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

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INTRODUCTION

- 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

OBJECTIVE

- 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

MATERIAL AND METHODS

Study 1 and Study 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 (IL/NIL)
- 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 Safety and Efficacy 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 0 (clear) or 1 (almost clear) 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

Figure 1. Study 1 and Study 2 Flowchart

Study 1
Mean age (standard deviation): 19.4 ± 6.41
Gender ratio: 52.1% female/47.9% male

Study 2
Mean age (standard deviation): 19.7 ± 6.3
Gender ratio: 57.3% female/42.7% male

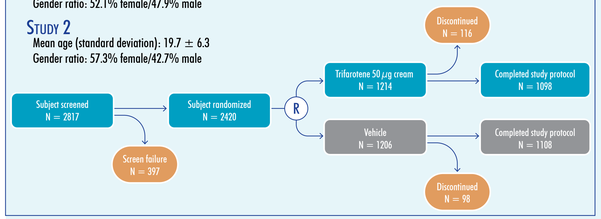
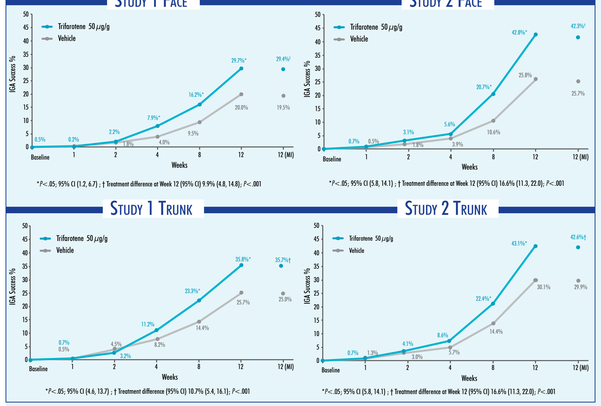


Figure 2. Efficacy comparison of trifarotene 50 μg/g cream and vehicle



*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

Efficacy:

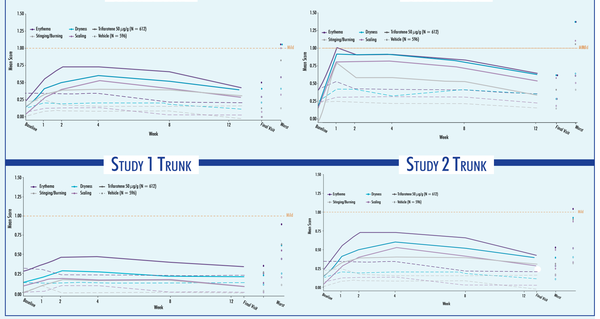
Efficacy assessments at week 12 were significant ($P<.001$) in favor of trifarotene 50 μg/g cream vs vehicle

- Study 1: Primary efficacy endpoints
- 29.4% IGA success rate in trifarotene 50 μg/g cream compared with 19.5% for vehicle
- Mean % change: -54.4% in facial ILs (baseline to week 12) for trifarotene 50 μg/g cream vs -44.8% for vehicle (MI)
- Mean % change: -49.7% in facial NILs count (baseline to week 12) for trifarotene 50 μg/g cream vs -35.7% for vehicle (MI) values used)
- Study 2: Primary efficacy endpoints
  - 42.3% trifarotene 50 μg/g cream IGA success rate vs 25.7% for vehicle
  - Mean % change: -66.2% in facial ILs (baseline to week 12) for trifarotene 50 μg/g cream vs -51.2% for vehicle
  - Mean % change: -57.7% in facial NILs (baseline to week 12) for trifarotene 50 μg/g cream vs -43.9% for vehicle (MI)

Safety

- Skin irritation with trifarotene 50 μg/g cream was transient, and consistent with expected retinoid response
  - Most common related AEs included irritation, pruritus, and sunburn (incidence ≥1%)
  - Severe AEs related to trifarotene 50 μg/g cream reported in 9 subjects vs 0 with vehicle, 0 serious AEs reported
  - Severe related AEs led to discontinuation in 1.9%/1.2% of subjects with trifarotene 50 μg/g cream in Study 1/Study 2

Figure 3. Study 1 and Study 2 safety data (score is from a 3-point scale)



RESULTS - Study 2

Figure 4. Long-term Safety and Efficacy Study flowchart

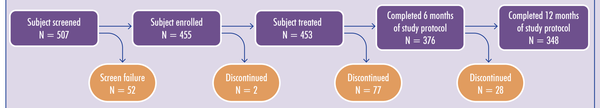


Figure 5. IGA/PGA success rates from Baseline to Week 52

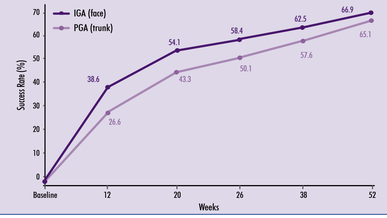
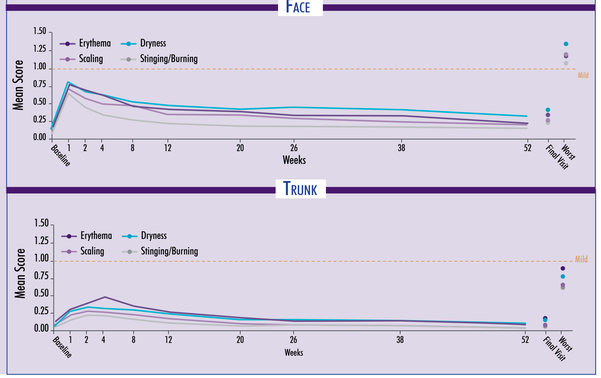


Figure 6. Local tolerability of trifarotene 50 μg/g cream

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



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]

REFERENCES

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