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# Efficacy and Safety of 1% Clascoterone Cream in Patients Aged ≥12 Years With Acne Vulgaris

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## ABSTRACT

**Background:** Two randomized phase 3 studies evaluated efficacy and safety of 1% clascoterone cream, a topical androgen receptor inhibitor, in patients aged ≥9 years with moderate-to-severe facial acne vulgaris after 12 weeks of treatment.

**Objectives:** To present a pooled data analysis of the efficacy and safety of 1% clascoterone cream after 12 weeks of treatment in patients aged ≥12 years from the 2 phase 3 trials.

**Methods:** Patients were randomized 1:1 to twice-daily treatment of the whole face with clascoterone or vehicle. Primary efficacy outcomes were proportion of patients achieving treatment success (Investigator's Global Assessment score of "clear" [0] or "almost clear" [1] with ≥2-point reduction from baseline) and absolute change from baseline (CFB) in noninflammatory lesion count and inflammatory lesion count; secondary efficacy outcomes included absolute CFB in total lesion count at week 12. Safety was assessed from treatment-emergent adverse events and local skin reactions.

**Results:** 709/712 patients age ≥12 years were treated with clascoterone/vehicle. After 12 weeks, clascoterone was efficacious compared with vehicle, based on proportion of patients achieving treatment success (19.9% vs 7.7%) and CFB in noninflammatory lesion count (−20.8 vs −11.9), inflammatory lesion count (−19.7 vs −14.0), and total lesion count (−40.0 vs −26.1; all $P<0.0001$). Frequencies of local skin reactions were low and similar between treatment arms, with no new safety signals.

**Conclusions:** Clascoterone is efficacious, with a favorable safety profile and low rates of local skin reactions in patients ≥12 years of age with facial acne vulgaris. (Clinicaltrials.gov NCT02608450 and NCT02608476)

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## INTRODUCTION

Acne vulgaris, the eighth most prevalent disease globally,[1,2] is a multifactorial skin condition characterized by the excess production of sebum, epithelial follicle hyperkeratinization, and inflammation.[1-3] Clinical manifestations of acne can range from mild to severe depending on the number of comedones, papules, pustules, or nodules, which most commonly affect the face, chest, and/or back.[3]

The onset of acne is associated with the fluctuation of hormones – including androgens, estrogens, progesterone, insulin, and insulin-like growth factor-1, adrenocorticotropic hormone, melanocortins, glucocorticoids, and growth hormone – and thus frequently begins at or before adrenarche or puberty.[2,4,5] The principal drivers of acne pathogenesis are androgens such as testosterone and dihydrotestosterone (DHT).[4,5] Androgens bind to their receptors on sebaceous glands, sebocytes, and

dermal papilla cells in the skin,[2,6,7] and regulate the transcription of genes involved in acne pathogenesis, including inflammatory cytokines and factors driving sebaceous gland proliferation and sebum production.[2,6,7] Serum dehydroepiandrosterone levels correlate with the presence of acne in prepubertal children and in adolescent girls (14-17 years of age) and with acne lesion counts in both male and female adults[8-10]; while DHT levels correlate positively with acne lesion counts in women (18-45 years of age).[8]

Topical 1% clascoterone cream (cortexolone 17α-propionate) is an androgen receptor inhibitor indicated for the topical treatment of acne in patients ≥12 years of age and is the first topical androgen receptor inhibitor approved by the US Food and Drug Administration (FDA) for acne treatment.[3,11,12] In vitro studies have shown that by binding to the androgen receptor, clascoterone competes with DHT and inhibits sebum production and downstream proinflammatory signaling pathways in primary human sebocytes and hair follicle dermal papilla cells.[13,14]

The efficacy and safety of 1% clascoterone cream in patients with moderate-to-severe facial acne vulgaris (grade 3 or 4 on the Investigator Global Assessment [IGA] scale) were demonstrated in 2 identical phase 3 studies (CB-03-01/25 [NCT02608450] and CB-03-01/26 [NCT02608476]) that included a total of 1440 patients ≥9 years of age.[2] The phase 3 clinical trial populations included only 19 patients aged ≥9 and <12 years, and clascoterone cream, 1% was subsequently approved in the United States for the treatment of acne vulgaris in patients ≥12 years of age. This paper presents post hoc pooled analyses of data from the 2 phase 3 randomized clinical trials on the efficacy and safety of 1% clascoterone cream after 12 weeks of treatment in 1421 patients ≥12 years of age.

