Unmet Needs in the Management of Acne Vulgaris: A Consensus Statement

Hilary Baldwin MD,[a] Aaron S. Farberg MD FAAD,[b] Cheri Frey MD,[c] Corey L. Hartman MD FAAD,[d] Edward Lain MD,[e] Rachel Meltzer MD MPH,[f] Zoe Draelos MD[g]

[a]Medical Director, The Acne Treatment and Research Center, Brooklyn NY, and Clinical Associate Professor of Dermatology, Rutgers Robert Wood Johnson Medical Center, New Brunswick, NJ
[b]Bare Dermatology, Dallas, TX, and Baylor Scott & White Health System, Dallas, TX
[c]Howard University, Washington, DC
[d]Skin Wellness Dermatology and University of Alabama at Birmingham Dermatology, Birmingham, AL
[e]Sanova Dermatology, Austin, TX
[f]Brigham and Women's Hospital and Harvard Medical School, Boston, MA
[g]Dermatology Consulting Services, High Point, NC

ABSTRACT

Acne vulgaris is the most common skin condition in the US, affecting up to 50 million Americans. The American Academy of Dermatology (AAD) guidelines on acne treatment were developed to provide recommendations for the diagnosis, grading, and treatment of acne in adolescents and adults to support clinicians in their therapeutic decision-making process. The most recent acne guidelines were published in 2016, and the approach to care and the therapeutic landscape of acne have evolved since that time. The Acne Management Consensus Roundtable was convened in 2022 to discuss unmet needs in the management of acne. The main focus of the meeting was the role of androgens in acne pathology; the evaluation of clascoterone, the first topical anti-androgen that specifically addresses sebum production in acne; and the identification of the place of clascoterone in therapy. Clascoterone was approved by the US Food and Drug Administration for the treatment of acne in patients 12 years and older in 2020. This report aims to highlight important limitations of the 2016 AAD treatment guidelines and to familiarize practitioners with clascoterone and its indication, efficacy and safety profile, and potential use across diverse patient populations. With its new mechanism of action, clascoterone may be able to fulfill important unmet needs in acne treatment.

J Drugs Dermatol. 2023;22(6):582-587. doi:10.36849/JDD.7587

INTRODUCTION

The most recent American Academy of Dermatology (AAD) guidelines on acne treatment were published in 2016.[1] The Acne Management Consensus Roundtable, a group of dermatologists, was convened in 2022 to discuss unmet needs in the management of acne. The meeting focused on the role of androgens in acne development; evaluation of the novel mechanism of action and clinical success of clascoterone, which was approved by the US Food and Drug Administration (FDA) in 2020 for the treatment of acne in patients 12 years and older; and identification of the place of clascoterone in acne therapy.

This report was developed to highlight unmet needs in acne treatment and to educate practitioners on how clascoterone, with its novel mechanism of action, may help to fill some of those gaps.

Pathogenesis of Acne

The pathophysiology of acne is multifactorial and involves 4 key, interrelated factors[2]: inflammation, follicular hyperkeratinization, increased sebaceous gland activity and sebum production, and colonization by *Cutibacterium acnes* (formerly *Propionibacterium acnes*).[3]

Abundant evidence indicates that androgen-stimulated sebum production drives acne pathogenesis by promoting growth, reproduction, and accumulation of skin cells in the hair follicle and providing an anaerobic environment that facilitates *C. acnes* proliferation and consequent inflammation[4,5]; androgens can also directly induce expression of inflammatory cytokines.[6] Increased levels of facial sebum secretion are observed in patients with acne compared with people without acne and positively correlate with lesion counts.[3,7-9] Alterations in sebum composition are also observed in patients with

acne and could contribute to the pathogenicity of sebum.[5] In order of abundance, human sebum mainly consists of esters of glycerol, wax, free fatty acids, squalene, and cholesterol.[10,11] Sebum analysis conducted in individuals with and without acne suggests that patients with acne generally have higher levels of squalene, and especially its pro-inflammatory oxidation byproducts,[12] and less linoleic acid in their sebum relative to patients without acne.[5,10,11,13,14] Triglycerides, lipoperoxides, and free fatty acids can promote *C. acnes* proliferation and inflammation by activation of the peroxisome proliferator-activated receptors signaling pathway.[7]

