

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

Marc Bloomenstein, OD, FAAO
Scottsdale, AZ

1

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, Viatrix, 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

2

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^{4,5}
- Demodex folliculorum and Demodex brevis are the only 2 species found in humans⁶
 - The life cycle of the Demodex mite is approximately 14 to 18 days from the egg to the larval stage followed by the adult stage⁶
 - The life span of the mite is limited outside the living body; direct contact is required for reinfestation⁶

D. folliculorum





0.3-0.4 mm length
Colonizes the base of the lash follicle⁶

D. brevis



0.1 mm length
Colonizes the meibomian gland⁶

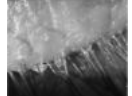




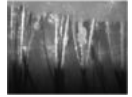
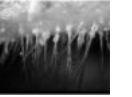
1. Mayo Clinic. Accessed June 28, 2022. <https://www.mayoclinic.org/diseases-conditions/blepharitis/symptoms-causes/ncgi-00270141>. 2. Zhang AC et al. Ophthalmic Physiol Opt. 2020;40(4):389-432. 3. Probstman SB et al. Clin Oculom (Auckl). 2018;10:57-63. 4. Truher W et al. Clin Ophthalmol. 2002;16:1105-1104. 5. Lewis D et al. Derm J Dermatol. 2017;23(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}

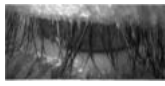





References: 1. Fromstein SR et al. Clin Oculom (Auckl). 2018;10:57-63. 2. Rhee MK et al. Eye Contact Lens. 2023;49(8):311-316.


4

DEMODEX BLEPHARITIS | Mechanisms of Disease




MECHANICAL

- Lash distension occurs as Demodex mites attach to follicles^{6,4}
- Demodex mites deposit debris and digestive enzymes, causing further irritation to the eyelid margin^{4,5}



BACTERIAL

- Demodex mites can contribute to blepharitis by carrying bacteria on their exterior^{6,7}




CHEMICAL

- Debris from Demodex mites can potentially lead to chronic inflammation and degeneration of conjunctival tissue⁶

1. Data on file. Images courtesy of Laura M. Perleman, MD, PhD. 2. Zhang AC et al. Ophthalmic Physiol Opt. 2020;40(4):389-432. 3. Liu J et al. Curr Opin Allergy Clin Immunol. 2011;11(2):202-210. 4. Probstman SB et al. Clin Oculom (Auckl). 2018;10:57-63. 5. Gao YF et al. JAMA Ophthalmol. 2019;37(10):1179-1183. 6. Gao YF et al. JAMA Ophthalmol. 2019;37(10):1179-1183. 7. Gao YF et al. JAMA Ophthalmol. 2019;37(10):1179-1183.


5

CLINICAL MANIFESTATIONS OF DEMODEX BLEPHARITIS




Disorders of Eyelashes²

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




Meibomian Gland Dysfunction²

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




Lid Margin Inflammation²

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



Conjunctival Inflammation²

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



Corneal Manifestations²

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

8. Liu J et al. Curr Opin Allergy Clin Immunol. 2003;3(2):105-110. 9. Cheng AM et al. Curr Opin Ophthalmol. 2013;24(2):265-270.

6

COLLARETTES ARE A PATHOGNOMONIC SIGN OF *DEMODEX* BLEPHARITIS

Collarettes, or cylindrical dandruff, are composed of mite waste products and eggs¹

- 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 overgrowth⁴
- Collarettes are composed of regurgitated undigested mite waste combined with epithelial cells, keratin, mite eggs, and secreted proteases and lipases that cause irritation³
- 100% of patients with collarettes have *Demodex* blepharitis^{1,5}

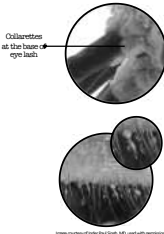


Image courtesy of John Paul Singh, MD, used with permission.

1. Zhang X et al. *Ophthalmology*. 2010;117(10):2004-2012. 2. Lee Y et al. *Invest Ophthalmol Vis Sci*. 2010;51(10):5699-5704. 3. Farnsworth M et al. *Ophthalmology*. 2010;117(10):2013-2017. 4. Bhatnagar V et al. *Journal of Cutaneous Medicine and Surgery*. 2011;17(10):1285-1288. 5. Tattler W et al. *Clin Ophthalmol*. 2022;16:1153-1164.

