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 ORIGINAL ARTICLE

Clascoterone Cream 1%: Mechanism of Action, Efficacy, and Safety of a Novel, First-in-Class Topical Antiandrogen Therapy for Acne

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ABSTRACT

Acne is a prevalent chronic inflammatory disease that can cause severe psychiatric effects and physical scarring of the skin. Historically, although systemic antiandrogen acne medications have been effective in women, the utility of these systemic medications has been limited due to potential systemic side effects in men and pregnant women. Therefore, research has been focused on developing topical formulations of antiandrogen therapy for acne. Topical clascoterone cream 1% is the first topical anti-androgen medication approved for the treatment of acne vulgaris in patients 12 years and older and represents a breakthrough in acne treatment.

Clascoterone, or cortexolone-17α propionate, is an androgen receptor inhibitor with highly localized activity. This medication is thought to compete with dihydrotestosterone (DHT) for androgen receptors located in pilosebaceous units, thus inhibiting the acnegenic downstream effects of DHT such as lipid synthesis and inflammatory cytokine production in a dose-dependent manner. Two phase III clinical trials have been conducted thus far; both trials have shown clascoterone 1% cream applied BID to be significantly more effective than placebo cream at treating acne vulgaris in patients ages 12 and older with moderate-to-severe acne. Clascoterone has also been shown to have a similar safety profile to that of placebo cream in clinical studies, without any systemic antiandrogenic effects observed in the clinical setting. Due to its novel mechanism of action and activity limited to the skin, clascoterone presents an exciting opportunity for dermatologists to further optimize care for eligible acne patients, either as a monotherapy or in combination with other anti-acne medications.

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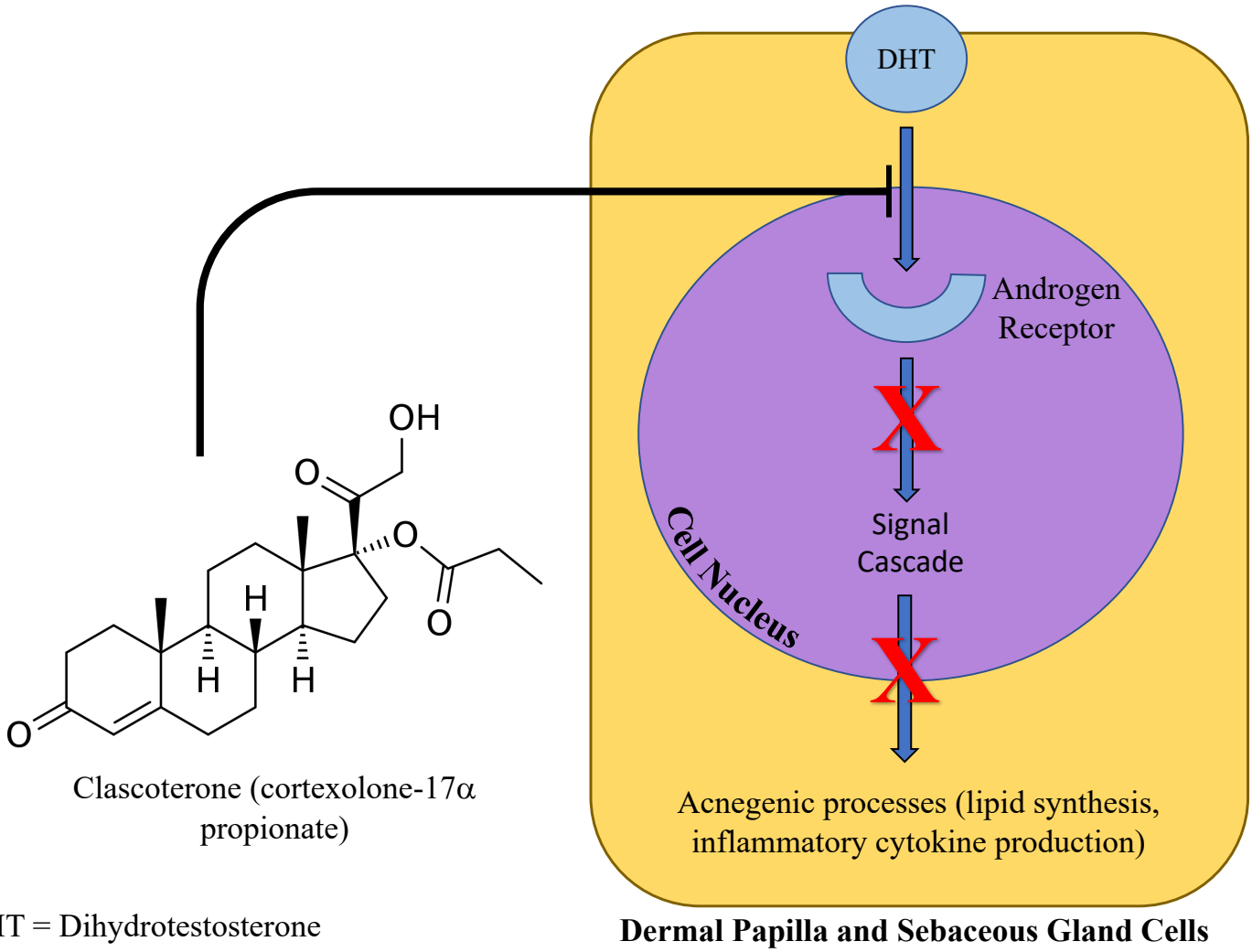
INTRODUCTION

