Efficacy and safety of clascoterone cream 1% in patients with acne vulgaris across subgroups defined by demographic characteristics

Lawrence F. Eichenfield[1], Adelaide A. Hebert[2], Linda Stein Gold[3], Martina Cartwright[4], Luigi Moro[5], Jenny Han[6], Nicholas Squittieri[7], Alessandro Mazzetti[5]

[1]University of California San Diego School of Medicine, La Jolla, CA, USA; Rady Children's Hospital San Diego, San Diego, CA, USA; [2]UTHealth McGovern Medical School, Houston, TX, USA; [3]Henry Ford Medical Center, Detroit, MI, USA; [4]Cassiopea Inc., San Diego, CA, USA; [5]Cassiopea S.p.A., Lainate, Italy; [6]Pharmapace Inc., San Diego, CA, USA; [7]Sun Pharmaceutical Industries, Inc., Princeton, NJ, USA

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, randomized, double-blind, vehicle-controlled, Phase 3 studies (studies 25 and 26) and an open-label extension study (study 27) in patients ≥9 years of age with moderate-to-severe acne vulgaris[2,3]
  - Twice-daily treatment with clascoterone cream 1% for 12 weeks resulted in significantly higher treatment success rates compared with vehicle cream treatment[2]
  - The safety of clascoterone twice daily was maintained for up to 12 months in the extension safety study[3]
- Although adolescents and young adults are most often affected by acne,[4] there has been growing awareness of the increasing prevalence and negative impacts of acne in adults[5,6]

OBJECTIVE

- To evaluate the safety and efficacy of clascoterone cream 1% twice daily in patients ≥12 years of age with moderate-to-severe facial acne vulgaris across subgroups defined by demographic characteristics

METHODS

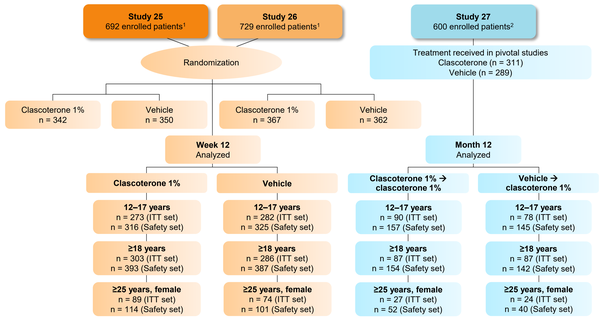
Study design, patients, and treatment

- Two identical, multicenter, randomized, vehicle-controlled Phase 3 studies evaluated the efficacy and safety of clascoterone cream 1% compared with vehicle cream twice daily for 12 weeks in patients with moderate-to-severe facial acne vulgaris
  - Male or nonpregnant female patients ≥9 years of age with a diagnosis of facial acne vulgaris and an Investigator's Global Assessment (IGA) score of 3 or 4 were eligible
- Patients who completed 1 of the 12-week Phase 3 pivotal trials could participate in an optional open-label extension study
  - All patients continuing into the extension study applied clascoterone cream 1% twice daily to the entire face for up to 9 additional months of treatment
  - Clascoterone treatment could be discontinued if the IGA score was 0 or 1 (clear/almost clear) and reinstated if/when acne worsened
  - Patients with any skin pathology or condition that could interfere with the study or who planned to use other topical or systemic antiacne preparations were excluded

Patient flow and analysis

- This analysis includes pooled data stratified by age and sex from the 2 pivotal studies and extension study in patients ≥12 years of age (**Figure 1**)
  - Total time applying clascoterone, including the Phase 3 studies, could be up to 12 months for patients originally randomized to clascoterone treatment

Figure 1. Patient flow diagram



[1]Number of patients ≥12 years of age enrolled in the pivotal studies (studies 25 and 26).
[2]Number of patients ≥12 years of age enrolled in the extension study (study 27).
Patients in the extension study are summarized based on the original treatment received in the pivotal studies.
Only 11 and 13 patients originally randomized to clascoterone and vehicle, respectively, were male and ≥25 years of age.
ITT, intention-to-treat.

- Efficacy was assessed at every in-clinic study visit using a 5-point IGA scale (0, clear; 4, severe)
  - Week 12 assessment: IGA score of 0 or 1 in all randomized patients ≥12 years of age (intention-to-treat [ITT] set) in the pivotal study
  - Month 12 assessment: IGA score of 0 or 1 in pivotal study ITT patients who entered the extension study and were assessed at Month 12
- Safety was evaluated from frequencies of treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) in patients ≥12 years of age who received at least 1 application of clascoterone (safety set)
- Missing data were not imputed

RESULTS

- Patient demographics are shown in **Table 1**. The majority of patients were female with mean ± standard deviation age of 19.8 ± 6.1 and 19.5 ± 6.1 years in patients originally treated with clascoterone and vehicle, respectively

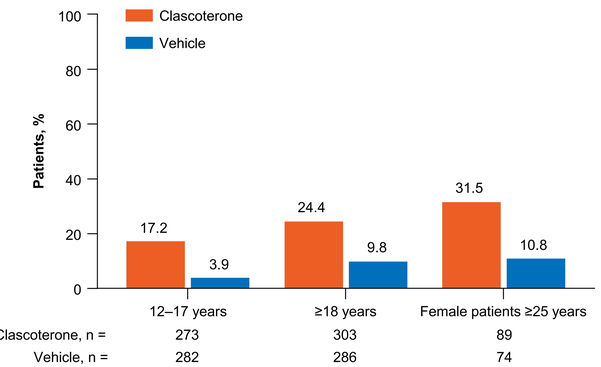
Table 1. Patient demographics

Characteristics	Clascoterone (n = 709)	Vehicle (n = 712)
Sex		
Male	256 (36.1)	282 (39.6)
Female	453 (63.9)	430 (60.4)
Age, years		
Mean ± SD	19.8 ± 6.1	19.5 ± 6.1
Median	18.0	18.0
Min, max	12, 58	12, 50
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)
Not Hispanic or Latino	601 (84.8)	624 (87.6)

Phase 3 pooled ITT population ≥12 years of age.
Data shown as n (%) unless otherwise specified.
ITT, intention-to-treat; max, maximum; min, minimum; SD, standard deviation.

