Rule These Out Before You Diagnose it as Dry Eye

Mile Brujic, OD, FAAO Bowling Green, OH

ARS Polling Instructions

Step 1 - Open the Vision East app and log in using your badge ID and last name

Step 2 - Head to the Connect & Learn tab and tap on All Education Sessions

Step 3 - Select the course you are attending from the list of sessions

Step 4 - Scroll to the bottom and select "Pre-course questions" prior to the session or "Post-course questions" after the session

Step 5 – Complete the survey question and Submit!

1

Disclosures

 I have received honoraria in the past 2 years for speaking, writing, participating in an advisory capacity, research or meeting support from: Apellis, ABB Optical, Alcon Laboratories, Allergan, Art Optical, Bausch + Lomb Health, Contamac, CooperVision, CSEye, Horizon Therapeutics, Johnson & Johnson Vision Care, Kala, Lenstech, Notal Vision, Novartis, Optovue, Oyster Point, RVL, Sun Pharma, Tarsus, Tangible Science, Santen, Visus, Walman Optical and Zea Vision.

· All relevant relationships have been mitigated

3

Epithelial Basement Membrane Dystrophy

- Also referred to as map-dot-fingerprint, Cogan's microcystic dystrophy, or anterior basement membrane dystrophy
- · Questions of true dystrophy versus degeneration
- Risk factors: family history (although difficult to track from patient history), ocular injuries (abrasions), ocular surgeries
- Basement membrane extend, abnormally, into the corneal epithelium
- This irregularity increases risk of recurrent corneal erosion (RCE), reduced vision, fluctuating vision

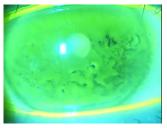
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Epithelial Basement Membrane Dystrophy



Epithelial Basement Membrane Dystrophy



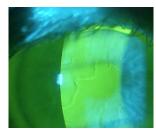
-Negative staining -Needs to be differentiated from TBUT -vision can be different on a day to day basis because of variation in corneal irregularities

Epithelial Basement Membrane Dystrophy

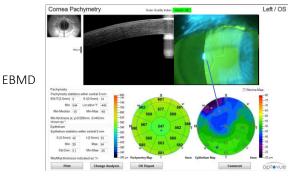


-Increased risk of RCE -Symptoms of eye discomfort can complicate diagnosis

Epithelial Basement Membrane Dystrophy



8



9

Epithelial Basement Membrane Dystrophy

- Lubrication
- Consider punctal occlusion
- Oinment in the evening (consider hyperosmotic agents)
- · Contact lenses (bandage and to improve vision quality)
- Amniotic membrane (consider for RCE)
- Oral doxycycline (consider for RCE)
- Scleral lenses
- Corneal debridement
- Phototherapeutic keratectomy (PTK)

10





Floppy Eyelid Syndrome

- •Extensive lid laxity secondary to decreased elastin content in tarsal plate
- •Spontaneous eversion of the lid can occur while sleeping
- •Can lead to chronic irritation of the lid
- •Critical to perform lid eversion on eye examination

Floppy Eyelid Syndrome

- •Low elastin levels and spontaneous eversion
- Will cause signs/symptoms of ocular discomfort
- •Has a strong association obstructive sleep apnea
- •Also associated with keratoconus, down syndrome

13

Floppy Eyelid Syndrome



14

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15





16



Floppy Eyelid Syndrome

- •Question about sleep patterns
- •Question about sleep apnea or confirm diagnosis
- •Refer to physician for appropriate testing
- Monitor optic nerves carefully for risk of glaucoma

Floppy Eyelid Syndrome

- •Ointment in the evening
- •Sleep rite
- Eye mask in the evening
- Blepharoplasty
- Lacriserts
- Punctal occlusion





20



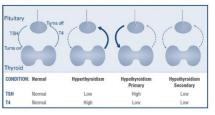
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Thyroid Function

- TSH is produced by pituitary gland
- Thyroid Gland Produces T4 which is converted to T3
- Alterations in hormonal balance can cause problems to arise