Acne is a prevalent chronic inflammatory disease that causes both severe psychiatric effects and physical scarring of the skin.[1-4] The 4 pathogenetic pathways that contribute to this condition are increased sebum production, inflammation, colonization by *Cutibacterium acnes*, and hyperkeratinization.[1,5] Acne treatment regimens can be topical or systemic, and they target one or more of these pathogenic pathways.[1] Examples of topical medications include retinoids, antibiotics, and salicylic acid, while systemic medications include isotretinoin, antibiotics, and combined oral contraceptive pills (OCPs).[1] However, no major breakthroughs in acne therapy have occurred since the introduction of isotretinoin in 1982, and current treatments are not without their shortcomings.[2,6] For example, while isotretinoin is effective and generally well-tolerated, its teratogenic properties make it complicated to prescribe and

FIGURE 1. Proposed mechanism of action of clascoterone.



monitor.[2] Additionally, increasing bacterial resistance to antibiotics has made it inadvisable to prescribe topical or systemic antibiotics as monotherapy or for longer than 3 to 6 months.[1,2,7]

Androgen hormones are involved in the increased sebum production and inflammation that lead to acne, but androgens have historically been difficult to target with medication.[8-11] For example, OCPs inhibit the production of androgens but can only be used in a subset of women and carry an undesirable side effect profile including increased cardiovascular side effects, headaches, and menstrual irregularities.[3,10,11] Spironolactone is another anti-androgen that can be prescribed off-label to treat hormonal acne, but this medication is often not tolerated in men due to its potential systemic side effects, including gynecomastia.[3,10,11] Neither OCPs nor spironolactone should be used during pregnancy due to their potential effects on fetal development.[3,6,9,12] Both of these medications are inseparable from their adverse effects because they are systemic in nature.[10]

Topical clascoterone cream 1% (also known by its brand name, Winlevi®) represents the first breakthrough in acne treatment in years and functions as a novel solution to targeting the androgen component of acne. Clascoterone is the first topical agent ever Food and Drug Administration (FDA)-approved that modulates sebum production in acne patients.[8] As the first topical androgen inhibitor available for use in both men and women, clascoterone avoids the systemic adverse effects of other anti-androgen medications such as OCPs and spironolactone, and exists as a promising treatment option since receiving FDA approval for treatment of acne vulgaris in patients 12 years old and older in 2020.[6,13,14]

Mechanism of Action

Clascoterone, also known as cortexolone-17α propionate, is an ester derivative of cortexolone and an androgen receptor inhibitor that shares a 4-ring backbone with the androgen dihydrotestosterone (DHT) and the androgen receptor inhibitor spironolactone.[8,9,12,13] Clascoterone functions as an androgen receptor inhibitor to counteract the effects of the androgenic effects of DHT in the skin.[5,6,14]