Role of Androgens in Acne

Testosterone and dihydrotestosterone (DHT) are produced by the testes or ovaries, adrenal glands, and locally within the pilosebaceous unit.[4,15] Testosterone produced by the testes is converted to DHT by 5α-reductase.[4] The ovaries release estrogen, progesterone, and androstenedione; androstenedione is first converted to testosterone, then to DHT by 5α-reductase.[16] Testosterone and DHT bind to androgen receptors in the pilosebaceous unit[15]; the androgen-receptor complex dimerizes and translocates to the cell nucleus,[15] where it promotes the expression of genes involved in the production of sebum and inflammatory cytokines.[4,15]

Ample evidence supports the role of androgens in acne pathogenesis in both male and female patients.[4,5] Some people with acne have elevated serum androgen levels, and the conversion of testosterone to DHT is more rapid in skin affected by acne relative to unaffected skin.[17,18] Patients with medical conditions characterized by high androgen levels, or patients receiving testosterone replacement therapy or anabolic steroids, are also prone to develop acne.[5] Acne is also a clinical manifestation of hyperandrogenism caused by polycystic ovary syndrome, congenital adrenal hyperplasia, and androgen-secreting tumors.[5,19,20] Acne without evidence of hyperandrogenism may be attributable to hypersensitivity of the androgen receptor[21]; in a prospective clinical study conducted between 2016 and 2017 in patients with severe and very severe acne (n = 199), there was a significant association between a CAG repeat polymorphism in the androgen receptor and nodulocystic acne in women without hormonal imbalance and hirsutism.[21] In support of the hypothesis that adequate control of androgen-stimulated sebum production can contribute to the success of acne treatment, oral contraceptives including combinations of ethinyl estradiol/drospirenone, ethinyl estradiol/desogestrel, ethinyl estradiol/chlormadinone, or ethinyl estradiol/cyproterone acetate can significantly reduce sebum excretion while improving several skin parameters (numbers of acne lesions, epidermal barrier function, pore size, and sebum production) in patients with acne.[22-25] Spironolactone (50–200 mg daily) also reduces sebum production in patients with severe acne.[26] Furthermore, acne remission was accompanied by reduced sebum excretion rates in a prospective study of patients with moderate to severe acne (n = 30) receiving isotretinoin treatment.[27]

The traditional anti-androgen therapies for acne include 4 combined oral contraceptive pills approved by the FDA for acne treatment in adult women who desire contraception. Spironolactone and flutamide are also used off-label for acne treatment due to their anti-androgenic properties. None of these are suitable for male or pregnant patients due to systemic anti-androgenic effects.[1] Acne therapies targeting this pathway may take time to result in improvement. Spironolactone efficacy has generally been evaluated only after 12 weeks,[28] and improvements in acne with oral contraceptives also take time, with significant effects usually observed after at least 3 cycles (28-day cycle, in a 24/4-day regimen).[1,29-31]

Current Acne Guidelines and Their Limitations

The AAD guidelines recommend a combination of multiple agents to target different aspects of acne pathogenesis as the first line of treatment.[1] Topical agents are recommended as the foundational treatment across all degrees of acne severity and may be used as monotherapy or in combination with other topical or oral treatments to address the different components of acne pathogenesis.[1] Based on the degree of acne severity, topical medications recommended for patients with mild and moderate acne include benzoyl peroxide, antibiotics, retinoids, and dapsone; topical azelaic acid is considered a useful adjunctive therapy, especially for the treatment of postinflammatory dyspigmentation.[1] For patients with moderate to severe acne, a combination of topical therapy plus oral medications, including oral contraceptives or spironolactone in female patients is recommended, with oral isotretinoin reserved for the most severe or refractory cases.[1]

