite the lack of randomized controlled trials, it remains a commonly prescribed therapy [93]. Benzoyl peroxide is also frequently used and recommended in combination with topical antibiotics and/or retinoids [5], with evidence supporting its use in truncal AV primarily derived from its efficacy in treating facial AV [104–107]. One of its disadvantages is its ability to bleach hair, clothing, and linens, with patients often preferring the wash-off formulation to minimize these effects.

5.1.2 Antibiotics

Topical antibiotics such as clindamycin, erythromycin, and minocycline are other anti-microbials utilized for AV. These agents function against the overgrowth of *C. acnes* through both antibacterial and anti-inflammatory mechanisms [108], but can induce bacterial resistance when used as monotherapies [109]. Studies demonstrated that combination therapy of topical antibiotics with BPO effectively decreased facial colonization of antibiotic-resistant strains of *C. acnes* [98], ultimately leading to treatment guidelines formally discouraging topical antibiotics as monotherapies [5]. Multiple trials have evaluated the superiority of fixed-combination treatments consisting of topical antibiotics and BPO (i.e., clindamycin 1% + BPO 5%) in facial AV [106, 110–115], but no similar trial has been conducted for truncal AV. Furthermore, topical minocycline in a 4% foam formulation has been recently US Food and Drug Administration (FDA) approved for the treatment of moderate-to-severe facial AV [116]. One of the major advantages of the topical formulation includes its favorable safety profile in comparison to systemic minocycline [117]. Pooled analyses from two phase III, randomized, vehicle-controlled studies ($n = 640$ [minocycline 4% foam] and $n = 321$ [vehicle] across both trials) demonstrated that topical minocycline applied once daily to the face for 12 weeks resulted in a greater Investigator's Global Assessment (IGA) success rate versus the vehicle control (5.17% vehicle-controlled rate; $p = 0.0188$) [118]. However, further studies will be required to assess the efficacy of topical minocycline for treating truncal AV.

5.1.3 Retinoids

Another class of topical therapeutics are retinoids such as tretinoin, adapalene, tazarotene, and trifarotene. Topical retinoids prevent microcomedones, normalize follicular keratinization, reduce inflammation, and are an effective core therapy for AV [119, 120]. Food and Drug Administration approved for facial AV, tazarotene 0.045% lotion has been recently evaluated for treating truncal acne. In a small non-controlled trial ($n = 19$), tazarotene resulted in 89% IGA success rates following a 12-week treatment period [95]. Moreover, trifarotene, a retinoic acid receptor-γ selective agonist, demonstrated safety and efficacy in treating both facial and truncal AV in multiple trials [76, 121], and has been FDA approved for truncal AV. In the PERFECT I and II trials ($n = 1214$ [trifarotene] and 1206 [vehicle] across both trials), Tan et al. report that trifarotene 0.005% cream applied once daily for 12 weeks resulted in a 35.7% Physician Global Assessment (PGA) success rate versus 25.0% with a vehicle control

Table 2 Topical and systemic agents that have been evaluated for the treatment of truncal acne vulgaris

Treatment modality	Agent	Study type	Outcome	References
Topical	Trifarotene 0.005% cream	Randomized controlled trials: PERFECT I and II (n = 1214 trifarotene and 1206 vehicle across both trials)	After 12 weeks, 10.7% vehicle-controlled PGA success rate ($p < 0.001$) in PERFECT I and 12.7% vehicle-controlled rate; ($p < 0.001$) in PERFECT II	[76]
	Trifarotene 0.005% cream	Long-term open-label trial (n = 453)	PGA success rates of 38.6% and 66.9% at 12 weeks and 52 weeks, respectively	[121]
	Tazarotene 0.045% lotion	Non-controlled pilot trial (n = 19)	89% IGA success rates following a 12-week treatment period	[95]
	Azelaic acid 15% foam	Open-label pilot trial (n = 18)	89% of patients exhibited a 1-grade IGA improvement after 16 weeks	[96]
	Azelaic acid 20% cream	Open-label trial (n = 251 women)	97% of patients exhibited an IGA of 0 (clear) or 1 (almost clear) on their chest and 94% exhibited an IGA of 0 or 1 on their back following 12 weeks	[131]
	Dapsone 7.5% gel	Open-label trial (n = 20)	45% IGA success rate following 16 weeks	[97]
Systemic	Sarecycline 1.5 mg/kg	Randomized controlled trials SC1401 (n = 483 sarecycline; n = 485 placebo) and SC1402 (n = 519 sarecycline; n = 515 placebo)	After 12 weeks, pooled analysis of the chest region from SC1401/1402 trials demonstrates 12.65% placebo-controlled IGA success rate ($p < 0.05$); pooled analysis of the back region from SC1401/1402 trials demonstrates 11.16% placebo-controlled IGA success rate ($p < 0.05$)	[150]
	Isotretinoin formulations 0.5 mg/kg/day for 4 weeks followed by 1.0 mg/kg/day for 16 weeks	Randomized controlled trial comparing Isotretinoin-Lidose (n = 464) to generic isotretinoin (n = 461)	After 20 weeks, 76.9% of patients achieved a 90% reduction in facial and truncal acne lesions following treatment with Isotretinoin-Lidose, while 81.0% of patients achieved the same outcome with generic isotretinoin	[152]
	Ethinyl estradiol 0.02 mg/drospirenone 3 mg	Randomized controlled trial	After 24 weeks, significant reductions in mean percent change in noninflammatory, inflammatory and total lesions by 52.1% ($p < 0.02$), 53.2% ($p < 0.05$), and 57.3% ($p < 0.02$), respectively compared with placebo. However, the success rate of achieving clear or almost clear skin did not reach statistical significance for COC vs placebo (53.3% vs 20%)	[179]
	Spironolactone <150 mg	Retrospective study (n = 70 women)	Improved lesions on the chest and back at both 6 and 12 months	[191]
	Spironolactone 100–200 mg	Retrospective study (n = 110 women)	Following 17 months, 85% of women exhibited improvement in their CASS score and 55% demonstrated completely clear skin. Patients displayed an average improvement of 73.1%, 75.9%, and 77.6% in facial, chest, and back lesions, respectively	[192]

CASS Comprehensive Acne Severity Scale, *COC* combined oral contraceptives, *IGA* Investigator's Global Assessment, *PGA* Physician's Global Assessment

PGA and IGA success is defined as achieving at least a 2-grade improvement from baseline and a rating of "clear" or "almost clear"

(10.7% vehicle-controlled rate; $p < 0.001$) in PERFECT I and 42.6% versus 29.9% (12.7% vehicle-controlled rate; $p < 0.001$) in PERFECT II [76]. Trifarotene also improved both inflammatory and non-inflammatory truncal lesions by week 4 in PERFECT I and by week 2 in PERFECT II, whereas PGA success rates reached statistical significance in both trials (PERFECT I 8.9% vehicle-controlled rate, $p < 0.05$; PERFECT II 8.0% vehicle-controlled rate; $p < 0.05$) by week 8 [76]. Of note, the exclusion criterion for trifarotene was the presence of severe acne, as evidenced by more than one nodule on the face or trunk. Long-term safety and efficacy were also evaluated in an independent 52-week open-label trial of 453 patients with moderate facial and truncal acne. In this study, once-daily topical trifarotene 0.005% resulted in truncal PGA success rates of 38.6% and 66.9% at 12 weeks (Fig. 3a, b) and 52 weeks, respectively [121]. The most common adverse effects to trifarotene treatment were mild pruritus (4.6%), irritation (4.2%), and sunburn (1.8%). Fixed combinations of topical retinoids with BPO or antibiotics have also been evaluated in the treatment of facial acne, but further trials need to be conducted in truncal AV [105, 106, 122–124].

5.1.4 Hormonal Topical Therapy

Clascoterone (cortexolone 17α-propionate) 1% cream is another topical AV therapy, and is FDA-approved for the treatment of facial acne [125]. Clascoterone decreases AV by preventing dihydrotestosterone from binding to local androgen receptors in the skin, thereby attenuating sebum production and downstream acnegenic pathways [126]. A major advantage of its topical formulation is that it demonstrates minimal systemic uptake [127, 128], circumventing the unwanted hormonal side effects of anti-androgenic therapy in male and pregnant patients (discussed in detail below with systemic spironolactone). This unique property may also be advantageous for treating AV in transgender men undergoing gender-affirming hormone therapy by targeting the hormonal pathogenesis of acne at the skin and avoiding systemic anti-androgenic effects [129]. In two randomized, phase III, vehicle-controlled trials ($n = 722$ [clascoterone 1% cream] and $n = 718$ [vehicle] across both trials), clascoterone 1% cream twice daily demonstrated a significant improvement of facial AV after 12 weeks of treatment in comparison to a vehicle ($p < 0.001$) [126]. An open-label extension study found that clascoterone 1% cream had a favorable long-term safety profile when applied to both the face and/or trunk [130]. However, long-term efficacy was not evaluated for either the face or trunk. Therefore, further trials are needed to assess whether clascoterone 1% is effective at treating truncal AV.

5.1.5 Azelaic Acid and Sulfone Agents

Topical azelaic acid and dapsone formulations have also been studied for treating truncal AV [96, 97, 131]. In small open-label trials of 15% azelaic acid foam twice daily ($n = 18$) or 20% cream twice daily ($n = 251$ women), patients exhibited improvement after 16 weeks [96] and 12 weeks [131], respectively. Although well tolerated in both studies, rare side effects included xerosis and skin tingling or burning. Likewise, 7.5% dapsone gel was evaluated in a three-center open-label trial of 20 patients with truncal AV with approximately half of patients demonstrating skin improvement following a once-daily application to the back for 16 weeks [97]. The medication was well tolerated without any reported side effects [97].

5.1.6 Advantages and Disadvantages of Topical Agents

As there is reduced systemic absorption from topical applications, advantages include potential long-term use without

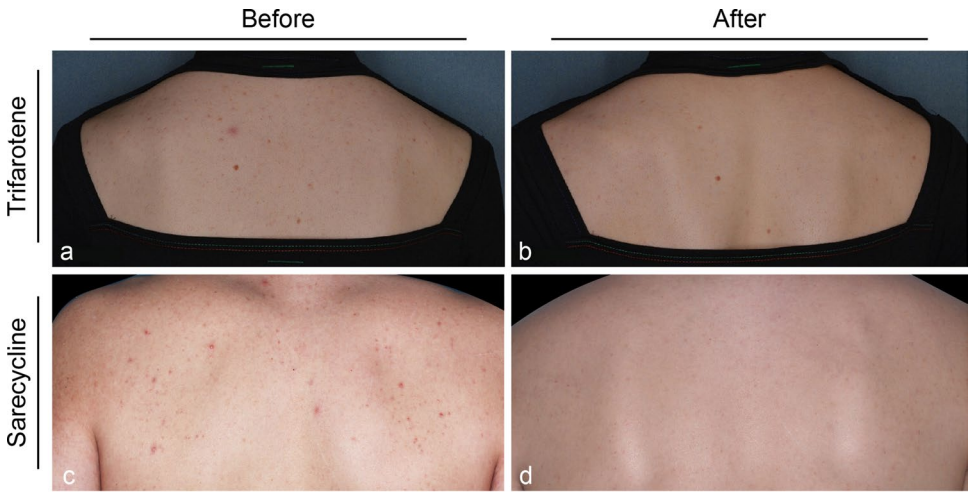

Fig. 3 Treatment of truncal acne with either topical trifarotene or oral sarecycline. Clinical images of truncal acne on the back of a patient before (**a**) and after a 12-week treatment (**b**) with topical trifarotene (0.005% daily) or before (**c**) and after a 12-week treatment (**d**) with oral sarecycline (1.5 mg/kg daily). Images from (**a**, **b**) adapted from Blume-Peytavi et al. [121]. Images from (**c**, **d**) are from a 12-week open-label clinical trial with oral sarecycline

significant systemic adverse effects, and compatibility with other medical comorbidities. Despite these advantages, limitations to topical therapies and factors contributing to possible low adherence include the difficulty for patients to self-administer medication, the large surface area requiring treatment, and irritation at the site of application, especially with retinoids. Moreover, the physical properties of topical formulations (i.e., gels, lotions, foams) play a significant role in patient preference and adherence [132]. Finally, while mild and moderate acne may respond well to topical treatment, limited evidence exists on the efficacy of topical agents in treating severe disease. Indeed, the PERFECT trials with topical trifarotene excluded patients with nodular acne [76], and guidelines do not recommend topicals as monotherapies for nodular AV [6]. Given these properties, oral medications may be more appropriate and in greater alignment with patient preferences.

5.2 Oral Therapy

The most widely utilized medication classes for oral therapy are antimicrobials, retinoids, and hormonal therapies, especially in moderate-to-severe cases. For truncal AV, clinicians often consider systemic treatment necessary, given the practical difficulties of treating extensive surface areas with topical agents alone. In clinical practice, it is also common to combine oral and topical treatments to address truncal involvement, such as the combination of systemic antibiotics and topical BPO. Importantly, oral therapy increases the possibility of systemic side effects, which may create difficulties for patients with multiple medical conditions.

