TRIFAROTENE 50 μg/g CREAM FOR TREATMENT OF ACNE VULGARIS – A SUMMARY OF TWO RANDOMIZED TRIALS AND A LONG-TERM SAFETY STUDY

Jerry Tan, MD[1]; James Del Rosso, DO[2]; Jonathan Weiss, MD[3]; Linda Stein Gold, MD[4]; Fran Cook-Bolden, MD[5]; Lawrence Eichenfield, MD[6]; Emil Tanghetti, MD[7]; Michael Graeber, MD[8]; Allesandra Alió Saenz, MD[8]; Faiz Ahmad[8]

[1]Department of Medicine, University of Western Ontario, Windsor ON, Canada, [2]JDR Dermatology Research/Thomas Dermatology, Las Vegas, NV; [3]Gwinnett Dermatology, Snellville, GA; [4]Henry Ford Medical Center Department of Dermatology, Detroit, MI; [5]Mount Sinai Hospital, New York, NY; [6]Department of Pediatric and Adolescent Dermatology, Rady Children's Hospital, University of California, San Diego, CA; [7]Center for Dermatology and Laser Surgery Sacramento, CA; [8]Galderma R&D, LLC, Fort Worth, TX

INTRODUCTION

Introduction to trifarotene 50 μg/g cream:[1]

- Retinoid receptor agonist that selectively targets retinoic acid receptor gamma
- Low systemic exposure after topical administration
- Once-daily cream developed for treatment of acne vulgaris on the face and trunk

Objectives:

- Study 1 and Study 2: Assess safety and efficacy of trifarotene 50 μg/g cream applied once daily for 12 weeks in subjects with acne vulgaris
- Long-term Safety and Efficacy Study: Evaluate long-term safety and efficacy of trifarotene 50 μg/g cream use over a period of 52 weeks

Figure 1. Study 1 and Study 2 Flowchart

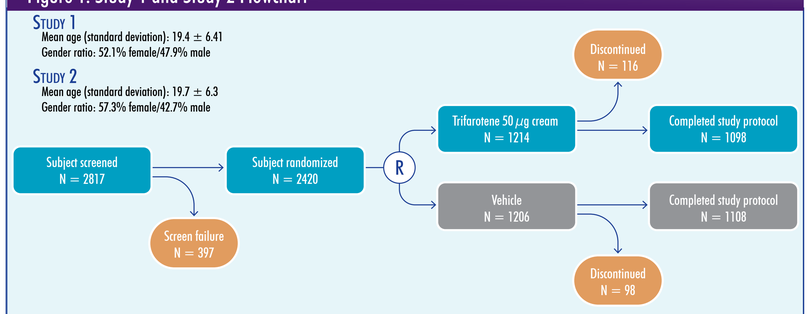
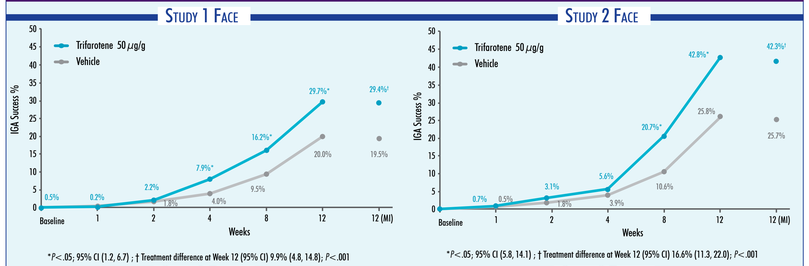


Figure 2. Efficacy Comparison of Trifarotene 50 μg/g Cream and Vehicle



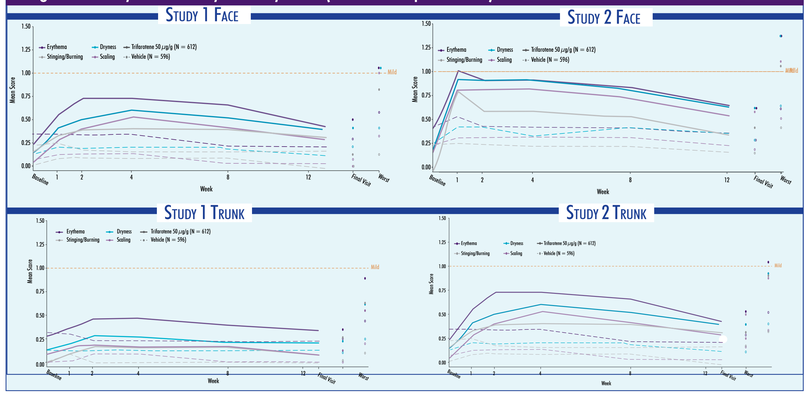
*P<.05; 95% CI (1.2, 6.7) ; † Treatment difference at Week 12 (95% CI) 9.9% (4.8, 14.8); P<.001