## MATERIALS AND METHODS

### Study Design and Treatment

The study design and methods were previously published in detail.[2] Briefly, both studies (CB-03-01/25 [NCT02608450] and CB-03-01/26 [NCT02608476]) were multicenter, randomized, double blind, and vehicle controlled.[2] The CB-03-01/25 study was conducted from January 21, 2016, to April 11, 2018 and the CB-03-01/26 study was conducted from November 16, 2015, to February 21, 2018.[2] Patients were randomized to apply 1% clascoterone cream or vehicle to the entire face twice daily for 12 weeks.[2]

### Study Population

Male or non-pregnant female patients ≥9 years of age with a diagnosis of facial acne vulgaris and an IGA score of 3 or 4 (0 [clear] to 4 [severe] scale) were eligible for enrollment in 2 phase 3 studies; 722 patients were allocated to treatment with 1% clascoterone cream and 718 patients to vehicle. Only patients ≥12 years of age were included in this analysis (709 patients treated with 1% clascoterone cream and 712 treated with vehicle). Key exclusion criteria included the presence of >2 facial nodules, nodulocystic acne, or any skin pathology or condition that could interfere with the study. Use of topical or systemic anti-acne preparations (ie, over-the-counter acne cleansers or treatments, retinoids, corticosteroids, or antibiotics) within 2 to 4 weeks of the initiation of treatment and use of spironolactone within 8 weeks of treatment were also reasons for exclusion.

### Assessments

*Efficacy Assessments*

The IGA was performed at each study visit (baseline and weeks 4, 8, and 12) using a 5-point scale (from 0 = clear to 4 = severe). Manual counting of noninflammatory lesions (NILCs) and inflammatory lesions (ILCs) was performed at each study visit (baseline and weeks 4, 8, and 12).[2]

*Safety Assessments*

Treatment-emergent adverse events (TEAEs) and local skin reactions (LSRs; edema, erythema/redness, pruritus, scaling/dryness, skin atrophy, stinging/burning, striae rubrae, and telangiectasia) were assessed at each study visit. TEAEs were summarized by treatment group and overall, and were classified using Medical Dictionary for Regulatory Activities (MedDRA) system organ class and preferred terms. The number and proportion of patients with any TEAE and the number of TEAEs were listed by preferred term, seriousness, relationship to test article, and severity. LSRs including edema, erythema/redness, scaling/dryness, skin atrophy, striae rubrae, and telangiectasia were assessed by the investigators and recorded on a 5-point scale. Patients rated the severity of stinging/burning and pruritus on a 4-point scale.

*Outcomes*

In the phase 3 studies, the coprimary efficacy outcomes were the proportion of patients achieving "success" (defined as an IGA score of "clear" [score = 0] or "almost clear" [score = 1] with a ≥2-point reduction in IGA score from baseline) and absolute change from baseline (CFB) in NILCs and ILCs at week 12. The secondary efficacy outcomes were absolute CFB in total lesion counts (TLCs) at week 12 and percent CFB in TLCs, NILCs, and ILCs at week 12. Safety outcomes included TEAEs and LSRs scored by frequency and severity at every visit (baseline and weeks 4, 8, and 12).

*Statistical Analysis*

Efficacy endpoints were analyzed in the intention-to-treat set, which included all randomized patients; subgroup analyses, reported in this paper, included patients ages ≥12, excluding 19 patients aged ≥9 and <12 years.

Comparisons between clascoterone and vehicle were analyzed using a logistic regression model for the proportion of subjects achieving "success" (defined by an IGA score 0/1 with a ≥2-point reduction in IGA score from baseline) and an analysis of covariance model for change and percent CFB in NILCs, ILCs, and TLCs, as previously described.[2] A multiple imputation method was used to impute missing values. Adjusted proportions and least-squares means derived from the models are presented with 2-sided nominal *P*-values; in the primary study, primary and secondary efficacy endpoints were analyzed using a prespecified hierarchical testing procedure for multiplicity control of type 1 error, which did not apply to this post hoc analysis.

