You *mite* want to consider treating that lid..

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Marc Bloomenstein's Disclosures

- Presenter is on speakers panel/Advisor of Alcon, Abbvie, J&J, Bausch + Lomb, Trukera, OcuSoft, Bruder, Reichert, LENZ, Visus, Tarsus, Azura, Viatris, Sight Sciences, Iveric, STAAR, Sun Pharma, Apellis, Topcon, Synedxis, Harrow
- Presenter has NO financial interest in any products mentioned
- And..all relevant materials have been mitigated

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DEMODEX BLEPHARITIS | A PERVASIVE AND DAMAGING EYE DISEASE

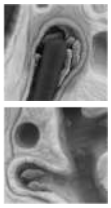
- **Blepharitis is the inflammation of the eyelids** causing irritation and redness
- **69% of blepharitis cases are due to *Demodex* infestation leading to *Demodex* blepharitis[1-4]**
  - *Demodex* mites are implicated in other diseases of the lid and lid margin, including blepharitis and meibomian gland dysfunction[2,3]
  - *Demodex* mites are associated with acne vulgaris, folliculitis, rosacea, seborrheic dermatitis, perioral and scalp hair loss, and basal cell carcinoma[1-3]
- ***Demodex folliculorum* and *Demodex brevis*** are the only 2 species found in humans[5]
  - The life cycle of the *Demodex* mite is approximately 14 to 18 days from the egg to the larval stage followed by the adult stage[5]
  - The life span of the mite is limited outside the living body; direct contact is required for transinfestation[5]

D. folliculorum

0.3-0.4 mm length
Colonizes the base of the lash follicle[2]

D. brevis

0.1 mm length
Colonizes the meibomian gland[2]

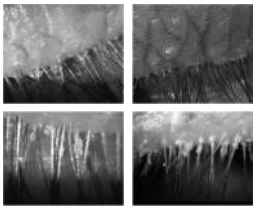


1. Mayo Clinic. Accessed June 28, 2022. https://www.mayoclinic.org/diseases-conditions/blepharitis/symptoms-causes/syc-20370141 **2.** Zhang AC et al. *Ophthalmic Physiol Opt.* 2020;40(4):389-432. **3.** Fromstein SR et al. *Clin Optom (Auckl).* 2018;10:57-63. **4.** Trattler W et al. *Clin Ophthalmol.* 2022;16:1153-1164. **5.** Litwin D et al. *Iran J Parasitol.* 2017;12(1):12-21.

3

What is *Demodex* blepharitis (DB)?

• DB is a common eyelid margin disease caused by an overgrowth of *Demodex* mites and characterized by collarettes, eyelid redness, inflammation, and ocular irritation.[1,2]



References: 1. Fromstein SR et al. Clin Optom (Auckl). 2018;10:57-63. 2. Rhee MK et al. Eye Contact Lens. 2023;49(8):311-318.

4

DEMODEX BLEPHARITIS | Mechanisms of Disease

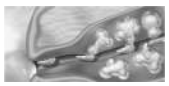
Image courtesy of Laura M. Periman, MD; used with permission.

MECHANICAL

- Lash distension occurs as *Demodex* mites attach to follicles[2-4]
- *Demodex* mites deposit debris and digestive enzymes, causing further irritation to the eyelid margin[4,6]

BACTERIAL

- *Demodex* mites can contribute to blepharitis by carrying bacteria on their exterior surface that may elicit immune responses[3,6,7]



CHEMICAL

- *Demodex* mites have been associated with altered meibum composition[8]
- Debris from *Demodex* mites can potentially lead to chronic inflammation and degeneration of conjunctival tissue[9]

1 Data on file. Images courtesy of Laura M. Periman, MD; 2022. **2.** Zhang AC et al. *Ophthalmic Physiol Opt.* 2020;40(4):389-432. **3.** Liu J et al. *Curr Opin Allergy Clin Immunol.* 2010;10(5):505-510. **4.** Fromstein SR et al. *Clin Optom (Auckl).* 2018;10:57-63. **5.** Gao YY et al. *Invest Ophthalmol Vis Sci.* 2005;46(9):3089-3094. **6.** Zhu M et al. *Front Microbiol.* 2018;9:1719. **7.** Li J et al. *Ophthalmology.* 2010;117(5):870-877. **8.** Gao R et al. *Transl Vis Sci Technol.* 2021;10(14):6. **9.** Turkowski W et al. *Biomed Res Int.* 2015;259103.

