Efficacy and safety of 1% clascoterone cream through 12 weeks in patients ≥12 years of age with facial acne vulgaris: pooled data analyses of two Phase 3 randomized clinical trials

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INTRODUCTION

- Acne vulgaris, the eighth most prevalent disease globally, is a multifactorial skin condition characterized by the excess production of sebum, epithelial follicle hyperkeratinization, and inflammation[1-3]
- Topical 1% clascoterone cream (cortexolone 17α-propionate) is a topical androgen receptor inhibitor approved by the US Food and Drug Administration for the treatment of acne in patients ≥12 years of age;[3,4] this is a novel mechanism of action for acne treatment[5]
- Two identical Phase 3 studies (CB-03-01/25 [S1] and CB-03-01/26 [S2]) evaluated 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)[2,3]

OBJECTIVE

- To present pooled data analyses of the efficacy and safety of 1% clascoterone cream after 12 weeks of treatment in the subgroup of patients ≥12 years of age from the two Phase 3 randomized clinical trials

METHODS

Study design

- Both studies were multicenter, randomized, double-blind, and vehicle-controlled
- Patients received 1% clascoterone cream or vehicle twice daily for 12 weeks
- The primary efficacy outcomes were the proportion of patients achieving "success" (defined as 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 noninflammatory lesion counts (NILCs) and inflammatory lesion counts (ILCs) at Week 12

Study population

Key inclusion criteria

- Male or nonpregnant 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; only patients 12 years of age and older were included in this analysis

Key inclusion criteria

- Patients with any skin pathology or condition that could interfere with the study or who had used topical or systemic anti-acne preparations (ie, over-the-counter acne cleansers or treatments, retinoids, corticosteroids, and antibiotics within 2–4 weeks of the initiation of treatment) were excluded

Assessments

- Efficacy was assessed from proportion of patients achieving an IGA 0/1 score with a ≥2-point reduction from baseline and absolute CFB in NILCs and ILCs at Week 12
- Safety was assessed from local skin reactions (LSRs [edema, erythema/redness, pruritus, scaling/dryness, skin atrophy, stinging/burning, striae rubrae, and telangiectasia]) through Week 12 (baseline and Weeks 4, 8, and 12)

Statistical analysis

- Efficacy analyses were performed on the intention-to-treat (ITT) set, which included all randomized patients, using a logistic regression model and an analysis of covariance model; subgroup analyses shown included patients aged 12 and older
- For efficacy endpoints, multiple imputation was used to impute missing values
- Safety analyses included all patients who received at least one application of the test treatment
- LSRs were summarized by the frequency of each individual reaction by treatment group and severity at each visit

RESULTS

Patient demographics

- Overall, 1421 patients ≥12 years of age were randomized; 709 patients were allocated to 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 balanced between treatment arms
  - The baseline IGA score was 3/4 in 82.5%/17.5% of clascoterone-treated patients vs 84.1%/15.9% of vehicle-treated patients (**Table 1**)
  - The most frequent local skin reactions were erythema and scaling/dryness

Table 1. Patients' baseline demographics and clinical characteristics

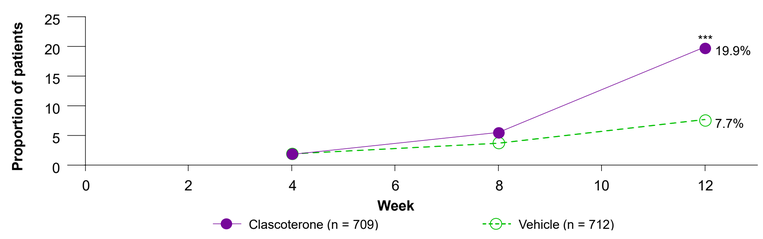
	Clascoterone (n = 709)	Vehicle (n = 712)
Sex, male	256 (36.1)	282 (39.6)
Age, years, mean ± SD	19.8 ± 6.1	19.5 ± 6.1
Race		
Caucasian	645 (91.0)	643 (90.3)
Asian	8 (1.1)	14 (2.0)
Black or African American	37 (5.2)	40 (5.6)
Other	19 (2.7)	15 (2.1)
Ethnicity		
Hispanic or Latino	108 (15.2)	88 (12.4)
Non-Hispanic 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		
TLC, mean ± SD	104 ± 25.4	104 ± 25.1
NILC, mean ± SD	61 ± 21.8	62 ± 21.3
ILC, mean ± SD	43 ± 12.0	42 ± 11.7

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.