Safety analyses included all patients who received ≥1 application of the test treatment. The LSRs were summarized by the frequency of each individual reaction by treatment group and severity at each visit. The TEAEs were summarized by treatment group at each visit; the number and proportion of subjects with any TEAE and the number of TEAEs were summarized by MedDRA system organ class and preferred term, seriousness, relationship to test article, and severity.

## RESULTS

### Patient Disposition and Demographics

Overall, 1421 patients ≥12 years of age were randomized; 709 patients were allocated to treatment with 1% clascoterone cream and 712 patients to vehicle. Among patients treated with clascoterone and vehicle, 63.9% and 60.4% were female, and 91.0% and 90.3% were white, with mean ± standard deviation (SD) age 19.8 ± 6.1 and 19.5 ± 6.1 years, respectively (Table 1). Baseline characteristics were generally balanced between treatment arms. At baseline, the IGA score was moderate (3) in 82.5% vs 84.1% and severe (4) in 17.5% vs 15.9% of patients treated with clascoterone vs vehicle, respectively (Table 1). The most frequent LSRs at baseline were erythema and scaling/dryness.

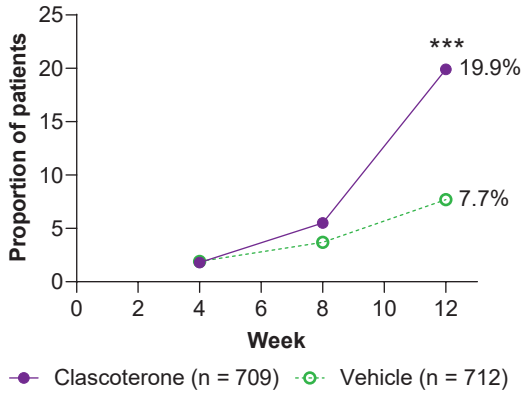
**TABLE 1.**

**Patients' Baseline Demographics and Clinical Characteristics**

| | Clascoterone (n = 709) | Vehicle (n = 712) |
|---|---|---|
| Sex, male | 256 (36.1) | 282 (39.6) |
| Age, years, mean ± SD | 19.8 ± 6.1 | 19.5 ± 6.1 |
| Race | | |
| White | 645 (91.0) | 643 (90.3) |
| Asian | 8 (1.1) | 14 (2.0) |
| Black or African American | 37 (5.2) | 40 (5.6) |
| Other | 19 (2.7) | 15 (2.1) |
| Ethnicity | | |
| Hispanic or Latino | 108 (15.2) | 88 (12.4) |
| Non-Hispanic or Latino | 601 (84.8) | 624 (87.6) |
| Fitzpatrick skin type | | |
| I | 14 (2.0) | 19 (2.7) |
| II | 230 (32.4) | 217 (30.5) |
| III | 290 (40.9) | 287 (40.3) |
| IV | 115 (16.2) | 117 (16.4) |
| V | 33 (4.7) | 41 (5.8) |
| VI | 27 (3.8) | 31 (4.4) |
| IGA score | | |
| 3 (moderate) | 585 (82.5) | 599 (84.1) |
| 4 (severe) | 124 (17.5) | 113 (15.9) |
| Lesion counts | | |
| NILC, mean ± SD | 61 ± 21.8 | 62 ± 21.3 |
| ILC, mean ± SD | 43 ± 12.0 | 42 ± 11.7 |
| TLC, mean ± SD | 104 ± 25.4 | 104 ± 25.1 |

ITT population, age 12 and over.
Data shown as n (%) unless otherwise noted.
IGA, Investigator Global Assessment; ILC, inflammatory lesion count; ITT, intention-to-treat; NILC, noninflammatory lesion count; SD, standard deviation; TLC, total lesion count.