While the exact mechanism of action remains unknown, in vitro studies have shown that clascoterone competes with DHT for the androgen receptors in the sebaceous glands of hair follicles and in dermal papilla cells.[6,8,9,12] DHT normally binds to androgen receptors present throughout the skin to increase sebum production from sebaceous glands and promote the development of nodular, cystic acne.[6,14] By competing with DHT for androgen receptors, clascoterone prevents DHT from activating transcription of androgen-responsive genes involved in inflammatory processes, such as genes involved in both lipid synthesis and inflammatory cytokine production; this process is illustrated in Figure 1.[3,6,8,9,12] As a result, less inflammation develops in the hair follicles and their associated sebaceous glands, preventing the development of acne.[15] These anti-inflammatory effects of clascoterone have been shown to be dose-dependent in prior in vitro studies, and clascoterone has not been found to be toxic to sebocyte cultures at the concentration needed to exhibit the above effects.[8,12] Additionally, in vitro studies have shown that clascoterone binds and inhibits androgen receptors with an even greater affinity than spironolactone.[12] Excretion of clascoterone has not been extensively studied in studies thus far.[16]

Notably, clascoterone is quickly hydrolyzed to its inactive metabolite, cortexolone, by esterases located in the epidermis, so the activity of this medication is highly localized to the area of its topical application.[6,8,10,15,17]

Efficacy

The prior clinical trials evaluating clascoterone cream are listed in Table 1. Early studies have demonstrated that clascoterone is an effective treatment for acne. For example, Trifu et al conducted a phase I clinical trial that showed that clascoterone worked faster and was better tolerated than tretinoin 0.05% or vehicle cream in adult men with moderate to severe facial acne.[18]

A 2019 phase II clinical trial evaluated the safety and efficacy of clascoterone at concentrations 0.1%, 0.5%, and 1% compared with placebo to determine the optimal concentration and dosing regimen.[19] Treatment efficacy was measured by changes in the inflammatory lesion count (ILC), non-inflammatory lesion count (NILC), Investigator's Global Assessment (IGA), and patient satisfaction with treatment.[19] Treatment success was defined as achieving an IGA score of 0 or 1 ("clear" or "almost clear") and an improvement from baseline by 2 or more IGA grades.[19]

This study demonstrated that clascoterone at concentrations of 0.1%, 0.5%, or 1% all led to significantly greater treatment success after 12 weeks than the placebo cream in 363 male and female patients 12 years and older with acne vulgaris.[19] Treatment success was highest for patients using clascoterone 1% BID and 0.1% BID, with a success rate of 8.6% and 8.3%, respectively, compared with 2.7% in patients using placebo cream.[19] The clascoterone treatment

TABLE 1.

Clinical Trials Studying Clascoterone Topical Cream for the Treatment of Acne Vulgaris

Citation	Study Type	n	Objective(s)	Duration	Outcomes
Trifu et al. 2011[18]	Phase I clinical trial	77 men	Compare efficacy of placebo cream vs tretinoin 0.05% cream vs clascoterone cream 1% for moderate-severe facial acne	8 weeks	Clascoterone 1% cream was well tolerated, significantly more effective than placebo cream, and faster at achieving 50% improvement than the other treatment groups
Mazzetti et al. 2019[22]	Phase IIa, open-label study	42 females and males ≥12 years old	Evaluate pharmacokinetic properties and adrenal suppression potential of clascoterone cream 1% in patients >18 years old and 12-18 years old	14 days	Clascoterone 1% cream was found to have a tolerable safety profile for both adolescents and adults when applied BID for 14 days
Mazzetti et al. 2019[19]	Phase IIb, randomized, double-blind vehicle controlled, dose escalation study	363 males and females ≥12 years old	Compare efficacy of clascoterone 0.1%, 0.5% or 1% vs placebo cream	12 weeks	All clascoterone cream concentrations were well-tolerated; the treatment regimen of clascoterone 1% BID was optimal
Hebert et al. 2020[6]	Two Phase III multicenter, randomized, vehicle-controlled, double-blind clinical studies	1,440 males and females ≥12 years old	Compare efficacy of clascoterone cream 1% vs placebo cream	12 weeks	Clascoterone cream 1% was found to be effective at treating moderate to severe facial acne compared with placebo, with a favorable safety profile
Eichenfield et al. 2020[5]	Open-label, long-term extension study	609 males and females ≥12 years old from the phase III clinical studies	Assess the safety of clascoterone cream 1% when used over an extended period of time	9 months	Clascoterone cream 1% was found to have a tolerable safety profile with a low frequency of treatment-emergent adverse events observed

groups also achieved statistically significant changes in ILC and NILC compared with the placebo group (P=0.0431 and P=0.0303, respectively). Participants using clascoterone 1% BID achieved the highest treatment success rate and greatest decrease in ILC (-13.5) and NILC (-17.5) compared with placebo.[19]