7

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 ahead⁴

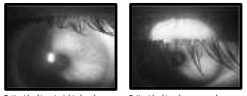


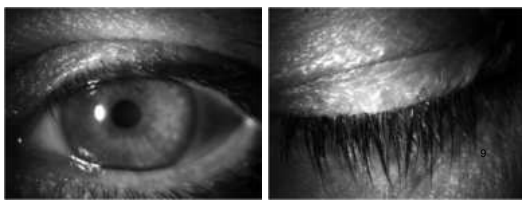
Image courtesy of Elizabeth Ho, MD, used with permission.

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 X et al. *Ophthalmology*. 2010;117(10):2004-2012. 2. Lee Y et al. *Invest Ophthalmol Vis Sci*. 2010;51(10):5699-5704. 3. Farnsworth M et al. *Ophthalmology*. 2010;117(10):2013-2017. 4. Bhatnagar V et al. *Journal of Cutaneous Medicine and Surgery*. 2011;17(10):1285-1288.

8

Diagnosing *Demodex* blepharitis (DB) is as simple as having your patients look down¹

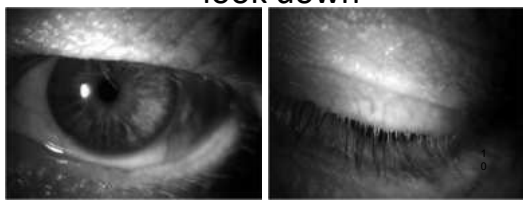


Images c/o Marc Bloomenstein, OD, FAAO

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

9

Diagnosing *Demodex* blepharitis (DB) is as simple as having your patients look down¹



Images c/o Marc Bloomenstein, OD, FAAO

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

10




Video c/o Marc Bloomenstein, OD, FAAO

36


11

Demodex blepharitis (DB) is highly prevalent, but underdiagnosed^{1,2}


- DB affects ~58% of eye care patients in the US¹
 - That's approximately 25 million patients²



~56% (n=245/440) of patients with cataracts have DB^{1,*}



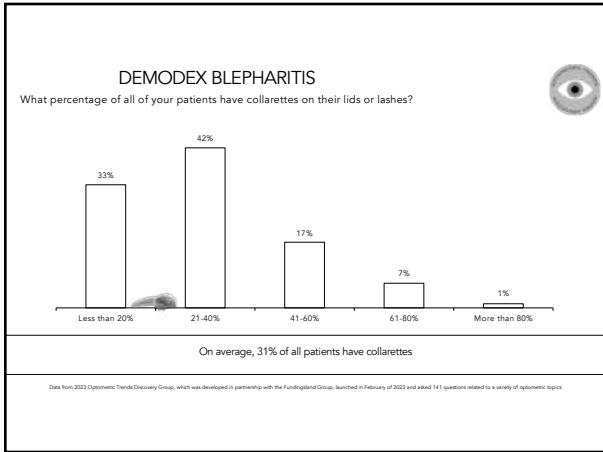
60% (n=135/225) of patients treated for dry eye also have DB^{1,*}



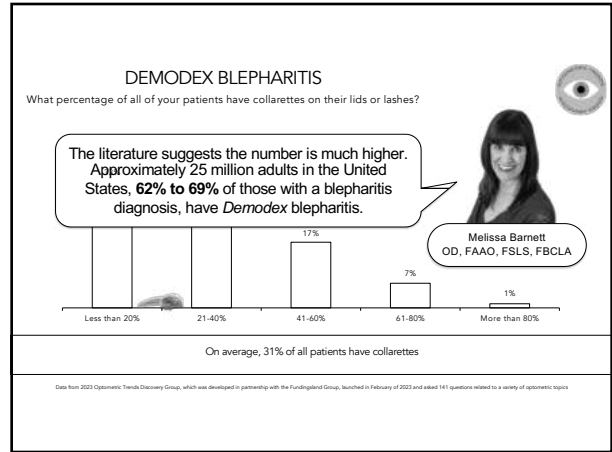
~93% (n=26/28) of patients with soft contact lens intolerance were found to have *Demodex*^{3†}

