



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, Aldeyra, Allergan, Art Optical, Avellino, Bausch + Lomb Health, Contamac, CooperVision, CSEye, Dompe, Horizon Therapeutics, Johnson & Johnson Vision Care, Kala, Lenstech, Notal Vision, Novartis, Oyster Point, Quidel, Radius XR, RVL, Sun Pharma, Tangible Science, Tarsus, Santen, Visus, Visionix, Walman Optical and Zea Vision.
- All relevant relationships have been mitigated

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InflammaDry

- Detects elevated levels of MMP-9 in tear fluid
- Rapid – 10 minute results
- Easy to use – can be performed by a nurse or technician
- In-office (point of care) test
- Low cost – no additional equipment required
- One time use – disposable
- Accurate – high sensitivity and specificity



InflammaDry is CE Marked and commercially available in Europe. At this time InflammaDry is pending 510(k) review by FDA and is not commercially available in the U.S.

4

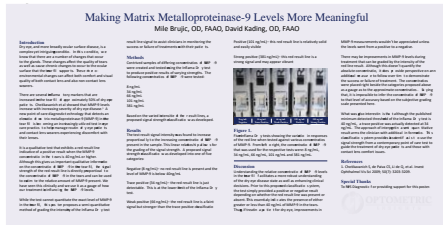
How to Use InflammaDry: Four-step Process

		<p>1. Gently dab the Sample Collector in 6-8 locations on the palpebral conjunctiva (lower eyelid) to collect a tear sample. Do not use a dragging motion.</p>
		<p>2. Snap the sample collector into the test cassette and press firmly where indicated.</p> <p>3. Dip the test cassette into the provided buffer vial for 20 seconds. Replace the cap.</p> <p>4. Read the results: 2 lines (1 red, 1 blue) = positive, 1 line (blue) = negative</p>

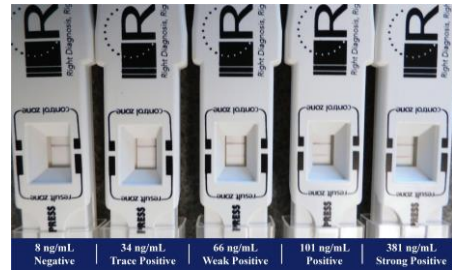
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7



Signal Strength

8

Osmolarity Digital Readout



9

Tear-Based Point-of-Care (T-POC) Quantitative Testing Platform

- Used to improve patient care in the areas of:
 - Dry eye disease (DED)
 - Ocular immunology,
 - Ocular allergy,
 - Ocular surgery, including LASIK
- With T-POC in your practice, patients can be diagnosed, treated, and monitored directly within your practice
 - Quantitative IgE and Lactoferrin results delivered within minutes
- Just a 1 microliter tear sample from each eye required
- Billable & reimbursable by Medicare and Private Insurance*
 - CPT 83520 (Lactoferrin)
 - CPT 82785 (IgE)

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T-POC Lactoferrin Testing Is it Aqueous Deficient or Evaporative Disease?

- Benefits of testing Lactoferrin levels in the tear film:
 - Low Lactoferrin levels (<0.9 ug/ml) directly correlates to DED caused by aqueous deficiency
 - Severity of DED can be determined by the Lactoferrin level
 - Low Lactoferrin levels indicate DED and depressed ocular immunity, which may represent an increased surgical risk
 - Low Lactoferrin levels may indicate the cause of contact lens intolerance
 - Changes in Lactoferrin levels may show the efficacy of the prescribed treatment
 - Dry eye is a relative contraindication for LASIK and other surgical procedures



Sensitivity: 93%
Specificity: 93%
Precision: 9% CV
Normal Lf = 0.9 mg/ml
Low Lf < 0.9 mg/ml
Shelf Life: 12 months

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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
 - 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
- IgE value is < 80 ng/mL (33 kIU), 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



Sensitivity: 93%
Specificity: 96%
High IgE = 94% CV
Test Time < 60 mg/ml
Normal IgE > 80 ng/ml
Shelf Life: 12 months

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Tear-Based POC Quantitative Testing

- 1 Rapid
- 2 Repeatable
- 3 Reproducible
- 4 Reimbursable



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No AMD
-No drusen or <10 small drusen (<63um) without pigment abnormalities

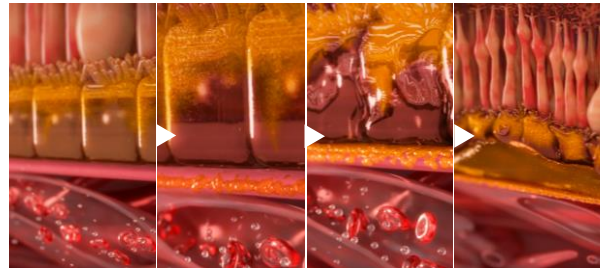
Early AMD
-Approximately >9 small drusen or <15 intermediate drusen (63-124um) or pigment abnormalities associated with AMD

Intermediate AMD
-Approximately >14 intermediate drusen or any large drusen (>124um)

Advanced AMD
-Geographic atrophy with involvement of the macular center or non-central GA atleast 350um in size

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Disease Process of AMD Starts Below the Surface



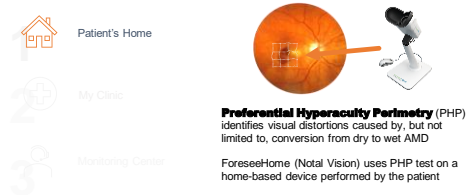
16

ForeseeHome



17

Real-World Remote Patient Monitoring Model
Preferential Hyperacuity Perimetry test for detecting visual abnormalities



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SYFOVRE[®] (pegcetacoplan injection) **APPROVED ON FEB 17, 2023**

INDICATION: SYFOVRE[™] (pegcetacoplan injection) is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

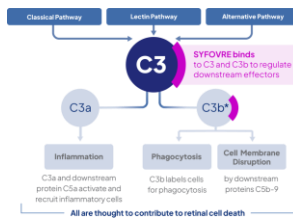
INTRAVITREAL INJECTION given monthly or every other month (EoM); Based upon doctor's discretion

DID YOU KNOW?