5.2.1 Systemic Antibiotics

Oral antibiotics are first-line treatments for moderate-to-severe facial and truncal AV, and are often used as a second-line therapy for mild AV that is unresponsive to topical agents. The most utilized class of antibiotics are the broad-spectrum tetracyclines, such as doxycycline and minocycline [133]. Tetracycline-based antibiotics treat AV by their direct antimicrobial activity against *C. acnes*, as well as their anti-inflammatory properties [133–135]. Doxycycline has been shown to be effective at 1.2–2.4 mg/kg for 12 weeks for moderate-to-severe acne [136]. However, the widespread use of broad-spectrum tetracycline-class antibiotics has led to resistance not only in *C. acnes*, but also in other commensal bacteria [137, 138]. Because of their broad-spectrum activity, doxycycline and minocycline can alter the cutaneous and gut microbiome, leading to dysbiosis [139, 140] and possibly contribute to the development of inflammatory bowel disease [141]. To help prevent antibiotic resistance, guidelines recommend using antibiotics for less than 3 months and with concomitant use of a topical retinoid and/or BPO [142].

More recently, sarecycline, a novel tetracycline-derived antibiotic with narrow-spectrum activity, was FDA approved for the treatment of moderate-to-severe AV [143, 144]. While its core molecular structure is similar to other tetracycline class antibiotics, sarecycline contains a unique C7 modification that imparts greater affinity for ribosomal binding, enhanced inhibition of bacterial protein synthesis through messenger RNA contact, and lower probability of inducing antibiotic resistance [145–147]. Sarecycline displays targeted antimicrobial activity against *C. acnes*, and other pathogenic Gram-positive bacteria, while exerting a 16- to 32-fold decrease in activity against enteric Gram-negative microbes as compared with doxycycline or minocycline [147]. Sarecycline was also shown to be four- to eightfold less active against anaerobes that typically colonize the human digestive tract in comparison to doxycycline [146]. These unique features may diminish the extent of skin and gut bacterial dysbiosis typically observed with broad-spectrum tetracyclines [139, 140], improving the patient experience by reducing the adverse effects from antibiotic therapy of AV [148].

The efficacy of sarecycline in treating patients with moderate-to-severe facial and truncal AV was evaluated in two, large randomized clinical trials (n = 2002 total), SC1401 (n = 483 sarecycline; n = 485 placebo) and SC1402 (n = 519 sarecycline; n = 515 placebo) [149]. In these studies, patients who received sarecycline 1.5 mg/kg for 12 weeks achieved greater truncal IGA success rates in comparison to placebo for both the back and chest. In a separate pooled analysis, sarecycline began demonstrating statistically significant improvements as early as 3 weeks for both the chest (4.13% placebo-controlled rate; $p < 0.05$) and back (5.09% placebo-controlled rate; $p < 0.05$) [150]. By 12 weeks, pooled analysis of the chest from SC1401/1402 trials demonstrated a 12.65% placebo-controlled IGA success rate ($p < 0.05$), while a pooled analysis of the back revealed an 11.16% placebo-controlled IGA success rate ($p < 0.05$) [150]. Clinical improvement following a 12-week treatment course with sarecycline in an open-label clinical trial can be readily seen as compared with baseline (Fig. 3c, d). Furthermore, sarecycline also demonstrated a favorable safety profile in comparison to doxycycline and minocycline [135].

5.2.2 Systemic Retinoids

Isotretinoin is the gold-standard oral medication FDA approved for the treatment of severe, recalcitrant, and scarring AV. Isotretinoin reduces sebum production; decreases sebocyte proliferation and activity; and normalizes keratinization to inhibit comedogenesis [151]. It is one of the most successful treatments for severe AV, reducing lesions [152], scarring [69, 153, 154], and the psychological sequelae of AV [155, 156]. However, despite its efficacy

during treatment, previous studies have reported relapse rates as high as 33% [69] and 39% [157]. While age, sex, or duration of acne prior to treatment did not influence relapse rates, patients who had truncal AV experienced greater relapses as compared with patients with facial AV (40% [truncal] vs 20% [facial]; $p < 0.05$) [157]. In this study, further analysis of the total cumulative dose of isotretinoin revealed that 82% of patients who had received <120 mg/kg relapsed in contrast to 30% of patients who received greater dosages ($p < 0.01$). This finding introduced the concept of cumulative dosing thresholds for isotretinoin treatment.

For severe, recalcitrant nodular AV, isotretinoin is often started at 0.5 mg/kg daily for 1 month and increased to 1.0 mg/kg daily, as tolerated, for 15–20 weeks to achieve a cumulative dose of 120–150 mg/kg [5, 158]; however, cumulative doses ≥200 mg/kg may be necessary for complete AV resolution. In cases of mild-to-moderate AV, lower doses have been evaluated in an effort to decrease adverse effects and costs [159, 160]. While previous studies did not a show a significant difference in treatment efficacy between 0.1 and 1.0 mg/kg daily for severe AV at the end of the trial period, patients who were treated with higher dosages (closer to 1.0 mg/kg daily) displayed reduced relapse rates than those who were treated with lower dosages (0.1 mg/kg daily) [69, 157, 161]; relapse rates were also decreased in patients who received a cumulative dose of 120–150 mg/kg [69]. Furthermore, other studies found that even higher cumulative doses of 220 mg/kg [162] or 290 mg/kg [163] may be necessary to maintain low rates of relapse.

However, whether current cumulative dosing standards influence treatment efficacy and relapse continues to be debated [154, 164, 165]. A prospective trial analyzing risk factors for relapse after isotretinoin found that treatment duration ($p = 0.50$), mean daily dose ($p = 0.86$), and sex ($p = 0.86$), did not influence relapse rates; instead, the presence of lesions following treatment ($p = 0.0011$), young age ($p = 0.0022$), and the presence of facial and truncal AV ($p = 0.036$) increased the risk of relapse [166]. Cunliffe and Norris also found that those who had truncal AV exhibited greater relapse rates versus those with facial AV (43% vs 27%; $p < 0.05$) [167]. One constant across multiple variables and analyses is that the presence of truncal AV remains a significant risk factor for relapse following isotretinoin treatment. Therefore, while isotretinoin is highly effective at eliminating both facial and truncal AV during the treatment period, it may not always provide long-term clearance for patients with truncal AV after a single treatment course.

The adverse effects associated with isotretinoin are dose dependent [168], and have been described elsewhere [169]. Cheilitis, xerosis, and dermatitis are among the most frequent mucocutaneous adverse effects. In fact, cheilitis is so common that its absence in the setting of therapy "failure" should raise suspicion of non-adherence [169]. Attempts to link isotretinoin use to depression, suicidal behavior, or inflammatory bowel disease have created angst among dermatologists and patients; however, these claims remain controversial and evidence-based medicine to date suggests the opposite [170–173]. The most serious adverse effect is its teratogenicity [174]. As a consequence, an isotretinoin registry named iPLEDGE was approved by the FDA in 2006 where prescribers and patients—both men and women—enroll to manage the risk of isotretinoin teratogenicity and prevent fetal exposure during pregnancy. Given this high safety burden, proper patient counseling and encouragement are imperative, especially in light of recent evidence showing that 31% of all female patients of childbearing potential admitted non-adherence with iPLEDGE pregnancy prevention measures [175]. Therefore, open discussions with patients are essential to weigh the risks and benefits of beginning isotretinoin therapy.

5.2.3 Systemic Hormonal Agents

Hormone therapies consist of combined oral contraceptives (COC) and spironolactone. Composed of ethinyl estradiol and progestin, COC exert their function in female patients via downregulating the hypothalamic–pituitary–gonadal axis to diminish androgen synthesis [176]; they also increase the expression of sex hormone-binding globulin, further decreasing the ability of free testosterone to activate sebum production [177]. A meta-analysis substantiated that COC are an effective monotherapy for facial AV, but that they demonstrate delayed treatment onset in comparison to oral antibiotics (6 months vs 3 months, respectively) [178]; however, the study found no difference in efficacy between the two treatment options after 6 months. For moderate truncal AV, a single-center, randomized, double-blinded trial studied the effect of ethinyl estradiol 0.02 mg/drospirenone 3 mg over the course of 24 weeks [179]. This study revealed a significant improvement in non-inflammatory, inflammatory, and total lesions with hormone therapy compared with placebo control, indicating that hormone therapy may be effective for truncal AV. However, the success rate of achieving clear or almost clear skin did not reach statistical significance for COC vs placebo (53.3% vs 20%). Therefore, larger multi-center studies are needed to better understand the effect of COC in treating truncal AV in comparison to facial AV.

Combined oral contraceptives are associated with an increased risk for vascular events such as venous thromboembolism (VTE). In a national cohort study from Denmark, investigators found a VTE incidence rate of 0.06 events per 100 person-years for COC users versus 0.03 events per 100 person-years for non-users [180]. Further analyses examining VTE incidences of specific COC formulations revealed

that drospirenone-containing contraceptives have an increased incidence rate (0.03 events per 100 person-years) in comparison to levonorgestrel-containing contraceptives (0.013 events per 100 person-years) [181]. Drospirenone-containing contraceptives have also demonstrated a greater relative risk of VTE compared with second- and third-generation COC [182]. The risk of cardiovascular events associated with COC use are also greater in women who smoke tobacco products, have genetic blood clotting defects, or have co-existing diabetes mellitus and/or hypertension [183, 184]. As such, a detailed medical/social history is necessary along with blood pressure measurement as COC are contraindicated in blood pressures exceeding 160/100 mmHg [185]. Furthermore, an increased risk of breast and cervical cancers has been reported with COC, especially with prolonged use [186]. A common misunderstanding is that the combination of a drospirenone-containing COC (an analog of spironolactone) with spironolactone may lead to hyperkalemia; however, no clinically significant increases in potassium have been observed [187].

While spironolactone is most commonly known for its diuretic effects, it also exerts anti-androgenic activity by decreasing testosterone production and competitively inhibiting both testosterone and dihydrotestosterone from binding to androgen receptors in the skin [188, 189]. Even though it has not been approved by the FDA for AV, it is commonly used and small studies have reported success in treating AV [190]. A retrospective study of 70 female individuals with adult acne revealed that low-dose spironolactone (< 150 mg daily) resulted in improved lesions on the chest and back at both 6 and 12 months [191]. Another study of 110 female patients found an average improvement of 73.1%, 75.9%, and 77.6% in facial, chest, and back lesions, respectively, following 17 months of spironolactone 100–200 mg daily [192]. Current guidelines recommend spironolactone for the treatment of acne in select women at a typical dosing of 50–200 mg daily [5].

Although spironolactone is generally well tolerated, potential side effects include diuresis, menstrual irregularities, fatigue, headache, and dizziness [193]. Furthermore, spironolactone may result in decreased libido, impotence, and gynecomastia, which limit its use in male patients, and is contraindicated in pregnancy because of an increased risk of feminization of male fetuses [194]. Hyperkalemia is extremely rare in healthy young adults [195], with one retrospective study reporting hyperkalemia in 0.72% of all recorded measurements [196]. Because of these findings, the authors conclude that regular potassium monitoring in young healthy women prescribed spironolactone for acne may not be necessary. A separate study also found that less than 1% of patients aged 18–45 years (n = 1/112) exhibited hyperkalemia while taking spironolactone, but a greater proportion of patients aged 46–65 years (16.7%; n = 2/12) showed signs of hyperkalemia [195], suggesting that monitoring may be needed in older patients. Furthermore, monitoring may be indicated in patients who are concurrently taking other hypertensive medications such as angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. Last, spironolactone may exhibit a slower onset of efficacy, which may not align with patient preferences for expeditious resolution of their acne [191].

6 Acne Scarring and Treatment

6.1 Scarring Rates

Affecting 87–95% of patients with acne, scarring is a detrimental consequence of AV and is positively correlated to both the severity and duration of acne lesions [84, 197]. Several grading scales exist to assess scar severity [82–84, 197]; however, there is no consensus on a single universal scale of choice. While the pathophysiology of post-acne scarring is still unknown, evidence supports the role of a delayed and prolonged inflammatory response to pathogenic antigens in individuals who develop scars in comparison to those who remain scar free [198].

Limited studies have evaluated scarring rates for truncal AV, especially in a site- and sex-specific manner. In one cohort of 185 patients (n = 101 female, 84 male), approximately 80% and 70% of men had scarring on their back and chest, respectively, as compared with 35% and 40% of women in these same truncal sites [197]. These findings suggest that men may have a predisposition for truncal scarring. Furthermore, the frequency of scarring appears to affect anatomical locations in unique ways. Specifically, the incidence of scarring was found to be greatest on the face in comparison to the back and chest [197]. In a subsequent study of 973 patients (n = 564 female, 409 male), the authors developed the SCAR-S evaluation tool to measure scar severity of the face, chest, and back, observing that 87%, 38%, and 51% of patients displayed scarring on the face, chest, and back, respectively [84], corroborating earlier findings that the face has a greater incidence of scarring compared with the trunk [197]. Moreover, the authors from these two studies also analyzed the correlation between the duration of untreated acne and scarring severity, finding that scar severity peaked after 2–3 years of untreated AV [84, 197]. Therefore, given the physical disfigurement and psychological sequelae associated with scarring, prompt treatment of both facial and truncal acne is imperative to help improve patients' quality of life and prevent the need for the procedural interventions described below.

