Long-term safety and efficacy of clascoterone cream 1% in patients ≥12 years old with acne vulgaris

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INTRODUCTION

- Clascoterone cream 1% is a topical androgen receptor inhibitor approved for the treatment of acne vulgaris in patients ≥12 years of age[1]
- Clascoterone efficacy and safety were evaluated in 2 identical, vehicle-controlled, Phase 3 studies (CB-03-01/25 and CB-03-01/26) in patients ≥9 years of age with moderate-to-severe facial acne vulgaris
  - Twice-daily treatment with clascoterone cream 1% for 12 weeks resulted in significantly higher treatment success rates and greater reduction in lesion counts compared with vehicle cream treatment[2]
  - Clascoterone was well tolerated, with a safety profile similar to that of vehicle
- Patients from the Phase 3 studies could enter an optional, long-term, open-label extension study; the safety results in patients ≥9 years of age are published[3]

OBJECTIVE

- To evaluate the long-term safety and efficacy of twice-daily clascoterone cream 1% in the subgroup of patients ≥12 years of age who entered the long-term extension study

METHODS

Study design and patients

- A multicenter, open-label, long-term extension study (CB-03-01/27) enrolled patients who completed 1 of the 12-week Phase 3 clinical trials (CB-03-01/25 and CB-03-01/26)
- Male or nonpregnant female patients who completed 1 of the 12-week, Phase 3, pivotal clinical trials (CB-03-01/25 and CB-03-01/26) and enrolled within 3 days of the final pivotal trial visit were eligible
  - Patients with any skin pathology or condition that could interfere with the study or who planned to use other topical or systemic anti-acne preparations or undergo procedures on the face (or trunk, if applicable) were excluded
  - This analysis includes only patients ≥12 years of age who entered the long-term extension study

Treatment administered

- Patients applied clascoterone cream 1% twice daily to the entire face and, if designated by the investigator and desired by the patient, to truncal acne, for 9 additional months of treatment
  - Total time applying clascoterone cream, including the Phase 3 studies, could be up to 12 months for patients originally randomized to clascoterone treatment
  - Clascoterone treatment could be discontinued if the Investigator's Global Assessment (IGA) score was 0 or 1 (clear/almost clear) and reinstated if/when acne worsened

Assessments

- Safety was evaluated from frequencies of treatment-emergent adverse events (TEAEs), serious adverse events, and local skin reactions (LSRs), including telangiectasia, skin atrophy, striae rubrae, erythema, edema, scaling/dryness, stinging/burning, and pruritus
  - Summarized in patients ≥12 years of age who received at least 1 application of clascoterone (safety population)
- Efficacy was evaluated from the IGA severity score for each treatment area, as applicable
  - Assessed at every in-clinic study visit (baseline and Months 1, 3, 6, and 9) using a 5-point IGA scale (0, clear; 4, severe)
  - Summarized in patients ≥12 years of age who completed the study without significant protocol violations (per-protocol [PP] population)

Statistical analysis

- For demographic, efficacy, and safety data, continuous variables were described by descriptive statistics, and categorical data by frequency counts and percentage of patients within each category
  - Patient demographics are reported in the subgroup of patients ≥12 years of age in the intention-to-treat (ITT) population
- Missing data were not imputed

RESULTS

Patient demographics

- A total of 600 patients ≥12 years of age enrolled in the extension study; 311 and 289 patients were originally randomized to treatment with clascoterone and vehicle, respectively, in the Phase 3 studies
  - The safety population included 598 patients treated with clascoterone (original randomization: clascoterone, 311; vehicle, 287)
  - The PP population included 319 patients, of whom 119 (37.3%) were on study for a total of 12 months
    - During the Phase 3 studies, 167 and 152 PP patients received clascoterone and vehicle, respectively
    - In the extension study, 124 PP patients also treated truncal acne, including 67 and 57 who received clascoterone and vehicle, respectively, during the Phase 3 studies
  - The majority of patients were female and White; mean ± standard deviation age in the ITT and PP populations was 19.3 ± 6.2 and 19.8 ± 6.6 years, respectively (**Table 1**)