- ~1M people are affected by GA in the US
- Vision loss from GA can occur before lesions reach the fovea
- The median time to foveal encroachment in GA patients was just 2.5 years

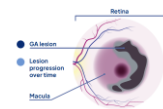
19

Mechanism of Action:
Targeting C3 within the Complement Cascade



20

RESULTS:
Monthly and EoM



Trial 1	
After 2 years, compared to those who did not receive SYFOVRE, SYFOVRE slowed lesion growth by	
▼ 22%	when taken monthly (n=202)
▼ 18%	when taken every other month (n=205)

Trial 2	
After 2 years, compared to those who did not receive SYFOVRE, SYFOVRE slowed lesion growth by	
▼ 18%	when taken monthly (n=201)
▼ 17%	when taken every other month (n=201)

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GATHER 1
GATHER 2

The Efficacy of Avacincaptad Pegol in Geographic Atrophy: GATHER1 and GATHER2 Results

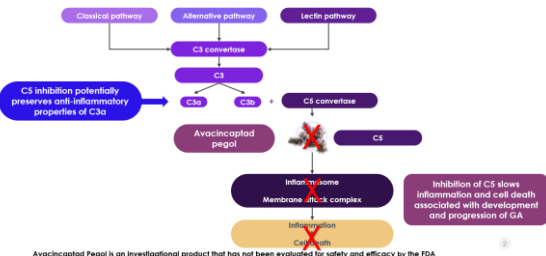
Arshad M Khanani, MD, MA¹; Sunit S Patel, MD, PhD²; Giovanni Staurenghi, MD³; Ramin Tadayoni, MD, PhD⁴; Carl J Danzaj, MD⁵; David R Lally, MD⁶; Anat Loewenstein, MD⁷; David S Boyer, MD⁸; Carl D Regillo, MD⁹; Tien P Wong, MD¹⁰; Glenn J Jaffe, MD¹¹; Justin Tang, PhD¹²; Liansheng Zhu, PhD¹³; Hersh Patel, OD¹⁴; Julie Clark, MD¹⁵

¹Shed Eye Associates, Reno, NV, USA; ²University of Nevada, Reno School of Medicine, Reno, NV, USA; ³West Texas A&M Consultants, Abilene, TX, USA; ⁴Tiger Clinic, Department of Biomedical and Clinical Sciences, "Gold School," University of Alberta, Edmonton, Alberta, Canada; ⁵Department of Ophthalmology, Harvard Medical School, Massachusetts Eye and Ear Infirmary, Boston, MA, USA; ⁶Department of Ophthalmology, Baylor University Medical Center, Baylor University, Fort Worth, Texas; ⁷Department of Ophthalmology, University of California, Los Angeles, CA, USA; ⁸Wills Eye Hospital, Philadelphia, PA, USA; ⁹Wills Eye Consultants of Texas, Retina Consultants of America, Houston Methodist Hospital, Houston, TX, USA; ¹⁰Department of Ophthalmology, Duke University, Durham, NC, USA; ¹¹North Bay, Parkersburg, WV, USA; ¹²The Retina Society, 2018 Annual Scientific Meeting, Prato, Italy, CA; ¹³November 2 - 5, 2022

MED-2200207
Avacincaptad Pegol is an investigational product that has not been evaluated for safety and efficacy by the FDA

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Avacincaptad pegol is a pegylated RNA aptamer designed to be a specific inhibitor of complement C5

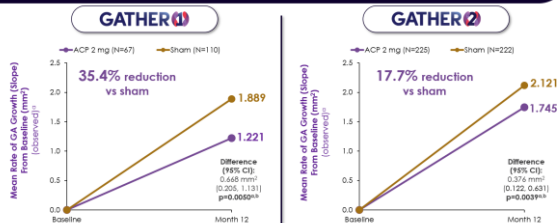


Avacincaptad Pegol is an investigational product that has not been evaluated for safety and efficacy by the FDA

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GATHER 1
GATHER 2

Mean rate of observed GA growth (slope analysis) demonstrated consistent efficacy results between the two studies



Note: The primary endpoint for GATHER1 (mean change in square root transformed GA area from baseline to month 12) (mm²) is consistent with this slope analysis (observed data). The slope analysis for GATHER1 (ACP 2 mg group vs sham) are from the MMRM model, drawing on all available data, including data from groups with different non-compliance rates in Part 1 and Part 2 of the trial. The slope analysis for GATHER2 (ACP 2 mg group vs sham) are from the MMRM model, drawing on all available data, including data from groups with different non-compliance rates in Part 1 and Part 2 of the trial. The slope analysis for GATHER2 (ACP 2 mg group vs sham) are from the MMRM model, drawing on all available data, including data from groups with different non-compliance rates in Part 1 and Part 2 of the trial.

Avacincaptad Pegol is an investigational product that has not been evaluated for safety and efficacy by the FDA

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Avacincaptad pegol (IZERVAY) is approved for the treatment of geographic atrophy secondary to age-related macular



- Efficacy and safety of IZERVAY were evaluated in 2 phase 3, randomized, multi-center, doublemasked, sham-controlled clinical trials
- IZERVAY safety profile was consistent, with a high rate of patient retention
- IZERVAY demonstrated significant reductions in GA growth in just 12 months

IZERVAY™ (avacincaptad pegol intravitreal solution) Prescribing Information, IVD/Celgene, Inc., Parsippany, NJ 07054

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New Data on Zeaxanthin

ORIGINAL RESEARCH
Prevention Surpasses Treatment: 5-year Follow-Up, Cost-Utility, and Cost-Benefit of Zeaxanthin Therapy for Neovascular Age-Related Macular Degeneration
 Gary C. Brown, D., Melissa M. Brown, Dennis Goehart, & Joseph Lim
 Received March 20, 2023 / Accepted May 22, 2023
 © The Author(s) 2023
ABSTRACT
Introduction: Oral administration of zeaxanthin (Z) 20 mg daily in patients with unilateral neovascular age-related macular degeneration (nAMD) treated with triple therapy (photodynamic therapy/intravitreal triamcinolone/anti-VEGF)
Methods: Consecutive, unilateral nAMD
Results: Zeaxanthin reduced follow-up 3-year nAMD incidence from 23 to 6% (p = 0.02) in a prior clinical trial. We questioned the long-term benefit and thus analyzed case-control 5-year patient data of trial participants and additional participants with 5-year follow-up, also performing cost-utility and cost-benefit analyses.