5

CLINICAL MANIFESTATIONS OF *DEMODEX* BLEPHARITIS

Disorders of Eyelashes[1,2]

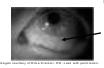
Infestation of the lash follicles can result in collarettes and may lead to malalignment, trichiasis, and madarosis

Meibomian Gland Dysfunction[1,2]

Blockage leads to filling, swelling, and many enlarged glands (cysts) or infection. Chalazia are common granulomatous responses

Lid Margin Inflammation[1,2]

Severe lid margin inflammation can be caused by mechanical blockage and a delayed host immune hypersensitivity reaction



Conjunctival Inflammation[1,2]

Without proper hygiene, lid margin inflammation may spread over to the conjunctiva producing a condition known as blepharoconjunctivitis

Corneal Manifestations[1,2]

D. brevis is commonly associated with inflammation that spreads to the cornea, causing sight-threatening corneal lesions, superficial vascularization, marginal infiltrates, phlyctenule-like lesions, opacity, and/or nodular scars

1. Liu J et al. *Curr Opin Allergy Clin Immunol.* 2010;10(5):505-510. **2.** Cheng AM et al. *Curr Opin Ophthalmol.* 2015;26(4):295-300.

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COLLARETTES ARE A PATHOGNOMONIC SIGN OF *DEMODEX* BLEPHARITIS

Collarettes, or cylindrical dandruff, are composed of mite waste products and eggs[1]

- Collarettes are translucent, solidified exudative excretions that form a cylindrical collar that cuffs around the base of the eyelash follicle[1-3]
- Collarettes are displaced along the shaft of the lash as it grows, and they are also displaced due to bacterial overgrowth[4]
- Collarettes are composed of regurgitated undigested mite waste combined with epithelial cells, keratin, mite eggs, and secreted proteases and lipases that cause irritation[3]
- **100%** of patients with collarettes have *Demodex* blepharitis[2,5]

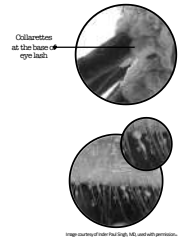

Image courtesy of Inder Paul Singh, MD, used with permission.

1. Zhang AC et al. *Ophthalmic Physiol Opt.* 2020;40(4):389-432. 2. Gao YY et al. *Invest Ophthalmol Vis Sci.* 2005;46(9):3089-3094. 3. Fromstein SR et al. *Clin Optom (Auckl).* 2018;10:57-63. 4. Bitton E et al. *Clinical and Experimental Optometry.* 2021;104(2):286-294. 5. Kheirkhah A et al. *Am J Ophthalmol.* 2017;182(1):112-127. 6. Data on file.

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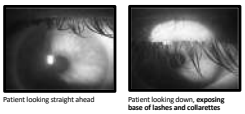
DEMODEX BLEPHARITIS CAN BE DIAGNOSED DURING SLIT LAMP EXAMINATION

Collarettes are hardened excretions around the base of the eyelashes visible during slit lamp examination[1-3]

Collarettes can be identified when the base of lashes on the upper lid are exposed as the patient **looks down[4]**

Collarettes may be missed during a slit lamp exam even with a lid lift if a patient is looking straight ahead[4]



Patient looking straight ahead | Patient looking down, **exposing base of lashes and collarettes**

Images courtesy of Elizabeth Yeu, MD, used with permission.

~~Asking a patient to look down during a slit lamp examination can reveal~~ diffuse collarettes and misdirected or missing lashes that are ~~strong signs of *Demodex*~~ blepharitis

1. Zhang AC et al. *Ophthalmic Physiol Opt.* 2020;40(4):389-432. 2. Gao YY et al. *Invest Ophthalmol Vis Sci.* 2005;46(9):3089-3094. 3. Fromstein SR et al. *Clin Optom (Auckl).* 2018;10:57-63. 4. Cataract & Refractive Surgery Today. Accessed June 29, 2022. https://crstoday.com/articles/cvi-2021/impact-of-demodex-blepharitis-and-importance-of-early-detection 5. Data on file. Image courtesy of Elizabeth Yeu, MD, 2022.

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Diagnosing *Demodex* blepharitis (DB) is as simple as having your patients look down[1]

Images c/o Marc Bloomenstein, OD, FAAO

Reference: 1. Trattler W et al. Clin Ophthalmol. 2022;16:1153-1164.