Table 1. Patient demographics, subgroup ≥12 years of age

	Original treatment assignment				Overall	
	Clascoterone		Vehicle			
	ITT	PP	ITT	PP	ITT	PP
Characteristic	n = 311	n = 167	n = 289	n = 152	N = 600	N = 319
Sex						
Male	118 (37.9)	70 (41.9)	109 (37.7)	55 (36.2)	227 (37.8)	125 (39.2)
Female	193 (62.1)	97 (58.1)	180 (62.3)	97 (63.8)	373 (62.2)	194 (60.8)
Race						
White	279 (89.7)	157 (94.0)	257 (88.9)	134 (88.2)	536 (89.3)	291 (91.2)
Asian	5 (1.6)	2 (1.2)	8 (2.8)	5 (3.3)	13 (2.2)	7 (2.2)
Black or African American	16 (5.1)	5 (3.0)	16 (5.5)	9 (5.9)	32 (5.3)	14 (4.4)
Other	11 (3.5)	3 (1.8)	8 (2.8)	4 (2.6)	19 (3.2)	7 (2.2)
Ethnicity						
Hispanic or Latino	26 (8.4)	9 (5.4)	15 (5.2)	7 (4.6)	41 (6.8)	16 (5.0)
Not Hispanic or Latino	285 (91.6)	158 (94.6)	274 (94.8)	145 (95.4)	559 (93.2)	303 (95.0)
Age, years						
Mean	19.3	19.7	19.3	19.9	19.3	19.8
Median	17.0	18.0	17.0	18.0	17.0	18.0
Standard deviation	5.77	6.13	6.68	7.04	6.22	6.57
Range	12–50	12–50	12–50	12–50	12–50	12–50

Patients are summarized overall and according to the original treatment they received in the Phase 3 pivotal studies.
Data shown as n (%) unless otherwise specified.
ITT, intention-to-treat; PP, per protocol.

Safety

- Overall, 108/598 (18.1%) patients in the safety population experienced a total of 187 TEAEs, with similar frequencies in patients previously treated with clascoterone compared with vehicle in the Phase 3 studies (**Table 2**)
  - The majority of TEAEs reported were mild or moderate in severity, and most were not considered related to clascoterone treatment
  - The most frequent TEAEs by percentage of patients affected were nasopharyngitis (2.8%) and upper respiratory tract infection (1.8%; **Table 3**)

Table 2. Summary of TEAEs in patients ≥12 years of age

	Original treatment assignment		Overall
	Clascoterone	Vehicle	
Category	n = 311	n = 287	N = 598
Patients with any TEAE	56 (18.0)	52 (18.1)	108 (18.1)
Mild	35 (11.3)	36 (12.5)	71 (11.9)
Moderate	27 (8.7)	23 (8.0)	50 (8.4)
Severe	4 (1.3)	3 (1.0)	7 (1.2)
Any test article–related TEAE	11 (3.5)	2 (0.7)	13 (2.2)
Any TEAE leading to discontinuation	9 (2.9)	0	9 (1.5)
Any serious TEAE	3 (1.0)	3 (1.0)	6 (1.0)
Any test article–related serious TEAE	0	0	0
Any serious TEAE leading to discontinuation	1 (0.3)	0	1 (0.2)
Any TEAE leading to death	0	0	0
Number of TEAEs, n	102	85	187
Related to test article	16	2	18
Not related to test article	86	83	169
Mild	55	53	108
Moderate	40	29	69
Severe	7	3	10

Patients are summarized overall and according to the original treatment they received in the Phase 3 pivotal studies.
Safety population. Data shown as n (%) unless otherwise specified.
TEAE, treatment-emergent adverse event.

Table 3. Most frequent TEAEs in patients ≥12 years of age

	Original treatment assignment					
	Clascoterone		Vehicle		Overall	
Category	n = 311		n = 287		N = 598	
Most frequent TEAEs	**Events, n**	**Patients**	**Events, n**	**Patients**	**Events, n**	**Patients**
Application site acne	4	4 (1.3)	0	0	4	4 (0.7)
Nasopharyngitis	7	6 (1.9)	14	11 (3.8)	21	17 (2.8)
Respiratory tract infection, viral	1	1 (0.3)	4	4 (1.4)	5	5 (0.8)
Sinusitis	3	3 (1.0)	2	2 (0.7)	5	5 (0.8)
Upper respiratory tract infection	9	8 (2.6)	3	3 (1.0)	12	11 (1.8)

Patients are summarized overall and according to the original treatment they received in the Phase 3 pivotal studies.
Safety population. Data shown as n (%) unless otherwise specified.
TEAE, treatment-emergent adverse event.

- The frequency of LSRs on the face and trunk was low; frequencies were similar in patients previously treated with clascoterone compared with vehicle in the Phase 3 studies
  - The most common new or worsening LSRs in patients previously treated with clascoterone/vehicle were scaling/dryness (face, 10.0%/7.3%; trunk, 3.5%/4.5%) and erythema (face, 8.0%/7.7%; trunk, 6.1%/7.3%; **Table 4**)
- No deaths were reported during the study

Table 4. New or worsening LSRs on the face and trunk in patients ≥12 years of age