Two identical phase III clinical trials have been completed for clascoterone so far, named CB-03-01/25 and CB-03-01/26 (NCT02608450 and NCT02608476 on ClinicalTrials.gov).[6] Occurring from November 2015 to April 2018, they were both multicenter, randomized, double-blind, vehicle-controlled, parallel-group studies that assessed the safety and efficacy of clascoterone 1% topical cream in males and non-pregnant females ages 9 and up with moderate to severe facial acne.[6,13] Eligible participants had an IGA score of 3 or 4, 30 to 75 inflammatory lesions, and 30 to 100 noninflammatory lesions.[6] Overall, 1,440 patients participated in the study and applied 1 g of either clascoterone 1% or placebo cream to the whole face daily for a treatment period of 12 weeks.[6] Patients were not permitted to use any other topical or systemic acne medications for the duration of the study.[6]

There were 3 coprimary efficacy endpoints assessed in this hierarchical order: the proportion of patients achieving treatment success at week 12, the absolute change from NILC at week 12, and the absolute change from baseline in ILC at week 12.[6] Treatment success was defined as achievement of an IGA score of 0 or 1, or an improvement in IGA score by 2 or more, or an absolute change in lesion counts from baseline.[6] The secondary endpoints for the studies were the percentage change from baseline in total lesion count (TLC), NILC, and ILC at week 12, as well as the absolute change in TLC from baseline at week 12.[6]

Overall, both phase III clinical trials found clascoterone 1% to be more effective than placebo cream at treating facial acne when applied twice daily for 12 weeks (P<0.001): a significantly greater number of patients receiving clascoterone 1% reached treatment success at week 12 compared with those using placebo cream in both phase III trials (18.4% vs 9.0%, P<0.001 in CB-03-01/25 and 20.3% vs 6.5%, P<0.001 in CB-03-01/26).6 Study participants using clascoterone 1% also achieved a significantly greater absolute reduction in noninflammatory lesion count compared with participants using the placebo cream (-19.4 vs -13.0, P<0.001 in CB-03-01/25 and -19.4 vs -10.8, P<0.001 in CB-03/01/26), as well as a significantly greater absolute reduction in inflammatory lesion count compared with placebo (-19.3 vs -15.5, P=0.003 in CB-03-01/25 and -20.0 vs -12.6, P<0.001 in CB-03-01/26).[6]

Secondary endpoints were also met because participants using clascoterone 1% achieved significantly greater absolute change in TLC from baseline to week 12 compared with participants using placebo cream (-39.1 vs -28.8, P<0.001 in CB-03-01/25 and -40.0 vs -23.6, P<0.001 in CB-03-01/26), as well as a significantly greater percentage change in NILC, ILC, and TLC compared with participants using placebo (NILC: -30.6% vs -21.6%, P=0.009 in CB-03-01/25 and -29.3% vs -15.6%, P<0.001 in CB-03-01/26. ILC: -44.8% vs -36.5%, P=0.005 in CB-03-01/25 and -46.9% vs -29.6%, P<0.001 in CB-03-01/26. TLC: -37.0 vs -28.4%, P=0.001 in CB-03-01/25 and -37.3% vs -22.1%, P<0.001 in CB-03-01/26).[6]

Some limitations of these clinical trials were that the sample sizes were small and did not permit subgroup analyses.[6] Additionally, these clinical trials did not include patient-reported outcomes as an outcome variable to evaluate the medication's impact on quality of life, and did not test clascoterone's efficacy when used with concomitant acne treatments.[6]

Safety

Clascoterone has been shown to have a similar safety profile to that of placebo cream in clinical studies.[6] In a prior phase I trial, all adverse events documented during the study were mild or moderate at most.[18] In phase II clinical trial, all concentrations of clascoterone at 0.1% BID, 0.5% BID, and 1% BID were well tolerated; the majority of documented adverse events were mild in severity and resolved by the end of the study.[19]