6.2 Treating AV Scarring

Similar to other aspects of AV, treatment of truncal acne scarring is largely based on facial studies. However, in the authors' experience, truncal scarring is more difficult to treat in comparison to facial scarring. As such, scar prevention by timely medical management as described above is key, considering that delayed treatment leads to increased scarring [84, 199]. Furthermore, it is essential to medically control acne before proceeding with scar treatments because the presence of active AV lesions reduces treatment efficacy.

Acne has several deleterious consequences, which include post-inflammatory erythema (PIE; also known as acne-induced macular erythema; AIME [200]), post-inflammatory hyperpigmentation (PIH; also known as acne-induced macular hyperpigmentation; AIMH [200]), atrophic scars (i.e., ice-pick, rolling, and boxcar scars), and hypertrophic scars [201, 202]. Moreover, particular scar morphologies have been shown to vary based on anatomical locations. While ice-pick, macular atrophic, hypertrophic, and keloid scars affect the face, back, and chest collectively, follicular macular atrophic scars due to perifollicular elastolysis were exclusive to the back and chest [197]. Post-inflammatory hyperpigmentation/acne-induced macular hyperpigmentation is more common in individuals with darker skin, while persistent PIE/AIME can be seen in those with lighter skin [201]. Scarring secondary to acne is thought to be a product of aberrant collagen production or degradation following cutaneous inflammation [198, 203]. Without prompt medical treatment, truncal AV can lead to severe and broad atrophic scars (Fig. 4a, b), as well as hypertrophic scars, particularly on the upper aspects of the back, chest, and shoulders [204]. Considering that multiple scar types are frequently present and respond differently to unique interventions, procedural treatment often requires a multimodal approach with combination therapies (Fig. 4c, d). The various modalities that can be utilized to treat the myriad sequalae of truncal acne are described in detail below.

6.2.1 Vascular Lasers

6.2.1.1 PDL The pulsed dye laser (PDL) is frequently used to treat acne and surgical scars. The PDL has a wavelength of 585 nm or 595 nm, which, via selective photothermolysis, targets oxyhemoglobin in red blood cells, leading to endothelial damage and coagulation of blood vessels [205, 206]. Therefore, if PIE/AIME is present, treatment with PDL is recommended to reduce the overall appearance of

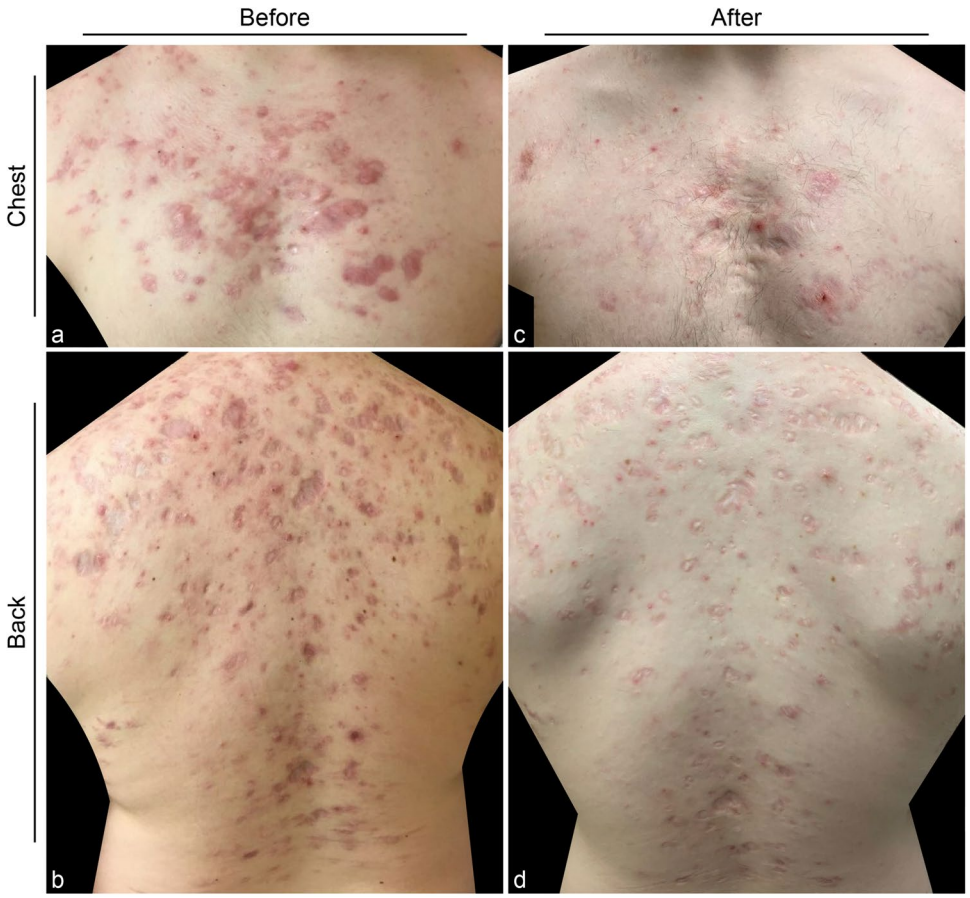

Fig. 4 Treatment of truncal acne scarring with multimodal interventions. Acne scarring on the chest and back before (**a**, **b**) and after (**c**, **d**) treatment. Patient received multiple intralesional injections with triamcinolone and treatments with non-ablative fractional resurfacing and pulsed dye laser

scars by reducing erythema. Alternatively, the potassium titanyl phosphate laser, which operates at 532 nm, also targets scar erythema by the same mechanism, but has a decreased depth of tissue penetration compared with PDL. In addition to treating PIE/AIME, PDL has been used to manage atrophic scars. For the face, a single PDL (585-nm) session demonstrated a 47.8% reduction in scar depth profilometry 120 days after treatment [207]. In a separate randomized, split-face controlled study, treatment with 595-nm PDL improved the clinical appearance of facial acne scars by 18.3% when assessed 8 weeks after a 6-week treatment period, an effect that was comparable to the 1064-nm long-pulsed Nd:YAG laser [208]. Interestingly, histological assessment of treatment areas demonstrated an increase in collagen deposition and upregulation of procollagen 1 and transforming growth factor beta-1 following application of both lasers. Even though no statistically significant difference was observed, the authors noted that PDL treatments trended in more favorable outcomes for ice-pick scars, while the Nd:YAG laser led to better responses for deep boxcar scars [208]. Last, PDL has also been effective against hypertrophic facial scars, resulting in improved scar volume, texture, and pliability [209–212].

6.2.1.2 IPL Intense pulsed light (IPL) does not meet the technical definition of a laser because of its wide emission spectrum (500–1200 nm); however, it is included amongst the vascular lasers given its efficacy against PIE/AIME. Furthermore, filters are typically employed to isolate a narrower range of wavelength, thereby emulating the monochromaticity of true lasers [213]. In clinical practice, IPL can be utilized as part of combination therapy or as a monotherapy. When combined with a topical 2% erythromycin solution, IPL accelerated the resolution of facial PIE/AIME when compared with topical erythromycin alone [214]. In a separate split-face study, Feng et al. found that combining IPL with a fractional 1064-nm Nd:YAG picosecond laser did not improve PIE/AIME in comparison to IPL monotherapy, indicating the effectiveness of IPL against erythema [215]. However, beyond PIE/AIME, the combination of IPL and the 1064-nm Nd:YAG picosecond laser led to a significant improvement in the severity of atrophic scars and pore count [215]. Intense pulsed light may also be combined with fractional CO_2 lasers, while IPL has been shown to reduce both inflammatory lesions and atrophic scar scores as a monotherapy, the addition of the CO_2 laser led to a greater improvement in atrophic scars [216]. Intense pulsed light is also effective against hypertrophic scars and keloids, diminishing the height, erythema, and firmness of the scars from various etiologies, including surgical scars, trauma, burns, and acne scars in 92.5% of the patients [217]. Last, IPL has been used successfully to treat acne vulgaris of the chest and back, but the treatment of truncal acne scars has not been evaluated [218].

6.2.2 Fractional Lasers

In contrast to PDL treatment, which selectively targets a chromophore in the skin, fractional lasers exert their effects by targeting tissue water [219]. In doing so, fractional lasers create numerous discrete columns of thermal damage, known as microscopic thermal zones, separated by unaffected areas that promote healing [220]. In general, fractional lasers are divided into ablative and non-ablative lasers (also known as non-ablative fractional resurfacing [NAFR]). The difference between these two laser modalities is that ablative lasers vaporize the aforementioned tissue columns while NAFR induces thermal injury.

6.2.2.1 Ablative Fractional CO_2 and 2940-nm Erbium:YAG lasers are most commonly used to treat acne scarring. The efficacy of fractional ablative lasers has been demonstrated mainly in the treatment of atrophic facial, not truncal, scars. In a prospective trial of 13 patients, investigators observed a mean scar improvement of 26–50% following two to three fractional CO_2 laser treatments [221]. However, common side effects included transient edema, oozing, and crusting, all of which resolved in 1 week [221]. Similarly, Chan et al. also found a statistically significant improvement in atrophic facial scars after one treatment with fractional CO_2 lasers [222]. Despite its positive effects, ablative resurfacing also carries a risk of hypertrophic scarring, and careful consideration of treatment settings, such as the coverage density and energy levels, is needed to prevent this adverse effect. Moreover, as demonstrated in a study of Asian patients with acne scars, fractional CO_2 lasers can also lead to PIH with 55.5% of patients showing signs of PIH at 1-month post-treatment and 11.1% at 6-months post-treatment [222]. Alternatively, treatment of atrophic facial scars in Asian patients with a 2940-nm Erbium:YAG resulted in a lower rate of PIH (3.0%), with patients rating their satisfaction as good-to-excellent after one treatment [223]. To improve response, fractional CO_2 lasers can be combined with NAFR in successive treatments [224], or concomitantly with radiofrequency [225]. Several studies also report more favorable outcomes when platelet-rich plasma was applied to areas treated with fractional CO_2 lasers [226–228].

6.2.2.2 Non-Ablative Non-ablative fractional resurfacing is frequently used to treat acne scars as it has less downtime and treatment-related side effects when compared with ablative fractional lasers. Non-ablative fractional resurfacing includes fractionated 1410-nm, 1440-nm Nd:YAG, 1540-nm and 1550-nm Erbium, and 1927-nm Thulium

lasers [229]. The 1540-nm Erbium:glass and 1550-nm Erbium-doped fiber fractional lasers are commonly utilized in clinical practice. In a study of 58 patients with moderate-to-severe facial atrophic scars, both 1540-nm Erbium-doped glass lasers and fractional CO_2 lasers improved scarring, but no significant difference was noted between either treatment condition [230]. Rather, patients who were treated with the non-ablative Erbium laser experienced a shorter downtime (i.e., crusting, scaling, erythema) and less pain as compared with the fractional CO_2 laser [230]. Likewise, a split-face trial comparing the efficacy of ablative CO_2 laser and 1565-nm Erbium glass laser treatment on the appearance of mild-to-moderate facial scars showed no significant difference between either treatment modality [231]. Again, patients reported less crusting, pain, and erythema on the facial side treated with the Erbium glass laser [231]. Sardana et al. also investigated the effectiveness of the Erbium glass laser on different types of scars, reporting that boxcar scars, rolling scars, and ice-pick scars showed 52.9%, 43.1%, and 25.9% improvement, respectively [232]. While there is still a concern for PIH with NAFR treatment, previous studies have demonstrated that NAFR can be an effective and safe treatment in various skin types by reducing the number of passes and total treatment density required [233, 234]. In addition, a larger total surface area can be treated with non-ablative resurfacing in a single treatment as compared with ablative resurfacing. Thus, a greater proportion of scarred skin can be treated in a single visit, which may lead to faster improvement in scar appearance. However, further studies are needed to determine the rate of scar resolution. In the authors' experience, NAFR is the treatment of choice for erythematous hypertrophic truncal acne scars, while ablative resurfacing is favored for atrophic scars.

6.2.2.3 Fractional Picosecond Lasers While picosecond lasers have largely been utilized in tattoo removal, more recent studies have evaluated their use in the treatment of acne scarring [235, 236]. Picosecond lasers with fractional modes (using a diffractive lens array or diffractive optical element) offer the benefit of photothermolysis and collagen synthesis in addition to the photomechanical effect [235, 236]. This is made possible by micro-lenses that split the picosecond pulses into columns with high fluence while the background areas receive lower-energy laser pulses, allowing for an overall reduction in treatment energy density [235].