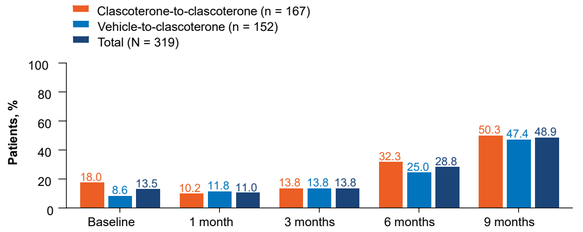
	Original treatment assignment			
	Clascoterone n = 311		Vehicle n = 287	
Symptom	Face	Trunk	Face	Trunk
Edema	5 (1.6)	1 (0.3)	5 (1.7)	5 (1.7)
Erythema	25 (8.0)	19 (6.1)	22 (7.7)	21 (7.3)
Pruritus	13 (4.2)	5 (1.6)	16 (5.6)	4 (1.4)
Scaling/dryness	31 (10.0)	11 (3.5)	21 (7.3)	13 (4.5)
Skin atrophy	3 (1.0)	1 (0.3)	4 (1.4)	4 (1.4)
Stinging/burning	11 (3.5)	1 (0.3)	8 (2.8)	2 (0.7)
Striae rubrae	1 (0.3)	2 (0.6)	2 (0.7)	1 (0.3)
Telangiectasia	3 (1.0)	1 (0.3)	4 (1.4)	1 (0.3)

Patients are summarized according to the original treatment they received in the Phase 3 pivotal studies.
Safety population. Data shown as n (%) unless otherwise specified.
LSR, local skin reaction.

Efficacy

- Among patients who completed the study without major protocol violations, the proportion with clear or almost-clear facial acne (IGA score 0/1) increased over time during treatment with clascoterone cream 1%; overall, 48.9% of patients had a facial IGA score of 0/1 at the end of the study (9 months; **Figure 1**)
  - Similar proportions of patients who originally received clascoterone or vehicle in the Phase 3 studies were clear or almost clear at the end of the study

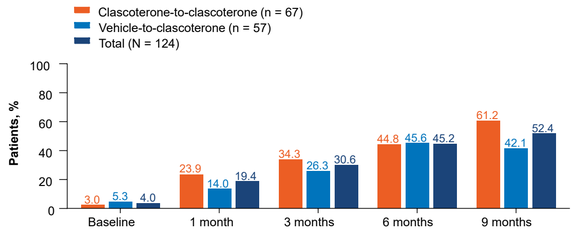
Figure 1. Percentage of patients ≥12 years of age with facial IGA 0/1 by visit



Patients are summarized overall and according to the original treatment they received in the Phase 3 pivotal studies.
Per-protocol population. Data shown as % unless otherwise specified.
IGA, Investigator's Global Assessment.

- The overall proportion of PP patients with clear or almost-clear truncal acne increased over time during clascoterone cream 1% treatment (**Figure 2**)
  - At the end of the study, the proportion of patients with a truncal IGA score of 0/1 was higher among those originally assigned to treatment with clascoterone vs vehicle (61.2% vs 42.1%, respectively)

Figure 2. Percentage of patients ≥12 years of age with truncal IGA 0/1 by visit



Patients are summarized overall and according to the original treatment they received in the Phase 3 pivotal studies.
Per-protocol population. Data shown as % unless otherwise specified.
IGA, Investigator's Global Assessment.

- Consistent with IGA results at each study visit, the overall proportions of PP patients who were clear or almost clear on the face increased with time on clascoterone treatment, with the greatest proportion of patients who were clear or almost clear observed in patients applying clascoterone for 12 months (67/119 [56.3%])

CONCLUSION

- Clascoterone cream 1% applied twice daily was well tolerated, and frequencies of TEAEs and LSRs were low throughout the study
  - Most reported TEAEs were mild in severity, and there was no accumulation of adverse events observed over time
  - No patient deaths were reported
- Among patients who completed the study without major protocol violations, the proportion achieving clear or almost-clear skin on the face and trunk increased with duration of clascoterone cream 1% treatment and was highest for patients on study for 12 months of treatment

REFERENCES

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DISCLOSURES

LFE, **AAH**, and **LSG** were study investigators. **LFE**, **AAH**, and **LSG** were also compensated advisors to Cassiopea. **AAH** is an employee of the McGovern Medical School of The University of Texas Health Science Center at 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. She also received personal fees for advisory, speaking, consulting, and/or other services from Almirall, Incyte, Pfizer, Aslan, Galderma Laboratories, Novartis, and Sun Pharma. **LFE** is an employee of the University of California San Diego, which received compensation from Cassiopea S.p.A. for study participation; he also served as an investigator, advisor, or consultant for Almirall, Dermata, Galderma Laboratories, and Ortho Dermatologics. **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 also received personal fees for advisory, speaking, consulting, research, and/or other services from Almirall, Foamix, Galderma Laboratories, Novartis, Sol-Gel, and Sun Pharma. **MC** is employed as the vice president of medical affairs at Novan Inc., was employed as the senior director of medical affairs at Cassiopea Inc. at the time of the study, received personal fees as a consultant from Cassiopea S.p.A., and receives personal fees as an adjunct faculty member from the University of Arizona. **LM** is an employee of Cassiopea S.p.A. and holds stock options in the company. **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, and served as the chief medical officer of Cosmo Pharmaceuticals.