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

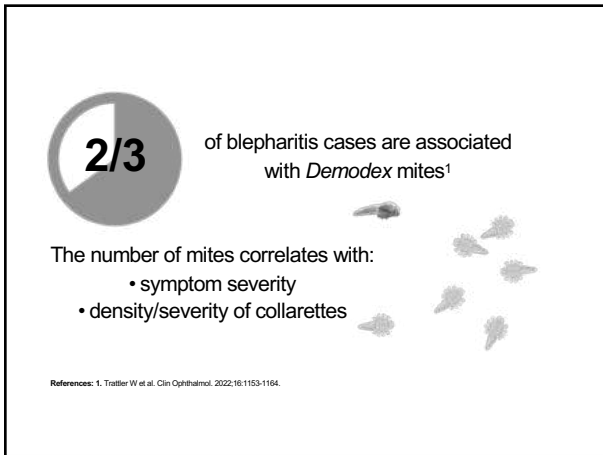
12



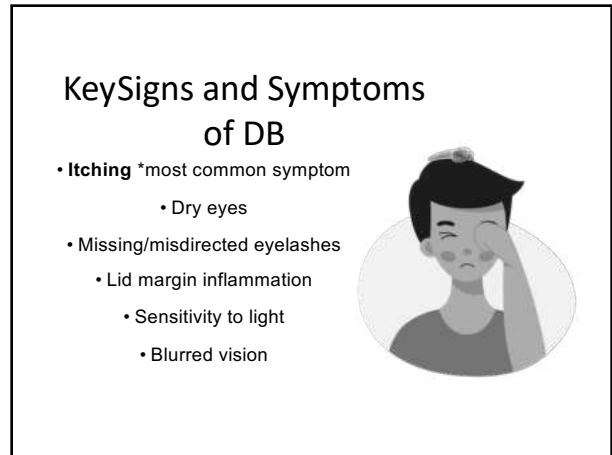
13



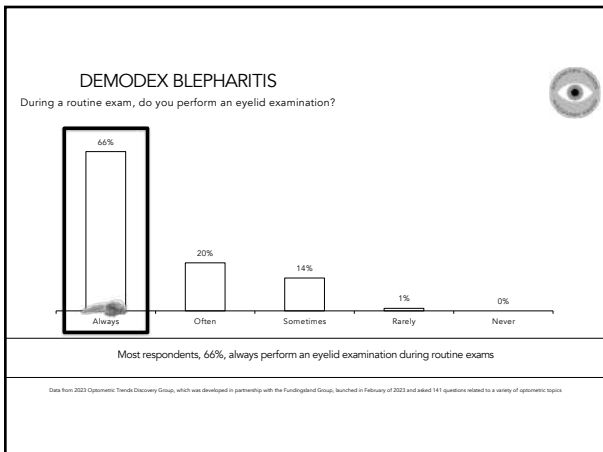
14



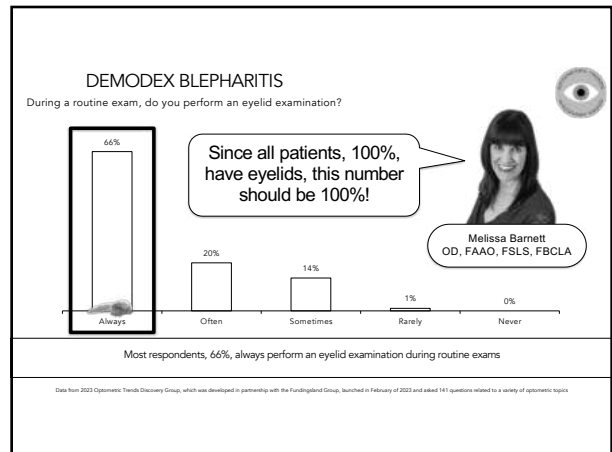
15



16




17



18

DB can cause eyelid redness and cylindrical deposits around the base of eyelashes (collarettes)^{1,2}



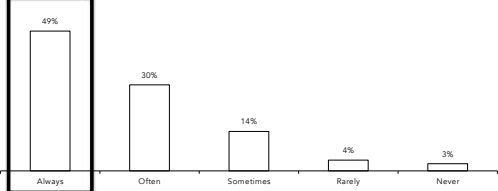
- Collarettes are the pathognomonic sign of DB^{1,2}
- Have patients look down during a routine slit lamp examination¹
- If you see collarettes, then you can confidently diagnose DB³

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. 2006;46(9):3089-3094.

