Twelve Innovations In Eye Care That You Need To Know About

Mile Brujic, OD, FAAO

Premier Vision Group

https://www.clientresourcesinc.com/2018/11/13/top-3-emerging-technologies/

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, Aldeyra, Allergan, Art Optical, Bausch + Lomb Health, Contamac, CooperVision, CSEye, Dompe, Dopavision, Glaukos, Horizon Therapeutics, Iveric Bio, Johnson & Johnson Vision Care, Lentechs, MDElite, Notal Vision, Novartis, Radius XR, RVL, Sun Pharma, Tangible Science, Tarsus, Santen, Viatris, Visus, Visionix, Walman Optical and Zea Vision.

All relevant relationships have been mitigated

#1 New Dry Eye Diagnostics and Treatment

https://www.clientresourcesinc.com/2018/11/13/top-3-emerging-technologies/

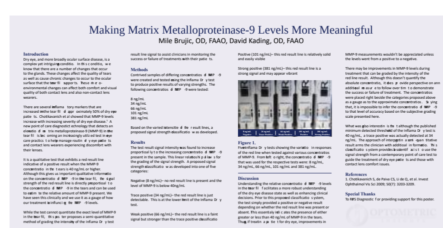
InflammaDry

- 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.

How to Use InflammaDry: Four-step Process

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.
2. Snap the sample collector into the test cassette and press firmly where indicated.
3. Dip the test cassette into the provided buffer vial for 20 seconds. Replace the cap.
4. Read the results: 2 lines (1 **red**, 1 **blue**) = positive, 1 line (**blue**) = negative



Making Matrix Metalloproteinase-9 Levels More Meaningful

Mile Brujic, OD, FAAO, David Kading, OD, FAAO

Introduction

Dry eye, and more broadly ocular surface disease, is a complex yet intriguing condition. In this condition, we know that there are a number of changes that occur to the glands. These changes affect the quality of tears as well as cause chronic changes to occur to the ocular surface that the tear film supports. These micro-environmental changes can affect both comfort and visual quality of both contact lens and also non-contact lens wearers.

There are several inflammatory markers that are increased in the tear film of approximately 50% of dry eye patients. Chotikavanich et al showed that MMP-9 levels increase with increasing severity of dry eye disease.[1] A new point of care diagnostict echnology that detects an elevation of matrix metalloproteinase-9 (MMP-9) in the tear film is becoming an increasingly utilized test in eye care practices to help manage routine dry eye patients and contact lens wearers experiencing discomfort with their lenses.

It is a qualitative test that exhibits a red result line indicative of a positive result when the MMP-9 concentration in the tears is 40 ng/mL or higher. Although this gives us important qualitative information on the concentration of MMP-9 in the tear film, the signal strength of the red result line is directly proportional to the concentration of MMP-9 in the tears and can be used to estimate the relative amount of MMP-9 present. We have seen this clinically and we use it as a gauge of how our treatment is influencing the MMP-9 levels.

While the test cannot quantitate the exact level of MMP-9 in the tear film, this poster proposes a semi-quantitative method of grading the intensity of the Inflamma Dry test result line signal to assist clinicians in monitoring the success or failure of treatments with their patients.

Methods

Contrived samples of differing concentrations of MMP-9 were created and tested using the Inflama Dry test to produce positive results of varying strengths. The following concentrations of MMP-9 were tested:

8 ng/mL
34 ng/mL
66 ng/mL
101 ng/mL
381 ng/mL

Based on the varied intensities of the result lines, a proposed signal strength classification was developed.

Results

The test result signal intensity was found to increase proportionally to the increasing concentration of MMP-9 present in the sample. This linear relationship allows for the grading of the signal strength. A proposed signal strength classification was developed into one of five categories:

Negative (8 ng/mL)– no red result line is present and the level of MMP-9 is below 40ng/mL

Trace positive (34 ng/mL)– the red result line is just detectable. This is at the lower limit of the Inflama Dry test.