9

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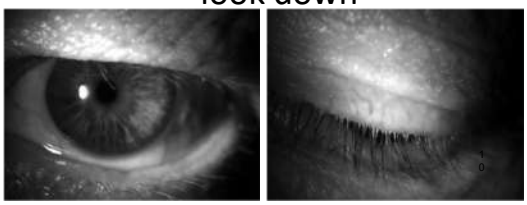

Images c/o Marc Bloomenstein, OD, FAAO

Reference: 1. Trattler W et al. Clin Ophthalmol. 2022;16:1153-1164.

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Demodex blepharitis (DB) is highly prevalent, but underdiagnosed[1,2]

- DB affects ~58% of eye care patients in the US[1]
  - That's approximately 25 million patients[2]

~56% (n=245/440) of patients with **cataracts have DB[1,*]**

60% (n=135/225) of patients **treated for dry eye also have DB[1,*]**

~93% (n=26/28) of patients with **soft contact lens intolerance were found to have *Demodex*[3,†]**

References: 1. Trattler W et al. Clin Ophthalmol. 2022;16:1153-1164. **2.** O'Dell L et al. Clin Ophthalmol. 2022;16:2979-2987. **3.** Tarkowski W et al. Biomed Res Int. 2015;2015:259109.

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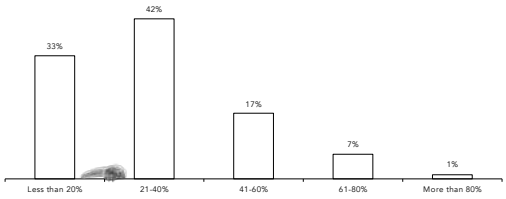
DEMODEX BLEPHARITIS

What percentage of all of your patients have collarettes on their lids or lashes?



On average, 31% of all patients have collarettes

Data from 2023 Optometric Trends Discovery Group, which was developed in partnership with the Fundingsland Group, launched in February of 2023 and asked 141 questions related to a variety of optometric topics

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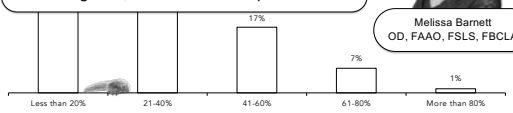
DEMODEX BLEPHARITIS

What percentage of all of your patients have collarettes on their lids or lashes?

The literature suggests the number is much higher. Approximately 25 million adults in the United States, **62% to 69%** of those with a blepharitis diagnosis, have *Demodex* blepharitis.

Melissa Barnett
OD, FAAO, FSLS, FBCLA



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of blepharitis cases are associated with *Demodex* mites[1]

The number of mites correlates with:

- symptom severity
- density/severity of collarettes

References: 1. Trattler W et al. Clin Ophthalmol. 2022;16:1153-1164.

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KeySigns and Symptoms of DB

- **Itching** *most common symptom
- Dry eyes
- Missing/misdirected eyelashes
- Lid margin inflammation
- Sensitivity to light
- Blurred vision

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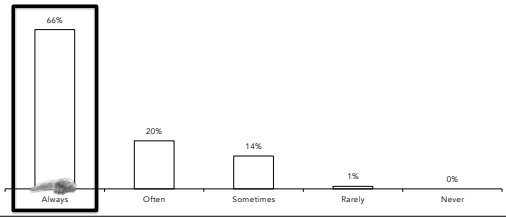
DEMODEX BLEPHARITIS

During a routine exam, do you perform an eyelid examination?



Most respondents, 66%, always perform an eyelid examination during routine exams

Data from 2023 Optometric Trends Discovery Group, which was developed in partnership with the Fundingsland Group, launched in February of 2023 and asked 141 questions related to a variety of optometric topics

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DEMODEX BLEPHARITIS

During a routine exam, do you perform an eyelid examination?

Since all patients, 100%, have eyelids, this number should be 100%!

Melissa Barnett
OD, FAAO, FSLS, FBCLA

Most respondents, 66%, always perform an eyelid examination during routine exams

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DB can cause eyelid redness and cylindrical deposits around the base of eyelashes (collarettes)[1,2]

Image c/o Marc Bloomenstein, OD, FAAO

- Collarettes are the pathognomonic sign of DB[1,2]
- Have patients look down during a routine slit lamp examination[1]
- If you see collarettes, then you can confidently diagnose DB[3]

References: 1. Trattler W et al. Clin Ophthalmol. 2022;16:1153-1164. **2.** Fromstein SR et al. Clin Optom (Auckl). 2018;10:57-63. **3.** Gao YY et al. Invest Ophthalmol Vis Sci. 2005;46(9):3089-3094.