19

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?



Response	Percentage
Always	49%
Often	30%
Sometimes	14%
Rarely	4%
Never	3%

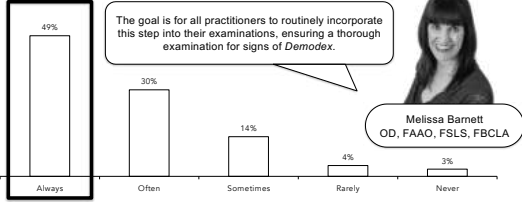
Nearly half of all respondents, 49%, always have the patient look down or close their lids to evaluate for collarettes or cylindrical dandruff when they do an eyelid examination

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

20

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?



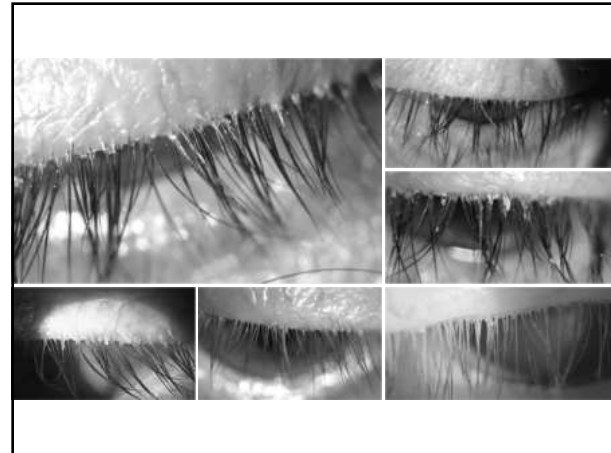
The goal is for all practitioners to routinely incorporate this step into their examinations, ensuring a thorough examination for signs of Demodex.

Melissa Barnett
OD, FAAO, FSL, FBCLA

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 Dictionary Group, which was developed in partnership with the FundRazrGroup, launched in February of 2023 and asked 141 questions related to a variety of optometric topics

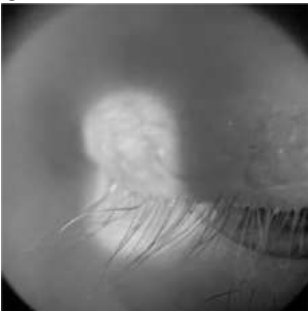
21



22

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

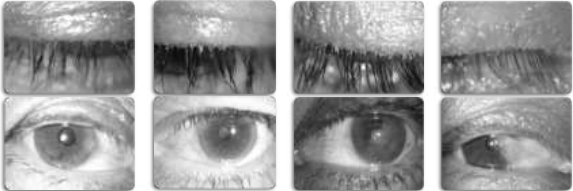


1. Fromstein SR, Hoffman JS, Poley J. Ophthol. Demodex blepharitis: clinical perspectives. Clin Optom (Auckl). 2018;10:57-64.
2. Weber CL, E'etu, MD

23

How health directly impacts the ocular surface

examples of demodex blepharitis and conjunctival/corneal disease



References: 1. Fromstein SR, Hoffman JS, Poley J. Ophthol. Demodex blepharitis: clinical perspectives. Clin Optom (Auckl). 2018;10:57-64. 2. Fromstein SR, Hoffman JS, Poley J. Ophthol. Demodex blepharitis: clinical perspectives. Clin Optom (Auckl). 2018;10:57-64. 3. Fromstein SR, Hoffman JS, Poley J. Ophthol. Demodex blepharitis: clinical perspectives. Clin Optom (Auckl). 2018;10:57-64.

24

Mixed blepharitis presentation

Collarettes, and Oily, Waxy scaling →
Seborrheic blepharitis

Collarettes, and flaky debris = "scurf" →
Staphylococcal (squamous) blepharitis

25

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 opacity⁵
- Other inflammatory diseases, such as rosacea, and blepharokeratitis and blepharoconjunctivitis.⁶

5. Shang XH, Cheng YH, He W, *et al.* / *QJMed* 2018;111:589-592. 6. Fromstein SR, Harburn JL, Patel J, *et al.* / *Clin Optom* (Aust) 2018;10:57-63.

26

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.