**FIGURE 1.** Proportion of patients achieving Investigator Global Assessment success through week 12.

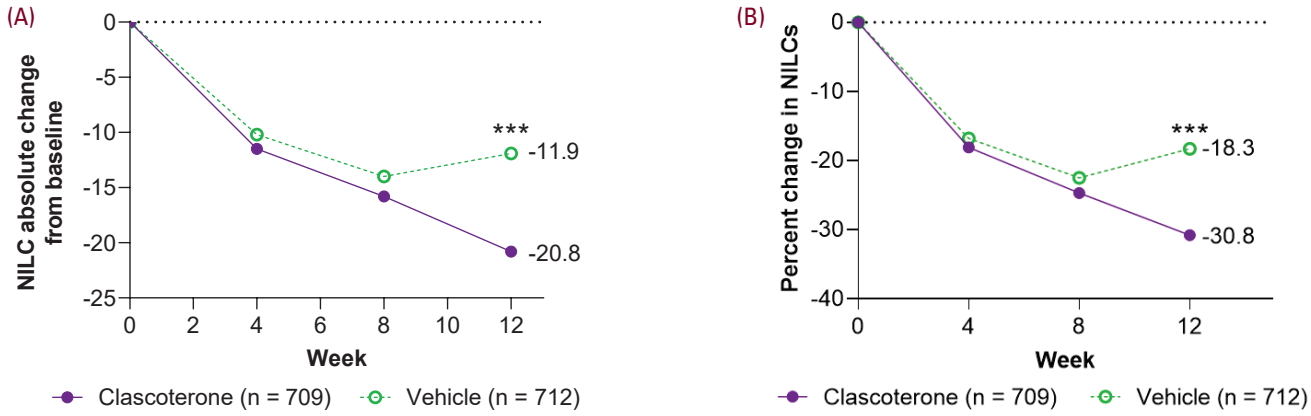



ITT population, age 12 and over. Data shown as %.
***$P$<0.0001.
ITT, intention-to-treat.

**Efficacy**

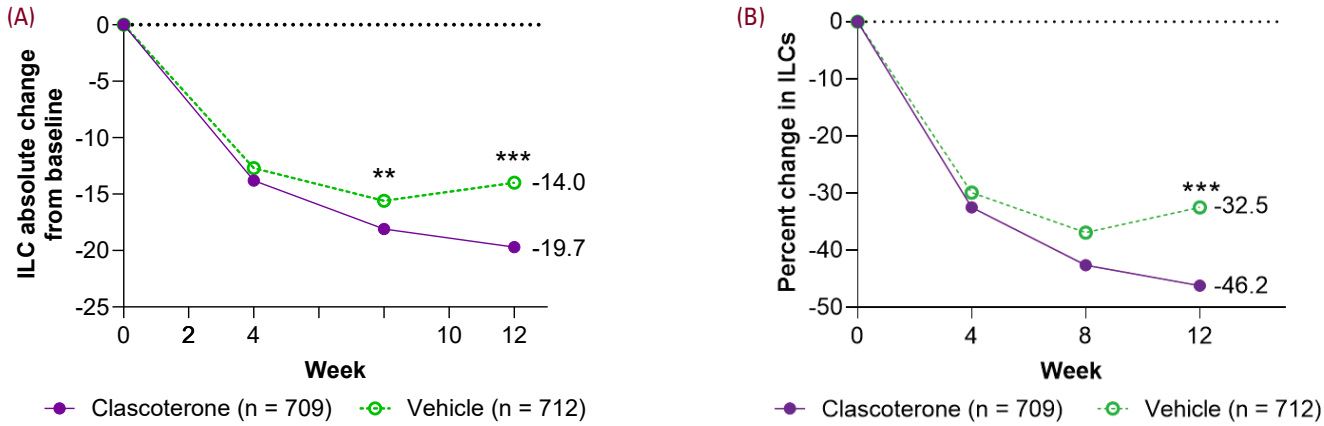
Clascoterone cream remained significantly more effective at week 12 compared with vehicle cream in the subgroup of patients 12 years of age and older. At week 12, 19.9% of clascoterone-treated patients achieved success based on IGA compared with 7.7% of vehicle-treated patients ($P$<0.0001; Figure 1). At week 12, the absolute CFB for patients treated with clascoterone vs vehicle was –20.8 vs –11.9 (percent change, –30.8% vs –18.3%; $P$<0.0001) for NILCs (Figures 2A and 2B) and –19.7 vs –14.0 (percent change, –46.2% vs –32.5%; $P$<0.0001) for ILCs, respectively (Figures 3A and 3B). The absolute CFB in TLC was –40.0 vs –26.1 for clascoterone-treated vs vehicle-treated patients (percent change, –37.8% vs –25.1%; $P$<0.0001) (Figures 4A and 4B).