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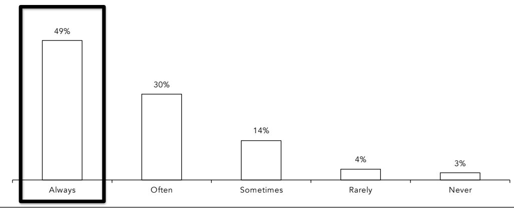
DEMODEX BLEPHARITIS

When you do an eyelid examination, do you have the patient look down or close their lids to evaluate for collarettes, or cylindrical dandruff, a pathognomonic sign of Demodex blepharitis?



Nearly half of all respondents, 49%, always have the patient look down or close their lids to evaluate for collarettes or cylindrical dandruff when they do an eyelid examination

Data from 2023 Optometric Trends Discovery Group, which was developed in partnership with the Fundingsland Group, launched in February of 2023 and asked 141 questions related to a variety of optometric topics

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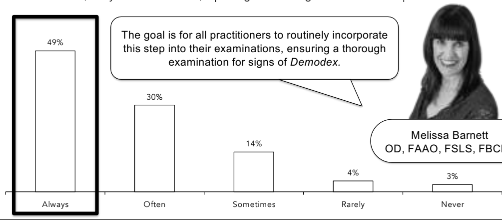
DEMODEX BLEPHARITIS

When you do an eyelid examination, do you have the patient look down or close their lids to evaluate for collarettes, or cylindrical dandruff, a pathognomonic sign of Demodex blepharitis?



The goal is for all practitioners to routinely incorporate this step into their examinations, ensuring a thorough examination for signs of *Demodex*.

Melissa Barnett
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Nearly half of all respondents, 49%, always have the patient look down or close their lids to evaluate for collarettes or cylindrical dandruff when they do an eyelid examination

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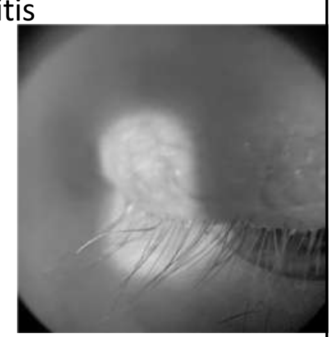
Demodex Blepharitis

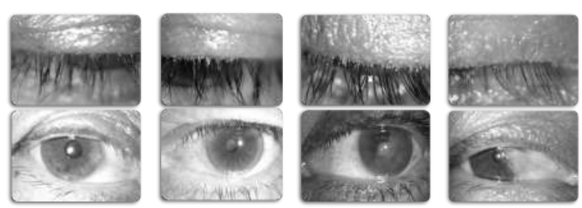
- Two species affect the eye
  - *Demodex folliculorum* ~0.3 to 0.4 mm in length, found in clusters around the lash root and lash follicle, where it feeds on sebum and follicular epithelial cells
  - *Demodex brevis* is shorter, more solitary, and prefers the meibomian glands.
- Mites ~2 weeks to mature from the egg to the larval stage, with an overall life span of up to 3 weeks
- Both species are translucent, elongated microscopic mites with four pairs of short, clawed legs[1]



1. Fromstein SR, Harthan JS, Patel J, Opitz DL. *Demodex* blepharitis: clinical perspectives. Clin Optom (Auckl). 2018 Jul 4;10:57-63.
1. Video c/o E. Yeu, MD

23

surface
examples of demodex blepharitis and conjunctival/corneal disease



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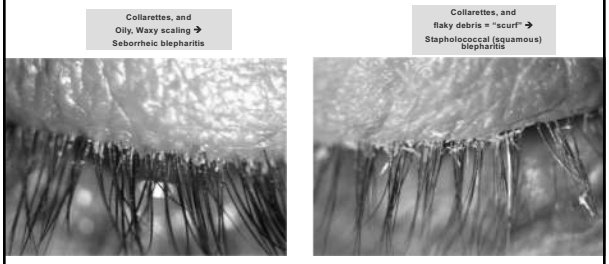
Mixed blepharitis presentation