22

Thyroid Gland Function

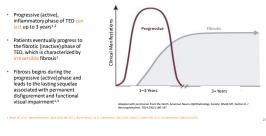


https://www.thyroid.org/thyroid-function-tests/

TED Is a Debilitating, Progressive, and Vision-threatening Autoimmune Disease



Inflammation During Progressive TED Advances to Chronic Fibrosis $^{\rm 1}$



25

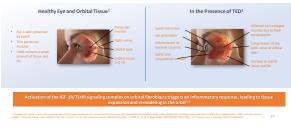
TED is Driven by Autoantibody Activation of IGF-1R

- Orbital fibroblasts, which are specialized cells responsible for tissue repair, are central to the pathophysiology of TED¹⁻³
- IGF-1R, a gatekeeper of orbital fibroblast activation, is overexpressed in TED orbital fibroblasts⁴
- IGF-1R and TSHR form a receptor-signaling complex and colocalize in orbital fibroblasts⁴
 Activation of IGF-1R stimulates release of inflammatory cytokines and production of hyaluronan and adipogenesis^{1,5,6}

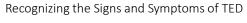


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Inflammation, Tissue Expansion, and Eye Muscle Changes May Lead to the Clinical Manifestations of TED



27



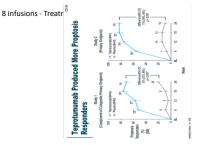


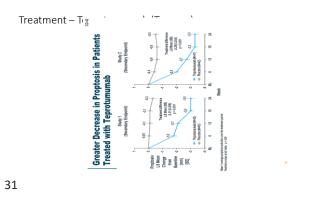
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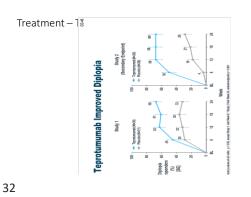
Ongoing Inflammation and Expansion of Orbital Tissues Leads to Changes in Physical Appearance

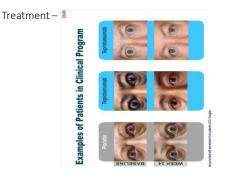


Treatment – Teprotumumab (Tepezza)

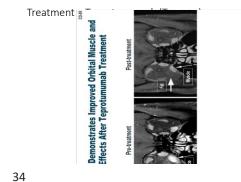












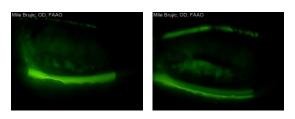
Kearns-Sayre Syndrome

- -Affects many parts of the body -Usually appears before 20 years old
- -Caused by mitochondrial DNA abnormalities
- -Causes progressive external ophthalmoplegia i.Paralysis of extraocular muscles ii.Ptosis
- -Pigmentary retinopathy

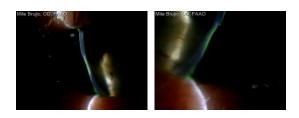
Kearns-Sayre Syndrome

Other systemic findings i.Cardiac conduction defects ii.Ataxia iii.Other muscle weakness iv.Deafness v.Kidney problems Occurs because of mitochondrial deficiencies Prevalence: 1-3/100,000

Kearns-Sayre Syndrome



Kearns-Sayre Syndrome



38

Kearns-Sayre Syndrome



39

Kearns-Sayre Syndrome

- Ointment in the evening
- •Sleep rite
- Eye mask in the evening
- Blepharoplasty
- Lacriserts
- Punctal occlusion

40

Mucous fishing syndrome

-Cyclical worsening of symptoms -Patients will "fish" mucous out of their eye usually from some irritant

-Mucous usually in the lower fornix

-Continual attempted removal causes more mucous to be formed

-Treatment often times requires educating patients to stop touching their eyes

Advancing Wavelike Epitheliopathy

-Wave like appearance of epithelium that extends from the limbal area into the central cornea -Is believed to be caused by toxic reaction of the cornea

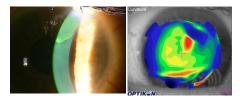
- -Differential diagnosis
- i.Superior limbic keratoconjunctivitis
- ii.Limbal stem cell disease
- iii.Epithelial basement membrane dystrophy

Advancing Wavelike Epitheliopathy

-Remove those substances believed to be causing the response -Silver nitrate application to the limbal area where the irregularity appears to be originating from



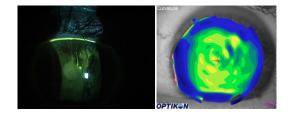
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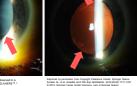


Presentation of Keratopathy (Microcyst-like Corneal Epithelial Changes)

