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NEWS, VIEWS, & REVIEWS

To Acne and Beyond: A Review of Sarecycline's Off-Label Uses

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INTRODUCTION

Sarecycline is a third-generation tetracycline that is only currently FDA-approved for the treatment of moderate to severe inflammatory acne vulgaris in patients ≥ 9 years old. It functions as a bacteriostatic translation inhibitor that targets gram-positive bacteria on the skin, most notably *Cutibacterium acnes*. Sarecycline shares anti-inflammatory properties with first- and second-generation tetracyclines, however, it is differentiated by its narrow spectrum of activity and less potent effect on gastrointestinal microbes. These features of sarecycline reduce the risk of antibiotic resistance and minimize side effects.[1-3] The most common side effects, nausea, nasopharyngitis, and headache, have been demonstrated by both short- and long-term safety investigations.[4-5] Importantly, sarecycline has comparable efficacy to older tetracyclines in reducing both inflammatory and non-inflammatory acne lesions on the face and trunk. Finally, the drug's once-daily administration helps to promote treatment adherence.

In addition to its use for acne, sarecycline has also been leveraged for the management of a myriad of other dermatologic conditions, including rosacea, perioral dermatitis, mucous membrane pemphigoid, and the papulopustular eruption of tyrosine kinase inhibitors.[6-10] Given that dermatologists have the highest antibiotic prescription rate per clinician among all medical specialties and that two-thirds of these prescriptions are for minocycline or doxycycline, dermatologists should be familiar with sarecycline's on- and off-label uses as part of their treatment armamentarium.[9]

Rosacea

Oral (and now even topical) tetracyclines are a mainstay in the treatment of the papulopustular subtype of rosacea due to their anti-inflammatory properties. However, given that the broad-spectrum action of older-generation tetracyclines poses risks of antibiotic resistance and off-target side effects, sarecycline is a viable alternative antibiotic choice.[12-13]

To further investigate the safety and efficacy of sarecycline in treating rosacea, a pilot study comparing sarecycline versus a multivitamin as a placebo in 102 subjects with rosacea was performed. The study found an improvement in Investigator's Global Assessment score of rosacea to clear or almost clear (P<0.0001) at week 12 of treatment, a reduction in total inflammatory lesion count (P<0.0001), a Subjective Global Assessment improvement reported by subjects (P<0.001), and greater reductions in erythema (P<0.0001), dryness (P=0.01), peeling (P=0.02), and burning (P=0.01) when compared with placebo. Adverse events did include gastroenteritis, however only in 2.6% of subjects.[6] While studies comparing sarecycline with older-generation tetracyclines have not been performed, this pilot study indicates that sarecycline could be a safe and effective option for the treatment of rosacea.

Perioral Dermatitis

As perioral dermatitis has previously been associated with a dysregulated skin microbiome, conventional treatment paradigms for treating severe perioral dermatitis include doxycycline.[14] Given the established role of tetracycline antibiotics in the treatment of perioral dermatitis and the challenging nature of managing this condition, sarecycline may function as a novel therapy for perioral dermatitis.

The first reported case of sarecycline use for the treatment of perioral dermatitis was documented in a patient with Crohn's disease, who exhibited clinical and symptomatic improvement within 5 days of treatment initiation and almost complete resolution within 13 days. Notably, sarecycline was chosen for this patient in part due to their history of inflammatory bowel disease to minimize the risk and sequelae of gut dysbiosis. Another published report demonstrated improvement in treatment-resistant steroid-induced perioral dermatitis after two months of treatment with sarecycline. Sarecycline was well tolerated in both cases.[7,8]

Mucous Membrane Pemphigoid

Treatment modalities for mucous membrane pemphigoid (MMP) vary but include systemic, topical, and intralesional corticosteroids and immune modifying agents.[16] The use of systemic minocycline has been reported as a therapeutic option for oral MMP, however, treatment success was limited by drug side effects.[17] In one report, a patient with MMP who was treated with sarecycline after previous unsuccessful treatment with doxycycline showed improvement in inflammation and disease activity. The patient was maintained on treatment for 3 months,

until discontinuation due to issues with insurance coverage, highlighting an important limiting factor of sarecycline: accessibility. Sarecycline is currently not available in a generic form, and the cost can be prohibitive for patients, especially compared with other tetracyclines.[7]

Papulopustular Eruption of Tyrosine Kinase Inhibitors

Tyrosine kinase inhibitors (TKIs) are oral agents that function through modulation of the epidermal growth factor receptor (EGFR) pathway and are used in the treatment of a variety of malignancies. Papulopustular eruptions (PPEs) are a common cutaneous toxicity associated with TKIs. Although PPEs are an indicator of drug efficacy, they can affect patients' quality of life and interfere with treatment adherence.[18] Tetracyclines are a component of the consensus guidelines for the prevention and treatment of PPE of TKI; however, their use is not without risks. One study of patients receiving oral tetracyclines for management of EGFR inhibitor-related PPE showed a "higher incidence of secondary skin infection with antibiotic-resistant bacteria compared with patients without prior antibiotic exposure (P=0.004)," and a "greater incidence of resistant infections…in patients with greater than 4 weeks of exposure."[19]

To overcome the limiting side effects of antimicrobial resistance in already immunosuppressed patients receiving TKIs for cancer treatment, sarecycline may be a viable alternative. One reported case demonstrated the successful clearance of a PPE after treatment with dasatinib, a TKI used for treating chronic myeloid leukemia and acute lymphoblastic leukemia. The patient in this case had no reported side effects, treatment interruptions, or changes to their dasatinib therapy.[10] These authors can also report the marked success of sarecycline for the treatment of a PPE of TKIs in a patient seen in our institution's supportive oncodermatology clinic.