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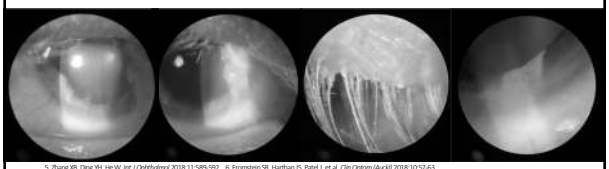
Demodex Blepharitis & Clinical Associations

- Also leads to **lid margin erythema**, **lid edema**, **eyelash misalignment or loss**, **recurrent chalazia** and, more rarely, **primary and recurrent pterygia**, **peripheral corneal vascularization**, **phlyctenule-like lesions** and **corneal opacity**[5]
- Other inflammatory diseases, such as **rosacea**, and **blepharokeratitis** and **blepharoconjunctivitis**.[6]



5. Zhang XB, Ding YH, He W. *Int J Ophthalmol* 2018;11:589-592. 6. Fromstein SR, Harthan JS, Patel J, et al. *Clin Optom (Auckl)* 2018;10:57-63.

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Explaining the DB Diagnosis to Patients

- There's a common misconception among patients that it's somehow their fault or caused by poor hygiene
- Patients don't always understand how the mites cause problems
- Many patients worry that the treatment process will be challenging.

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Keys Points when Delivering the DB Diagnosis to Patients

1. DB is a prevalent condition and not a reflection of personal negligence.[1-3]
2. The condition results from an increase in tiny mites that can harm the eyelids.[1,4,5]
3. Treatment is straightforward and effective.[6]

References: 1. Trattler W et al. Clin Ophthalmol. 2022;16:1153-1164. **2.** O'Dell L et al. Clin Ophthalmol. 2022;16:2979-2987. **3.** Liu J et al. Curr Opin Allergy Clin Immunol. 2010;10(5):505-510. **4.** Gao YY et al. Invest Ophthalmol Vis Sci. 2005;46(9):3089-3094. **5.** Fromstein SR et al. Clin Optom (Auckl). 2018;10:57-63. **6.** XDEMVY [prescribing information]. Tarsus Pharmaceuticals, Inc; 2023.

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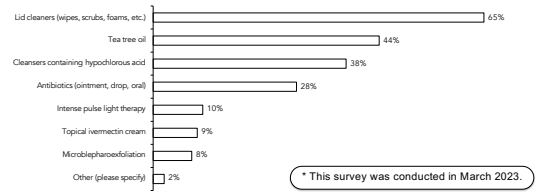
DEMODEX BLEPHARITIS

What are your TOP 2 treatment recommendations for a patient with Demodex blepharitis? (Select 2)



Lid cleaners and tea tree oil are the top 2 treatment recommendations for a patient with Demodex blepharitis

Data from 2023 Optometric Trends Discovery Group, which was developed in partnership with the Fundingsland Group, launched in February of 2023 and asked 141 questions related to a variety of optometric topics

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Common Treatments for *Demodex* Blepharitis

At-Home

- Tea tree oil
- Lid wipes
- Topical ivermectin cream
- Cleansers containing hypochlorous acid
- Lid scrubs
- Antibiotics

In-Office

- Intense pulsed light therapy
- Microblepharoexfoliation

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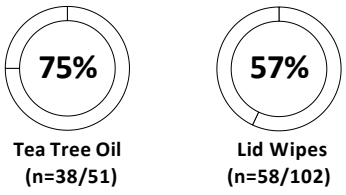
Tea Tree Oil and Lid Wipes Manage the Collarettes but Aren't Treating the Root Cause



Reference: 1. Trattler W et al. Clin Ophthalmol. 2022;16:1153-1164.

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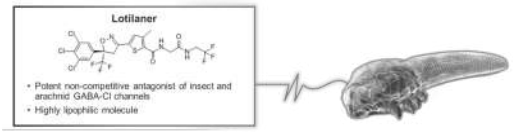
Lotilaner ophthalmic solution,0.25%

- The first and only FDA-approved treatment for *Demodex* blepharitis (July 2023)
- Paralyzes and eradicates *Demodex* mites by selectively inhibiting parasite-specific GABA-Cl channels



Reference: Tarsus Pharmaceuticals, Inc; 2023.