Microcyst-like corneal epithelial changes (MECs) may be identified during ophthalmic slit lamp exams¹ MECs can appear in both symptomatic and asymptomatic patients²

Document whether MECs are³:

 Confluent (ie, merging or clumped) Nonconfluent (ie, sepa or distinct) Figure. Arrows denote comeal microcysts observed in a 52 commonly regime for any star providers \$1 \$10000774 4



minology Criteria for Adverse Events (CTCAE): Version 5.0. Intelescentric, applications/docs/CTCAE_v6_Duick_Reference_5x7.pdf. Massionis LiA, et al. Clin Cancer Res. 2019;25(8):1727-1736. 2. US Department of Health and Human Services. Common Ten US Department of Health and Human Services; 2017. Accessed September 29, 2022. https://tspc.noc.or.go/public/accidevelopment 5. LIAHERE. Proceeding International Control Science Science Science Science (2019):251701:177.

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 Please see Indication on silde 2 and Important Safety Information on sildes 17-22, and accompanying full Prescribing Information, including BOXED WARNING.

49

Why Your Patients Are on ELAHERE™



ELAHERE is a therapy approved to treat certain patients with advanced ovarian cancer

ELAHERE is indicated for the treatment of adult patients with folate receptor-alpha (FR_d) positive, platinum-resistant epithelial ovarian, failopian tube, or primary peritoneal cancer, who have received one to three prior systemic treatme regimens. Select patients for therapy based on an FDA-approved test

This indication is approved under accelerated approval based on tumor response rate and durability of response Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial

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Why Eye Care Is Important for Patients Receiving ELAHERE™



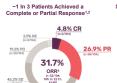
BOXED WARNING: OCULAR TOXICITY ELAHERE can cause severe ocular toxicities, including visual impairment, keratopathy, dry eye, photophobia, eye pain, and uveitis.

- Conduct an ophthalmic exam including visual acuity and slit lamp exam prior to initiation of ELAHERE, every other cycle for the first 8 cycles, and as clinically indicated.
- Administer prophylactic artificial tears and ophthalmic topical steroids.
- Withhold ELAHERE for ocular toxicities until improvement and resume at the same or reduced dose.
- Discontinue ELAHERE for Grade 4 ocular toxicities.

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51

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What Patients Can Expect With ELAHERE™

Safety Profile:

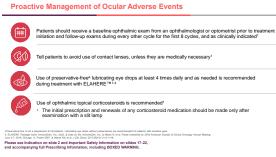
and y Prome: Serious adverse events occurred in 31% of patients The most common (22%) adverse events, including laboratory abnormalities, were vision inaparient, fatigue, increased AST, nauses, increased ALT, karatopathy, adhodminal pain, decreased inymhorytes, peripheral neuropathy, diambe, adcreased albumin, constipation, increased alkaine phosphatase, dry eye, decreased magnesium, decreased leukocytes, decreased neutrophis, and decreased hemoglobin¹ 11% of batients discontinued due to an adverse event

- 11% of patients discontinued due to an adverse event
 <1% discontinued due to an ocular event!
- · Dose delays and reductions occurred in 39% and 20% of patients, respectively
- Ocular adverse events will be detailed later in this presentation

Encrement Prager was attracted to 102, 2022, 2 UNE of the International Inc.
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52

46.2% SD (n=48/304)



Recommended Schedule for Eye Drops



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What to Look for in the Baseline Ophthalmic Exam

A baseline ophthalmic examination should include a visual acuity test and slit lamp exam
 Document the patient's current symptoms and visual acuity prior to the initiation of ELAHERE ⁷⁴



Note presidence signs and symptoms of ocular surface disease ELAVERE. Package intert. ImmunoGen. Inc.: 2022.