- Group randomized to 20mg of Zeaxanthin (ZX) per day + AREDS 2 vs just AREDS 2
- Patients developing nAMD in the non-affected eye in that time period (5 years)
 -22% of ZX
 -48% of non-ZX

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New IOP, VF and MPOD devices

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iCare HOME2 and HOME feature comparison



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iCare HOME2 and HOME
 Available measurement positions
 The new iCare HOME2 enables measurement freedom.



iCare HOME2



- Measurements are possible in sitting, reclined and supine positions

iCare HOME

- Measurements are possible in sitting position only

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iCare HOME2 and HOME
 Measurement guidance before the measurement

 <p>iCare HOME2 Smart light guide enables active positioning guidance for the patient. The light rings help find the correct measurement distance.</p> <ul style="list-style-type: none"> • Solid red light means the device is not level and cannot take a measurement • Visible blue light ring indicates that the probe is too far from the eye • When the patient sees a symmetrical green light ring, the device is positioned in correct angle 	 <p>iCare HOME Probe base light to help level the tonometer</p> <ul style="list-style-type: none"> • Solid red light means the device is not level and cannot take a measurement • When the patient sees a symmetrical green light ring, the device is level and centered
--	--

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iCare HOME2 and HOME
Taking measurements

iCare HOME2

- Patient is self-taught or has minimal assistance from technician on proper use of device
- A successful measurement is indicated with a check mark, shown on the display screen and single long beep
- A measurement sequence consists of six measurements
- Take the measurement sequence by
 - pressing Measure button 6 individual times or
 - pressing and holding the Measure button down

iCare HOME

- A technician instructs patient on proper use of device
- A successful measurement is indicated with a small check mark and single long beep
- A measurement sequence consists of six measurements
- Take the measurement sequence by
 - pressing Measure button 6 individual times or
 - pressing and holding the Measure button down



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Wearable Devices for VF

Radiusxr
Olleyes
M&S Technologies



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Study on Effect of Nutrition on Computer Symptoms

- 360 participants
- Randomized to 4 groups that utilized 1 of four nutritional formulations for 90 days
- Measurements were taken at baseline, 45 days later and 90 days later
 - 1 - Placebo
 - 2 - 6 mg Lutein, 1.2mg Zeaxanthin, 75mg chrysanthemum extract, 75mg goji berry extract, 100mg black current extract
 - 3 - 10 mg Lutein, 2 mg Zeaxanthin, 125mg chrysanthemum extract, 125mg goji berry extract, 167mg black current extract
 - 4 - 14 mg Lutein, 2.8 mg Zeaxanthin, 175mg chrysanthemum extract, 175mg goji berry extract, 233mg black current extract

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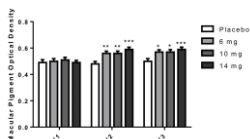
Results

- Improved eye fatigue symptoms
- Improved Schirmer test
- Improved macular pigment optical density (MPOD)

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4. Improved Macular Pigment Optical Density (MPOD)

- All baseline measurements for all groups were identical
- All treatment groups demonstrated significant increase in MPOD over placebo at second visit (45 days after beginning nutrition)



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Summary

- Nutritional supplementation improves eye fatigue symptoms, visuognosis persistence, Schirmer strip test and MPOD levels
- Some of symptom and sign improvement likely secondary to MPOD changes
- MPOD has traditionally been considered a biomarker for risk factors associated with long term disease development and progression
- MPOD may be an appropriate functional marker for eye fatigue
- Understanding the massive amount of screen time currently being performed by everyone, this is becoming an increasingly important area for eye care providers to intervene when appropriate

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ELM – Eye Lipid Mobilizer (Not Yet Available)



<https://www.eyedotec.com/>

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AZR-MD-001

- **Mechanism of action:** Contains selenium sulfide, a keratolytic agent also found in some anti-dandruff shampoos.
- **Safety/efficacy:**
 - An interim data analysis from a double-masked, vehicle-controlled trial presented at ARVO 2021 found a significantly greater change in OSDI score of at least 4.5 units in the group receiving 1.0% AZR concentration (85.7%) vs vehicle group (22.2%, $P=0.03$)
 - Change from baseline in Meibomian Gland Score was also significantly higher with 1.0% AZR vs control ($P=0.03$)

Quinn PK, et al. Clin Ophthalmol. 2021;15:4389-4394. <https://doi.org/10.1097/ICL.0000000000002724>
<https://clinicaltrials.gov/ct2/show/study/NCT03825557> Terms: azr md001 & azr md001

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NOV03 (Currently Available – Miebo)

- **Mechanism of action:** Sole ingredient is perfluorohexyloctane, which covers the tear film to limit aqueous evaporation and penetrates meibomian glands, reportedly dissolving altered meibum
- **Safety/efficacy:**
 - Results of the phase 3 double-masked GOBI study presented at the 2022 ASCRS annual meeting showed that adults with MGD-related DED in the treatment group vs placebo group had significantly improved total corneal fluorescein staining (2.0 vs -1.0) and visual analog scale dryness score (-27.4 vs -19.7), $P<0.001$ for both on Day 57.
 - Blurred vision was the only adverse event more likely in treated subjects (3.0% vs 0.3%).
 - Topline data of the phase 3 MOJAVE trial announced in 2021 also included significant change on these efficacy outcomes versus control on day 57 ($P<0.001$ for both)

Tucker J, et al. Cornea. 2021;40(8):1432-1441. <https://doi.org/10.1097/ICO.0000000000002724> <https://www.eyedotec.com/news/2021/09/30/2021-09-30-113908676>