Fractional 1064-nm picosecond lasers are effective in treating atrophic scars [215, 237, 238], with similar outcomes as the fractional 1550-nm Erbium laser [238]. In another split-face trial, the use of a fractional 1064-nm picosecond laser resulted in comparable improvements to fractional CO_2 laser treatment for facial atrophic acne scars in patients with Fitzpatrick skin type III–V, but with a greater safety profile [239]. Importantly, there was no evidence of PIH following treatment with the picosecond laser, while 24% of patients experienced PIH with the fractional CO_2 laser [239]. Other picosecond devices have also demonstrated positive effects on facial scars. Three-dimensional volumetric analysis of atrophic scars revealed a mean improvement of 24.3%, along with an increased density of elastic fibers and dermal collagen on histology, after six treatments with the fractional 755-nm alexandrite picosecond laser [240]. However, despite the numerous studies demonstrating amelioration of facial scarring with fractional picosecond lasers, there are limited data evaluating its efficacy for truncal scars. Yet analysis of histological data from both the face and trunk after picosecond laser treatment suggest that these two anatomical sites may respond similarly to picosecond laser treatments. Indeed, a paralleled upregulation of collagen and elastic fibers in both the face [240] and back [237] following treatment with fractional picosecond lasers indicate that the clinical improvements observed for facial scarring may also translate to the trunk. Overall, fractional picosecond lasers have the potential to be an effective treatment option for patients with truncal acne scars, particularly in individuals with darker skin. However, further studies are needed considering the paucity of available data for truncal scarring.

6.2.3 Non-Laser Fractional Radiofrequency

Radiofrequency uses electric current to cause thermal damage. As it does not target a specific chromophore, it can be used safely in all skin types [241]. Fractional radiofrequency uses an array of electrodes or microneedles to create fractional thermal damage and has been shown to improve atrophic acne scars, including ice-pick and boxcar scars [242–246]. The combination of fractional FR and fractional CO_2 laser is frequently utilized to treat atrophic acne scars, which has led to improved patient satisfaction [247–249].

6.2.3.1 Microneedling Microneedling causes epidermal and dermal injury by puncturing the skin with fine sharp needles that vary in size, and can be adjusted for a desired depth of penetration. Microneedling helps improve shallow atrophic scars and has a low risk of hyperpigmentation [250–252]. Cachafeiro et al. also demonstrated that microneedling yielded comparable results to a fractional non-ablative 1340-nm Erbium laser when treating atrophic facial acne scars and resulted in a lower rate of PIH [253]. While microneedling can be utilized as a monotherapy for acne scars, it is frequently combined with other treatments, including platelet-rich plasma [254–256] and chemical peels such as glycolic acid [257, 258]. Indeed, co-administration of microneedling and topical treatments is hypothesized to enhance the penetration of topical ther-

apies. However, it is important to note again that these studies have focused on facial acne scars and the efficacy of microneedling for truncal acne has yet to be evaluated.

6.2.4 Injection Treatments

6.2.4.1 Intralesional Injections Intralesional injections of corticosteroids such as triamcinolone acetonide (TAC) and/or 5-FU are effective against hypertrophic scars and keloids. The recommended dosing of TAC varies from 10 to 40 mg/mL, with 40 mg/mL commonly used for keloid scars on the trunk [204, 259]. In a study comparing the use of intralesional injection of 5-FU (50 mg/mL) or TAC (40 mg/mL) for keloid scars, Saha and Mukhopadhyay found a comparable reduction in scar volume, though patients reported more frequent injection-related pain with 5-FU than with TAC [204]. Alternatively, the combination of intralesional TAC and 5-FU is more effective for the treatment of hypertrophic scars and keloids, as demonstrated in a randomized trial of 150 patients comparing intralesional TAC (40 mg/mL) alone or with 5-FU (45 mg) [260]. Furthermore, topical formulations of 5-FU or TAC may also be used in the treatment of keloids and hypertrophic scars through laser-assisted delivery. In a prospective case series of 15 patients with hypertrophic scars ($n = 2/15$ with acne scars), patients underwent five treatments of fractional CO_2 lasers, immediately followed by application of topical TAC (10 or 20 mg/mL) [261]. With this treatment modality, the authors observed a >50% improvement in texture, hypertrophy, and dyschromia of hypertrophic scars [261]. Similarly, monthly treatment with topical 5-FU (5%) combined with the ablative fractional Erbium:YAG laser led to improved hypertrophic scar height, pliability, and vascularity [262]. However, pain and ulceration also occurred at a higher rate with combination therapy than with topical 5-FU alone [262]. Further studies have also compared laser-assisted delivery of topical TAC (20 mg/mL) and 5-FU (50 mg/mL) with a fractional ablative CO_2 laser, finding no significant decrease in scar surface area between the two treatment arms [263].

6.2.5 Fillers

The use of various fillers, including calcium hydroxyapatite, poly-L-lactic acid (PLLA), and polymethylmethacrylate (PMMA), for soft-tissue augmentation has also been employed to improve acne scars.

6.2.5.1 PLLA The treatment of more significant atrophic scars can be augmented by intralesional injections of PLLA [264], or through laser-assisted delivery of topical PLLA [265]. In the case of facial acne scarring, fractional CO_2 laser-assisted delivery of PLLA resulted in at least a 33% improvement of scar atrophy and contour [265].

6.2.5.2 PMMA Polymethylmethacrylate is a FDA-approved treatment for acne scars and has shown significant benefit in ameliorating atrophic scarring [266]. In a randomized trial of moderate-to-severe rolling facial atrophic scars, prompt improvement was observed after an intralesional PMMA injection, with a sustained response up to 6 months post-treatment [267]. Facial scar treatment with the combination of PMMA and microneedling also showed a significant improvement compared with microneedling alone [268], indicating the clinical benefits of a multimodal approach.

6.3 Conclusions for Evaluation and Treatment of Acne Scarring

Overall, many therapeutic options exist for treating acne scarring; however, the vast majority of these interventions, except for intralesional injections of TAC and 5-FU, have been evaluated for treating scars on the face rather than on the trunk. Furthermore, navigating each treatment option can be challenging and requires careful analysis of scar characteristics to select the most optimal treatment plan (Fig. 5). Vascular lasers such as PDL and IPL are recommended if PIE/AIME is present. While not discussed above, sun protection is critical for PIH/AIMH, and hydroquinone or fractional picosecond lasers may be used as an adjunct therapy. In the case of atrophic scars, ablative and non-ablative fractional lasers, fractional picosecond lasers, fractional radiofrequency, and microneedling can be utilized. Fillers may also have an additional role, especially in the case of large rolling and boxcar scars. In the authors' experience, the improvement seen with truncal acne scar treatment is modest and often necessitates a multimodal approach (Fig. 4). Therefore, clinicians and patients should engage in open discussions about the limitations surrounding treatment options and undergo shared decision making regarding cosmetic goals and expectations. While further research is needed to develop and optimize more effective interventions to treat truncal acne scarring, the best clinical course of action currently available is scar prevention via prompt medical management of acne lesions.

7 Conclusions

Even though truncal AV occurs in roughly half of patients with acne and leads to significant rates of disfigurement, it remains a largely neglected clinical concern, as compared with facial AV. As such, current guidelines for the treatment of truncal lesions are mainly derived from facial studies, which have led to sub-optimal outcomes. When truncal AV

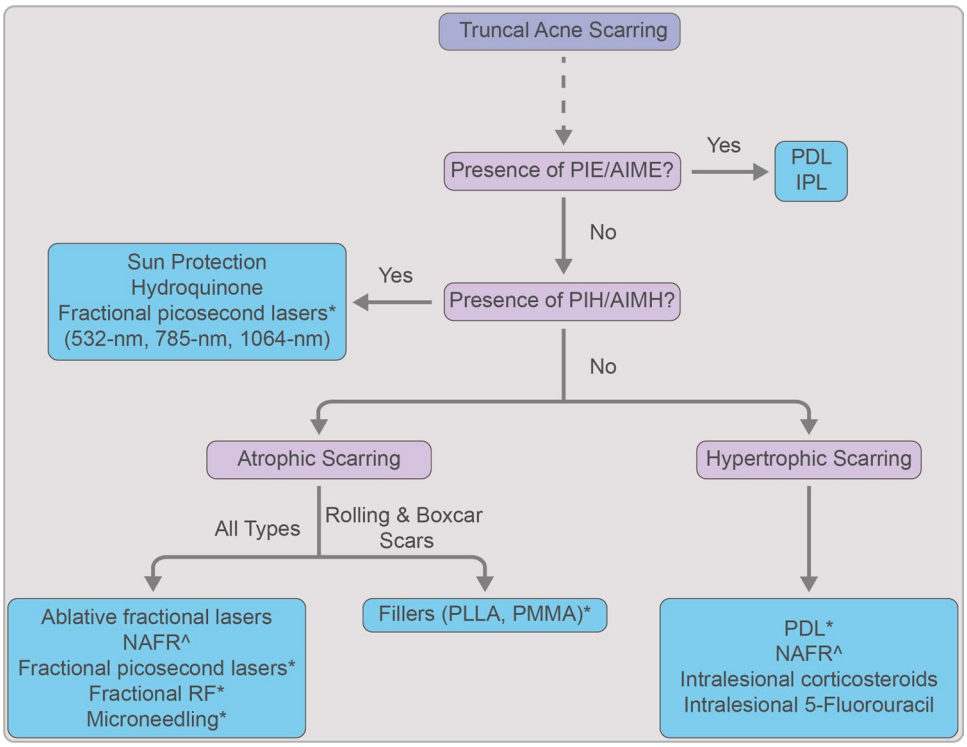

Fig. 5 Flow diagram for the evaluation and treatment of truncal acne scarring. Combination treatments, such as ablative fractional lasers and topical poly-L-lactic acid (PLLA), can be used to improve outcome. *IPL* intense pulsed light, *NAFR* non-ablative fractional, *nm* nanometer, *PDL* pulsed dye laser, *PIE* post-inflammatory erythema, *AIME* acne-induced macular erythema, *PIH* post-inflammatory hyperpigmentation, *AIMH* acne-induced macular hyperpigmentation, *PMMA* polymethylmethacrylate, *RF* radiofrequency, ^risks of PIH can be reduced by lowering density and number of passes, *safe in Fitzpatrick type III–V skin

goes untreated, it can quickly lead to scar formation and reduced quality of life for patients. Currently, isotretinoin and oral tetracycline-class antibiotics are the most effective treatments for truncal acne owing to their rapid onset of efficacy and ease of use. If medical therapy is delayed or suboptimal, current corrective procedures for truncal scarring are available, with the caveat they may be limited in efficacy because they were primarily developed for facial scars. As dermatology moves deeper into the precision medicine era, especially for inflammatory disorders such as psoriasis vulgaris and atopic dermatitis, it is important that truncal AV therapy continues to receive the proper research and clinical attention it deserves. New targeted, effective, and safe therapies for truncal AV, along with its scarring sequelae, are much needed to enhance the quality of life of patients with AV.

Acknowledgments We thank the Yale Department of Dermatology Resident Slide Collection for providing clinical images. We thank Drs. T. Orlowski, H.H. Reynolds, and L.V. Graham for providing clinical images of truncal demodicosis. This work was supported by the NIH/NIGMS Medical Scientist Training Grant T32GM136651 for SGD.

Declarations

Funding No sources of funding were received for the preparation of this article.

Conflicts of interest SGD, SRK, AG, and KCS have no disclosures; AYM has received funds, honoraria, or research grants as an advisory board member (A), consultant (C), clinical study investigator (I), and/or speaker (SP) for Almirall, Biofronterra, and Galderma; CGB has served as an (I) for Almirall; a (C) for AbbVie, Almirall, Arcutis, EpiHealth, LEO Pharma, Sanofi-Regeneron, and UCB; and a (SP) for and received honoraria from Allergan, Almirall, LEO Pharma, and UCB. These engagements did not influence the writing of this manuscript.

Ethics Approval Not applicable.

Consent to Participate Not applicable.

Consent for Publication Not applicable.

Availability of Data and Material Not applicable.

Code Availability Not applicable.

Authors' Contributions SGD, SRK, AG, AYM, KCS, and CGB researched and/or provided data for the article. SGD and SRK wrote the first draft of the article. All authors contributed substantially to discussion of the content and reviewed and/or edited the manuscript before submission.

References

1. Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380:2163–96.
2. McConnell RC, Fleischer AB Jr, Williford PM, et al. Most topical tretinoin treatment is for acne vulgaris through the age of 44 years: an analysis of the National Ambulatory Medical Care Survey, 1990–1994. J Am Acad Dermatol. 1998;38:221–6.