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Plea and What to Monitor During Scheduled Follow-up Ophthalmic Exams



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Timing of Onset

56

Types of Ocular Adverse Events That May Occur With ELAHERE™

Ocular adverse event	All grades, %	Grade 3, %	Grade 4, %
Visual impairment ^b	50	6.6	0
Keratopathy	37	8.5	0.9
Dry eyed	27	1.9	0
Cataract	18	2.8	0
Photophobia	17	0	0
Eye pain ^e	10	0	0
Adverse events that required o impairment (9%) and keratopa	dose reductions in ≥	3% of patients in	cluded visual
No patients had permanent or	ular sequelae ³		

 Coular adverse events was Soular adverse events was Soular adverse events (signed, flow) Soular adverse events Soular adverse event

Integrated Safety Analysis of Patients Treated With ELAHERE (N=464)^a



 Ocular adverse events led to permanent discontinuation of ELAHERE in 0.6% of patients¹

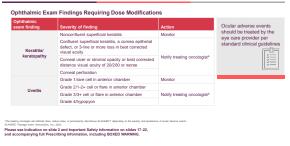
What to Expect With Ocular Events Associated With ELAHERE™

Impact

58

Monitoring Ocular Adverse Events

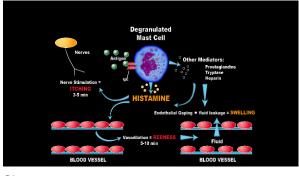
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Coordinating With the Treating Oncologist



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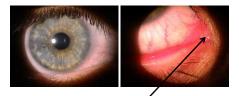
Types of Allergic Eye Disease

- Acute allergic conditions Seasonal Allergic Conjunctivitis (Hay Fever) - SAC Perennial Allergic Conjunctivitis – PAC
- Chronic allergic conditions Vernal Conjunctivitis - VKC Atopic Conjunctivitis - AKC Giant Papillary Conjunctivitis - GPC

62

64

Misunderstanding the Itchy Eye

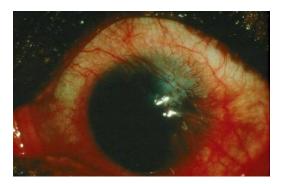


Allergic Conjunctivitis: Seasonal / Perennial

- Causes: Environmental Genetic predisposition Findings: Family history No eosinophils found in scrapings Spike in tear histamine Normal histaminase function
- Signs/Symptoms: Itching Redness Chemosis Lid swelling Tearing

63





Atopic Keratoconjunctivitis (AKC)

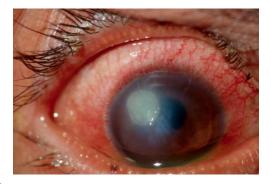
Causes: Associated with atopic dermatitis May be perennial Genetic predisposition Environmental antigens

Clinical Findings: Initiates between 20 and 50 years

of age Elevated levels of eosinophils, TH₂, lymphocytes, and mast cells Signs/Symptoms: Itching Redness Photophobia Keratopathy SPK/Ulcers Keratoconus Anterior polar cataracts Mucous discharge Atopic blepharitis



69



68

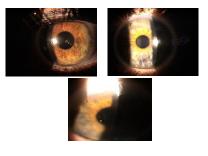
Vernal Keratoconjunctivitis (VKC)

Causes:

Genetic predisposition, atopy Seasonal/perennial allergens (IgE) Nonspecific hypersensitivity

Clinical Findings: Most predominant in males from 3 to 20 years old Increased levels of superficial mast cells, eosinophils, and lymphocytes Decreased levels of histaminase Signs/Symptoms: Ptosis Ropy mucous discharge Photophobia Large, nonuniform cobblestone papillae Trantas dots Limbal nodules Neovascularization Shield ulcers Itching

Contact Lenses



70



Giant Papillary Conjunctivitis (GPC)

Causes:

Repeated mechanical irritation caused by: Contact lens edge Exposed sutures Extruded scleral buckle Ocular foreign bodies

Aggravated by concomitant allergy

Can also aggravate ocular allergy

Clinical Findings: Increased chronic inflammatory cells Signs/Symptoms: Decreased CL tolerance Blurred vision Foreign body sensation Small, uniform papillae on upper tarsal plate Thick mucous build-up

Treatment Options

Topical Medications

- Antihistamine/ Mast Cell Stabilizer Combinations
 - · Blocks Histamine receptors on blood vessels, nerve endings, etc
 - Inhibits histamine degranulation from sensitized mast cells so that when these cells are challenged with antigen, they do not degranulate
 - Patanol, Pataday, Elestat, Zaditor, Lastacaft, Bepreve

RASP Inhibitors

- www.aldeyra.com
- Aldehyde is a product of metabolism
- Normally rapidly broken down
- With inflammation, is produced in quantities that are difficult to breakdown efficiently
- RASP Reactive aldehyde species
- Reproxalap Is a RASP inhibitor

73

74

76

Tear-Based POC Quantitative Testing



T-POC IgE Testing: Is There An Allergic Component?