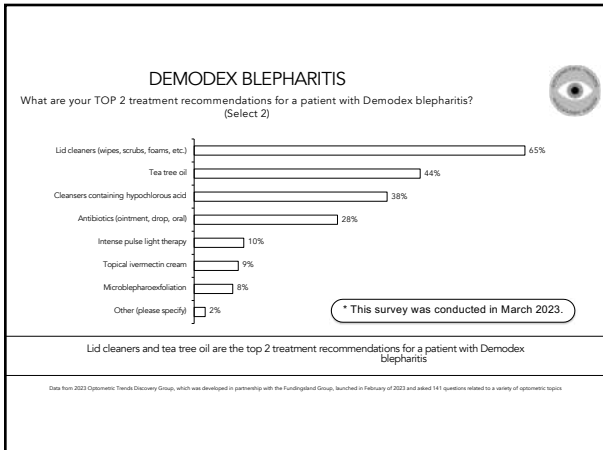
27

Keys Points when Delivering the DB Diagnosis to Patients

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

References: 1. Trailler 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(6):550-510. 4. Gao YY *et al.* / *Invest Ophthalmol Vis Sci*. 2005;46(9):3089-3094. 5. Fromstein SR *et al.* / *Clin Optom* (Aust). 2018;10:57-63. 6. XDEM/V [prescribing information]. Tarsus Pharmaceuticals, Inc. 2023.

28



29

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


30

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



75%

Tea Tree Oil
(n=38/51)



57%

Lid Wipes
(n=58/102)

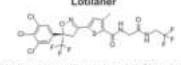
Reference: 1. Trattler W et al. Clin Ophthalmol. 2022;16:1153-1164.

31


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

Lotilaner



- Potent non-competitive antagonist of insect and arachnid GABA-Cl channels
- Highly lipophilic molecule

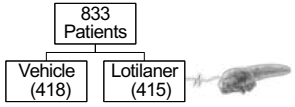


Reference: Tarsus Pharmaceuticals, Inc. 2023.

32

Studies to Know: SATURN-1 and 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. You 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. Sadr, E. Castillo, RM, and Jalal, P. Presented at ASCRS 2023, May 5-8, 2023, San Diego, CA.

33

SATURN-1 and SATURN-2 Study Results

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


References: 1. You 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. Sadr, E. Castillo, RM, and Jalal, P. Presented at ASCRS 2023, May 5-8, 2023, San Diego, CA.

34

SATURN-1 and SATURN-2 Study Results


- Collarette Reduction (≤ 2 collarettes)**
 - 50% compared with 10% vehicle

AVERAGE BASELINE
~100 COLLARETTES



→

≤ 2 COLLARETTES

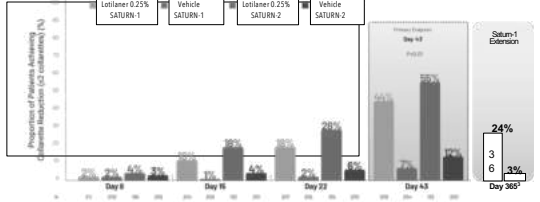


References: 1. You E, et al. Cornea. 2023 Apr 1:42(4):435-43. 2. Gaddie IB, et al. Ophthalmology. 2023 Oct 1:130(10):1015-23. 3. Sadr, E. Castillo, RM, and Jalal, P. Presented at ASCRS 2023, May 5-8, 2023, San Diego, CA.

35

SATURN-1 and SATURN-2 Study Results

- Collarette Reduction (≤ 2 collarettes)**
 - 50% compared with 10% vehicle



Proportion of Patients Achieving Collarette Reduction (≤ 2 collarettes) (%)

Day 0 Day 15 Day 30 Day 45 Day 60

Lotilaner 0.25% SATURN-1 Vehicle SATURN-1 Lotilaner 0.25% SATURN-2 Vehicle SATURN-2

May 14 P=0.02 Saturn1 Extension

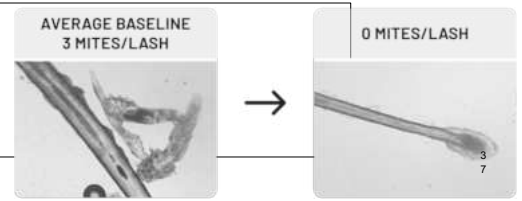
24%
3
6 2%

References: 1. You 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. Sadr, E. Castillo, RM, and Jalal, P. Presented at ASCRS 2023, May 5-8, 2023, San Diego, CA.

