DEMODEX BLEPHARITIS

Long-term treatment and the condition's relation to rosacea.

BY ANGIE WEN, MD

LONG-TERM OUTCOMES OF 6-WEEK TREATMENT OF LOTILANER OPHTHALMIC SOLUTION, 0.25%, FOR *DEMODEX* BLEPHARITIS: A NONINTERVENTIONAL EXTENSION STUDY

Sadri E, Paauw J, Ciolino J, et al[1]
Industry support: Tarsus Pharmaceuticals

ABSTRACT SUMMARY

This noninterventional extension study evaluated the long-term outcomes of lotilaner ophthalmic solution 0.25% (Xdemvy, Tarsus Pharmaceuticals) for the treatment of *Demodex* blepharitis. A total of 239 patients who completed the Saturn-1 study[2] were assessed at the 180- and 365-day follow-up visits. In the original Saturn-1 study, 421 patients with *Demodex* blepharitis were randomly assigned to receive 6 weeks of treatment with either lotilaner 0.25% or a vehicle control. Investigators analyzed 115 and 105 patients in the treatment and control groups, respectively.

The posttreatment study was conducted at 11 US clinical sites. All patients who completed the Saturn-1 study were invited to participate. They were enrolled if they met the eligibility criteria and agreed to comply with the study protocol. Patients were asked not to place cosmetics at the eyelid margin for the duration of the study. There was no restriction on their use of concomitant medications or contact lens wear.

Collarettes and erythema of the eyelid margin were evaluated according to the same criteria used in the original Saturn-1 study. Adverse events were recorded.

At day 180, the proportion of patients with collarette cure (0–2 collarettes = collarette grade 0) was 39.8% in the treatment group and 2.7% in the control group ($P < .0001$). At day 365, the proportion was 23.5% in the treatment group and 2.9% in the control group ($P < .0001$). The number of patients who experienced a reduction to 10 or fewer collarettes (grade 0 or 1) was also significantly greater in the treatment versus control group on day 180 (70.3% vs 18.0%, $P < .0001$) and day 365 (62.6% vs 21.9%, $P < .0001$). Erythema cure (grade 0) for the upper eyelid was observed in a greater percentage of the treated versus control patients on day 180 (21.1% vs 6.3%, $P = .0005$) and day 365 (28.7% vs 14.3%, $P = .0049$).

There were no clinically significant adverse effects with regard to corneal staining scores, IOP, or dilated fundus findings. One patient in the treatment group experienced blurred vision, and one patient in the control group experienced instillation pain; both events were described as mild.

STUDY IN BRIEF

- An observational extension study of a prospective, randomized, double-masked study evaluated the long-term outcomes of lotilaner ophthalmic solution 0.25% (Xdemvy, Tarsus Pharmaceuticals) for the treatment of *Demodex* blepharitis. Compared to patients treated with the vehicle control, a higher proportion of those treated with lotilaner had collarette cure (grade 0–2) and reduction (≤ 10) at 180 days. No long-term adverse effects were observed.

WHY IT MATTERS

The study suggests that lotilaner ophthalmic solution 0.25% may be effective against and provide control of *Demodex* blepharitis beyond the 6-week treatment course. Coupled with the long-term safety data, this finding is encouraging for patients and physicians seeking a lasting solution to a prevalent external ocular disease.

DISCUSSION

Demodex blepharitis affects 55% to 58% of patients who present to a US ophthalmologist. Patients often experience itching, irritation, foreign body sensation, and eyelid margin inflammation.[3] This prevalent form of lid margin disease is caused by mites that infest the eyelash follicles. The pathognomonic sign is collarettes, cylindrical sleeves of material at the base of the eyelashes. Collarettes are composed of partially digested epithelial cells, mite waste, and eggs.[4]

Xdemvy became the first and only US FDA-approved treatment for *Demodex* blepharitis in July 2023. The drug's effectiveness was demonstrated in the Saturn-1 and phase 3 Saturn-2 studies.[5] In addition to measuring collarettes and lid erythema, the Saturn studies examined epilated eyelashes under the microscope for mite eradication (0 mites/lash).