3. Collier CN, Harper JC, Cafardi JA, et al. The prevalence of acne in adults 20 years and older. J Am Acad Dermatol. 2008;58:56–9.
4. Moradi Tuchayi S, Makrantonaki E, Ganceviciene R, et al. Acne vulgaris. Nat Rev Dis Primers. 2015;1:15029.
5. Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol. 2016;74:945–73.
6. Nast A, Dreno B, Bettoli V, et al. European evidence-based (S3) guideline for the treatment of acne: update 2016: short version. J Eur Acad Dermatol Venereol. 2016;30:1261–8.
7. Del Rosso JQ, Bikowski JB, Baum E, et al. A closer look at truncal acne vulgaris: prevalence, severity, and clinical significance. J Drugs Dermatol. 2007;6:597–600.
8. Del Rosso JQ, Stein-Gold L, Lynde C, et al. Truncal acne: a neglected entity. J Drugs Dermatol. 2019;18:205–1208.
9. Tan J, Beissert S, Cook-Bolden F, et al. Impact of facial and truncal acne on quality of life: a multi-country population-based survey. JAAD Int. 2021;3:102–10.
10. Papadopoulos L, Walker C, Aitken D, Bor R. The relationship between body location and psychological morbidity in individuals with acne vulgaris. Psychol Health Med. 2000;5:431–8.
11. Hassan J, Grogan S, Clark-Carter D, et al. The individual health burden of acne: appearance-related distress in male and female adolescents and adults with back, chest and facial acne. J Health Psychol. 2009;14:1105–18.
12. Tan JJK, Tang J, Fung K, et al. Prevalence and severity of facial and truncal acne in a referral cohort. J Drugs Dermatol. 2008;7:551–6.
13. Dreno B, Jean-Decoster C, Georgescu V. Profile of patients with mild-to-moderate acne in Europe: a survey. Eur J Dermatol. 2016;26:177–84.
14. Goncalves G, Amado JM, Matos ME, et al. The prevalence of acne among a group of Portuguese medical students. J Eur Acad Dermatol Venereol. 2012;6:514–7.
15. Tan J, Del Rosso JQ, Weiss JS, et al. Prevalence and demographics of truncal involvement among acne patients: survey data and a review of the literature. J Clin Aesthet Dermatol. 2022;15:62–7.
16. Isaacsson VC, Almeida JRHL, Duquia RP, et al. Dissatisfaction and acne vulgaris in male adolescents and associated factors. An Bras Dermatol. 2014;89:576–9.
17. Dreno B, Thiboutot D, Layton AM, et al. Large-scale international study enhances understanding of an emerging acne population: adult females. J Eur Acad Dermatol Venereol. 2015;29:1096–106.
18. Radi R, Gold S, Acosta JP, et al. Treating acne in transgender persons receiving testosterone: a practical guide. Am J Clin Dermatol. 2022;23:219–29.
19. Wierckx K, Van de Peer F, Verhaeghe E, et al. Short- and long-term clinical skin effects of testosterone treatment in trans men. J Sex Med. 2014;11:222–9.
20. Plewig G, Melnik B, Chen W. Acne-mimicking diseases, Plewig and Kligman's acne and rosacea. Cham: Springer International Publishing; 2019. p. 299–410.
21. Wu DC, Chan WW, Metelitsa AI, et al. Pseudomonas skin infection: clinical features, epidemiology, and management. Am J Clin Dermatol. 2011;12:157–69.
22. Boni R, Nehrhoff B. Treatment of gram-negative folliculitis in patients with acne. Am J Clin Dermatol. 2003;4:273–6.
23. Luelmo-Aguilar J, Santandreu MS. Folliculitis: recognition and management. Am J Clin Dermatol. 2004;5:301–10.
24. Back O, Faergemann J, Hornqvist R. Pityrosporum folliculitis: a common disease of the young and middle-aged. J Am Acad Dermatol. 1985;12:56–61.
25. Ayers K, Sweeney SM, Wiss K. Pityrosporum folliculitis: diagnosis and management in 6 female adolescents with acne vulgaris. Arch Pediatr Adolesc Med. 2005;159:64–7.
26. Ponka D, Baddar F. Wood lamp examination. Can Fam Physician. 2012;58:976.
27. Durdu M, Guran M, Ilkit M. Epidemiological characteristics of Malassezia folliculitis and use of the May-Grunwald-Giemsa stain to diagnose the infection. Diagn Microbiol Infect Dis. 2013;76:450–7.
28. Poli F. Differential diagnosis of facial acne on black skin. Int J Dermatol. 2012;51(24–26):27–9.
29. Jacinto-Jamora S, Tamesis J, Katigbak ML. Pityrosporum folliculitis in the Philippines: diagnosis, prevalence, and management. J Am Acad Dermatol. 1991;24:693–6.
30. Hald M, Arendrup MC, Svejgaard EL, et al. Evidence-based Danish guidelines for the treatment of Malassezia-related skin diseases. Acta Derm Venereol. 2015;95:12–9.
31. Rosenthal D, LeBoit PE, Klumpp L, et al. Human immunodeficiency virus-associated eosinophilic folliculitis: a unique dermatosis associated with advanced human immunodeficiency virus infection. Arch Dermatol. 1991;127:206–9.
32. Parker SR, Parker DC, McCall CO. Eosinophilic folliculitis in HIV-infected women: case series and review. Am J Clin Dermatol. 2006;7:193–200.
33. Bull RH, Harland CA, Fallowfield ME, et al. Eosinophilic folliculitis: a self-limiting illness in patients being treated for haematological malignancy. Br J Dermatol. 1993;129:178–82.
34. Evans TR, Mansi JL, Bull R, et al. Eosinophilic folliculitis occurring after bone marrow autograft in a patient with non-Hodgkin's lymphoma. Cancer. 1994;73:2512–4.
35. Teraki Y, Konohana I, Shiohara T, et al. Eosinophilic pustular folliculitis (Ofuji's disease): immunohistochemical analysis. Arch Dermatol. 1993;129:1015–9.
36. Ellis E, Scheinfeld N. Eosinophilic pustular folliculitis: a comprehensive review of treatment options. Am J Clin Dermatol. 2004;5:189–97.
37. Paichitrojjana A. Demodicosis imitating acne vulgaris: a case report. Clin Cosmet Investig Dermatol. 2022;15:497–501.
38. Chen W, Plewig G. Human demodicosis: revisit and a proposed classification. Br J Dermatol. 2014;170:1219–25.
39. Forton F, Seys B. Density of Demodex folliculorum in rosacea: a case-control study using standardized skin-surface biopsy. Br J Dermatol. 1993;128:650–9.
40. Huang HP, Hsu CK, Lee JY. A new superficial needle-scraping method for assessing Demodex density in papulopustular rosacea. J Cosmet Dermatol. 2020;19:896–900.
41. Aktas Karabay E, Aksu CA. Demodex folliculorum infestations in common facial dermatoses: acne vulgaris, rosacea, seborrheic dermatitis. An Bras Dermatol. 2020;95:187–93.
42. Salem DA, El-Shazly A, Nabih N, et al. Evaluation of the efficacy of oral ivermectin in comparison with ivermectin-metronidazole combined therapy in the treatment of ocular and skin lesions of Demodex folliculorum. Int J Infect Dis. 2013;17:e343–7.
43. Sarac G. A comparison of the efficacy and tolerability of topical agents used in facial Demodex treatment. J Cosmet Dermatol. 2019;18:1784–7.
44. Bikowski JB, Del Rosso JQ. Demodex dermatitis: a retrospective analysis of clinical diagnosis and successful treatment with topical crotamiton. J Clin Aesthet Dermatol. 2009;2:20–5.
45. Jacot W, Bessis D, Jorda E, et al. Acneiform eruption induced by epidermal growth factor receptor inhibitors in patients with solid tumours. Br J Dermatol. 2004;151:238–41.
46. Hurwitz RM. Steroid acne. J Am Acad Dermatol. 1989;21:1179–81.
47. Nielsen JN, Licht RW, Fogh K. Two cases of acneiform eruption associated with lamotrigine. J Clin Psychiatry. 2004;65:1720–2.
48. Yeung CK, Chan HH. Cutaneous adverse effects of lithium: epidemiology and management. Am J Clin Dermatol. 2004;5:3–8.

49. Bieber T, Simpson EL, Silverberg JI, et al. Abrocitinib versus placebo or dupilumab for atopic dermatitis. N Engl J Med. 2021;384:1101–12.
50. Kazandjieva J, Tsankov N. Drug-induced acne. Clin Dermatol. 2017;35:156–62.
51. Du-Thanh A, Kluger N, Bensalleh H, et al. Drug-induced acneiform eruption. Am J Clin Dermatol. 2011;12:233–45.
52. Scope A, Agero AL, Dusza SW, et al. Randomized double-blind trial of prophylactic oral minocycline and topical tazarotene for cetuximab-associated acne-like eruption. J Clin Oncol. 2007;25:5390–6.
53. Wenzel FG, Horn TD. Nonneoplastic disorders of the eccrine glands. J Am Acad Dermatol. 1998;38:1–17.
54. Carter R 3rd, Garcia AM, Souhan BE. Patients presenting with miliaria while wearing flame resistant clothing in high ambient temperatures: a case series. J Med Case Rep. 2011;5:474.
55. Ale I, Lachapelle JM, Maibach HI. Skin tolerability associated with transdermal drug delivery systems: an overview. Adv The. 2009;26:920–35.
56. Hu CH, Michel B, Farber EM. Transient acantholytic dermatosis (Grover's disease): a skin disorder related to heat and sweating. Arch Dermatol. 1985;121:1439–41.
57. French LE, Piletta PA, Etienne A, et al. Incidence of transient acantholytic dermatosis (Grover's disease) in a hospital setting. Dermatology. 1999;198:410–1.
58. Parsons JM. Transient acantholytic dermatosis (Grover's disease): a global perspective. J Am Acad Dermatol. 1996;35:653–66.
59. Quirk CJ, Heenan PJ. Grover's disease: 34 years on. Australas J Dermatol. 2004;45:83–6.
60. Orlowski TJR, Graham LV. Truncal demodex folliculitis. Skin. 2020;2:365–8.
61. Hafsi W, Badri T. Acne conglobata. Treasure Island: StatPearls; 2022.
62. Yiu ZZ, Madan V, Griffiths CE. Acne conglobata and adalimumab: use of tumour necrosis factor-alpha antagonists in treatment-resistant acne conglobata, and review of the literature. Clin Exp Dermatol. 2015;40:383–6.
63. Dessinioti C, Katsambas A. Difficult and rare forms of acne. Clin Dermatol. 2017;35:138–46.
64. Melnik B, Jansen T, Grabbe S. Abuse of anabolic-androgenic steroids and bodybuilding acne: an underestimated health problem. J Dtsch Dermatol Ges. 2017;5:110–7.
65. Weimann E, Bohles HJ. Acute acne fulminans et conglobata after the end of high-dose testosterone therapy for hereditary tall stature. Klin Padiatr. 1999;211:410–2.
66. Chicarilli ZN. Follicular occlusion triad: hidradenitis suppurativa, acne conglobata, and dissecting cellulitis of the scalp. Ann Plast Surg. 1987;18:230–7.
67. Vasanth V, Chandrashekar BS. Follicular occlusion tetrad. Indian Dermatol Online J. 2014;5:491–3.
68. Musumeci ML, Fiorentini F, Bianchi L, et al. Follicular occlusion tetrad in a male patient with pachyonychia congenita: clinical and genetic analysis. J Eur Acad Dermatol Venereol. 2019;33(Suppl. 6):36–9.
69. Peck GL, Olsen TG, Butkus D, et al. Isotretinoin versus placebo in the treatment of cystic acne. A randomized double-blind study. J Am Acad Dermatol. 1982;6:735–45.
70. Gollnick HP, Graupe K, Zaumseil RP. Comparison of combined azelaic acid cream plus oral minocycline with oral isotretinoin in severe acne. Eur J Dermatol. 2011;11:538–44.
71. Tan MG, Worley B, Kim WB, et al. Drug-induced intracranial hypertension:a systematic review and critical assessment of drug-induced causes. Am J Clin Dermatol. 2020;21:163–72.
72. Sand FL, Thomsen SF. Adalimumab for the treatment of refractory acne conglobata. JAMA Dermatol. 2013;149:1306–7.
73. Shirakawa M, Uramoto K, Harada FA. Treatment of acne conglobata with infliximab. J Am Acad Dermatol. 2006;55:344–6.
74. Greywal T, Zaenglein AL, Baldwin HE, et al. Evidence-based recommendations for the management of acne fulminans and its variants. J Am Acad Dermatol. 2017;77:109–17.
75. Li AW, Antaya RJ. Isotretinoin-induced acne fulminans without systemic symptoms with concurrent exuberant granulation tissue. Pediatr Dermatol. 2018;35:257–8.
76. Tan J, Thiboutot D, Popp G, et al. Randomized phase 3 evaluation of trifarotene 50 mug/g cream treatment of moderate facial and truncal acne. J Am Acad Dermatol. 2019;80:1691–9.
77. Mallon E, Newton JN, Klassen A, et al. The quality of life in acne: a comparison with general medical conditions using generic questionnaires. Br J Dermatol. 1999;140:672–6.
78. Tan JK, Zhang X, Jones E, et al. Correlation of photographic images from the Leeds revised acne grading system with a six-category global acne severity scale. J Eur Acad Dermatol Venereol. 2013;27:e414–9.
79. Obrien SCL, Cunliffe WJ. The Leeds revised acne grading system. J Dermatol Treat. 1998;9:215–20.
80. Allen BS, Smith JG Jr. Various parameters for grading acne vulgaris. Arch Dermatol. 1982;118:23–5.
81. Tan JK, Tang J, Fung K, et al. Development and validation of a comprehensive acne severity scale. J Cutan Med Surg. 2007;11:211–6.
82. Dreno B, Khammari A, Orain N, et al. ECCA grading scale: an original validated acne scar grading scale for clinical practice in dermatology. Dermatology. 2007;214:46–51.
83. Goodman GJ, Baron JA. Postacne scarring: a qualitative global scarring grading system. Dermatol Surg. 2006;32:1458–66.
84. Tan JK, Tang J, Fung K, et al. Development and validation of a scale for acne scar severity (SCAR-S) of the face and trunk. J Cutan Med Surg. 2010;14:156–60.
85. Gupta MA, Johnson AM, Gupta AK. The development of an Acne Quality of Life scale: reliability, validity, and relation to subjective acne severity in mild to moderate acne vulgaris. Acta Derm Venereol. 1998;78:451–6.
86. Martin AR, Lookingbill DP, Botek A, et al. Health-related quality of life among patients with facial acne: assessment of a new acne-specific questionnaire. Clin Exp Dermatol. 2001;26:380–5.
87. Tan JKL, Jones E, Allen E, et al. Evaluation of essential clinical components and features of current acne global grading scales. J Am Acad Dermatol. 2013;69:754–61.
88. Barratt H, Hamilton F, Car J, et al. Outcome measures in acne vulgaris: systematic review. Br J Dermatol. 2009;160:132–6.
89. Doshi A, Zaheer A, Stiller MJ. A comparison of current acne grading systems and proposal of a novel system. Int J Dermatol. 1997;36:416–8.
90. Bernardis E, Shou H, Barbieri JS, et al. Development and initial validation of a multidimensional acne global grading system integrating primary lesions and secondary changes. JAMA Dermatol. 2020;156:296–302.
91. Auffret N, Nguyen JM, Leccia MT, et al. TRASS: a global approach to assess the severity of truncal acne. J Eur Acad Dermatol Venereol. 2022;2:2.
92. Burke BM, Cunliffe WJ. The assessment of acne vulgaris: the Leeds technique. Br J Dermatol. 1984;111:83–92.
93. Tan J, Alexis A, Baldwin H, et al. Gaps and recommendations for clinical management of truncal acne from the Personalising Acne: Consensus of Experts Panel. JAAD Int. 2021;5:33–40.
94. Poli F, Auffret N, Leccia MT, et al. Truncal acne, what do we know? J Eur Acad Dermatol Venereol. 2020;34:2241–6.
95. Kircik L. Efficacy and safety of tazarotene lotion, 0.045% in the treatment of truncal acne vulgaris. J Drugs Dermatol. 2021;21:713–6.