Unfortunately, although topical medications are the mainstay of acne treatment, none of those currently recommended by the guidelines address all 4 key factors of acne pathogenesis[32]; in fact, no topical medications target excess sebum production.[32] Among oral medications, hormonal therapy can successfully moderate sebum production and related inflammation but has no direct effect on hyperkeratinization and *C. acnes* colonization; isotretinoin is the only treatment that can act on all 4 contributors to acne pathogenesis.[1,32] Although these systemic treatment options can be effective, they are not suitable for all patients. Isotretinoin is teratogenic and is contraindicated in patients who are pregnant and those who can become pregnant and are not willing to take contraceptives.[1,32] Hormonal therapies are not recommended for men, pregnant or lactating patients, and women ≥35 years old who are heavy smokers, and they are not advisable in patients receiving testosterone.[1,32,33] Spironolactone is associated with adverse effects including, diuresis, menstrual irregularities, breast tenderness, and gynecomastia, and may

block the masculinizing effects of testosterone therapy.[1,33] Considering the clinical and management gap in acne treatment, the authors recognize an unmet need for FDA-approved treatments that can safely address all key components of acne in a wide variety of patients (Table 1).

Guideline Limitations

Despite being developed based on the best available evidence, the current guidelines rely on studies that used different study designs, definitions of acne, and acne severity grading systems.[1] Most acne clinical trials did not specifically include vulnerable patient groups requiring additional considerations with regard to the benefits and risks of acne medications, and therefore, these special populations, including patients who are menopausal, lactating, pregnant, or receiving androgen therapy, are not adequately represented in the current guidelines. Truncal acne is not specifically discussed in the guidelines despite 30% to 60% of patients with facial acne having truncal involvement as well.[34-36] The skin on the trunk has different characteristics from facial skin, and different treatment recommendations could be more appropriate.[37] The guidelines also lack a dedicated section discussing novel therapies[1] and are therefore behind clinical practice and the present state of knowledge. Although many of these therapies are in various stages of development and lack high-quality evidence, the publication of a special issue of interim guidelines entirely dedicated to the introduction of new treatment options could be highly beneficial to increase practitioners' awareness.

Considerations for Healthcare Providers

The panel members noted that treatment of acne is challenging and that many factors influence treatment choices in addition to treatment guidelines and practitioners' clinical experience. These include sex (as systemic oral hormonal therapies cannot be used in male and transmasculine patients), skin sensitivity, skin type (ie, dry, oily vs nonoily, and phototype), anatomic sites affected, sebum production, presence of scarring, family history, underlying pathophysiology, patients' quality-of-life impact, patients' prior treatments, and special populations (ie, people who are menopausal, lactating, or pregnant; people with menstruation-associated acne; adolescents younger than 11 years of age; children below 8 years of age; and patients receiving testosterone). The panel has the following additional recommendations for healthcare providers:

Awareness That All Acne Is Fundamentally Hormone-Driven

A common misperception among practitioners is the belief that "hormonal" acne is limited to women, despite all acne having a hormonal basis. Healthcare practitioners should be aware that acne is often hormone-driven in male patients and in patients receiving exogenous androgen therapy, regardless of their gender.[33]

Ongoing Education on New Treatment Options

The authors note that education regarding acne therapy about medications starts early in residency and is dependent on the knowledge base of the attending physicians and exposure to new pharmaceutical options. In the authors' experience, education is important to ensure that practitioners learn about new therapeutic options. Healthcare providers should continue to learn how to optimize their patients' skin, mental health, and quality-of-life outcomes.