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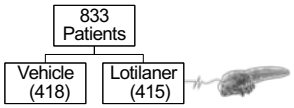
Studies toKnow: SATURN-1and SATURN-2

- Two 6-week, randomized, multicenter, double-masked, vehicle-controlled studies



- Patients were randomized to either lotilaner or vehicle at a 1:1 ratio, dosed twice daily in each eye

References: 1. Yeu E, et al. Cornea. 2023 Apr 1;42(4):435-43. **2.** Gaddie IB, et al. Ophthalmology. 2023 Oct 1;130(10):1015-23. **3.** Sadri, E. Castillo, RM, and Jalalat, P. Presented at ASCRS 2023; May 5-8, 2023; San Diego, CA.

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SATURN-1 and SATURN-2 Study Results

1. Collarette Reduction (≤2 collarettes)
   - 50% compared with 10% vehicle
2. Mite Eradication (0 mites/lash)
   - 60% compared with 16% vehicle
3. Erythema Cure (Grade 0)
   - 25% compared with 8% vehicle
4. Collarette Reduction (≤10 collarettes)
   - 85% compared with 28% vehicle

References: 1. Yeu E, et al. Cornea. 2023 Apr 1;42(4):435-43. **2.** Gaddie IB, et al. Ophthalmology. 2023 Oct 1;130(10):1015-23. **3.** Sadri, E. Castillo, RM, and Jalalat, P. Presented at ASCRS 2023; May 5-8, 2023; San Diego, CA.

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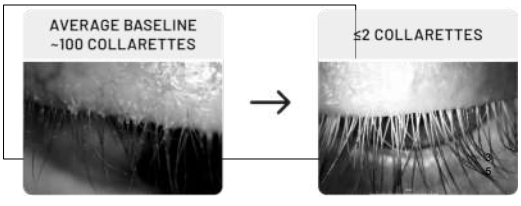

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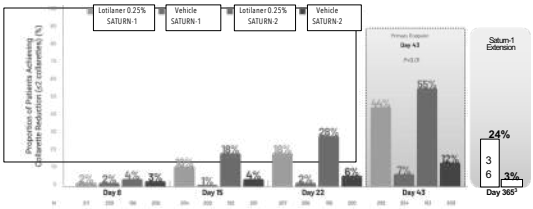
   - 50% compared with 10% vehicle



References: 1. Yeu E, et al. Cornea. 2023 Apr 1;42(4):435-43. **2.** Gaddie IB, et al. Ophthalmology. 2023 Oct 1;130(10):1015-23. **3.** Sadri, E. Castillo, RM, and Jalalat, P. Presented at ASCRS 2023; May 5-8, 2023; San Diego, CA.

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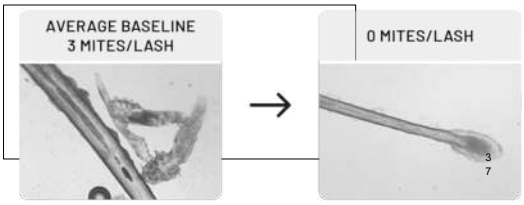
SATURN-1 and SATURN-2 Study Results

2. Mite Eradication (0 mites/lash)
- 60% compared with 16% vehicle



References: 1. Yeu E, et al. Cornea. 2023 Apr 1;42(4):435-43. **2.** Gaddie IB, et al. Ophthalmology. 2023 Oct 1;130(10):1015-23. **3.** Sadri, E. Castillo, RM, and Jalalat, P. Presented at ASCRS 2023; May 5-8, 2023; San Diego, CA.

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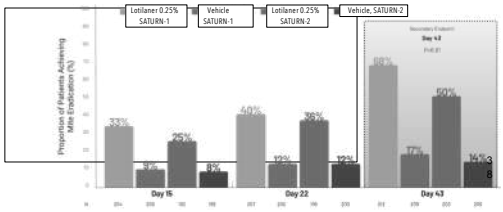

References: 1. Yeu E, et al. Cornea. 2023 Apr 1;42(4):435-43. **2.** Gaddie IB, et al. Ophthalmology. 2023 Oct 1;130(10):1015-23. **3.** Sadri, E. Castillo, RM, and Jalalat, P. Presented at ASCRS 2023; May 5-8, 2023; San Diego, CA.