The 2 aforementioned phase III clinical trials also found that clascoterone 1% is generally well-tolerated.[8,13] Any adverse events that were recorded were mostly mild, with no systemic adverse events or changes in electrocardiograms (ECGs) observed.[6] Across both studies, the most common adverse effects reported in patients receiving the medication included local skin irritation such as erythema (occurring in 12.2% of participants using clascoterone vs 15.4% using placebo), scaling or dryness (occurring in 10.5% of participants using clascoterone vs 10.4% using placebo), and pruritus (occurring in 7.7% of participants using clascoterone vs 8.2% using placebo), all of which occurred at similar rates compared with patients who received placebo.[8,13]

The most common treatment-emergent adverse events (TEAEs) observed were nasopharyngitis (occurring in 1.7% of participants using clascoterone vs 3.7% of participants using placebo in CB-01-03/25, and in 1.1% vs 1.9% in CB-01-03/26), headache (0.6% in clascoterone group vs 0.3% in placebo group in CB-01-03/25 and 1.1% vs 0.8% in CB-01-03/26), oropharyngeal pain (0.6% in clascoterone group vs 0.3% in placebo group in CB-01-03/25 and 1.1% vs 1.1% in CB-01-03/26), and vomiting (0.6% in clascoterone group vs 0.6% in placebo group in CB-01-03/25 and 0.5% vs 0.3% in CB-01-03/26).[8] Overall, clascoterone 1% was found to have a similar safety profile compared with the placebo cream.[6]

At this time clascoterone is only approved for use in patients ages 12 years and above.[13] This medication is not mutagenic or carcinogenic.[13]

To date, no clinical evidence suggests Hypothalamus-Pituitary-Adrenal (HPA) axis suppression by clascoterone.[20,21] A 2019 open-label phase II clinical trial studied clascoterone's potential to cause adrenal suppression if used for 2 weeks in 42 subjects ages 12 and older with moderate-to-severe acne vulgaris.[22] Primary safety endpoints were defined as HPA axis response to cosyntropin at day 1 compared with day 14, and pharmacokinetic evaluation in the form of concentration-time profiles of clascoterone and cortexolone; secondary safety endpoints included clinical laboratory testing, local and systemic adverse events, physical exams, vital signs, and ECGs.[22] This study found that, while 3 out of 42 subjects in the study demonstrated evidence of abnormal HPA axis responses to cosyntropin at the endpoint of day 14, no clinical evidence of adrenal suppression was ever observed.[22] Additionally, these 3 subjects all demonstrated normal HPA axis responses 4 weeks after the study's conclusion.[22] Finally, laboratory testing showed that cortexolone plasma concentrations were consistently below the lower limit of quantitation, confirming that no correlation exists between systemic clascoterone exposure and HPA axis suppression.[22] Similar to prior study observations, the majority of recorded local skin reactions (LSRs) were mild, with one case of moderate pruritus noted.[22] Thus, this phase II clinical trial concluded that clascoterone is safe and tolerable for use.[22]

One open-label, long-term extension clinical trial has been conducted to evaluate the safety of clascoterone. This clinical study occurred from March 2016 to August 2018, where participants from the phase III clinical studies detailed above had the option to continue applying their assigned study medication (either clascoterone 1% cream or placebo cream) twice daily to the face and/or trunk for up to 9 months.[5] The study participants were assessed at 1, 3, 6, and 9 months, and if they were found to have an IGA score of 1 or 0, they entered an off-treatment period until the next study assessment.[5] Any patients who planned to use other acne medications, planned to undergo procedures involving the face and/or trunk, or had other skin pathologies that could interfere with the skin assessments were excluded.[5] This was a multinational study with 324 subjects participating from 75 sites.[5]

At the end of 9 months, no systemic adverse events from the medication were observed, and TEAEs occurred at low rates.[5] Additionally, TEAEs were found to occur at similar rates between the placebo cream and the clascoterone 1% cream.[5] LSRs included erythema,

scaling, and pruritus, and occurrence rates of these were low; additionally, since clascoterone does not function as a corticosteroid, no topical side effects of corticosteroids such as skin atrophy or striae were observed.[5] Finally, none of the side effects associated with systemic antiandrogenic medications were observed, such as feminization or decreased libido.[5,23] The proportion of patients with IGA scores of 0 or 1 also increased with time spent using clascoterone 1% cream, with 48.1% of patients meeting this criteria by the end of the study.[5] As a result, clascoterone 1% cream has been found to have a favorable safety and efficacy profile for males and non-pregnant females ages 12 and up for up to 12 months of continuous use (12 weeks in phase III clinical trials and 9 months in the open-label long-term extension trial).[5]