*P<.05; 95% CI (5.8, 14.1) ; † Treatment difference at Week 12 (95% CI) 16.6% (11.3, 22.0); P<.001

*P<.05; 95% CI (4.6, 13.7) ; † Treatment difference (95% CI) 10.7% (5.4, 16.1); P<.001

*P<.05; 95% CI (5.8, 14.1) ; † Treatment difference at Week 12 (95% CI) 16.6% (11.3, 22.0); P<.001

Figure 3. Study 1 and Study 2 Safety Data (score is a 3-point scale)



METHODS

Study 1 and 2

- Two identical multi-center, double-blind, randomized 12-week studies of subjects with moderate facial and truncal acne comparing vehicle with once-daily trifarotene 50 μg/g cream; N = 2,420
- Study 1: conducted at 109 sites, majority United States
- Study 2: conducted at 80 sites, majority Europe
- Primary efficacy endpoints (face) measured at Baseline and Weeks 1, 2, 4, 8, and 12:
  - Success rate: percentage of subjects with Investigator Global Assessment (IGA) of clear (0) or almost clear (1) and at least a 2-grade improvement
  - Absolute change in facial inflammatory/non-inflammatory lesion count
- Secondary efficacy endpoints (trunk) measured at Baseline and Weeks 1, 2, 4, 8, and 12:
  - Success rate: percentage of subjects with Physician Global Assessment (PGA) of clear (0) or almost clear (1) and at least a 2-grade improvement
  - Absolute change in truncal inflammatory/non-inflammatory lesion count
- Safety endpoints:
  - Incidence of adverse events and local tolerability[1]

Long-term Efficacy and Safety Study

- A long-term safety and efficacy study conducted over 52 weeks for once-daily use of trifarotene 50 μg/g cream in patients with moderate facial and truncal acne; N = 455
- Efficacy and tolerability measured at Baseline and Weeks 12, 20, 26, 38, and 52
- Primary endpoints (safety) included:
  - Local tolerability (erythema, scaling, dryness, stinging/burning) on face and trunk
  - Adverse events
- Secondary endpoints (efficacy) included:
  - Success rate: IGA/PGA score of clear (0) or almost clear (1) and at least a 2-grade IGA/PGA improvement from Baseline
  - Grade change from baseline of IGA and PGA
  - Subject's assessment of facial acne improvement[2]

RESULTS

Study 1 and 2

Efficacy:

Results of all efficacy assessments at Week 12 significant ($P < .001$) in favor of trifarotene 50 μg/g cream versus vehicle

- Study 1: Primary efficacy endpoints (MI)
  - 29.4% IGA success rate in trifarotene 50 μg/g cream compared with 19.5% for vehicle
  - Mean percent change of -54.4% in facial inflammatory lesion count from Baseline to Week 12 for trifarotene 50 μg/g cream, compared with -44.8% for vehicle
  - Mean percent change of -49.7% in facial non-inflammatory lesion count from Baseline to Week 12 for trifarotene 50 μg/g cream, compared with -35.7% for vehicle (multiple imputation values used)
- Study 2: Primary efficacy endpoints
  - 42.3% trifarotene 50 μg/g cream IGA success rate compared with 25.7% for vehicle
  - Mean percent change of -66.2% in facial inflammatory lesion count from Baseline to Week 12 for trifarotene 50 μg/g cream, compared with -51.2% for vehicle
  - Mean percent change of -57.7% in facial non-inflammatory lesion count from Baseline to Week 12 for trifarotene 50 μg/g cream, compared with -43.9% for vehicle (multiple imputation values used)

Safety:

- Skin irritation related to trifarotene 50 μg/g cream was transient, and consistent with known patterns of topical retinoid dermatitis
  - Most common related AEs included irritation, pruritus, and sunburn (incidence ≥1%)
  - Severe AEs related to trifarotene 50 μg/g cream reported in nine subjects versus none in the vehicle group, with no serious AEs reported
  - Severe related AEs led to subject discontinuation in 1.9% of the trifarotene 50 μg/g cream group in Study 1, and in 1.2% of the trifarotene 50 μg/g cream group in Study 2
- Tolerability signs related to trifarotene 50 μg/g cream assessed as mostly mild to moderate by investigator

Long-term Efficacy and Safety Study

Efficacy:

- Both IGA and PGA success rates improved over time
  - IGA success rates increased from 26.6% at Week 12 to 65.1% at Week 52
  - PGA success rates increased from 38.6% at Week 12 to 66.9% at Week 52
  - At Week 52, 57.9% of patients had both IGA and PGA success[2]

Safety:

- Majority of treatment emergent adverse events (TEAEs) occurred during the first three months of the study
- Most common TEAEs included pruritus, irritation, and sunburn
- No serious TEAEs were related to trifarotene 50 μg/g cream[2]

Figure 4. Long-term Safety and Efficacy Study flowchart

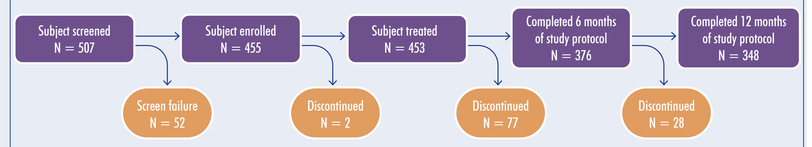


Figure 5. IGA/PGA success rates from Baseline to Week 52

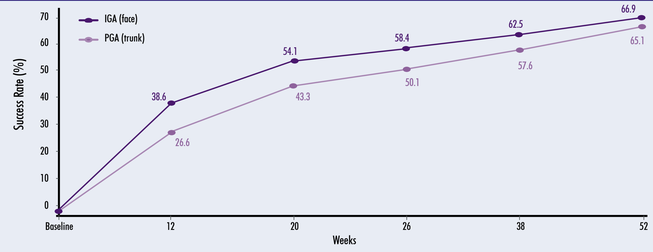
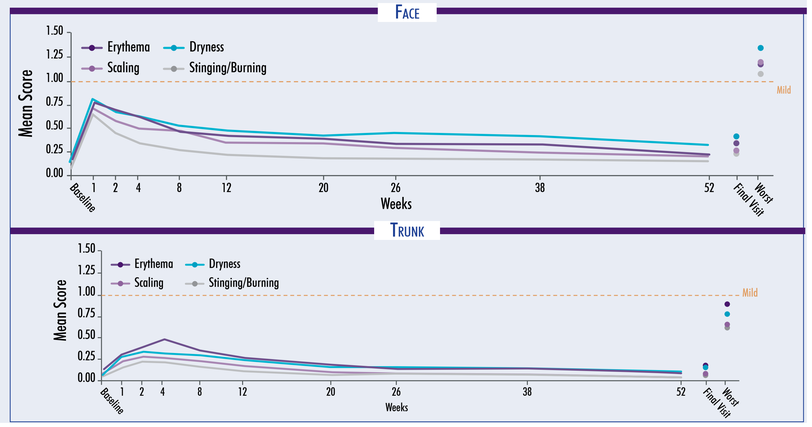


Figure 6. Local tolerability of trifarotene 50 μg/g cream

Severity scale score: 0 (none), 1 (mild), 2 (moderate), 3 (severe)



REFERENCES

We wish to thank our colleagues in Galderma International, Galderma R&D in Sophia Antipolis, and Galderma Laboratories and the trifarotene study group, as well as all investigators in the United States, Canada, Europe, and Russia who participated in these clinical trials.

1. Tan J, Thiboutot D, Popp G, Gooderham M, Lynde C, Del Rosso J, et al. Randomized phase 3 evaluation of trifarotene 50 mg/g cream treatment of moderate facial and truncal acne. *J Am Acad Dermatol.* 2019;80:1691-9.
2. Blume-Peytavi U, Fowler J, Lajos K, Draelos Z, Cook-Bolden F, Dirschka T, et al. Long-term safety and efficacy of trifarotene 50μg/g cream, a first-in-class RAR-γ selective topical retinoid, in patients with moderate facial and truncal acne. *J Eur Acad Dermatol Venereol.* 2019:(In preparation).

SUMMARY

- In Study 1 and Study 2, trifarotene 50 μg/g cream had a rapid effect, with significant reduction in lesion counts on the face as early as Week 1, and on the trunk as early as Week 2
- Subjects in the Long-term Safety and Efficacy Study demonstrated continuous clinical improvement over the course of the 52-week study period
- Trifarotene 50 μg/g cream is well tolerated and efficacious for treatment of facial and truncal acne, compared with vehicle
- Treatment with trifarotene 50 μg/g cream was observed to be safe and tolerable in both the 12- and 52-week studies[1, 2]

ALT.P-RD18250-08

ACKNOWLEDGEMENTS Study funded by Galderma R&D, LLC. Medical writing supported by Galderma Laboratories, L.P.