96. Hoffman LK, Del Rosso JQ, Kircik LH. The efficacy and safety of azelaic acid 15% foam in the treatment of truncal acne vulgaris. J Drugs Dermatol. 2017;16:534–8.
97. Del Rosso JQ, Kircik L, Tanghetti E. Management of truncal acne vulgaris with topical dapsone 7.5% gel. J Clin Aesthet Dermatol. 2018;11:45–50.
98. Leyden JJ, Wortzman M, Baldwin EK. Antibiotic-resistant Propionibacterium acnes suppressed by a benzoyl peroxide cleanser 6%. Cutis. 2008;82:417–21.
99. Leyden JJ, Preston N, Osborn C, et al. In-vivo effectiveness of adapalene 0.1%/benzoyl peroxide 2.5% gel on antibiotic-sensitive and resistant Propionibacterium acnes. J Clin Aesthet Dermatol. 2011;4:22–6.
100. Gollnick H, Cunliffe W, Berson D, et al. Management of acne: a report from a global alliance to improve outcomes in acne. J Am Acad Dermatol. 2003;49:1–37.
101. Bikowski J. A review of the safety and efficacy of benzoyl peroxide (5.3%) emollient foam in the management of truncal acne vulgaris. J Clin Aesthet Dermatol. 2010;3:26–9.
102. Leyden JJ. Efficacy of benzoyl peroxide (5.3%) emollient foam and benzoyl peroxide (8%) wash in reducing Propionibacterium acnes on the back. J Drugs Dermatol. 2010;9:622–5.
103. Leyden JJ, Del Rosso JQ. The effect of benzoyl peroxide 9.8% emollient foam on reduction of Propionibacterium acnes on the back using a short contact therapy approach. J Drugs Dermatol. 2012;11:830–3.
104. Tanghetti E, Abramovits W, Solomon B, et al. Tazarotene versus tazarotene plus clindamycin/benzoyl peroxide in the treatment of acne vulgaris: a multicenter, double-blind, randomized parallel-group trial. J Drugs Dermatol. 2006;5:256–61.
105. Keating GM. Adapalene 0.1%/benzoyl peroxide 2.5% gel: a review of its use in the treatment of acne vulgaris in patients aged >/= 12 years. Am J Clin Dermatol. 2011;12:407–20.
106. Zouboulis CC, Fischer TC, Wohlrab J, et al. Study of the efficacy, tolerability, and safety of 2 fixed-dose combination gels in the management of acne vulgaris. Cutis. 2009;84:223–9.
107. Yang Z, Zhang Y, Lazic Mosler E, et al. Topical benzoyl peroxide for acne. Cochrane Database Syst Rev. 2020;3:11154.
108. Toyoda M, Morohashi M. An overview of topical antibiotics for acne treatment. Dermatology. 1998;6:130–4.
109. Mills O Jr, Thornsberry C, Cardin CW, et al. Bacterial resistance and therapeutic outcome following three months of topical acne therapy with 2% erythromycin gel versus its vehicle. Acta Derm Venereol. 2002;82:260–5.
110. Webster G, Rich P, Gold MH, et al. Efficacy and tolerability of a fixed combination of clindamycin phosphate (1.2%) and low concentration benzoyl peroxide (2.5%) aqueous gel in moderate or severe acne subpopulations. J Drugs Dermatol. 2009;8:736–43.
111. Thiboutot D, Zaenglein A, Weiss J, et al. An aqueous gel fixed combination of clindamycin phosphate 1.2% and benzoyl peroxide 2.5% for the once-daily treatment of moderate to severe acne vulgaris: assessment of efficacy and safety in 2813 patients. J Am Acad Dermatol. 2008;59:792–800.
112. Lookingbill DP, Chalker DK, Lindholm JS, et al. Treatment of acne with a combination clindamycin/benzoyl peroxide gel compared with clindamycin gel, benzoyl peroxide gel and vehicle gel: combined results of two double-blind investigations. J Am Acad Dermatol. 1997;37:590–5.
113. Tschen EH, Katz HI, Jones TM, et al. A combination benzoyl peroxide and clindamycin topical gel compared with benzoyl peroxide, clindamycin phosphate, and vehicle in the treatment of acne vulgaris. Cutis. 2001;67:165–9.
114. Leyden JJ, Hickman JG, Jarratt MT, et al. The efficacy and safety of a combination benzoyl peroxide/clindamycin topical gel compared with benzoyl peroxide alone and a benzoyl peroxide/erythromycin combination product. J Cutan Med Surg. 2001;5:37–42.
115. Pariser DM, Rich P, Cook-Bolden FE, et al. An aqueous gel fixed combination of clindamycin phosphate 1.2% and benzoyl peroxide 3.75% for the once-daily treatment of moderate to severe acne vulgaris. J Drugs Dermatol. 2014;13:1083–9.
116. F.P. Ltd. Foamix receives FDA approval of Amzeeq™ topical minocycline treatment for millions of moderate to severe acne sufferers, PR Newswire, 2019.
117. Martins AM, Marto JM, Johnson JL, et al. A review of systemic minocycline side effects and topical minocycline as a safer alternative for treating acne and rosacea. Antibiotics (Basel). 2021;10:2.
118. Gold LS, Dhawan S, Weiss J, et al. A novel topical minocycline foam for the treatment of moderate-to-severe acne vulgaris: Results of 2 randomized, double-blind, phase 3 studies. J Am Acad Dermatol. 2019;80:168–77.
119. Kolli SS, Pecone D, Pona A, et al. Topical retinoids in acne vulgaris: a systematic review. Am J Clin Dermatol. 2019;20:345–65.
120. Leyden J, Stein-Gold L, Weiss J. Why topical retinoids are mainstay of therapy for acne. Dermatol Ther (Heidelb). 2017;7:293–304.
121. Blume-Peytavi U, Fowler J, Kemeny L, et al. Long-term safety and efficacy of trifarotene 50 mug/g cream, a first-in-class RAR-gamma selective topical retinoid, in patients with moderate facial and truncal acne. J Eur Acad Dermatol Venereol. 2020;34:166–73.
122. Richter JR, Forstrom LR, Kiistala UO, et al. Efficacy of the fixed 1.2% clindamycin phosphate, 0.025% tretinoin gel formulation (Velac) and a proprietary 0.025% tretinoin gel formulation (Aberela) in the topical control of facial acne. J Eur Acad Dermatol Venereol. 1998;11:227–33.
123. Zouboulis CC, Derumeaux L, Decroix J, et al. A multicentre, single-blind, randomized comparison of a fixed clindamycin phosphate/tretinoin gel formulation (Velac) applied once daily and a clindamycin lotion formulation (Dalacin T) applied twice daily in the topical treatment of acne vulgaris. Br J Dermatol. 2000;143:498–505.
124. Dreno B, Bettoli V, Ochsendorf F, et al. Efficacy and safety of clindamycin phosphate 1.2%/tretinoin 0.025% formulation for the treatment of acne vulgaris: pooled analysis of data from three randomised, double-blind, parallel-group, phase III studies. Eur J Dermatol. 2014;24:201–9.
125. Dhillon S. Clascoterone: first approval. Drugs. 2020;80:1745–50.
126. Hebert A, Thiboutot D, Stein Gold L, et al. Efficacy and safety of topical clascoterone cream, 1%, for treatment in patients with facial acne: two phase 3 randomized clinical trials. JAMA Dermatol. 2020;156:621–30.
127. Ferraboschi P, Legnani L, Celasco G, et al. A full conformational characterization of antiandrogen cortexolone-17 alpha-propionate and related compounds through theoretical calculations and nuclear magnetic resonance spectroscopy. Medchemcomm. 2014;5:904–14.
128. Mazzetti A, Moro L, Gerloni M, et al. Pharmacokinetic profile, safety, and tolerability of clascoterone (cortexolone 17-alpha propionate, CB-03-01) topical cream, 1% in subjects with acne vulgaris: an open-label phase 2a study. J Drugs Dermatol. 2019;18:563.
129. Marks DH, Mansh MD. Potential role for topical antiandrogens in the management of acne among patients receiving masculinizing hormone therapy. JAMA Dermatol. 2020;156:1380–1.
130. Eichenfield L, Hebert A, Gold LS, et al. Open-label, long-term extension study to evaluate the safety of clascoterone (CB-03-01)