- Benefits of testing IgE levels in the tear film:
 Presence of IgE indicates the diagnosis of allergic conjunctivitis
- allergic conjunctivitis Levels of IgE increase with the severity of the allergic response IgE testing can help differentiate allergic conjunctivitis from DED Changes in IgE levels may show the efficacy of prescribed treatment
- of prescribed treatment [gE value is < 80 ng/mL (33 klU), there is a 95.7% probability that the patient does not have an ocular allergy IgE value is > 80 ng/mL, there is a 92.9% probability that this elevated IgE is indicative of an ocular allergy



75

Trichiasis



Trichiasis



Low Mag

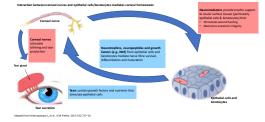
High Mag

Trichiasis

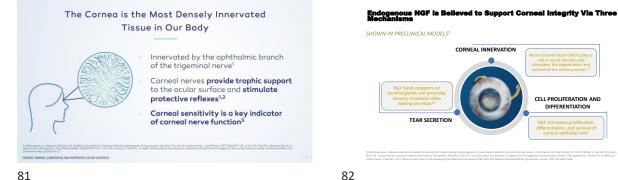


79

Ocular Surface BEYOND the TEARS



80



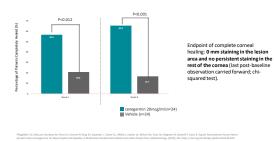
82 MEDICAL HISTORY





CELL PROLIFERATION AND DIFFERENTIATION

65.2% of Patients Had Complete Corneal Healing at week 8

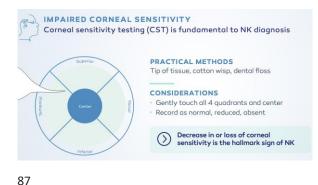




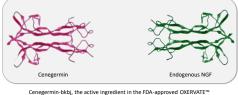
aesthesiometer



86



Cenegermin Mimics the Structure of Endogenous NGF in the Ocular Tissues



Cenegermin-bkbj, the active ingredient in the FDA-approved OXERVATE™ (cenegermin-bkbj ophthalmic solution) 0.002% (20 mcg/mL), is structurally identical to the human NGF protein found in ocular tissues

88



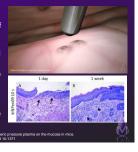
1.Warms Meibum

- 2. Emits Energy that absorbed by chromophores in hemoglobin and closes abnormal vessels in the eyelid margin and adjacent conjunctiva. Prevents release of inflammatory factors by the vessels 3.Reduces inflammatory factors in tears (interleukin 17A. Interleukin-6,
- prostaglandin E2) (up-regulates expression of anti-inflammatory agents while downregulating pro-inflammatory argents)
- 4. Activates fibroblasts and enhance collagen production
- 5.Reduce inflammatory or neurogenic pain 6.Reduction in bacterial load and demodex to reduce inflammation

Thank you Dr. Laura Periman for the following slides on conjunctivochalasis plasty

Plasma Pen CCh-plasty

- · Used extensively in aethetics, dermatology for non-invasive treatment of mild to moderate rhytids, skin tags, AK, xanthelasma, angioma, telangiectasias acne scars, skin tightening ("non surgical blepharoplasty")
- · Controlled plasma arc that induces tissue contraction and triggers fibroblast collagen remodeling
- Highly controlled contraction of the conjunctiva with minimal thermal damage



92



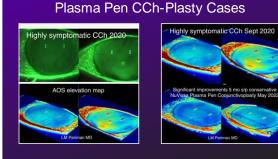
Plasma Pen CCH-plasty Technique · Pre-Procedure: Lid scrub, Pre-Procedure: Lid scrub, proparacaine soaked proparacaine soaked pledget, brimonidine, pledget, brimonidine, moxifloxacin or tobra-dex moxifloxacin or tobra-dex drops drops Post-Procedure: combination antibiotic-steroid, antibiotic-steroid, perflurohexyloctane perflurohexyloctane Tylenol for pain control Tylenol for pain control Patients report relief in CCh Patients report relief in CCh symptoms starting day 3 symptoms starting day 3

