Long-term Safety and Tolerability of Sarecycline for the Treatment of Acne Vulgaris: Results from a Phase III, Multicenter, Open-Label Study and a Phase I Phototoxicity Study

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Introduction

- Sarecycline is a narrow-spectrum tetracycline-class antibiotic designed for the treatment of moderate-to-severe acne.
- Sarecycline’s narrow-spectrum anti-bacterial activity and lipophilicity may minimize side effects commonly associated with broad-spectrum tetracyclines, such as minocycline and doxycycline.
- Here, we report the results of 2 identically designed, phase 3 pivotal trials, SC1401 and SC1402, to evaluate the efficacy and safety of once-daily sarecycline (n=2002).

Methods

- Patients (n=483) aged 9 years or older with moderate-to-severe acne who completed one of two prior pivotal Phase III, double-blind, placebo-controlled, 12-week trials in which they received sarecycline 1.5mg/kg/day or placebo once daily were continued on once daily sarecycline for up to 40 weeks. Study visits: weeks 2, 6, 12, 18, 24, 32, and 40.
- Excluded: Receiving/planning to receive any systemic acne vulgaris medication, systemic retinoids, systemic corticosteroids or any androgen/anti-androgenic therapy (e.g. testosterone, spironolactone).
- Included: Allowed use of topical acne vulgaris medications.
- The primary assessment was the safety of sarecycline 1.5mg/kg/day for 40 weeks as indicated by adverse events (AEs), vital signs, electrocardiograms, clinical laboratory tests, and physical examinations.
- Patterns of sarecycline use were a secondary assessment.
- Subjects treated until adequate improvement obtained as per Investigator judgment (eg. IGA score of 0 or 1) and re-initiated if acne recurred (eg. IGA score ≥ 3).

Results

- TEAEs of Interest Safety Population
  - Placebo/Sarecycline (N=236), n (%)
  - Sarecycline/Sarecycline (N=247), n (%)
  - Total (N=483), n (%)

Common TEAEs (≥2% of patients in either group)
- Nasopharyngitis
- Upper-respiratory tract infection
- Headache
- Urinary tract infection

Gastrointestinal
- Nausea
- Vomiting
- Diarrhea
- Constipation

Vestibular
- Dizziness
- Vertigo
- Tinnitus

Sunburn and skin hyperpigmentation
- Sunburn
- Skin hyperpigmentation

Vaginal yeast infections in females
- Vulvovaginal mycotic infection
- Genital fungal infection
- Genital candidiasis

Conclusion

- Sarecycline was associated with low rates of TEAEs, with nasopharyngitis, upper-respiratory-tract infection, headache, and nausea being the only TEAEs reported ≥2% or more of patients with moderate-to-severe acne vulgaris aged nine years or older treated with sarecycline once daily for up to 40 weeks.
- Rates of TEAEs commonly associated with other tetracycline antibiotics were low. Rates of TEAEs commonly associated with other tetracycline antibiotics were for dizziness (0.4%) and sunburn (0.2%), and for gastrointestinal TEAEs, nausea (2.1%), vomiting (1.9%), and diarrhea (1.0%). Vulvovaginal mycotic infection (0.8%).
- Sarecycline has low potential to cause clinically significant phototoxicity.
- No clinically meaningful safety findings were noted.

Phase-1 Phototoxicity

Synopsis

- 19 Subjects (healthy; non-smoker, men, aged 18 to 45 years) received placebo or 240mg of sarecycline in a random order in each of the two treatment periods (not weight based).
- A two-treatment, two-period, two-sequence crossover design. Treatment periods were separated by at least nine days.
- At three hours after administration of the study treatment, a previously unexposed area of each subject’s back was irradiated with 16J/cm² of UVA, after which point, another area was irradiated with UVA/UVB at 50 percent of the subject’s minimum erythemal dose (MED).
- UV-exposed skin was assessed visually at 24, 48, and 72 hours after irradiation, and UV-induced skin reaction was evaluated using dermal response score scale.

Results: Dermal response to UV exposure did not exceed mild erythema with either sarecycline or placebo at any time point, and the mean and maximum UV-induced dermal response scores for both sarecycline and placebo were low. No TEAEs or serious AEs were reported in the phototoxicity study.

Phase-3 Long-term Safety (40-week)