cream, 1% twice daily, in patients with acne vulgaris. J Am Acad Dermatol. 2020;83:477–85.
131. Kainz JT, Berghammer G, Auer-Grumbach P, et al. Azelaic acid 20 % cream: effects on quality of life and disease severity in adult female acne patients. J Dtsch Dermatol Ges. 2016;14:1249–59.
132. Eastman WJ, Malahias S, Delconte J, et al. Assessing attributes of topical vehicles for the treatment of acne, atopic dermatitis, and plaque psoriasis. Cutis. 2014;94:46–53.
133. Tan HH. Antibacterial therapy for acne: a guide to selection and use of systemic agents. Am J Clin Dermatol. 2003;4:307–14.
134. Webster GF, McGinley KJ, Leyden JJ. Inhibition of lipase production in Propionibacterium acnes by sub-minimal-inhibitory concentrations of tetracycline and erythromycin. Br J Dermatol. 1981;104:453–7.
135. Armstrong AW, Hekmatjah J, Kircik LH. Oral tetracyclines and acne: a systematic review for dermatologists. J Drugs Dermatol. 2020;19:s6-13.
136. Leyden JJ, Bruce S, Lee CS, et al. A randomized, phase 2, dose-ranging study in the treatment of moderate to severe inflammatory facial acne vulgaris with doxycycline calcium. J Drugs Dermatol. 2013;12:658–63.
137. Patel M, Bowe WP, Heughebaert C, et al. The development of antimicrobial resistance due to the antibiotic treatment of acne vulgaris: a review. J Drugs Dermatol. 2010;9:655–64.
138. Del Rosso JQ, Webster GF, Rosen T, et al. Status report from the Scientific Panel on Antibiotic Use in Dermatology of the American Acne and Rosacea Society: part 1: antibiotic prescribing patterns, sources of antibiotic exposure, antibiotic consumption and emergence of antibiotic resistance, impact of alterations in antibiotic prescribing, and clinical sequelae of antibiotic use. J Clin Aesthet Dermatol. 2016;9:18–24.
139. Thompson KG, Rainer BM, Antonescu C, et al. Minocycline and its impact on microbial dysbiosis in the skin and gastrointestinal tract of acne patients. Ann Dermatol. 2020;32:21–30.
140. Francino MP. Antibiotics and the human gut microbiome: dysbioses and accumulation of resistances. Front Microbiol. 2015;6:1543.
141. Margolis DJ, Fanelli M, Hoffstad O, et al. Potential association between the oral tetracycline class of antimicrobials used to treat acne and inflammatory bowel disease. Am J Gastroenterol. 2010;105:2610–6.
142. Farrah G, Tan E. The use of oral antibiotics in treating acne vulgaris: a new approach. Dermatol Ther. 2016;29:377–84.
143. US Food and Drug Administration. Seysara® (sarecycline) tablets for oral use (package insert). Approved prescribing information. Almirall LLC.
144. Deeks ED. Sarecycline: first global approval. Drugs. 2019;79:325–9.
145. Batool Z, Lomakin IB, Polikanov YS, et al. Sarecycline interferes with tRNA accommodation and tethers mRNA to the 70S ribosome. Proc Natl Acad Sci U S A. 2020;117:20530–7.
146. Bunick CG, Keri J, Tanaka SK, et al. Antibacterial mechanisms and efficacy of sarecycline in animal models of infection and inflammation. Antibiotics (Basel). 2021;10:2.
147. Zhanel G, Critchley I, Lin LY, et al. Microbiological profile of sarecycline, a novel targeted spectrum tetracycline for the treatment of acne vulgaris. Antimicrob Agents Chemother. 2019;63:2.
148. Grada A, Bunick CG. Spectrum of antibiotic activity and its relevance to the microbiome. JAMA Netw Open. 2021;4: e215357.
149. Moore A, Green LJ, Bruce S, et al. Once-daily oral sarecycline 1.5 mg/kg/day is effective for moderate to severe acne vulgaris: results from two identically designed, phase 3, randomized, double-blind clinical trials. J Drugs Dermatol. 2018;17:987–96.
150. Del Rosso JQ, Stein Gold L, Baldwin H, et al. Management of truncal acne with oral sarecycline: pooled results from two phase-3 clinical trials. J Drugs Dermatol. 2021;20:634–40.
151. Nelson AM, Gilliland KL, Cong Z, et al. 13-cis Retinoic acid induces apoptosis and cell cycle arrest in human SEB-1 sebocytes. J Invest Dermatol. 2006;126:2178–89.
152. Webster GF, Leyden JJ, Gross JA. Results of a phase III, double-blind, randomized, parallel-group, non-inferiority study evaluating the safety and efficacy of Isotretinoin-Lidose in patients with severe recalcitrant nodular acne. J Drugs Dermatol. 2014;13:665–70.
153. Peck GL, Olsen TG, Yoder FW, et al. Prolonged remissions of cystic and conglobate acne with 13-cis-retinoic acid. N Engl J Med. 1979;300:329–33.
154. Layton A. The use of isotretinoin in acne. Dermatoendocrinol. 2009;1:162–9.
155. Rubinow DR, Peck GL, Squillace KM, et al. Reduced anxiety and depression in cystic acne patients after successful treatment with oral isotretinoin. J Am Acad Dermatol. 1987;17:25–32.
156. Marron SE, Tomas-Aragones L, Boira S. Anxiety, depression, quality of life and patient satisfaction in acne patients treated with oral isotretinoin. Acta Derm Venereol. 2013;93:701–6.
157. Layton AM, Knaggs H, Taylor J, et al. Isotretinoin for acne vulgaris: 10 years later: a safe and successful treatment. Br J Dermatol. 1993;129:292–6.
158. Goldsmith LA, Bolognia JL, Callen JP, et al. American Academy of Dermatology Consensus Conference on the safe and optimal use of isotretinoin: summary and recommendations. J Am Acad Dermatol. 2004;50:900–6.
159. Borghi A, Mantovani L, Minghetti S, et al. Low-cumulative dose isotretinoin treatment in mild-to-moderate acne: efficacy in achieving stable remission. J Eur Acad Dermatol Venereol. 2011;25:1094–8.
160. Amichai B, Shemer A, Grunwald MH. Low-dose isotretinoin in the treatment of acne vulgaris. J Am Acad Dermatol. 2006;54:644–6.
161. Strauss JS, Rapini RP, Shalita AR, et al. Isotretinoin therapy for acne: results of a multicenter dose-response study. J Am Acad Dermatol. 1984;10:490–6.
162. Blasiak RC, Stamey CR, Burkhart CN, et al. High-dose isotretinoin treatment and the rate of retrial, relapse, and adverse effects in patients with acne vulgaris. JAMA Dermatol. 2013;49:1392–8.
163. Cyrulnik AA, Viola KV, Gewirtzman AJ, et al. High-dose isotretinoin in acne vulgaris: improved treatment outcomes and quality of life. Int J Dermatol. 2012;51:1123–30.
164. Rademaker M. Isotretinoin: dose, duration and relapse. What does 30 years of usage tell us? Australas J Dermatol. 2013;54:157–62.
165. Zouboulis CC. The truth behind this undeniable efficacy: recurrence rates and relapse risk factors of acne treatment with oral isotretinoin. Dermatology. 2006;212:99–100.
166. Quereux G, Volteau C, N'Guyen JM, et al. Prospective study of risk factors of relapse after treatment of acne with oral isotretinoin. Dermatology. 2006;212:168–76.
167. Cunliffe WJ, Norris JF. Isotretinoin: an explanation for its long-term benefit. Dermatologica. 1987;175(Suppl. 1):133–7.
168. Rademaker M. Adverse effects of isotretinoin: a retrospective review of 1743 patients started on isotretinoin. Australas J Dermatol. 2010;51:248–53.
169. Ellis CN, Krach KJ. Uses and complications of isotretinoin therapy. J Am Acad Dermatol. 2001;45:S150–7.
170. Marqueling AL, Zane LT. Depression and suicidal behavior in acne patients treated with isotretinoin: a systematic review. Semin Cutan Med Surg. 2007;26:210–20.
171. Chia CY, Lane W, Chibnall J, et al. Isotretinoin therapy and mood changes in adolescents with moderate to severe acne: a cohort study. Arch Dermatol. 2005;141:557–60.

172. Rashtak S, Khaleghi S, Pittelkow MR, et al. Isotretinoin exposure and risk of inflammatory bowel disease. JAMA Dermatol. 2014;150:1322–6.
173. Paljarvi T, McPherson T, Luciano S, et al. Isotretinoin and adverse neuropsychiatric outcomes: retrospective cohort study using routine data. Br J Dermatol. 2022;187:64–72.
174. Dai WS, LaBraico JM, Stern RS. Epidemiology of isotretinoin exposure during pregnancy. J Am Acad Dermatol. 1992;26:599–606.
175. Collins MK, Moreau JF, Opel D, et al. Compliance with pregnancy prevention measures during isotretinoin therapy. J Am Acad Dermatol. 2014;70:55–9.
176. Thorneycroft IH, Stanczyk FZ, Bradshaw KD, et al. Effect of low-dose oral contraceptives on androgenic markers and acne. Contraception. 1999;60:255–62.
177. Panzer C, Wise S, Fantini G, et al. Impact of oral contraceptives on sex hormone-binding globulin and androgen levels: a retrospective study in women with sexual dysfunction. J Sex Med. 2006;3:104–13.
178. Koo EB, Petersen TD, Kimball AB. Meta-analysis comparing efficacy of antibiotics versus oral contraceptives in acne vulgaris. J Am Acad Dermatol. 2014;71:450–9.
179. Palli MB, Reyes-Habito CM, Lima XT, et al. A single-center, randomized double-blind, parallel-group study to examine the safety and efficacy of 3mg drospirenone/0.02 mg ethinyl estradiol compared with placebo in the treatment of moderate truncal acne vulgaris. J Drugs Dermatol. 2013;2:633–7.
180. Lidegaard O, Lokkegaard E, Svendsen AL, et al. Hormonal contraception and risk of venous thromboembolism: national follow-up study. BMJ. 2009;339: b2890.
181. Jick SS, Hernandez RK. Risk of non-fatal venous thromboembolism in women using oral contraceptives containing drospirenone compared with women using oral contraceptives containing levonorgestrel: case-control study using United States claims data. BMJ. 2011;342: d2151.
182. Gronich N, Lavi I, Rennert G. Higher risk of venous thrombosis associated with drospirenone-containing oral contraceptives: a population-based cohort study. CMAJ. 2011;183:E1319–25.
183. Katsambas AD, Dessinioti C. Hormonal therapy for acne: why not as first line therapy? Facts and controversies Clin Dermatol. 2010;28:17–23.
184. van Vlijmen EF, Veeger NJ, Middeldorp S, et al. Thrombotic risk during oral contraceptive use and pregnancy in women with factor V Leiden or prothrombin mutation: a rational approach to contraception. Blood. 2011;118:2055–61; quiz 2375.
185. Svoboda RM, Nawaz N, Zaenglein AL. Hormonal treatment of acne and hidradenitis suppurativa in adolescent patients. Dermatol Clin. 2022;40:167–78.
186. Gierisch JM, Coeytaux RR, Urrutia RP, et al. Oral contraceptive use and risk of breast, cervical, colorectal, and endometrial cancers: a systematic review. Cancer Epidemiol Biomarkers Prev. 2013;22:1931–43.
187. Krunic A, Ciurea A, Scheman A. Efficacy and tolerance of acne treatment using both spironolactone and a combined contraceptive containing drospirenone. J Am Acad Dermatol. 2008;58:60–2.
188. Menard RH, Stripp B, Gillette JR. Spironolactone and testicular cytochrome P-450: decreased testosterone formation in several species and changes in hepatic drug metabolism. Endocrinology. 1974;94:1628–36.
189. Boisselle A, Dionne FT, Tremblay RR. Interaction of spironolactone with rat skin androgen receptor. Can J Biochem. 1979;57:1042–6.
190. Layton AM, Eady EA, Whitehouse H, et al. Oral spironolactone for acne vulgaris in adult females: a hybrid systematic review. Am J Clin Dermatol. 2017;18:169–91.
191. Isvy-Joubert A, Nguyen JM, Gaultier A, et al. Adult female acne treated with spironolactone: a retrospective data review of 70 cases. Eur J Dermatol. 2017;27:393–8.
192. Charny JW, Choi JK, James WD. Spironolactone for the treatment of acne in women, a retrospective study of 110 patients. Int J Womens Dermatol. 2017;3:111–5.
193. Shaw JC, White LE. Long-term safety of spironolactone in acne: results of an 8-year followup study. J Cutan Med Surg. 2002;6:541–5.
194. Elsaie ML. Hormonal treatment of acne vulgaris: an update. Clin Cosmet Investig Dermatol. 2016;9:241–8.
195. Thiede RM, Rastogi S, Nardone B, et al. Hyperkalemia in women with acne exposed to oral spironolactone: a retrospective study from the RADAR (Research on Adverse Drug Events and Reports) program. Int J Womens Dermatol. 2019;5:155–7.
196. Plovanich M, Weng QY, Mostaghimi A. Low usefulness of potassium monitoring among healthy young women taking spironolactone for acne. JAMA Dermatol. 2015;151:941–4.
197. Layton AM, Henderson CA, Cunliffe WJ. A clinical evaluation of acne scarring and its incidence. Clin Exp Dermatol. 1994;19:303–8.
198. Holland DB, Jeremy AH, Roberts SG, et al. Inflammation in acne scarring: a comparison of the responses in lesions from patients prone and not prone to scar. Br J Dermatol. 2004;150:72–81.
199. Goodman GJ. Postacne scarring: a review of its pathophysiology and treatment. Dermatol Surg. 2000;26:857–71.
200. Layton A, Alexis A, Baldwin H, et al. Identifying gaps and providing recommendations to address shortcomings in the investigation of acne sequelae by the Personalising Acne: Consensus of Experts panel. JAAD Int. 2021;5:41–8.
201. Connolly D, Vu HL, Mariwalla K, et al. Acne scarring: pathogenesis, evaluation, and treatment options. J Clin Aesthet Dermatol. 2017;10:12–23.
202. Jacob CI, Dover JS, Kaminer MS. Acne scarring: a classification system and review of treatment options. J Am Acad Dermatol. 2001;45:109–17.
203. Jemec GB, Jemec B. Acne: treatment of scars. Clin Dermatol. 2004;22:434–8.
204. Saha AK, Mukhopadhyay M. A comparative clinical study on role of 5-flurouracil versus triamcinolone in the treatment of keloids. Indian J Surg. 2012;74:326–9.
205. Forbat E, Al-Niaimi F. Nonvascular uses of pulsed dye laser in clinical dermatology. J Cosmet Dermatol. 2019.
206. Yoon HJ, Lee DH, Kim SO, et al. Acne erythema improvement by long-pulsed 595-nm pulsed-dye laser treatment: a pilot study. J Dermatolog Treat. 2008;19:38–44.
207. Patel N, Clement M. Selective nonablative treatment of acne scarring with 585 nm flashlamp pulsed dye laser. Dermatol Surg. 2002;28:942–5.
208. Lee DH, Choi YS, Min SU, et al. Comparison of a 585-nm pulsed dye laser and a 1064-nm Nd:YAG laser for the treatment of acne scars: a randomized split-face clinical study. J Am Acad Dermatol. 2009;60:801–7.
209. Alster TS. Improvement of erythematous and hypertrophic scars by the 585-nm flashlamp-pumped pulsed dye laser. Ann Plast Surg. 1994;32:186–90.
210. Khatri KA, Mahoney DL, McCartney MJ. Laser scar revision: a review. J Cosmet Laser Ther. 2011;13:54–62.
211. Vrijman C, van Drooge AM, Limpens J, et al. Laser and intense pulsed light therapy for the treatment of hypertrophic scars: a systematic review. Br J Dermatol. 2011;165:934–42.
212. Kono T, Ercocen AR, Nakazawa H, et al. The flashlamp-pumped pulsed dye laser (585 nm) treatment of hypertrophic scars in Asians. Ann Plast Surg. 2003;51:366–71.