93

Plasma Pen CCH-plasty Technique

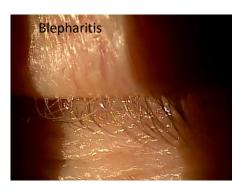
Post-Procedure: combination

94



Inferior CCH-plasty Improved SLK





Blepharitis



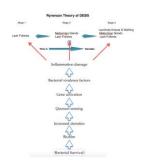
Low Mag

High Mag









MICROBLEPHAROEXFOLIATION (MBE)





103

Lid Margin Hygiene Protocol

1) Identify condition

- 2) Photo document (video capture at slit lamp)
- Discussion with patient
- Rx antibiotic/steroid combination 1 gtt bid to qid OU rubbing medication into lid margin after instillation or tea tree oil
- 5) Patient to return in 1 week for follow up
- 6) Return for microblepharoexfoliation procedure
- 7) Photo document (video capture at slit lamp) pre and post procedure
- 8) Use medication for one more day
- 9) Continue on maintenance therapy (Hypochlorous Acid)

104

Microblepharoexfoliation Protocol

- 1) Prepare blephex
- 2) Place 1 gtt proparacaine OU
- 3) Blephex upper and lower left lid margin
- 4) Rinse with addipak solution (non-preserved NaCl)
- 5) Blephex upper and lower right lid margin
- 6) Rinse with addipak solution (non-preserved NaCl)
- 7) 1 gtt lumify OU
- 8) Photodocument lid margins

105

Lotilaner Ophthalmic Solution 0.25%



106

Objective

Eye rinsing has been an effective method to reduce Matrix Metalloproteinase-9 (MMP-9), a hallmark of surface inflammation

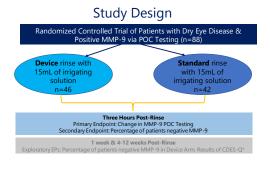
A **single** ocular rinse assisted via **irrigating eyelid retractor** effect on MMP-9

Effectiveness of a Singular Ocular Rinse via Irrigating Eyelid Retractor to Reduce MMP-9 in Patients with Dry Eye Disease

> Nandini Venkateswaran, MD ABO Natasha Mayer, BSc



San Diego, California



Eligibility Criteria

Inclusion Criteria	Exclusion Criteria
 218 years of age with dry eye complaints Positive MMP-9 via Point-of-care testing 	Anti-inflammatory medication usage Artificial tear or topical ocular medication usage within the past 14 days Intraocular surgery within the past 6 months Contraindication to MMP-9 POC testing Acute allergic or infectious conjunctivitis Histoy of 55 or cicatricial conjunctiviti Severe dry eye preventing wetting of the POC testing

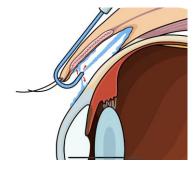
Irrigating Eyelid Retractor

Fixed to a syringe, the retractor has 5 ports which aim fluid at the palpebral conjunctiva, bulbar conjunctiva and conjunctival fornix.

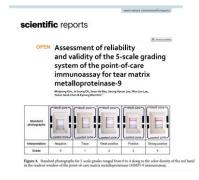


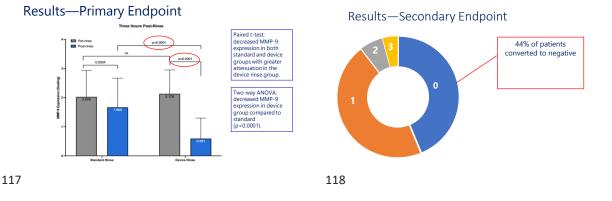












116

Conclusion

A novel irrigating eyelid retractor rinse of the ocular surface statistically reduces MMP-9 levels compared to baseline and is superior to a standard eye rinse.

- Use of an irrigating eyelid retractor may be a therapeutic avenue for those patients with dry eye disease.
- Further work on the durability of these findings is ongoing.

ARS Polling Instructions

Step 1 - Open the Vision East app and log in using your badge ID and last name

Step 2 - Head to the Connect & Learn tab and tap on All Education Sessions

Step 3 - Select the course you are attending from the list of sessions

Step 4 - Scroll to the bottom and select "Pre-course questions" prior to the session or "Post-course questions" after the session

Step 5 – Complete the survey question and Submit!

2/5/2024

Thank you

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