- A significantly greater proportion of clascoterone-treated vs vehicle-treated patients achieved clear or almost clear skin (IGA 0/1) at Week 12 among patients 12 to 17 years (P <0.0001), ≥18 years (P <0.0001), and female patients ≥25 years of age (P = 0.002; **Figure 2**)

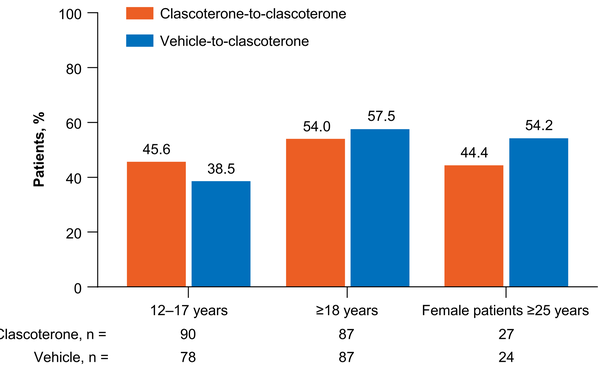
Figure 2. Proportion of patients ≥12 years of age who achieved IGA 0/1 at Week 12 by age and sex



Phase 3 pooled ITT population. Male patients ≥25 years of age are not shown due to the small number of patients in this subgroup. Data shown as percent.
IGA, Investigator's Global Assessment; ITT, intention-to-treat.

- The proportion of patients achieving IGA 0/1 among those assessed at each visit increased throughout the extension study in all subgroups (**Figure 3**)

Figure 3. Proportion of patients ≥12 years of age who achieved IGA 0/1 at Month 12 by age and sex



Phase 3 pooled ITT population that completed Month 12. Male patients ≥25 years of age are not shown due to the small number of patients in this subgroup. Patients are summarized according to the original treatment received in the Phase 3 studies. Treatment through Month 12 includes 3 months in the Phase 3 studies. Data shown as percent.
IGA, Investigator's Global Assessment; ITT, intention-to-treat.

- The frequency of TEAEs through Week 12 across subgroups is shown in **Table 2**
  - SAEs occurred in <0.5% of patients in any subgroup, and none were related to study drug

Table 2. Summary of TEAEs through 12 weeks in patients ≥12 years of age by age and sex

Category	12–17 years		≥18 years		≥25 years, female	
	Clascoterone n = 316	Vehicle n = 325	Clascoterone n = 393	Vehicle n = 387	Clascoterone n = 114	Vehicle n = 101
All TEAEs	34 (10.8)	46 (14.2)	45 (11.5)	45 (11.6)	11 (9.6)	13 (12.9)
SAEs	0	1 (0.3)	0	1 (0.3)	0	0
TEAEs related to study drug	5 (1.6)	6 (1.8)	7 (1.8)	16 (4.1)	4 (3.5)	4 (4.0)
TEAEs leading to dose modification	1 (0.3)	1 (0.3)	4 (1.0)	6 (1.6)	2 (1.8)	2 (2.0)
TEAEs leading to discontinuation	2 (0.6)	5 (1.5)	3 (0.8)	9 (2.3)	2 (1.8)	2 (2.0)

Phase 3 pooled safety population. Data shown as n (%).
SAE, serious adverse event; TEAE, treatment-emergent adverse event.

- TEAE frequency through Month 12 was comparable between patients originally randomized to treatment with clascoterone vs vehicle across all subgroups
  - No patient deaths were reported during the study

CONCLUSIONS

- The efficacy and safety of clascoterone cream 1% were maintained for up to 12 months of twice-daily use in adolescent and adult patients ≥12 years of age, including female patients ≥25 years of age
  - The proportion of patients with clear or almost clear skin was greatest after 12 months of treatment in patients 18 years of age or older

REFERENCES

1) WINLEVI® (clascoterone cream 1%) Prescribing Information. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; 2020.
2) Hebert A, et al. *JAMA Dermatol.* 2020;156(6):621-630.
3) Eichenfield L, et al. *J Am Acad Dermatol.* 2020;83(2):477-485.
4) Lynn DD, et al. *Adolesc Health Med Ther.* 2016;7:13-25.
5) Collier CN, et al. *J Am Acad Dermatol.* 2008;58(1):56-59.
6) Altunay IK, et al. *Acta Derm Venereol.* 2020;100:adv00051.

ACKNOWLEDGMENTS

The authors thank the patients, investigators, and sites for their participation. The studies were funded by Cassiopea S.p.A. Medical writing and editorial support were provided by Dana Lengel, PhD, of AlphaBioCom, a Red Nucleus company, and funded by Sun Pharma.

DISCLOSURES

LFE, AAH, and **LSG** were study investigators. **LFE, AAH**, and **LSG** were also compensated advisors to Cassiopea. **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, Dermata, Galderma Laboratories, and Ortho Dermatologics. **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; she has also received personal fees for advisory, speaking, consulting, and/or other services from Almirall, Incyte, Pfizer, Aslan, Galderma Laboratories, Novartis, and Sun Pharma. **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 services with 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., holds stock options in the company, and has served as the chief medical officer of Cosmo Pharmaceuticals.