CONSISTENT EFFICACY AND SAFETY IN FOUR DOUBLE-BLIND, VEHICLE-CONTROLLED STUDIES OF IVERMECTIN 1% CREAM IN THE TREATMENT OF MODERATE TO SEVERE PAPULOPUSTULAR ROSACEA

INTRODUCTION

Rosacea is a chronic inflammatory disease.

- Rosacea has traditionally been classified as either erythematotelangiectatic (ETR), papulopustular (PPR), phymatous, or ocular rosacea.
- PPR is characterized by facial papules, pustules, and persistent erythema.

The pathogenesis of PPR is not yet completely understood; however, current studies indicate that underlying causes may include dysregulation of the innate immune system, overgrowth of commensal skin organisms, aberrant neurovascular signaling, and the production of inflammatory mediators in basal skin.

- Ivermectin 1% cream (IVM) is an effective and safe topical therapy approved to treat the inflammatory lesions of rosacea.

- During the development of IVM, 2 Phase 2 and 2 Phase 3 vehicle-controlled studies were conducted in more than 1600 subjects.

METHODS

Study Design

- Objectives:
  - This analysis reviews the consistency of efficacy and safety results of 4 (two phase 2 and 2 phase 3) 12-week, vehicle-controlled studies (N = 1683) conducted during the development of IVM.

- Methods:
  - Phase 2, Study 1:
    - 6-arm, 12-week, double-blind, placebo-controlled, investigator-blind, vehicle- and active-controlled study.
    - Subjects were male or female, ≥ 18 years of age, with PPR (≥ 15 lesions).
    - For the sake of consistency of this analysis, only data from the Ivermectin 1% and vehicle arms are reported here.
  - Phase 2, Study 2:
    - 12-week, multi-center, double-blind, placebo-controlled study.
    - Subjects were male or female, ≥ 18 years of age, with PPR (≥ 15 lesions).
    - Discontinuations Due to AEs in the IVM arm
      - Phase 2, Study 1: 1 (1.9%) subjects.
    - Adverse events
      - Discontinuations Due to AEs in the vehicle arm
        - Phase 2, Study 1: 1 (1.9%) subjects.

- Phase 3, Study 1:
- Phase 3, Study 2:

RESULTS

Efficacy

- 1603 subjects in 4 studies (two phase 2 and two phase 3) are included in this analysis.
- All 4 studies confirmed the statistically superior efficacy of IVM vs vehicle.
- Success rate (IGA 0 or 1) was statistically superior for IVM vs vehicle in all 4 studies (Figure 1).
- Week 2, Phase 2, Study 1: 7 (2.6%) subjects.
- Week 12, Phase 2, Study 1: 1 (0.4%) subjects vs vehicle.
- Week 12, Phase 2, Study 2: 1 (0.4%) subjects vs vehicle.
- Week 12, Phase 3, Study 1: 6 (1.0%) subjects vs vehicle.
- Week 12, Phase 3, Study 2: 4 (1.7%) subjects vs vehicle.
- Ivermectin 1%:
  - Week 12, Phase 3, Study 1: 1 (0.1%) subject.
  - Week 12, Phase 3, Study 2: 1 (0.2%) subject.

Safety

- The treatment was highly tolerable in all 4 studies, and there were few study discontinuations (Table 1).

- Discontinuations Due to AEs in the IVM arm
  - Phase 2, Study 1: 1 (1.9%) subjects.
  - Phase 2, Study 2: 0 (0.0%) subjects.
  - Phase 3, Study 1: 1 (1.6%) subjects.
  - Phase 3, Study 2: 6 (1.3%) subjects.

- No serious adverse events related to IVM were observed in any of the 4 studies.

- The incidences of treatment-related AEs were low, and comparable in both treatment groups.
  - Related AEs: Phase 2, Study 1: Vehicle: 5 (5 subjects, 4.8%); IVM: 5 (5 subjects, 4.7%).
  - Related AEs: Phase 2, Study 2: Vehicle: 6 (6 subjects, 10.9%); IVM: 6 (6 subjects, 10.9%).
  - Related AEs: Phase 3, Study 1: Vehicle: 24 (19 subjects, 4.9%); IVM: 25 (18 subjects, 28%).
  - Related AEs: Phase 3, Study 2: Vehicle: 17 (12 subjects, 2.6%); IVM: 20 (15 subjects 6.5%).

Figure 1. Significant IGA Success

Figure 2. Mean Percent Lesion Reduction

REFERENCES


2. Henry Ford Medical Center, Dept. of Dermatology, Detroit, MI, *Galderma Laboratories, L.P., Fort Worth, TX, **Galderma R&D, Sophia Antipolis, France

SUMMARY

- In phase 4 studies, IVM demonstrated strong efficacy, tolerability, and safety.
- The data supporting efficacy, tolerability, and safety was replicated with a high level of consistency.
- The low incidence of AEs, good tolerability, and high efficacy make IVM an excellent treatment choice for PPR.