Weak positive (66 ng/mL)– the red result line is a faint signal but stronger than the trace positive classification

Positive (101 ng/mL)– this red result line is relatively solid and easily visible

Strong positive (381 ng/mL)– this red result line is a strong signal and may appear vibrant

Figure 1.
Five Inflama Dry tests showing the variation in responses of the red line when tested against various concentrations of MMP-9. From left to right, the concentration of MMP-9 that was used for the respective tests were: 8 ng/mL, 34 ng/mL, 66 ng/mL, 101 ng/mL and 381 ng/mL.

Discussion

Understanding the relative concentration of MMP-9 levels in the tear film facilitates a more robust understanding of the dry eye disease state as well as enhancing clinical decisions. Prior to this proposed classification system, the test simply provided a positive or negative result depending on whether the red result line was present or absent. This essentially indicates the presence of either greater or less than 40 ng/mL of MMP-9 in the tears. Thus, if treating a patient for dry eye, improvements in MMP-9 measurements wouldn't be appreciated unless the levels went from a positive to a negative.

There may be improvements in MMP-9 levels during treatment that can be graded by the intensity of the red line result. Although this doesn't quantify the absolute concentration, it does provide perspective on an additional measure to follow over time to demonstrate the success or failure of treatment. The concentrations were placed right beside the categories proposed above as a gauge as to the approximate concentrations. Saying that, it is impossible to infer the concentration of MMP-9 to that level of accuracy based on the subjective grading scale presented here.

What was also interesting is that although the published minimum detected threshold of the Inflama Dry test is 40 ng/mL, a trace positive was actually detected at 34 ng/mL. The approach of interpreting a semi-quantitative result arms the clinician with additional information. This classification system provides a scientific basis to use the signal strength from a contemporary point of care test to guide the treatment of dry eye patients and those with contact lens comfort issues.

References

1. Chotikavanich S, de Paiva CS, Li de Q, et al. Invest Ophthalmol Vis Sci 2009; 50(7): 3203-3209.

Special Thanks

To RPS Diagnostics for providing support for this poster.

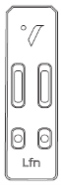
Osmolarity Digital Readout

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)

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: 83%
Specificity: 98%
Precision: < 9% CV
Normal Lf: > 0.9 mg/ml
Low Lf: < 0.9 mg/ml
Shelf Life: 12 months

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: < 9% CV
Test Time: < 80 ng/ml
Normal IgE: > 80 ng/ml
Shelf Life: 12 months

Tear-Based POC Quantitative Testing

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

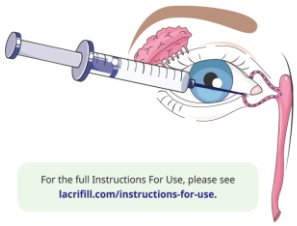
Lacrifill (Nordic Pharma)

- Cross-linked hyaluronic acid gel that allows patient's eyes to be bathed in their own natural tears
- Customized for each individual patient
- Provides a full fill of the canalicular system
- Lasts for 6 months
- In-office procedure reimbursed through existing CPT code (68761)

Procedure

Instructions for Use

1. LACRIFILL comes in a pre-filled injector with enough gel to treat the lower and upper canaliculi.
2. The cannula tip is placed in the punctum and the LACRIFILL gel is inserted.
3. The gel flows through the punctum into the lacrimal sac.
4. If you see the gel extruding from the upper punctum, you know that both the upper and lower puncta have been blocked.