Blepharitis can be a chronic, debilitating disease that has significant clinical, functional and psychosocial effects on patients.[6] Evidence showing up to 1 year of efficacy after the initiation of lotilaner therapy is encouraging. The study by Sadri et al also confirms the medication's long-term safety profile.

EVIDENCE FOR THE CLINICAL ASSOCIATION BETWEEN *DEMODEX* AND ROSACEA: A REVIEW

Wei F, Li L, Kong Y, et al[7]
Industry support: None

ABSTRACT SUMMARY

This systematic review and meta-analysis of 23 case-controlled studies revealed a close relationship between *Demodex* and rosacea in humans.

Noninvasive skin testing techniques such as superficial skin biopsy, confocal microscopy, and fluorescence video dermatoscopy have confirmed a significantly higher *Demodex* density in rosacea patients. Additionally, Lacey cultured live *Demodex* mites with human sebaceous cells and found that Toll-like receptor 2 immune responses were downregulated with low mite numbers and proinflammatory responses were activated with increased mite numbers.[8] Kim found increased interleukin 17 cytokine release in patients with *Demodex* blepharitis, a response that can induce the production of vascular endothelial growth factor A and thereby cause the telangiectasias associated with rosacea.[9]

There was also some overlap between the efficacious treatments for rosacea and *Demodex*. Proven rosacea treatments generally have direct antiparisitic effects (eg, permethrin), antiinflammatory effects (eg, metronidazole), or both properties (eg, topical 1% ivermectin cream). Studies have shown that ivermectin treatment reduces the *Demodex* burden and improves rosacea, with decreased expression of inflammatory cytokines such as interleukin 8, Toll-like receptor 4, and tumor necrosis factor alpha observed during the same time periods. Ivermectin was more effective than topical metronidazole for the treatment of severe pustular rosacea, which suggests that eliminating *Demodex* mites is beneficial for treating rosacea.[10,11]

The concomitant presence of rosacea and *Demodex* infestation may lead to an imbalance between types 1 and 2 T helper cell immunity, allowing *Demodex* to proliferate rapidly, causing severe inflammatory responses and papular pustular rosacea and leading to a vicious circle of disease.[12] Wei et al recommended the early use of ivermectin, which has acaricidal as well as antiinflammatory properties, along with topical type 1 T helper cell inhibitors to block the progression of the inflammatory response and break the cycle.

DISCUSSION

Rosacea affects the skin and eyes in humans. The exact pathogenesis of this chronic inflammatory condition is unclear. Greater than 50% of patients with cutaneous rosacea also have ocular rosacea, which can cause permanent vision loss if left untreated.[13]

Ocular rosacea can lead to telangiectasias, thickening of the lid margin, and meibomian gland dysfunction with concomitant evaporative dry eye disease. Some have theorized that the development of rosacea is linked to *Demodex*, a commensal organism that resides in hair follicles and sebaceous glands and is a known cause of inflammatory blepharitis.

Demodex blepharitis is a significant cause of ocular morbidity. It manifests as eyelid margin erythema, meibomian gland dysfunction, disruptions to the tear film, and peripheral corneal vascularization.[14] According to the review article by Wei et al, many studies have suggested a potentiating effect between cutaneous rosacea and *Demodex*, highlighting the need to examine patients with evidence of blepharitis for both conditions and to consider targeted treatments for both disease processes to achieve optimal control. Close collaboration between eye care providers and dermatologists might prove beneficial as well. ■

STUDY IN BRIEF

- A review article summarized the possible role of *Demodex* mites in the pathogenesis of rosacea. The disease seemed to favor the proliferation of *Demodex*, and the overgrowth of *Demodex*, in turn, exacerbated the symptoms of rosacea, creating a vicious circle.

WHY IT MATTERS

Ocular rosacea and *Demodex* blepharitis are significant sources of eye disease burden and morbidity. Recognizing the potentiation of disease in patients who have both conditions highlights the need for combined, targeted, acaricidal, and antiinflammatory treatment.

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