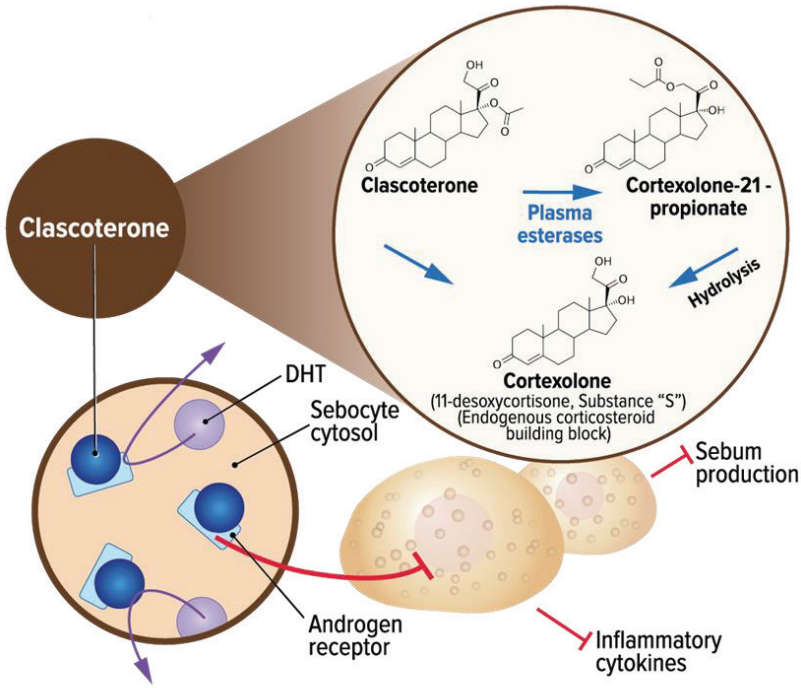
Attention to Patient Perceptions

In addition to physical effects, acne profoundly affects patients' quality of life.[38] Healthcare providers should be mindful of patients' emotional well being and also consider patients' goals and expectations. This comprehensive approach is crucial to the identification of an individualized and more successful treatment strategy.[38]

Clascoterone: Evaluating Clinical Success

Clascoterone 1% topical cream is an androgen receptor inhibitor designed for topical use. Although the exact mechanism of clascoterone for the treatment of acne is not known, preclinical evidence indicates clascoterone binds to and blocks the androgen receptor to decrease androgen-driven sebum production, making it the first approved topical anti-androgen acne therapy (Figure 1).[39] In vitro studies have shown that clascoterone competes with DHT for binding to the androgen receptor, reducing production of inflammatory cytokines and sebum components with efficacy comparable to that of spironolactone within the same donor.[39,40] Notably, clascoterone is rapidly metabolized in the skin into cortexolone, an endogenous bioproduct, which has no androgen activity and only weak glucocorticoid activity.[39,41] In the Phase 2 trials of clascoterone, cortexolone plasma levels were generally below or near the lower limit of quantitation, confirming a localized effect of clascoterone at the site of topical application with consequent minimal systemic anti-androgenic effects.[42] The Phase 3 clinical trials for clascoterone further demonstrated efficacy and safety in moderate to severe facial acne in both male and female patients through week 12.[43] In the 2 identical studies, clascoterone significantly reduced both inflammatory lesion counts and noninflammatory lesion counts as well as Investigator's Global Assessment score.[43] Moreover, the tolerability and safety profile of clascoterone was consistent with those of vehicle cream in both male and female patients, supporting the therapeutic value of clascoterone as a new treatment option for acne in potentially more diverse patient populations.[43] Evidence from the subsequent 9-month extension study (CB-03-01/27) enrolling clascoterone- and vehicle-treated patients from the two Phase 3 trials confirmed the potential of clascoterone for long-term use and suggested that this topical androgen receptor inhibitor could also be used safely to treat truncal acne.[44] The significant systemic effects seen with oral

FIGURE 1. Clascoterone mechanism of action.



DHT, dihydrotestosterone

anti-androgen agents, including reduced libido and feminization in male patients, were not observed with topical clascoterone treatment.[44] The most frequently observed new or worsening local skin reactions were erythema and scaling/dryness, but no systemic adverse reactions were reported.[43,44] The long-term safety profile of clascoterone applied to the face and/or trunk was favorable and consistent with previous trials, with no sex-related differences reported; most treatment-related adverse events were mild or moderate.[44]

Based on these data, clascoterone cream 1% was approved by the FDA in 2020 for the topical treatment of acne vulgaris in patients 12 years of age and older.[45]

Identification of the Place of Clascoterone in Acne Therapy: Expert Perspectives and Considerations

Clascoterone has potential as a foundational drug for the treatment of moderate to severe comedonal and inflammatory acne in patients ≥12 years of age of any sex at any level of acne severity.