213. Rao J. Treatment of acne scarring. Facial Plast Surg Clin North Am. 2011;19:275–91.
214. Faghihi G, Isfahani AK, Hosseini SM, et al. Efficacy of intense pulsed light combined with topical erythromycin solution 2% versus topical erythromycin solution 2% alone in the treatment of persistent facial erythematous acne macules. Adv Biomed Res. 2012;1:70.
215. Feng H, Wu Y, Jiang M, et al. The efficacy and safety of fractional 1064 nm Nd:YAG picosecond laser combined with intense pulsed light in the treatment of atrophic acne scar: a split-face study. Lasers Surg Med. 2021;3:1356–63.
216. Wang B, Wu Y, Luo YJ, et al. Combination of intense pulsed light and fractional CO(2) laser treatments for patients with acne with inflammatory and scarring lesions. Clin Exp Dermatol. 2013;38:344–51.
217. Erol OO, Gurlek A, Agaoglu G, et al. Treatment of hypertrophic scars and keloids using intense pulsed light (IPL). Aesthetic Plast Surg. 2008;32:902–9.
218. Piccolo D, Kostaki D, Dianzani C, et al. Effective intense pulsed light protocol in the treatment of moderate to severe acne vulgaris of the chest and back. J Clin Aesthet Dermatol. 2022;15:22–5.
219. Salameh F, Shumaker PR, Goodman GJ, et al. Energy-based devices for the treatment of acne scars: 2022 international consensus recommendations. Lasers Surg Med. 2022;54:10–26.
220. Cohen BE, Brauer JA, Geronemus RG. Acne scarring: a review of available therapeutic lasers. Lasers Surg Med. 2016;48:95–115.
221. Chapas AM, Brightman L, Sukal S, et al. Successful treatment of acneiform scarring with CO2 ablative fractional resurfacing. Lasers Surg Med. 2008;40:381–6.
222. Chan NP, Ho SG, Yeung CK, et al. Fractional ablative carbon dioxide laser resurfacing for skin rejuvenation and acne scars in Asians. Lasers Surg Med. 2010;42:615–23.
223. Hu S, Hsiao WC, Chen MC, et al. Ablative fractional erbium-doped yttrium aluminum garnet laser with coagulation mode for the treatment of atrophic acne scars in Asian skin. Dermatol Surg. 2011;37:939–44.
224. Kim S, Cho KH. Clinical trial of dual treatment with an ablative fractional laser and a nonablative laser for the treatment of acne scars in Asian patients. Dermatol Surg. 2009;35:1089–98.
225. Cameli N, Mariano M, Serio M, et al. Preliminary comparison of fractional laser with fractional laser plus radiofrequency for the treatment of acne scars and photoaging. Dermatol Surg. 2014;40:553–61.
226. Faghihi G, Keyvan S, Asilian A, et al. Efficacy of autologous platelet-rich plasma combined with fractional ablative carbon dioxide resurfacing laser in treatment of facial atrophic acne scars: a split-face randomized clinical trial. Indian J Dermatol Venereol Leprol. 2016;82:162–8.
227. Gawdat HI, Hegazy RA, Fawzy MM, et al. Autologous platelet rich plasma: topical versus intradermal after fractional ablative carbon dioxide laser treatment of atrophic acne scars. Dermatol Surg. 2014;40:152–61.
228. Lee JW, Kim BJ, Kim MN, et al. The efficacy of autologous platelet rich plasma combined with ablative carbon dioxide fractional resurfacing for acne scars: a simultaneous split-face trial. Dermatol Surg. 2011;37:931–8.
229. Preissig J, Hamilton K, Markus R. Current laser resurfacing technologies: a review that delves beneath the surface. Semin Plast Surg. 2012;26:109–16.
230. Elsaie ML, Ibrahim SM, Saudi W. Ablative fractional 10 600 nm carbon dioxide laser versus non-ablative fractional 1540 nm erbium-glass laser in Egyptian post-acne scar patients. J Lasers Med Sci. 2018;9:32–5.
231. Cheng X, Yang Q, Su Y, et al. Comparison of 1565-nm nonablative fractional laser and 10600-nm ablative fractional laser in the treatment of mild to moderate atrophic acne scars. Dermatol Surg. 2021;47:392–6.
232. Sardana K, Manjhi M, Garg VK, et al. Which type of atrophic acne scar (ice-pick, boxcar, or rolling) responds to nonablative fractional laser therapy? Dermatol Surg. 2014;40:288–300.
233. Chan NP, Ho SG, Yeung CK, et al. The use of non-ablative fractional resurfacing in Asian acne scar patients. Lasers Surg Med. 2010;42:710–5.
234. Alexis AF, Coley MK, Nijhawan RI, et al. Nonablative fractional laser resurfacing for acne scarring in patients with Fitzpatrick skin phototypes IV-VI. Dermatol Surg. 2016;42:392–402.
235. Torbeck RL, Schilling L, Khorasani H, et al. Evolution of the picosecond laser: a review of literature. Dermatol Surg. 2019;45:183–94.
236. Lee CH, Jin EM, Seo HS, et al. Efficacy and safety of treatment with fractional 1,064-nm picosecond laser with diffractive optic element for wrinkles and acne scars: a clinical study. Ann Dermatol. 2021;33:254–62.
237. Choi ME, Paik SH, Lee WJ, et al. Treatment of acne scars with a fractional 1064-nm Nd:YAG picosecond laser and histopathologic findings. Dermatol Ther. 2020;33: e13297.
238. Chayavichitsilp P, Limtong P, Triyangkulsri K, et al. Comparison of fractional neodymium-doped yttrium aluminum garnet (Nd:YAG) 1064-nm picosecond laser and fractional 1550-nm erbium fiber laser in facial acne scar treatment. Lasers Med Sci. 2020;35:695–700.
239. Sirithanabadeekul P, Tantrapornpong P, Rattakul B, et al. Comparison of fractional picosecond 1064-nm laser and fractional carbon dioxide laser for treating atrophic acne scars: a randomized split-face trial. Dermatol Surg. 2021;47:e58-65.
240. Brauer JA, Kazlouskaya V, Alabdulrazzaq H, et al. Use of a picosecond pulse duration laser with specialized optic for treatment of facial acne scarring. JAMA Dermatol. 2015;151:278–84.
241. Boen M, Jacob C. A review and update of treatment options using the Acne Scar Classification System. Dermatol Surg. 2019;45:411–22.
242. Nitayavardhana S, Wanitphakdeedecha R, Ng JNC, et al. The efficacy and safety of fractional radiofrequency nanoneedle system in the treatment of atrophic acne scars in Asians. J Cosmet Dermatol. 2020;19:1636–41.
243. Goel A, Gatne V. Use of nanofractional radiofrequency for the treatment of acne scars in Indian skin. J Cosmet Dermatol. 2017;16:186–92.
244. Simmons BJ, Griffith RD, Falto-Aizpurua LA, et al. Use of radiofrequency in cosmetic dermatology: focus on nonablative treatment of acne scars. Clin Cosmet Investig Dermatol. 2014;7:335–9.
245. Min S, Park SY, Yoon JY, et al. Comparison of fractional microneedling radiofrequency and bipolar radiofrequency on acne and acne scar and investigation of mechanism: comparative randomized controlled clinical trial. Arch Dermatol Res. 2015;307:897–904.
246. Katz BE. The fate of active acne and acne scars following treatment with fractional radiofrequency. J Drugs Dermatol. 2019;18:1268–72.
247. Kacar N, Dursun R, Akbay M, et al. The early and late efficacy of single-pass fractional carbondioxide laser, fractional radiofrequency, and their combination in acne scars: a prospective, split-face, single-blinded, controlled clinical study. Dermatol Ther. 2020;33: e14444.
248. Tatliparmak A, Aksoy B, Shishehgarkhaneh LR, et al. Use of combined fractional carbon dioxide laser and fractional microneedle radiofrequency for the treatment of acne scars: a retrospective analysis of 1-month treatment outcome on

scar severity and patient satisfaction. J Cosmet Dermatol. 2020;19:115–21.
249. Kim J, Lee YI, Kim J, et al. Safety of combined fractional microneedle radiofrequency and CO2 as an early intervention for inflammatory acne and scarring treated with concomitant isotretinoin. Dermatol Surg. 2020;46:e71–7.
250. Minh PPT, Bich DD, Hai VNT, et al. Microneedling therapy for atrophic acne scar: effectiveness and safety in Vietnamese patients. Open Access Maced J Med Sci. 2019;7:293–7.
251. El-Domyati M, Barakat M, Awad S, et al. Microneedling therapy for atrophic acne scars: an objective evaluation. J Clin Aesthet Dermatol. 2015;8:36–42.
252. Dogra S, Yadav S, Sarangal R. Microneedling for acne scars in Asian skin type: an effective low cost treatment modality. J Cosmet Dermatol. 2014;13:180–7.
253. Cachafeiro T, Escobar G, Maldonado G, et al. Comparison of nonablative fractional erbium laser 1,340 nm and microneedling for the treatment of atrophic acne scars: a randomized clinical trial. Dermatol Surg. 2016;42:232–41.
254. Asif M, Kanodia S, Singh K. Combined autologous platelet-rich plasma with microneedling verses microneedling with distilled water in the treatment of atrophic acne scars: a concurrent split-face study. J Cosmet Dermatol. 2016;15:434–43.
255. Ibrahim MK, Ibrahim SM, Salem AM. Skin microneedling plus platelet-rich plasma versus skin microneedling alone in the treatment of atrophic post acne scars: a split face comparative study. J Dermatolog Treat. 2018;29:281–6.
256. Schoenberg E, O'Connor M, Wang JV, et al. Microneedling and PRP for acne scars: a new tool in our arsenal. J Cosmet Dermatol. 2020;19:112–4.
257. Rana S, Mendiratta V, Chander R. Efficacy of microneedling with 70% glycolic acid peel vs microneedling alone in treatment of atrophic acne scars: a randomized controlled trial. J Cosmet Dermatol. 2017;16:454–9.
258. Sharad J. Combination of microneedling and glycolic acid peels for the treatment of acne scars in dark skin. J Cosmet Dermatol. 2011;10:317–23.
259. Morelli Coppola M, Salzillo R, Segreto F, et al. Triamcinolone acetonide intralesional injection for the treatment of keloid scars: patient selection and perspectives. Clin Cosmet Investig Dermatol. 2018;11:387–96.
260. Khan MA, Bashir MM, Khan FA. Intralesional triamcinolone alone and in combination with 5-fluorouracil for the treatment of keloid and hypertrophic scars. J Pak Med Assoc. 2014;64:1003–7.
261. Waibel JS, Wulkan AJ, Shumaker PR. Treatment of hypertrophic scars using laser and laser assisted corticosteroid delivery. Lasers Surg Med. 2013;45:135–40.
262. Tawfik AA, Fathy M, Badawi A, et al. Topical 5 fluorouracil cream vs combined 5 fluorouracil and fractional erbium YAG laser for treatment of severe hypertrophic scars. Clin Cosmet Investig Dermatol. 2019;12:173–80.
263. Waibel JS, Wulkan AJ, Rudnick A, et al. Treatment of hypertrophic scars using laser-sssisted corticosteroid versus laser-assisted 5-fluorouracil delivery. Dermatol Surg. 2019;45:423–30.
264. Beer K. A single-center, open-label study on the use of injectable poly-L-lactic acid for the treatment of moderate to severe scarring from acne or varicella. Dermatol Surg. 2007;33(Suppl. 2):S159–67.
265. Rkein A, Ozog D, Waibel JS. Treatment of atrophic scars with fractionated CO2 laser facilitating delivery of topically applied poly-L-lactic acid. Dermatol Surg. 2014;40:624–31.
266. Epstein RE, Spencer JM. Correction of atrophic scars with artefill: an open-label pilot study. J Drugs Dermatol. 2010;9:1062–4.
267. Karnik J, Baumann L, Bruce S, et al. A double-blind, randomized, multicenter, controlled trial of suspended polymethylmethacrylate microspheres for the correction of atrophic facial acne scars. J Am Acad Dermatol. 2014;71:77–83.
268. Biesman BS, Cohen JL, DiBernardo BE, et al. Treatment of atrophic facial acne scars with microneedling followed by polymethylmethacrylate-collagen gel dermal filler. Dermatol Surg. 2019;45:1570–9.