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Meivertter



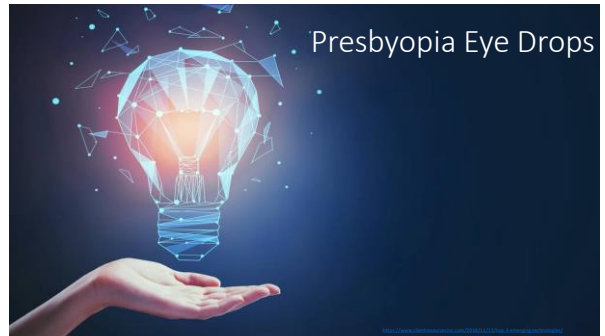
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Quality of Life

Acta Ophthalmologica
Acta Ophthalmologica 2014

Review Article

Review of the impact of presbyopia on quality of life in the developing and developed world

Arturo D. Goerz,¹ William C. Stewart,² William R. Burns,³ Susanna A. Stewart¹ and Lindsay A. Nelson¹

¹University of Nevada, Las Vegas, Nevada, USA
²US Pharmaceutical Research Network, LLC, Cheshire, Wyoming, USA
³Victory Vision, Inc., Fort Worth, Texas, USA

ABSTRACT. (October 2013). Review: overall purpose: To examine the public health impact of presbyopia regarding the effect on quality of life (QoL) and society in both the developed and developing worlds. **Background.** A population-based cross-sectional study of patients, the Canadian Elderly and Midlife Vision using the following search terms: presbyopia, QoL, cross-sectional, impact, eye, presbyopia, treatment and public health. **Methods.** were assessed into the literature of their addressed needs and public health.

Goerz AD, Stewart WC, Burns WR, Stewart SA, Nelson LA. Review of the impact of presbyopia on quality of life in the developing and developed world. Acta Ophthalmol. 2014 Sep;92(8):497-500.

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Current Treatments (Non-surgical)

- Glasses
 - Reading glasses
 - Advantages – low cost, easily accessible, convenient
 - Disadvantages – inconvenient, are dependent on them
- Bifocals
 - Advantages – have correction on all the time (both distance and near)
 - Disadvantages – sometimes current environment isn't conducive to this design; cosmetic component
- Progressive addition glasses
 - Advantages – have correction on all the time (both distance and near)
 - Disadvantages - sometimes current environment isn't conducive to this design

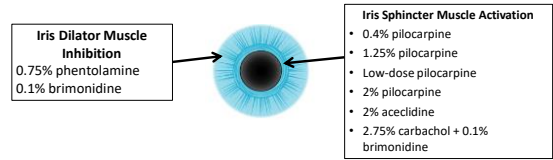
48

Current Treatments (Non-surgical)

- **Contact Lenses**
 - **Single Vision Distance**
 - Advantages – provides visual freedom from spectacles
 - Disadvantages – need optical correction for near vision
 - **Monovision**
 - Advantages - provides visual freedom from spectacles
 - Disadvantages – some visual compromise
 - **Multifocals**
 - Advantages - provides visual freedom from spectacles
 - Disadvantages – some cannot adapt to multifocal optics

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MOAs of Different Miotics In Development For Presbyopia



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Topical Presbyopia Treatment Approaches

FDA Approved	Phase 3	Phase 2	
Allergan/AbbVie 1.25% pilocarpine	Orasis low dose pilocarpine	Visus brimonidine + carbachol	Ocuphire 0.75% phentolamine + 0.4% pilocarpine
	Eyenovia microdose 1% or 2% pilocarpine	LENZ aceclidine	Novartis 1.5% lipolic acid choline ester
		Glaukos transdermal delivery of pilocarpine	

Chamman WN. Ophthalmic Physiol Opt. 2019;39(1):1-10.

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Ocular Surface Inflammation

- Commercially available as Restasis
- 0.05% concentration
- Preservative free
 - Single vials
 - Multi-dose bottle
 - Patented non-preserved system that maintains its sterility
- Is an immunosuppressive agent
- Available as generic

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Restasis (Cyclosporine 0.05%)



54

Cyclosporine 0.09%

- Commercially available as Cequa
- Unit dose vials
- Unique delivery mechanism
- N-cell technology

55

Cequa (cyclosporine 0.09%)



56

Klarity-C Drops PF

- 0.1% cyclosporine
- Preservative free
- Imprimis Rx
- 5.5mL multidose bottle



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Verkazia

- 0.1% cyclosporine
- Approved for vernal keratoconjunctivitis
- Dosed four times/day



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Cyclosporine 0.1%

- Novaliq
- VEVEE
- FDA approved for the signs and symptoms of dry eye
- Water free

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Ocular Surface Inflammation

- Intercellular adhesion molecule-1 (ICAM-1) is found on surface cells of the conjunctiva and cornea
- ICAM-1 is overexpressed in dry eye disease
- LFA-1 and ICAM-1 binding is believed to be propagate inflammatory cascade on the ocular surface
 - Is believed to do so by T-cell activation and migration to target tissues

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Ocular Surface Inflammation

- Lifitegrast applied topically is believed to prevent the interaction between LFA-1 on T-cells and ICAM-1 on the ocular surface
- Has been shown to improve both signs and symptoms of dry eye within a 12 week time period
- Commercially available as Xiidra
 - 5% concentration
 - non-preserved sterile unit dose vials
- It is a lymphocyte functioning antigen-1 (LFA-1) antagonist

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Tyrvaya



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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

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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

ASCRS 2023

San Diego, California

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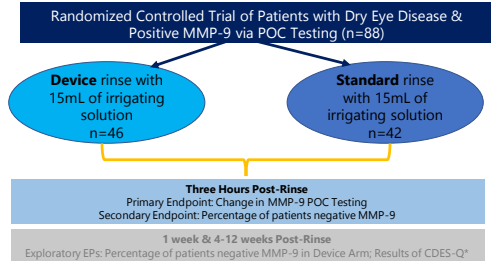
Objective