CONCLUSION

Sarecycline, with its distinctive anti-inflammatory properties and demonstrated efficacy, stands poised to address significant gaps in the treatment of various dermatologic conditions as well as selectively replace its broader-spectrum counterparts. Despite its narrow spectrum of action, sarecycline's targeted approach not only enhances its therapeutic potential but also positions sarecycline as a valuable addition to the dermatologist's arsenal. Interestingly, given the use of tetracyclines in hidradenitis suppurativa (HS), these authors were surprised that no cases of sarecycline for the treatment of HS have been reported. Looking forward, the curious yet cautious dermatologist may uncover even more uses for sarecycline.

DISCLOSURE

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References

1. Haidari W, Bruinsma R, Cardenas-de la Garza JA, et al. Sarecycline review. *Ann Pharmacother.* 2020;54(2):164-170. doi:10.1177/1060028019873111.
2. Batool Z, Lomakin IB, Polikanov YS, et al. Sarecycline interferes with tRNA accommodation and tethers mRNA to the 70S ribosome. *Proc Natl Acad Sci U S A.* 2020;117(34):20530-20537. doi:10.1073/pnas.2008671117.
3. Swallow MA, Fan R, Cohen JM, et al. Antibiotic resistance risk with oral tetracycline treatment of acne vulgaris. *Antibiotics (Basel).* 2022;11(8):1032. doi:10.3390/antibiotics11081032.
4. Moore AY, Charles JEM, Moore S. Sarecycline: A narrow spectrum tetracycline for the treatment of moderate-to-severe acne vulgaris. *Future Microbiol.* 2019;14(14):1235-1242. doi:10.2217/fmb-2019-0199.
5. Harper JC, Armstrong A, Fried RG, et al. Patient-reported outcomes with sarecycline treatment for acne vulgaris: Pooled analysis of phase 3 clinical studies. *J Am Acad Dermatol.* 2023;89(4):832-834. doi:10.1016/j.jaad.2023.04.075.
6. Rosso JQ, Draelos ZD, Effron C, et al. Oral sarecycline for treatment of papulopustular rosacea: Results of a pilot study of effectiveness and safety. *J Drugs Dermatol.* 2021;20(4):426-431. doi:10.36849/JDD.2021.5923.
7. Graber E, Kay CR. Successful treatment of periorificial dermatitis with novel narrow spectrum sarecycline. *J Drugs Dermatol.* 2021;20(1):98-100. doi:10.36849/JDD.5678.
8. Sher A, Kresch M, Bitterman D, et al. Sarecycline as a potential treatment for steroid-induced rosacea/perioral dermatitis: A case report. *J Drugs Dermatol.* 2024;23(2) doi:10.36849/JDD.7638.
9. Grada A, Ghannoum MA, Bunick CG. Sarecycline demonstrates clinical effectiveness against staphylococcal infections and inflammatory dermatoses: Evidence for improving antibiotic stewardship in dermatology. *Antibiotics (Basel).* 2022;11(6):722. doi:10.3390/antibiotics11060722.
10. Poplausky D, Young JN, Dubin DP, et al. Dasatinib-associated acneiform eruption successfully treated with sarecycline in a patient with chronic myeloid leukemia. *Cureus.* 2023;15(9) doi:10.7759/cureus.45697.
11. Picardo M, Eichenfield LF, Tan J. Acne and rosacea. *Dermatol Ther (Heidelb).* 2017;7(Suppl 1):43-52. doi:10.1007/s13555-016-0168-8.
12. Sharma A, Kroumpouzos G, Kassir M, et al. Rosacea management: A comprehensive review. *J Cosmet Dermatol.* 2022;21(5):1895-1904. doi:10.1111/jocd.14816.
13. Choe J, Barbieri JS. Emerging medical therapies in rosacea: A narrative review. *Dermatol Ther (Heidelb).* 2023;13(12):2933-2949. doi:10.1007/s13555-023-01048-1.
14. Searle T, Ali FR, Al-Niaimi F. Perioral dermatitis: Diagnosis, proposed etiologies, and management. *J Cosmet Dermatol.* 2021;20(12):3839-3848. doi:10.1111/jocd.14060.
15. Ahmed AR, Kurgis BS, Rogers RS 3rd. Cicatricial pemphigoid. *J Am Acad Dermatol.* 1991;24(6 Pt 1):987-1001. doi:10.1016/0190-9622(91)70159-y.
16. Kirtschig G, Murrell D, Wojnarowska F, et al. Interventions for mucous membrane pemphigoid and epidermolysis bullosa acquisita. *Cochrane Database Syst Rev.* 2003;2003(1) doi:10.1002/14651858.CD004056.
17. Carrozzo M, Arduino P, Bertolusso G, et al. Systemic minocycline as a therapeutic option in predominantly oral mucous membrane pemphigoid: A cautionary report. *Int J Oral Maxillofac Surg.* 2009;38(10):1071-1076. doi:10.1016/j.ijom.2009.06.021.
18. Lacouture ME, Anadkat MJ, Bensadoun RJ, et al. Clinical practice guidelines for the prevention and treatment of EGFR inhibitor-associated dermatologic toxicities. *Support Care Cancer.* 2011;19(8):1079-1095. doi:10.1007/s00520-011-1197-6.
19. Hirotsu K, Dang TM, Li S, et al. Association of antibiotic resistance with antibiotic use for epidermal growth factor receptor inhibitor-related papulopustular eruption. *JAMA Dermatol.* 2019;155(7):848-850. doi:10.1001/jamadermatol.2019.0063.

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