**FIGURE 2.** (A) Absolute and (B) Percent change from baseline in noninflammatory lesion counts through week 12



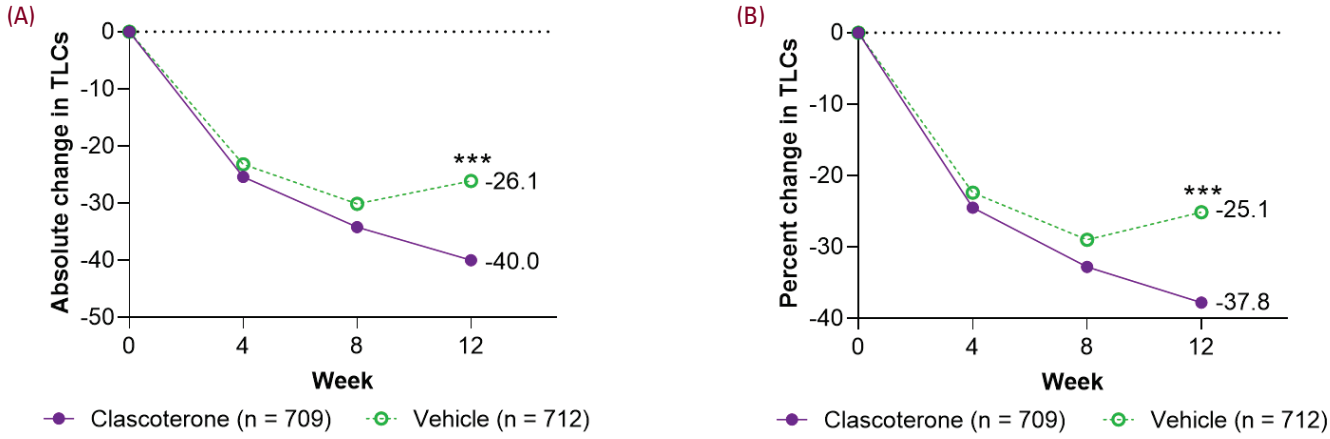

ITT population, age 12 and over. Data shown as change from baseline in absolute and percent lesion counts.
***$P$<0.0001.
NILC, noninflammatory lesion count; ITT, intention-to-treat.

**FIGURE 3.** (A) Absolute and (B) Percent change from baseline in inflammatory lesion counts through week 12.




ITT population, age 12 and over. Data shown as CFB in absolute and percent lesion counts.
**$P$ = 0.0031; ***$P$<0.0001.
CFB, change from baseline; ILC, inflammatory lesion count; ITT, intention-to-treat.

**FIGURE 4.** (A) Absolute and (B) Percent change from baseline in total lesion counts through week 12.




ITT population, age 12 and over. Data shown as CFB in absolute and percent lesion counts.
***$P<0.0001$.
CFB, change from baseline; TLC, total lesion count; ITT, intention-to-treat.

**TABLE 2.**

**Summary of Treatment-Emergent Adverse Events Through Week 12**

| | Clascoterone (n = 709) | Vehicle (n = 712) |
|---|---|---|
| ≥1 TEAE | 79 (11.1) | 91 (12.8) |
| Mild | 60 (8.5) | 57 (8.0) |
| Moderate | 19 (2.7) | 31 (4.4) |
| Severe | 0 | 3 (0.4) |
| Serious TEAEs | 0 | 2 (0.3) |
| TEAEs related to study drug | 12 (1.7) | 22 (3.1) |
| TEAEs leading to study drug discontinuation | 5 (0.7) | 12 (1.7) |
| Most frequent TEAEs | | |
| Nasopharyngitis | 10 (1.4) | 20 (2.8) |
| Headache | 6 (0.8) | 4 (0.6) |
| Oropharyngeal pain | 6 (0.8) | 5 (0.7) |

Individual events shown as n (%) of patients. Includes patients who received ≥1 application of the test treatment during the study.
TEAE, treatment-emergent adverse event.