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

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Study Design



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Eligibility Criteria

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none"> ≥18 years of age with dry eye complaints Positive MMP-9 via Point-of-care testing 	<ul style="list-style-type: none"> Anti-inflammatory medication usage Artificial tear or topical ocular medication usage within the past 14 days Intraocular surgery within the past 6 months Contact lens wear within past 12 hours Contraindication to MMP-9 POC testing Acute allergic or infectious conjunctivitis History of SJS or cicatricial conjunctival disease Severe dry eye preventing wetting of the POC testing

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Baseline Characteristics

	Device Arm (n=46)	Standard Arm (n=42)	Total (n=88)
Sex, n (%)			
Male	10 (22%)	6 (14%)	16 (18%)
Female	36 (78%)	36 (86%)	72 (82%)
Race, n (%)			
White	43 (94%)	40 (95%)	83 (94%)
Age, Mean (SD), years	47.4 ± 3.4	45.9 ± 4.2	46.6 ± 3.2

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Irrigating Eyelid Retractor

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



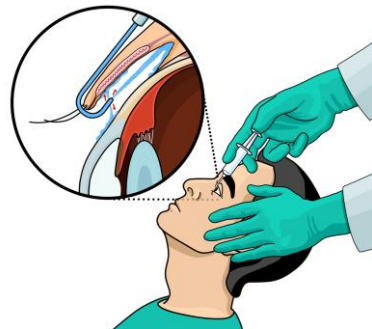
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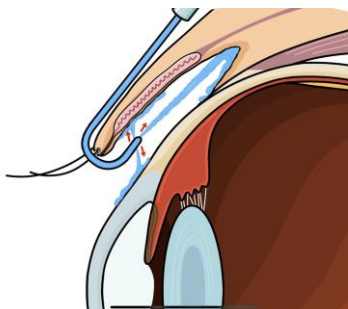
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scientific reports

OPEN Assessment of reliability and validity of the 5-scale grading system of the point-of-care immunoassay for tear matrix metalloproteinase-9

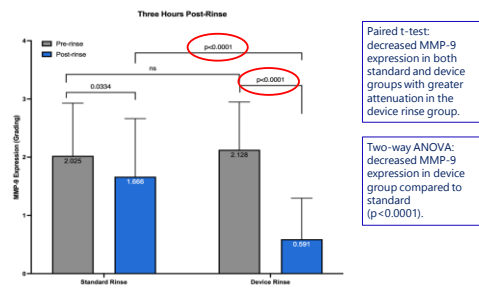
Milgrom-Gil, M, Huang, QJ, Sauer, M, Ben, S, Seong-Hyeon Lee, Woo Jun Lee, Yeon Seok Choi & Kyung Woo Kim

Standard photographs	Control zone	Control zone	Control zone	Control zone	Control zone
Interpretation	Negative	Trace	Weak positive	Positive	Strong positive
Grade	0	1	2	3	4

Figure 4. Standard photographs for 5-scale grades ranged from 0 to 4 along to the color density of the red band in the readout window of the point-of-care metalloproteinase (MMP)-9 immunoassay.

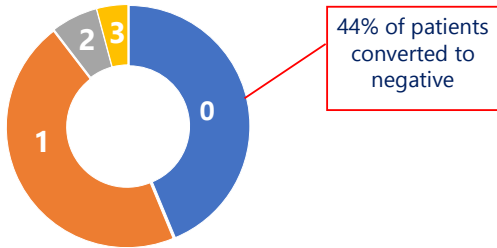
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Results—Primary Endpoint



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Results—Secondary Endpoint



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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.

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No AMD
-No drusen or <10 small drusen (<63um) without pigment abnormalities

Early AMD
-Approximately >9 small drusen or <15 intermediate drusen (63-124um) or pigment abnormalities associated with AMD

Intermediate AMD
-Approximately >14 intermediate drusen or any large drusen (>124um)

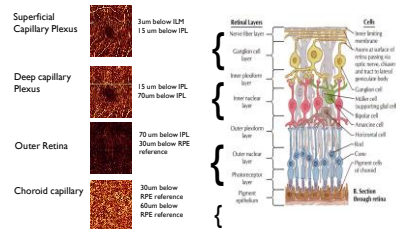
Advanced AMD
-Geographic atrophy with involvement of the macular center or non-central GA atleast 350um in size

82



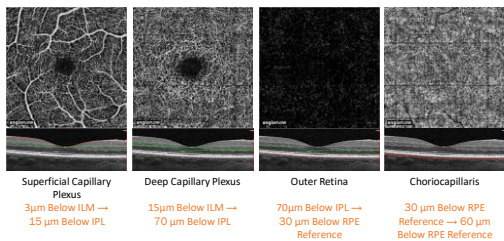
83

Visualize Retinal Vasculature



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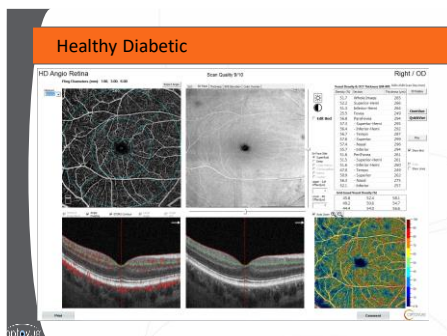
Normal Retinal Vasculature