Some factors regarding the safety of clascoterone remain unknown. For example, no available data exists on the use of clascoterone during pregnancy to evaluate for drug-associated risk of adverse maternal and fetal outcomes; also, no data are available on the absorption of clascoterone or its metabolites into breastmilk and subsequent effects on breastfed infants.[13,21] Additionally, no drug interaction studies have been completed to evaluate how clascoterone affects other acne medications and vice versa; this could be a relevant point of concern for dermatologists because acne treatment is typically multimodal in nature.[10,13,21]

A systematic review found that topical clascoterone is both effective at treating acne vulgaris and safe for use.[3] Specifically, the study evaluated the five randomized controlled clinical trials for clascoterone discussed thus far; baseline characteristics of 2457 study participants, efficacy outcomes, and safety outcomes were extracted from each clinical trial.[3] The study concluded that there was a low risk of bias in these clinical trials, and their pooled analysis confirmed that clascoterone has a tolerably similar safety profile compared with placebo.[3] Additionally, clascoterone cream was found to significantly reduce noninflammatory lesion counts and led to significantly greater improvement in IGA scores compared with placebo cream.[3]

Real-world Use of Clascoterone

Existing evidence points towards clascoterone as a novel, effective treatment for patients with acne. As the first topical anti-androgen medication ever approved for treatment of acne, clascoterone presents an exciting opportunity for treatment of patients who have been excluded from anti-androgen therapy in the past, such as men.[6,9,12] Similar to other topical antiacne medications, clascoterone can also be used for acne of any severity.[11]

Clascoterone may be used as a monotherapy or as an adjunctive medication for patients on additional acne medications.[24,25] It functions as a useful alternative to systemic anti-androgen medications as a method of controlling sebum production. Because clascoterone targets a different mechanism of action from other topical medications, it can also be synergistic when used in combination with other topical acne medications such as retinoids for treatment of both inflammatory and non-inflammatory acne lesions.[4,14] Additionally, clascoterone may also be used as an alternative to antibiotics in patients who are not good candidates for oral tetracycline therapy or when concern for resistance to topical antibiotics exists.[3] Clascoterone can also be used in place of tretinoin given its greater tolerability and the lower incidence of LSRs associated with its use.[18] Clascoterone is not included in the AAD recommendations for acne because it received FDA approval after the most recent recommendations were released in 2016; nevertheless, it is currently included in decision-making algorithms as an option for mild papulopustular or mixed comedonal and papulopustular acne that does not respond to other medications such as topical retinoids, benzoyl peroxide, topical antibiotics, or topical dapsone.[25,26]

Clascoterone functions as an effective, safe option to both target one of the more difficult-to-treat components of acne and treat patient populations that have previously been excluded from the use anti-androgen medications. As such, clascoterone presents an exciting opportunity for dermatologists to further optimize care for eligible acne patients.

DISCLOSURES

April W Armstrong MD MPH has served as a research investigator, scientific advisor, or speaker to AbbVie, Almirall, Arcutis, ASLAN, Beiersdorf, BI, BMS, EPI, Incyte, Leo, UCB, Janssen, Lilly, Mindera, Nimbus, Novartis, Ortho Dermatologics, Sun, Dermavant, Dermira, Sanofi, Regeneron, and Pfizer.

Hannah Peterson BS has no conflicts of interest to disclose.

Leon Kircik MD has served as either a speaker, consultant, advisor or an investigator for Allergan, Abbvie, Bausch Health, Cipher Canada, Galderma, GSK, J&J, Novartis, Ortho Dermatologics, Pfizer, Promius, Primus, Sun Pharma, Taro.