Clascoterone is the first topical hormonal medication that specifically addresses sebum production in acne[40] and has a favorable safety profile in adult and adolescent patients, including males.[43] Because of its rapid hydrolysis to cortexolone, clascoterone can target androgen-stimulated sebaceous gland activity and improve acne with limited systemic anti-androgenic

TABLE 1.

Topical and Oral Acne Medications and Their Impact on Different Factors of Acne Pathogenesis				
Therapies	**Sebum Production**	**Hyperkeratinization**	**Inflammation**	***Cutibacterium acnes***
Topical Medications				
Retinoids	--	X	X	--
BP	--	X	X	X
Antibiotics	--	X	X	X
Oral Medications				
Antibiotics	--	X	X	X
Hormonal therapy	X	X	Indirect	Indirect
Isotretinoin	X	X	X	X

BP, benzoyl peroxide

activity.[39,43] For these reasons, based on the authors' clinical experience, clascoterone could be suitable in the following specific populations: patients with moderate to severe acne who do not wish to take antibiotics, transmasculine patients for whom medications such as spironolactone could interfere with their gender-affirming care, gender minority patients, other patients receiving androgen therapy, mature patients of any gender with acne (ages 29–40 years), patients for whom isotretinoin is not indicated, and patients who do not wish to use oral medications.

The authors agree that clascoterone may represent a new category of acne medication that should be included in a multimodal approach to acne therapy.

CONCLUSION

Treatment of acne is challenging, and there is an unmet need for FDA-approved medications targeting sebum production that can be used safely in a variety of patients. New acne treatments continue to be developed, and treatment guidelines often fall behind clinical practice. Clascoterone, with its unique mechanism of action, fills an important role in acne treatment. Clinical trials of clascoterone support its efficacy and safety in both male and female patients. However, more studies are needed to achieve a better understanding of the mechanism of action of clascoterone in the treatment of acne vulgaris.

DISCLOSURES

HB serves as an advisor for Galderma, Ortho Dermatologics, Sun Pharma, LaRoche-Posay, Journey, EPI, and Cutera. ASF serves as an advisor for Sun Pharma, Ortho Dermatologics, Galderma, Novartis, and Pfizer Inc. CF serves as a consultant for Sun Pharma, Proctor & Gamble, CeraVe, Galderma, SpoiledChild, Recell, and Regeneron. CLH serves as an advisor for Allergan, Galderma, Skinceuticals, Revision Skincare, Paula's Choice, Unilever, Johnson & Johnson, Versed, Dial, and Neutrogena. EL serves as a consultant and/or speaker for Sun Pharma, L'Oreal, JJCI, Galderma, Ortho Dermatologics, Pfizer, AbbVie, Incyte, BMS, Dermavant, and Almirall. RM serves as a consultant for Sun Pharma. ZD has received grants from Sun Pharma, Dr. Reddy's, and Ortho Dermatologics.

ACKNOWLEDGMENT

The Acne Management Consensus Roundtable meeting was funded by Sun Pharma. Medical writing support was provided by Elisabetta Lauretti PhD, of AlphaBioCom, a Red Nucleus company, and funded by Sun Pharma.