85

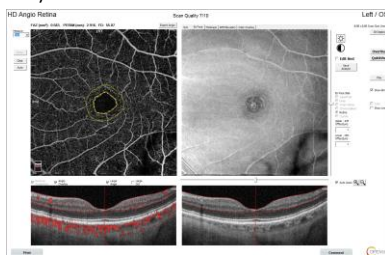


86



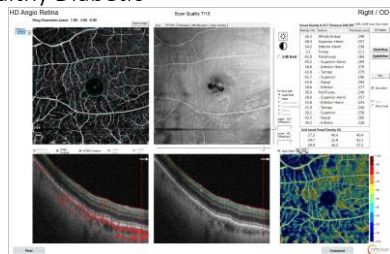
87

Unhealthy Diabetic



88

Unhealthy Diabetic

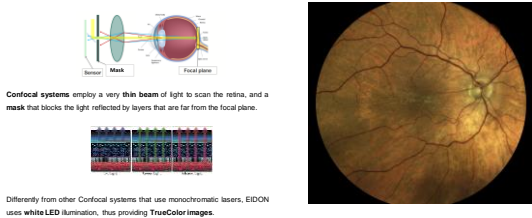


89



90

TrueColor Confocality



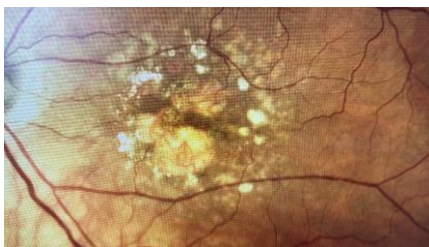
91

New Standards for Detecting Change



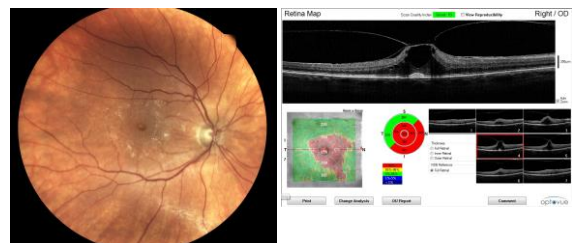
92

Flicker Functionality



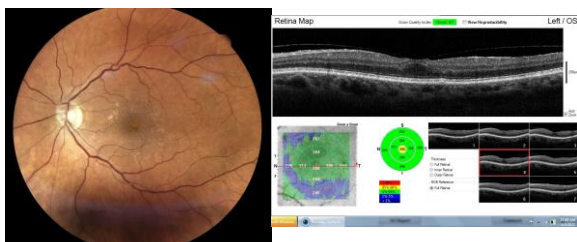
93

Macular findings

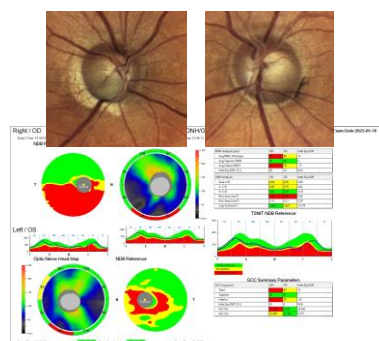


94

Macular findings



95



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Choroidal Nevus

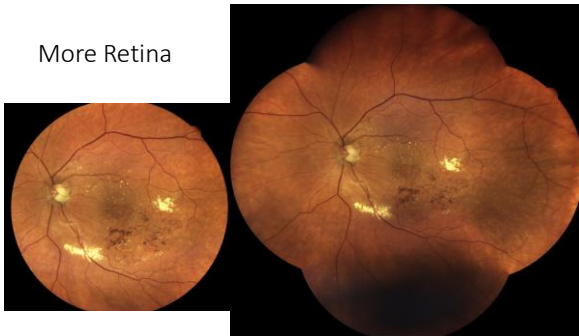


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More Retina



99

Retinoschisis change??



100

Retinoschisis change??



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Chronic macular edema



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Headache help

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PERCEPT MiWear®

MiWear is a unique **migraine therapy** that uses special lens filters in eyewear that only allows a very **narrow band of green light**. nbGL has been shown in research to provide **therapeutic effects** for the migraine sufferer. This is important because migraine can be debilitating and MiWear may improve their quality of life by allowing these sufferers to continue in their daily activities.

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Severe Headache & Migraine Sufferers: Breakthrough
Burstein et al

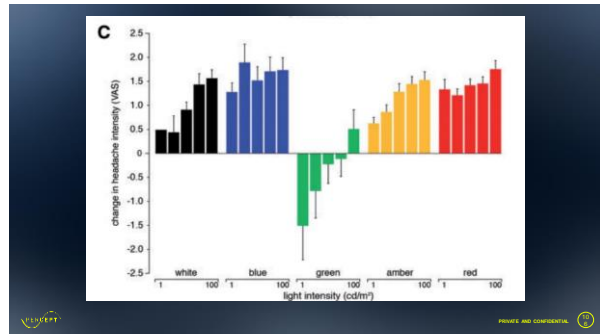
BRAIN
A JOURNAL OF NEUROLOGY

Migraine photophobia originating in cone-driven retinal pathways

Rodrigo Noveda,^{1,2} Carolyn A. Bernstein,^{1,2} Rony-Reuven Nir,³ Alice J. Lee,⁴ Anne B. Fulton,^{2,5} Suzanne M. Bertisch,^{2,6} Alexandra Hovagimian,⁷ Dean M. Cestari,^{2,8} Rodrigo Saavedra-Walker,^{2,9} David Borsook,^{2,8} Bruce L. Doran,¹⁰ Catherine Buetner^{2,8} and Rami Burstein^{1,2}

Migraine headache is strongly exacerbated by light. Using psychophysical assessments in patients with normal vision we found that green light exacerbates migraine headache significantly less than white, blue, amber or red light. To delineate mechanisms, we used electroretinography and visual evoked potential recording in patients, and multi-unit recording of cone- and light-sensitive thalamic neurons in rats to show that green activates cone-driven retinal pathways to a lesser extent than white, blue and red. Thalamic neurons are most responsive to blue and least responsive to green and that cortical responses to green are significantly smaller than those generated by blue, amber and red light. These findings suggest that patients experience with colour and migraine photophobia could originate in cone-driven retinal pathways, first-order relay thalamic neurons outside the main visual pathway, and processed by the cortex. Additionally, the findings provide solutions for the working effects of **nbGL**.