REFERENCES

1. Fox L, Csongradi C, Aucamp M, et al. Treatment modalities for acne. *Molecules*. 2016;21(8). doi:10.3390/molecules21081063.
2. Habeshian KA, Cohen BA. Current issues in the treatment of acne vulgaris. *Pediatrics*. 20222020;145(Suppl 2):S225-S230. doi:10.1542/peds.2019-2056L.
3. Alkhodaidi ST, Al Hawsawi KA, Alkhudaidi IT, et al. Efficacy and safety of topical clascoterone cream for treatment of acne vulgaris: a systematic review and meta-analysis of randomized placebo-controlled trials. *Dermatol Ther*. 2021;34(1):e14609. doi:10.1111/dth.14609.
4. Leung AK, Barankin B, Lam JM, et al. Dermatology: how to manage acne vulgaris. *Drugs Context*. 2021;10:2021-8-6. doi: 10.7573/dic.2021-8-6.
5. 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. doi:10.1016/j.jaad.2020.04.087.
6. 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. doi:10.1001/jamadermatol.2020.0465.
7. Adler BL, Kornmehl H, Armstrong AW. Antibiotic resistance in acne treatment. *JAMA Dermatol*. 2017;153(8):810-811. doi: 10.1001/jamadermatol.2017.1297.
8. Dhillon S. Clascoterone: First approval. *Drugs*. 2020;80(16):1745-1750. doi:10.1007/s40265-020-01417-6.
9. Kircik LH. Game changer in acne treatment. *J Drugs Dermatol*. 2020;19(3):28.
10. Sanchez C, Keri J. Androgen receptor inhibitors in the treatment of acne vulgaris: efficacy and safety profiles of clascoterone 1% cream. *Clin Cosmet Investig Dermatol*. 2022;15:1357-1366. doi: 10.2147/CCID.S289750.
11. Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2016;74(5):945-73 e33. doi: 10.1016/j.jaad.2015.12.037.
12. Rosette C, Agan FJ, Mazzetti A, et al. Cortexolone 17α-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.
13. WINLEVI (clascoterone) cream, Full Prescribing Information. Federal Drug Administration. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213433s000lbl.pdf. Accessed December 3, 2022.
14. Drake L, Reyes-Hadsall S, Barbieri JS, et al. New developments in topical acne therapy. *Am J Clin Dermatol*. 2022;23(2):125-136. doi:10.1007/s40257-021-00666-9.
15. Burma N, Woo T, Parsons L. Topical clascoterone for acne vulgaris. *Skin Ther Lett*. 2022-02-01 2022;27(1):1-3.
16. Kim ES, Keam SJ. Clascoterone 1% cream in acne vulgaris: a profile of its use. *Drugs & Therapy Perspectives*. 2021;37(5):194-198. doi: 10.1007/s40267-021-00831-4.
17. 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. doi:10.1055/s-0031-1297043.
18. Trifu V, Tiplica GS, Naumescu E, et al. Cortexolone 17alpha-propionate 1% cream, a new potent antiandrogen for topical treatment of acne vulgaris. A pilot randomized, double-blind comparative study vs placebo and tretinoin 0.05% cream. *Br J Dermatol*. 2011;165(1):177-83. doi: 10.1111/j.1365-2133.2011.10332.x.
19. Mazzetti A, Moro L, Gerloni M, et al. A phase 2b, randomized, double-blind vehicle controlled, dose escalation study evaluating clascoterone 0.1%, 0.5%, and 1% topical cream in subjects with facial acne. *J Drugs Dermatol*. 2019;18(6):570.
20. Han JJ, Faletsky A, Barbieri JS, et al. New acne therapies and updates on use of spironolactone and isotretinoin: a narrative review. *Dermatol Ther (Heidelb)*. 2021;11(1):79-91. doi:10.1007/s13555-020-00481-w.
21. Harris C. Clascoterone (Winlevi) for the treatment of acne. *Am Fam Physician*. 2021;104(1):93-94.
22. 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.
23. Elsaie ML. Hormonal treatment of acne vulgaris: an update. *Clin Cosmet* Investig Dermatol. 2016;9:241-8. doi: 10.2147/CCID.S114830
24. Purvis CG, Balogh EA, Feldman SR. Clascoterone: How the novel androgen receptor inhibitor fits into the acne treatment paradigm. *Ann Pharmacother*. 2021;55(10):1297-1299. doi: 10.1177/1060028021992055.
25. Piszczatoski CR, Powell J. Topical clascoterone: the first novel agent for acne vulgaris in 40 years. *Clin Ther*. 2021;43(10):1638-1644.
26. UpToDate. Acne vulgaris: overview of management. Available at: https://www.uptodate.com/contents/acne-vulgaris-overview-of-management?search=clascoterone&source=searchresult&selectedTitle=1~5&usage_type=default&display_rank=. Accessed December 29, 2022.

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