Efficacy

- At W12, 19.9% of clascoterone-treated patients achieved success based on IGA compared with 7.7% of vehicle-treated patients (*P* <0.0001; **Figure 1**)

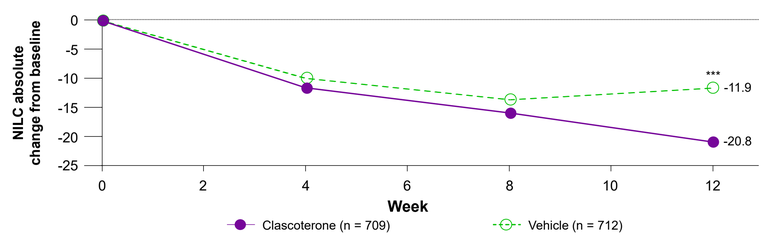
Figure 1. Proportion of patients achieving IGA success through Week 12



ITT population, age 12 and over. Data shown as %.
***P <0.0001. IGA, Investigator Global Assessment; ITT, intention-to-treat.

- The absolute change from baseline in NILCs for clascoterone-treated patients was −20.8 vs −11.9 in vehicle-treated patients (*P* <0.0001; **Figure 2A**)

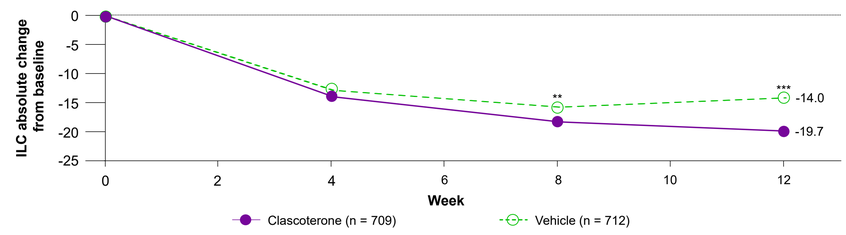
Figure 2A. Absolute change from baseline in noninflammatory lesion count through Week 12



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

- The absolute change from baseline in ILCs was −19.7 for clascoterone-treated patients vs −14.0 for vehicle-treated patients (*P* <0.0001; **Figure 2B**)

Figure 2B. Absolute change from baseline in inflammatory lesion count through Week 12



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

Safety

- The majority of patients in each treatment group remained free of LSRs through Week 12 (**Table 2**)
  - At Week 12, the majority of LSRs observed were minimal or mild in severity; the most frequent were erythema, scaling/dryness, and skin atrophy
  - No local skin reaction was considered moderate-to-severe in >1.7% of patients (**Table 2**)

Table 2. Summary of local skin reactions on the face by symptoms and severity at Week 12

By severity, n (%)	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)
Moderate	11 (1.6)	9 (1.3)
Mild	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 at least one application of the test treatment during the study.

CONCLUSIONS

- Topical 1% clascoterone cream has favorable efficacy and safety in the treatment of facial acne vulgaris in patients aged 12 and older and represents a novel mechanism of action for acne treatment
  - Frequencies of LSRs were low, and the majority were mild in severity
- These Phase 3 studies did not contemplate the concomitant use of 1% clascoterone cream with other anti-acne medications
- Larger studies are necessary to investigate the long-term efficacy and safety of 1% clascoterone cream alone or in combination with other topical acne medications

REFERENCES

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DISCLOSURES

MC is 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 Abbott Nutrition, NICO Corporation, and Menlo Therapeutics. **LM** is an employee of Cassiopea S.p.A. and holds stock options in the company. **EF** is a former employee of Cassiopea S.p.A. and may hold stock. **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.