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PERCEPT MiWear®

- Migraine
 - Estimated annual costs of \$17 billion (U.S.)
 - Affects more than 40 million people (U.S.)
- Opportunity to help migraine sufferers live and function without optical noise

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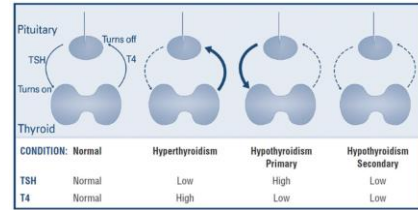
108

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

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Thyroid Gland Function

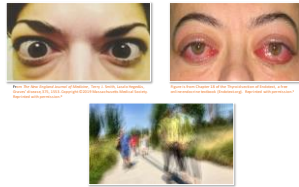


<https://www.thyroid.org/thyroid-function-tests/>

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

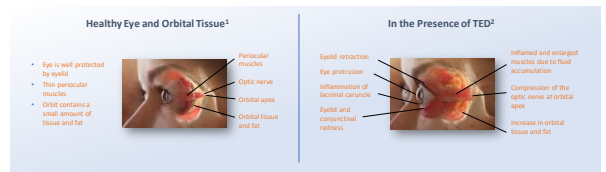
- Patients may experience^{1,7}:
 - Poor ophthalmic clinical outcomes
 - Disfigurement
 - Vision-threatening complications
 - Psychosocial distress
 - Restrictions in daily activities and ability to work



1. Bellizzi AS, et al. Ophthalmology. 2009;116:103-110. 2. Moller-Nielsen L, et al. JAMA Ophthalmol. 2012;30:1519-1524. 3. Baranovskiy L, et al. Invest Ophthalmol Vis Sci. 2010;51:2439-2445. 4. Baranovskiy L, et al. Invest Ophthalmol Vis Sci. 2010;51:2439-2445. 5. Baranovskiy L, et al. Invest Ophthalmol Vis Sci. 2010;51:2439-2445. 6. Baranovskiy L, et al. Invest Ophthalmol Vis Sci. 2010;51:2439-2445. 7. Baranovskiy L, et al. Invest Ophthalmol Vis Sci. 2010;51:2439-2445.

111

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



Activation of the IGF-1R/TSHR signaling complex on orbital fibroblasts triggers an inflammatory response, leading to tissue expansion and remodeling in the orbit^{1,2}

1. Baranovskiy L, et al. Ophthalmology. 2010;117:103-110. 2. Baranovskiy L, et al. Ophthalmology. 2010;117:103-110. 3. Baranovskiy L, et al. Ophthalmology. 2010;117:103-110. 4. Baranovskiy L, et al. Ophthalmology. 2010;117:103-110. 5. Baranovskiy L, et al. Ophthalmology. 2010;117:103-110. 6. Baranovskiy L, et al. Ophthalmology. 2010;117:103-110. 7. Baranovskiy L, et al. Ophthalmology. 2010;117:103-110.

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Recognizing the Signs and Symptoms of TED

Eyelid^{1,3}

- Upper eyelid retraction: 91% of patients affected
- Eyelid swelling
- Pain
- Lagophthalmos (incomplete closure of eyelid)

Orbital Tissue^{1,3,4}

- Exophthalmos (proptosis): Occurs in 62% of patients
- Pain/deep ache
- Disfigurement

1. Baranovskiy L, et al. Ophthalmology. 2010;117:103-110. 2. Baranovskiy L, et al. Ophthalmology. 2010;117:103-110. 3. Baranovskiy L, et al. Ophthalmology. 2010;117:103-110. 4. Baranovskiy L, et al. Ophthalmology. 2010;117:103-110.

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

Conjunctiva and Cornea^{1,3}

- Chemosis (swelling of the conjunctiva)
- Conjunctival hyperemia (redness)
- Photophobia (light sensitivity)
- Pain
- Foreign body sensation (gritiness)
- Exposure keratopathy
- Swollen lacrimal canuncle
- Dry eye and tearing

Extraocular Muscle^{1,5}

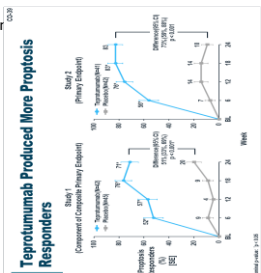
- Restricted ocular motility: Occurs in ~40% of patients
- Strabismus (misalignment of eye)
- Diplopia (double vision)
- Pain
- Retro-orbital ache
- Decreased vision and depth perception

1. Baranovskiy L, et al. Ophthalmology. 2010;117:103-110. 2. Baranovskiy L, et al. Ophthalmology. 2010;117:103-110. 3. Baranovskiy L, et al. Ophthalmology. 2010;117:103-110. 4. Baranovskiy L, et al. Ophthalmology. 2010;117:103-110. 5. Baranovskiy L, et al. Ophthalmology. 2010;117:103-110.

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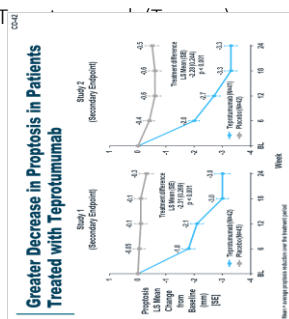
Treatment – Teprotumumab (Tepezza)

8 infusions - Treat



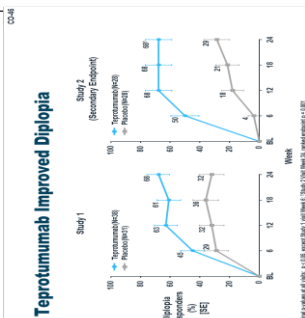
115

Treatment – T



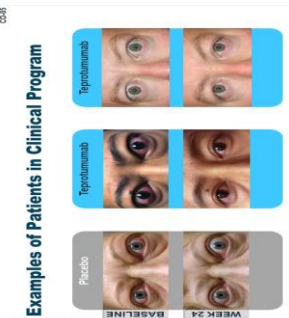
116

Treatment –



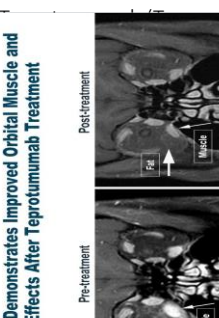
117

Treatment –



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Treatment



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GlobalNewsWire

Osmotica Pharmaceuticals plc Receives FDA Approval for Upneeq™ (oxymetazoline hydrochloride ophthalmic solution), 0.1% for Acquired Blepharoptosis (Droopy Eyelid) in Adults

Profile: Osmotica Holdings US LLC

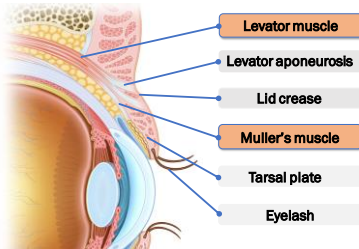
July 19, 2023 09:51 ET | Source: Osmotica Holdings US LLC



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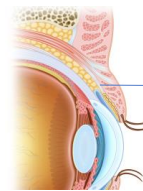
Lid Anatomy: Two Muscles Lift the Eyelid



Frederick et al. *Anesth Pain Surg*. 2003; 7:183-204.