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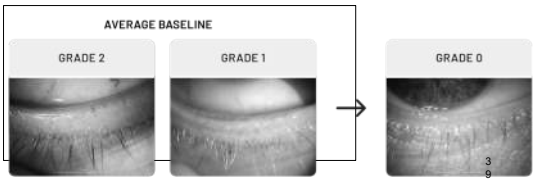
SATURN-1 and SATURN-2 Study Results

3. Erythema Cure (Grade 0)
- 25% compared with 8% vehicle



References: 1. Yeu E, et al. Cornea. 2023 Apr 1;42(4):435-43. **2.** Gaddie IB, et al. Ophthalmology. 2023 Oct 1;130(10):1015-23. **3.** Sadri, E. Castillo, RM, and Jalalat, P. Presented at ASCRS 2023; May 5-8, 2023; San Diego, CA.

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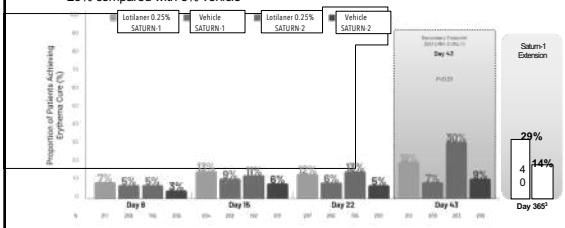

References: 1. Yeu E, et al. Cornea. 2023 Apr 1;42(4):435-43. **2.** Gaddie IB, et al. Ophthalmology. 2023 Oct 1;130(10):1015-23. **3.** Sadri, E. Castillo, RM, and Jalalat, P. Presented at ASCRS 2023; May 5-8, 2023; San Diego, CA.

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SATURN-1 and SATURN-2 Study Results

4. Collarette Reduction (≤10 collarettes)
- 85% compared with 28% vehicle

References: 1. Yeu E, et al. Cornea. 2023 Apr 1;42(4):435-43. **2.** Gaddie IB, et al. Ophthalmology. 2023 Oct 1;130(10):1015-23. **3.** Sadri, E. Castillo, RM, and Jalalat, P. Presented at ASCRS 2023; May 5-8, 2023; San Diego, CA.

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SATURN-1 and SATURN-2 Study Results

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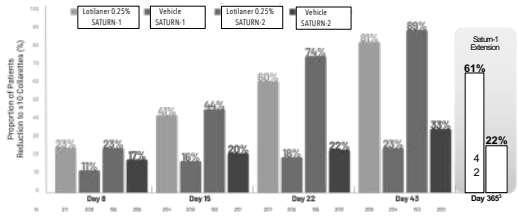

References: 1. Yeu E, et al. Cornea. 2023 Apr 1;42(4):435-43. **2.** Gaddie IB, et al. Ophthalmology. 2023 Oct 1;130(10):1015-23. **3.** Sadri, E. Castillo, RM, and Jalalat, P. Presented at ASCRS 2023; May 5-8, 2023; San Diego, CA.

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Patients Tolerate Lotilaner Drops

~90% of patients in both trials in the lotilaner and vehicle groups reported the drop as neutral to very comfortable

References: 1. Yeu E, et al. Cornea. 2023 Apr 1;42(4):435-43. **2.** Gaddie IB, et al. Ophthalmology. 2023 Oct 1;130(10):1015-23. **3.** Sadri, E. Castillo, RM, and Jalalat, P. Presented at ASCRS 2023; May 5-8, 2023; San Diego, CA.

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DEMODEX BLEPHARITIS KEY TAKEAWAYS

- *Demodex* mites may be present in 69% of all blepharitis cases
- It is a disease that is often misdiagnosed and underdiagnosed
- *Demodex* blepharitis is prevalent in cataract, dry eye, and contact lens patients and has a substantial impact on the daily lives of patients, including psychosocial and clinical burden
- Eradicating the root cause (the *Demodex* mite) rather than just addressing symptoms is crucial
- Current options for managing *Demodex* blepharitis do not eradicate mites and are poorly tolerated
- Confidently and definitively diagnose *Demodex* blepharitis by looking for collarettes
- Look for collarettes by having every patient **look down during a slit lamp examination**
- Provide patient education and understand their current struggles with comfort and lid hygiene compliance
- TP-03, if approved, may be an emerging safe and effective treatment for *Demodex* blepharitis, and has demonstrated patient comfort and shown effective collarette cure, mite eradication and erythema cure in 2 pivotal studies

WHAT CAN WE ALL DO?

- Look for collarettes during every slit lamp exam – collarettes are the pathognomonic sign of *Demodex* blepharitis
- Share images of collarettes with your peers to equip them with knowledge to properly diagnose *Demodex* blepharitis

Image courtesy of Inder Paul Singh, MD, used with permission.

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Thank you

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