**Safety**

Topical 1% clascoterone cream maintained a favorable safety profile in patients 12 years of age and older. The incidence of TEAEs was similar between treatment arms. Most TEAEs were mild or moderate in severity; there were no serious TEAEs in patients treated with clascoterone, but 2 (0.3%) vehicle-treated patients experienced serious TEAEs. The most frequent TEAEs in clascoterone-treated vs vehicle-treated patients were nasopharyngitis (1.4% vs 2.8%), headache (0.8% vs 0.6%), and oropharyngeal pain (0.8% vs 0.7%), respectively (Table 2). The majority of patients in each treatment group remained free of LSRs through week 12 (Table 3). The majority of LSRs observed were minimal or mild in severity, and the most frequent were erythema, scaling/dryness, and skin atrophy. The most frequent LSRs considered moderate in severity were pruritus and erythema, in 1.7% and 1.5% of vehicle-treated patients and in 1.1% and 0.8% clascoterone-treated patients, respectively. Pruritus was considered severe in only 0.4% of vehicle-treated and 0.3% of clascoterone-treated patients (Table 3).

**TABLE 3.**

**Summary of Local Skin Reactions on Face by Symptoms and Severity at Week 12**

| By Severity | Clascoterone (n = 709) | Vehicle (n = 712) |
|---|---|---|
| Erythema | | |
| None | 485 (68.4) | 487 (68.4) |
| Minimal | 86 (12.1) | 92 (12.9) |
| Mild | 40 (5.6) | 30 (4.2) |
| Moderate | 6 (0.8) | 11 (1.5) |
| Severe | 0 | 0 |
| Scaling/dryness | | |
| None | 567 (80.0) | 565 (79.4) |
| Minimal | 39 (5.5) | 46 (6.5) |
| Mild | 11 (1.6) | 9 (1.3) |
| Moderate | 0 | 0 |
| Severe | 0 | 0 |
| Skin atrophy | | |
| None | 555 (78.3) | 569 (79.9) |
| Trace | 39 (5.5) | 37 (5.2) |
| Mild | 18 (2.5) | 9 (1.3) |
| Moderate | 3 (0.4) | 4 (0.6) |
| Severe | 2 (0.3) | 1 (0.1) |
| Pruritus | | |
| None | 584 (82.4) | 588 (82.6) |
| Mild | 22 (3.1) | 17 (2.4) |
| Moderate | 8 (1.1) | 12 (1.7) |
| Severe | 2 (0.3) | 3 (0.4) |
| Striae rubrae | | |
| None | 587 (82.8) | 595 (83.6) |
| Trace | 19 (2.7) | 22 (3.1) |
| Mild | 11 (1.6) | 2 (0.3) |
| Moderate | 0 | 1 (0.1) |
| Severe | 0 | 0 |
| Edema | | |
| None | 590 (83.2) | 591 (83.0) |
| Minimal | 16 (2.3) | 20 (2.8) |
| Mild | 11 (1.6) | 7 (1.0) |
| Moderate | 0 | 2 (0.3) |
| Severe | 0 | 0 |
| Telangiectasia | | |
| None | 599 (84.5) | 596 (83.7) |
| Trace | 11 (1.6) | 19 (2.7) |
| Mild | 7 (1.0) | 4 (0.6) |
| Moderate | 0 | 1 (0.1) |
| Severe | 0 | 0 |
| Stinging/burning | | |
| None | 608 (85.8) | 609 (85.5) |
| Mild | 6 (0.8) | 9 (1.3) |
| Moderate | 0 | 0 |
| Severe | 2 (0.3) | 2 (0.3) |

Individual events shown as n (%) of patients. Includes patients who received ≥1 application of the test treatment during the study.

