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

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	13 (5.5)	5 (2.0)	18 (3.7)
Upper-respiratory-tract infection	7 (3.0)	9 (3.6)	16 (3.3)
Headache	9 (3.8)	5 (2.0)[b]	14 (2.9)[b]
Urinary tract infection	2 (0.8)	5 (2.0)	7 (1.4)
Gastrointestinal			
Nausea	4(1.7)	6(2.4)	10(2.1)
Vomiting	3(1.3)	6(2.4)	9(1.9)
Diarrhea	3 (1.3)	2 (0.8)	5 (1.0)
Constipation	2 (0.8)	0	2 (0.4)
Vestibular			
Dizziness	1(0.4)	1(0.4)	2(0.4)
Vertigo	0	0	0
Tinnitus	0	0	0
Sunburn and skin hyperpigmentation			
Sunburn	0	1(0.4)	1(0.2)
Skin hyperpigmentation	1(0.4)	0	1(0.2)
Vaginal yeast infections in females			
Vulvovaginal mycotic infection	0	2(1.6)	2(0.8)
Genital fungal infection	0	1(0.4)	1(0.2)
Genital candidiasis	1(0.4)	0	1(0.2)

The safety population included 483 patients; 354 patients (73.3%) completed the study 1

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/cm^2 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
- Mean and maximum numerical UV-induced dermal response scores were determined for sarecycline and placebo

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

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 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.

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