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Oxymetazoline Acts at Müller's Muscle to Lift the Upper Eyelid

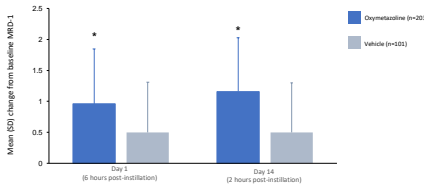


- Oxymetazoline is a potent, direct-acting α -adrenergic receptor agonist^{1,2}
 - ~5-fold greater affinity for α_2 receptors^{3*}
- Selectively activates α -adrenergic receptors in Müller's muscle⁴

*Receptor binding affinity is defined via in vitro binding assays.
 1. Hershbach B, et al. *Fundam Clin Pharmacol*. 2010;24(6):729-739. 2. Sugden D, et al. *Br J Pharmacol*. 1996;118(5):1246-1252. 3. Weston LO, et al. *Chin Chem Lett*. 2020;51:2027-2035. 4. Upneeq™ (oxymetazoline hydrochloride ophthalmic solution), 0.1% (Prescribing Information), PSL, Pharmaceuticals, Inc. 2020.

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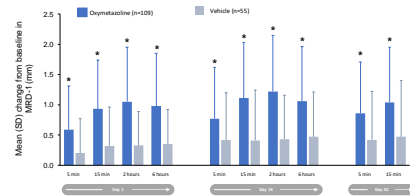
Oxymetazoline Significantly Increased Upper Eyelid Lift in Two Clinical Studies



Posted data from two 6-week, randomized, double-masked, placebo-controlled clinical trials; $p < 0.0001$ vs. vehicle from an ANCOVA model with study and treatment as fixed factors and baseline score as a covariate. Patients with congenital ptosis, Horner syndrome, myasthenia gravis, mechanical ptosis, ptosis/blepharospasm or substantial dermatomal/ataxia independent eyelid pain occurring within 3 mm of the upper eyelid margin, or visual field loss from any cause other than ptosis, were excluded from both trials.
 Steven CB, et al. *JAMA Ophthalmol*. 2020;38(11):1168-1175.

125

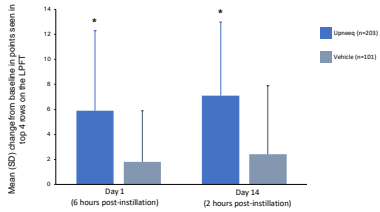
Oxymetazoline Provided a Rapid and Sustained Effect Over 42 Days



Data from 6-week, randomized, double-masked, placebo-controlled clinical trial (NCT02012021) $p < 0.05$ vs. vehicle from an ANCOVA model with treatment as a fixed factor and baseline score as a covariate.
 Hershbach J, et al. *Chin J Ophthalmol*. 2021;15:2743-2751.

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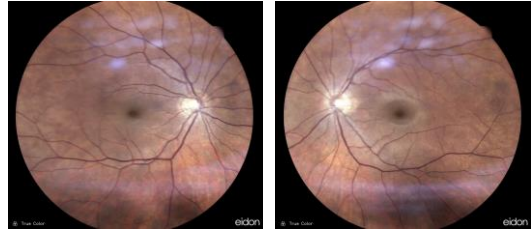
Oxymetazoline Significantly Improved Superior Visual Field Deficits



Posted data from two 6-week, randomized, double-masked, placebo controlled clinical trials; p<0.0001 vs. vehicle, from an ANCOVA model with study and treatment as fixed factors and baseline score as a covariate.
 Sivren CE, Foster S, Jarama M, et al. JAMA Ophthalmol. 2020;138(11):1168-1175.

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Examples of Patient Photo's

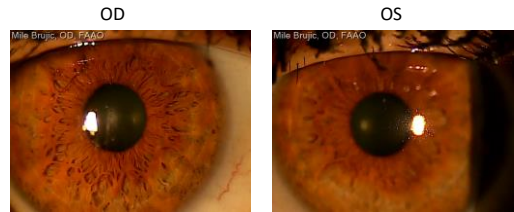


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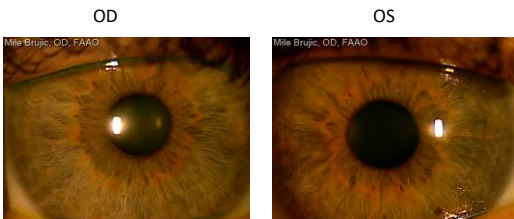
Examples of Patient Photos



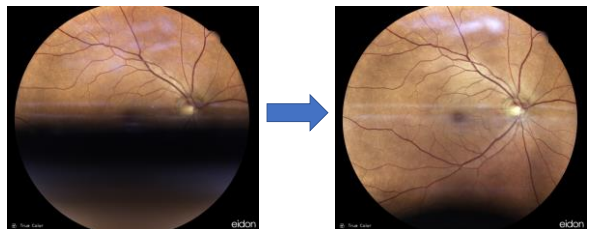
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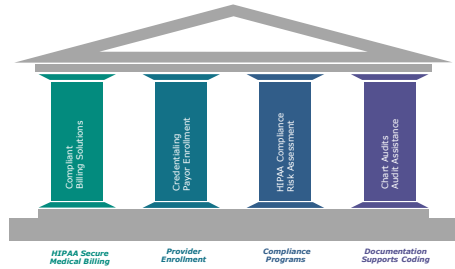
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HOW IT WORKS



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Cost Effective Staffing
For Optometry

What Can We Do?

- Inbound Calls
- Outbound Calls
- Insurance Verification

TE-M

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