## DISCUSSION

The efficacy of 1% clascoterone cream applied topically twice daily for 12 weeks for the treatment of facial acne vulgaris remained superior compared with vehicle treatment in patients aged 12 and older. The primary and secondary efficacy endpoints were met. Topical 1% clascoterone cream was well tolerated, with a comparable safety profile to that of vehicle; no new safety concerns were identified. The majority of TEAEs were mild or moderate in severity; the most common were nasopharyngitis, headache, and oropharyngeal pain. The majority of LSRs were minimal or mild in severity. The incidence of treatment-related TEAEs was low (1.7% for 1% clascoterone cream vs 3.1% for vehicle cream), and no serious TEAE was considered related to study treatment.

There is considerable evidence on the role of androgens in the pathogenesis of acne. Available options for antiandrogen therapy include inhibition of androgen receptors (androgen receptor blockers such as oral spironolactone, flutamide, and cyproterone acetate) and/or inhibition of androgen production by the ovary or adrenal gland (oral contraceptives and low-dose glucocorticoids).[12,15] Several clinical trials have assessed the efficacy of combined oral contraceptives (COCs) in reducing both inflammatory and comedonal lesion counts in patients with acne and linked this to their antiandrogenic properties.[12] However, despite being effective, the oral therapies targeting the androgen pathway are associated with systemic adverse events and are not indicated as monotherapy[4]; moreover, COCs and spironolactone are recommended only for women.[12,16] The use of spironolactone can also cause menstrual irregularities, low blood pressure, and breast tenderness in women,[17] and is contraindicated during pregnancy due to the increased risk of hypospadias and feminization of a male fetus.[4]

Clascoterone is the first topical androgen receptor inhibitor to be approved by the FDA.[18] Topical 1% clascoterone represents a novel mechanism of action for the treatment of acne and is the first topical agent targeting the hormonal pathway that may be used safely in males.[19] Clascoterone cream is applied topically, and serious drug-related systemic side effects were not observed in this analysis or in previous studies.[2,20,21] Clascoterone is metabolized quickly, and the primary metabolite, cortexolone, is inactive. These properties support local action with minimal systemic exposure and side effects.[20] Antiandrogenic effects such as reduced libido or feminization in male participants were not observed.[19] Currently, 1% clascoterone cream is the only approved topical antiandrogen treatment for acne.

The design of the phase 3 studies excluded patients with concomitant use of other anti-acne medications.[2] Clascoterone cream should be investigated for potential use as a first-line foundation medication in conjunction with other existing acne topical and/or oral therapies including retinoids, benzoyl peroxide, and antibiotics. Additionally, impact of clascoterone use on quality of life was not assessed and should be considered for future trials.

The favorable efficacy and safety profiles of topical 1% clascoterone cream for the treatment of facial acne vulgaris were confirmed in patients aged ≥12 years. Frequencies of LSRs were low, and the majority were mild in severity. Further studies are needed to investigate the efficacy and safety of 1% clascoterone cream in combination with other topical acne medications.