REFERENCES

1. Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol.* 2016;74(5):945-973 e933.
2. Oge LK, Broussard A, Marshall MD. Acne vulgaris: diagnosis and treatment. *Am Fam Physician.* 2019;100(8):475-484.
3. Jung IS, Yun SJ, Lee JB. The difference in sebum secretion affecting development of acne. *Ann Dermatol.* 2019;31(4):426-433.
4. Lai JJ, Chang P, Lai KP, et al. The role of androgen and androgen receptor in skin-related disorders. *Arch Dermatol Res.* 2012;304(7):499-510.
5. Shannon JF. Why do humans get acne? A hypothesis. *Med Hypotheses.* 2020;134:109412.
6. Lee WJ, Jung HD, Chi SG, et al. Effect of dihydrotestosterone on the upregulation of inflammatory cytokines in cultured sebocytes. *Arch Dermatol Res.* 2010;302(6):429-433.
7. Goh C, Cheng C, Agak G, et al. Acneiform disorders. In: Kang S, Amagai M, Bruckner AL, et al, eds, *Fitzpatrick's Dermatology,* 9th ed New York, NY: McGraw Hill Education. 2019:1391-1418.
8. Choi CW, Choi JW, Park KC, et al. Facial sebum affects the development of acne, especially the distribution of inflammatory acne. *J Eur Acad Dermatol Venereol.* 2013;27(3):301-306.
9. Okoro OE, Adenle A, Ludovici M, et al. Lipidomics of facial sebum in the comparison between acne and non-acne adolescents with dark skin. *Sci Rep.* 2021;11(1):16591.
10. Picardo M, Ottaviani M, Camera E, Mastrofrancesco A. Sebaceous gland lipids. *Dermatoendocrinol.* 2009;1(2):68-71.
11. Greene RS, Downing DT, Pochi PE, et al. Anatomical variation in the amount and composition of human skin surface lipid. *J Invest Dermatol.* 1970;54(3):240-247.
12. Ottaviani M, Alestas T, Flori E, et al. Peroxidated squalene induces the production of inflammatory mediators in HaCaT keratinocytes: a possible role in acne vulgaris. *J Invest Dermatol.* 2006;126(11):2430-2437.
13. Pappas A, Johnsen S, Liu JC, et al. Sebum analysis of individuals with and without acne. *Dermatoendocrinol.* 2009;1(3):157-161.
14. Morello AM, Downing DT, Strauss JS. Octadecadienoic acids in the skin surface lipids of acne patients and normal subjects. *J Invest Dermatol.* 1976;66(5):319-323.
15. Alwyn DD. Androgens have forgotten and emerging roles outside of their reproductive functions, with implications for diseases and disorders. *J Endocr Disord.* 2014;1(1):1005.
16. Lam C, Zaenglein AL. Contraceptive use in acne. *Clin Dermatol.* 2014;32(4):502-515.
17. Henze C, Hinney B, Wuttke W. Incidence of increased androgen levels in patients suffering from acne. *Dermatology.* 1998;196(1):53-54.
18. Sansone G, Reisner RM. Differential rates of conversion of testosterone to dihydrotestosterone in acne and in normal human skin–a possible pathogenic factor in acne. J *Invest Dermatol.* 1971;56(5):366-372.
19. Housman E, Reynolds RV. Polycystic ovary syndrome: a review for dermatologists: Part I. Diagnosis and manifestations. *J Am Acad Dermatol.* 2014;71(5):847 e841-847 e810; quiz 857-848.
20. Degitz K, Placzek M, Arnold B, et al. Congenital adrenal hyperplasia and acne in male patients. *Br J Dermatol.* 2003;148(6):1263-1266.
21. Demirkan S, Sayin DB, Gunduz O. CAG polymorphism in the androgen receptor gene in women may be associated with nodulocystic acne. *Postepy Dermatol Alergol.* 2019;36(2):173-176.
22. Katz HI, Kempers S, Akin MD, et al. Effect of a desogestrel-containing oral contraceptive on the skin. *Eur J Contracept Reprod Health Care.* 2000;5(4):248-255.
23. Kerscher M, Reuther T, Bayrhammer J, et al. Effects of an oral contraceptive containing chlormadinone and ethinylestradiol on acne-prone skin of women of different age groups: an open-label, single-centre, phase IV study. *Clin Drug Investig.* 2008;28(11):703-711.
24. Kranzlin HT, Nap MA. The effect of a phasic oral contraceptive containing Desogestrel on seborrhea and acne. *Eur J Contracept Reprod Health Care.* 2006;11(1):6-13.
25. Palombo-Kinne E, Schellschmidt I, Schumacher U, et al. Efficacy of a combined oral contraceptive containing 0.030 mg ethinylestradiol/2 mg dienogest for the treatment of papulopustular acne in comparison with placebo and 0.035 mg ethinylestradiol/2 mg cyproterone acetate. *Contraception.* 2009;79(4):282-289.
26. Goodfellow A, Alaghband-Zadeh J, Carter G, et al. Oral spironolactone improves acne vulgaris and reduces sebum excretion. *Br J Dermatol.* 1984;111(2):209-214.
27. Hughes BR, Cunliffe WJ. A prospective study of the effect of isotretinoin on the follicular reservoir and sustainable sebum excretion rate in patients with acne. *Arch Dermatol.* 1994;130(3):315-318.
28. Kim GK, Del Rosso JQ. Oral spironolactone in post-teenage female patients with acne vulgaris: practical considerations for the clinician based on current data and clinical experience. *J Clin Aesthet Dermatol.* 2012;5(3):37-50.
29. Koltun W, Lucky AW, Thiboutot D, et al. Efficacy and safety of 3 mg drospirenone/20 mcg ethinylestradiol oral contraceptive administered in 24/4 regimen in the treatment of acne vulgaris: a randomized, double-blind, placebo-controlled trial. *Contraception.* 2008;77(4):249-256.