36

SATURN-1 and SATURN-2 Study Results

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

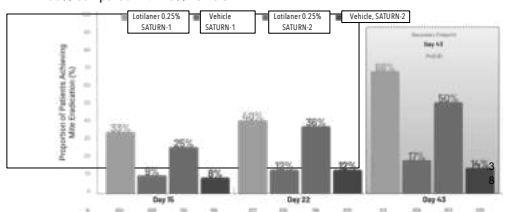


References: 1. You E, et al. Cornea. 2023 Apr 1:42(4):435-43. 2. Gaddie IB, et al. Ophthalmology. 2023 Oct 1:130(10):1015-23. 3. Sadrì, E. Castillo, RM, and Jalilat, P. Presented at ASCRS 2023, May 5-8, 2023, San Diego, CA

37

SATURN-1 and SATURN-2 Study Results

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

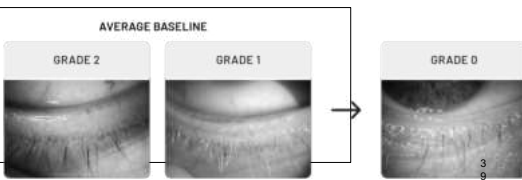


References: 1. You E, et al. Cornea. 2023 Apr 1:42(4):435-43. 2. Gaddie IB, et al. Ophthalmology. 2023 Oct 1:130(10):1015-23. 3. Sadrì, E. Castillo, RM, and Jalilat, P. Presented at ASCRS 2023, May 5-8, 2023, San Diego, CA

38

SATURN-1 and SATURN-2 Study Results

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

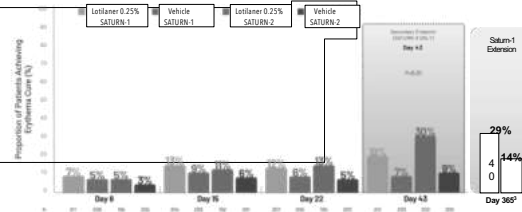


References: 1. You E, et al. Cornea. 2023 Apr 1:42(4):435-43. 2. Gaddie IB, et al. Ophthalmology. 2023 Oct 1:130(10):1015-23. 3. Sadrì, E. Castillo, RM, and Jalilat, P. Presented at ASCRS 2023, May 5-8, 2023, San Diego, CA

39

SATURN-1 and SATURN-2 Study Results

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

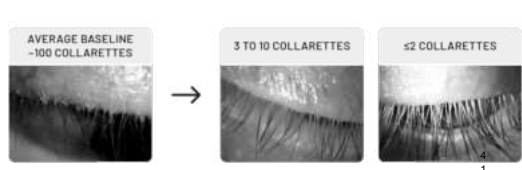


References: 1. You E, et al. Cornea. 2023 Apr 1:42(4):435-43. 2. Gaddie IB, et al. Ophthalmology. 2023 Oct 1:130(10):1015-23. 3. Sadrì, E. Castillo, RM, and Jalilat, P. Presented at ASCRS 2023, May 5-8, 2023, San Diego, CA

40

SATURN-1 and SATURN-2 Study Results

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

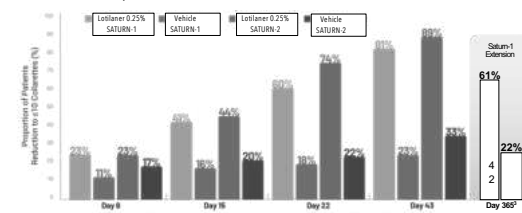


References: 1. You E, et al. Cornea. 2023 Apr 1:42(4):435-43. 2. Gaddie IB, et al. Ophthalmology. 2023 Oct 1:130(10):1015-23. 3. Sadrì, E. Castillo, RM, and Jalilat, P. Presented at ASCRS 2023, May 5-8, 2023, San Diego, CA

41

SATURN-1 and SATURN-2 Study Results

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



References: 1. You 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. Sadrì, E. Castillo, RM, and Jalilat, P. Presented at ASCRS 2023, May 5-8, 2023, San Diego, CA

42

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. You 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 Jalalati, P. Presented at ASCRS 2023, May 5-8, 2023, San Diego, CA

43

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 that has been ineffective 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 our Full Page 10, 2023 presentation

44

Thank you

45