## DISCLOSURES

AAH, LFE, LSG, DT, SV, and YM were study investigators. AAH, LFE, and LSG were also compensated advisors to Cassiopea; DT served in the past as a consultant to Cassiopea, Inc. AAH is an employee of the McGovern Medical School of The University of Texas Health Science Center in Houston, which received compensation from Cassiopea S.p.A. for study participation; she also received an honorarium for serving on the Cassiopea advisory board; all research grant funds were paid to her institution. LFE is an employee of the University of California San Diego, which received compensation from Cassiopea S.p.A. for study participation; he has also served as an investigator, advisor, or consultant for Almirall, Galderma Laboratories, L'Oreal, and Ortho Dermatologics. DT is an employee of the College of Medicine at The Pennsylvania State University in Hershey, which received compensation from Cassiopea S.p.A. for study participation; she has also received honoraria from Galderma Laboratories, and Novartis. LSG is an employee of the Henry Ford Health System in Detroit, Michigan, which received compensation from Cassiopea S.p.A. for study participation; she has also received personal fees for advisory, speaking, consulting, research, and/or other ties with Almirall, Foamix, Galderma Laboratories, Novartis, Sol-Gel, and Sun Pharmaceuticals. MC is employed as the Vice President, Medical Affairs at Novan Inc.; was employed as the senior director of medical affairs for Cassiopea, Inc.; received personal fees as a consultant from Cassiopea S.p.A.; receives personal fees as an adjunct faculty member from the University of Arizona; holds stock options in Cassiopea S.p.A.; and was a previously contracted employee of Anacor-Pfizer and consultant to Menlo Therapeutics, NICO Corporation, and Abbott Nutrition. LM is an employee of Cassiopea S.p.A., and holds stock options in the company. EF was an employee of Cassiopea S.p.A. JH is an employee of Pharmapace Inc. NS is an employee of Sun Pharmaceutical Industries, Inc. AM is employed as the chief medical officer for Cassiopea S.p.A., and holds stock options in the company; is a board member of Cassiopea S.p.A.; and has served as the chief medical officer of Cosmo Pharmaceuticals.

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## REFERENCES

1. Tan JK, Bhate K. A global perspective on the epidemiology of acne. *Br J Dermatol.* 2015;172( Suppl 1):3-12.
2. 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.
3. Kalabalik-Hoganson J, Frey KM, Ozdener-Poyraz AE, Slugocki M. Clascoterone: a novel topical androgen receptor inhibitor for the treatment of acne. *Ann Pharmacother.* 2021;55(10):1290-1296.
4. Elsaie ML. Hormonal treatment of acne vulgaris: an update. *Clin Cosmet Investig Dermatol.* 2016;9:241-248.
5. Lynn DD, Umari T, Dunnick CA, Dellavalle RP. The epidemiology of acne vulgaris in late adolescence. A*dolesc Health Med Ther.* 2016;7:13-25.
6. 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.
7. Zouboulis CC. Acne and sebaceous gland function. *Clin Dermatol.* 2004;22(5):360-366.
8. Cappel M, Mauger D, Thiboutot D. Correlation between serum levels of insulin-like growth factor 1, dehydroepiandrosterone sulfate, and dihydrotestosterone and acne lesion counts in adult women. *Arch Dermatol.* 2005;141(3):333-338.
9. Ceruti JM, Leirós GJ, Balañá ME. Androgens and androgen receptor action in skin and hair follicles. *Mol Cell Endocrinol.* 2018;465:122-133.
10. Aizawa H, Nakada Y, Niimura M. Androgen status in adolescent women with acne vulgaris. *J Dermatol.* 1995;22(7):530-532.
11. Winlevi® (clascoterone cream 1%). full prescribing information. Cassiopea inc. 2021.
12. 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. e33.
13. 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.
14. Rosette C, Rosette N, Mazzetti A, et al. Cortexolone 17α-propionate (clascoterone) is an androgen receptor antagonist in dermal papilla cells in vitro. *J Drugs Dermatol.* 2019;18(2):197-201.
15. Thiboutot D, Chen W. Update and future of hormonal therapy in acne. *Dermatology.* 2003;206(1):57-67.
16. Hauk L. Acne vulgaris: treatment guidelines from the AAD. *Am Fam Physician.* 2017;95(11):740-741.
17. Ayatollahi A, Samadi A, Bahmanjahromi A, Robati RM. Efficacy and safety of topical spironolactone 5% cream in the treatment of acne: a pilot study. *Health Sci Rep.* 2021;4(3):e317.
18. Piszczatoski CR, Powell J. Topical clascoterone: the first novel agent for acne vulgaris in 40 years. *Clin Ther.* 2021;43(10):1638-1644.
19. Santhosh P, George M. Clascoterone: a new topical anti-androgen for acne management. *Int J Dermatol.* 2021;60(12):1561-1565.
20. Mazzetti A, Moro L, Gerloni M, Cartwright M. 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.
21. Alkhodaidi ST, Al Hawsawi KA, Alkhudaidi IT, Magzoub D, Abu-Zaid A. 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.

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