30. Koltun W, Maloney JM, Marr J, et al. Treatment of moderate acne vulgaris using a combined oral contraceptive containing ethinylestradiol 20 µg plus drospirenone 3 mg administered in a 24/4 regimen: a pooled analysis. *Eur J Obstet Gynecol Reprod Biol.* 2011;155(2):171-175.
31. Plewig G, Cunliffe WJ, Binder N, et al. Efficacy of an oral contraceptive containing EE 0.03 mg and CMA 2 mg (Belara) in moderate acne resolution: a randomized, double-blind, placebo-controlled Phase III trial. *Contraception.* 2009;80(1):25-33.
32. Savage LJ, Layton AM. Treating acne vulgaris: systemic, local and combination therapy. *Expert Rev Clin Pharmacol.* 2010;3(4):563-580.
33. Radi R, Gold S, Acosta JP, et al. Treating acne in transgender persons receiving testosterone: a practical guide. *Am J Clin Dermatol.* 2022;23(2):219-229.
34. 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(10):62-67.
35. 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(6):1096-1106.
36. 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(6):597-600.
37. Kim SA, Kim BR, Chun MY, et al. Relation between pH in the trunk and face: truncal pH can be easily predicted from facial pH. *Ann Dermatol.* 2016;28(2):216-221.
38. Brownstone M. Acne updates. Pearls on treating acne from a recent Maui Derm Conference. *Dermatology Times.* 2022;43(8).
39. 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(6):563.
40. Rosette C, Agan FJ, Mazzetti A, et al. Cortexolone 17alpha-propionate (clascoterone) is a novel androgen receptor antagonist that inhibits production of lipids and inflammatory cytokines from sebocytes in vitro. *J Drugs Dermatol.* 2019;18(5):412-418.
41. Celasco G, Moro L, Bozzella R, et al. Biological profile of cortexolone 17alpha-propionate (CB-03-01), a new topical and peripherally selective androgen antagonist. *Arzneimittelforschung.* 2004;54(12):881-886.
42. Center for Drug Evaluation and Research. US Food and Drug Administration. Accessed May, 2023. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/213433Orig1s000MultidisciplineR.pdf.
43. 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(6):621-630.
44. 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(2):477-485.
45. WINLEVI (clascoterone) cream, for topical use [full prescribing information]. Princeton, NJ: Sun Pharmaceutical Industries, Inc.; 2021.

AUTHOR CORRESPONDENCE

Hilary Baldwin MD
E-mail:..... HBaldwin@acnetrc.com