For the full Instructions For Use, please see **lacrifill.com/instructions-for-use.**

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

Real-World Remote Patient Monitoring Model

Preferential Hyperacuity Perimetry test for detecting visual abnormalities

1. Patient's Home
2. My Clinic
3. Monitoring Center

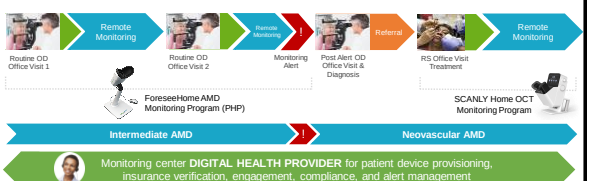
Preferential Hyperacuity Perimetry (PHP) identifies visual distortions caused by, but not limited to, conversion from dry to wet AMD

ForeseeHome (Notal Vision) uses PHP test on a home-based device performed by the patient

[16]

Digital healthcare services for AMD patients

Dedicated remote monitoring programs with advanced, AI-based technologies support Optometrist diagnosis of acute nAMD conversion and monitoring of chronic therapy between office visits



Monitoring center **DIGITAL HEALTH PROVIDER** for patient device provisioning, insurance verification, engagement, compliance, and alert management

SCANLY Home OCT Device

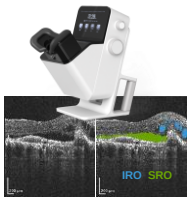
EASY-TO-USE PATIENT SELF-OPERATED CONNECTED DEVICE

Key Features

- Portable device: size 14"x11"x14" (WxDxH), weight <16 lbs.
- Patient self-setup and self-operation
- Automatic data transmission via built-in wireless connection
- AI-enabled estimation of hypo-reflective spaces

Imaging System Specifications

- Spectral-domain optical coherence tomography (SD-OCT)
- Scan area: 10 x 10 degree (3mm x 3mm)
- High density volume scan with up to 88 B-scans and 34 µm spacing
- Self-imaging time < 1 minute per eye[1]



1. https://clinicaltrials.gov/study/NCT04907409

IRO: Intra-retinal hypo-reflective spaces | **SRO**: Sub-retinal hypo-reflective spaces

DID YOU KNOW?

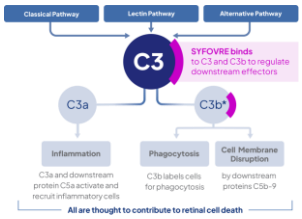
- ~1M people are affected by GA in the US
- Vision loss from GA can occur before lesions reach the fovea
- The median time to foveal encroachment in GA patients was just 2.5 years

SYFOVRE (pegcetacoplan injection) APPROVED ON FEB 17, 2023

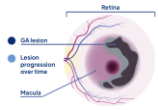
INDICATION: SYFOVRE™ (pegcetacoplan injection) is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

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

Mechanism of Action:
Targeting C3 within the Complement Cascade



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)

GATHER1 GATHER2

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

Arshad M Khanani, MD, MA[1]; Sunil S Patel, MD, PhD[2]; Giovanni Staurenghi, MD[3]; Ramin Tadayoni, MD, PhD[4]; Carl J Danzig, MD[5]; David R Lally, MD[6]; Anat Loewenstein, MD[7]; David S Boyer, MD[8]; Carl D Regillo, MD[9]; Tien P Wong, MD[10]; Glenn J Jaffe, MD[11]; Justin Tang, PhD[12]; Liansheng Zhu, PhD[12]; Hersh Patel, OD[12]; Julie Clark, MD[12]

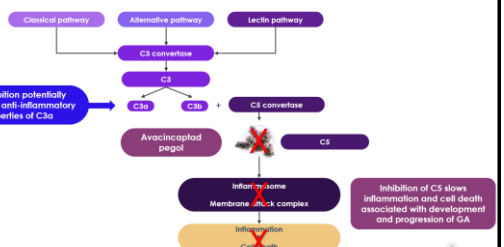
[1]Sierra Eye Associates, Reno, NV, USA; University of Nevada, Reno School of Medicine, Reno, NV, USA. [2]West Texas Retina Consultants, Abilene, TX, USA. [3]Eye Clinic, Department of Biomedical and Clinical Sciences "Luigi Sacco," University of Milan, Milan, Italy. [4]Université de Paris, Ophthalmology Department, AP-HP, Hôpital Lariboisière, Paris, France. [5]Rand Eye Institute, Deerfield Beach, FL, USA; Florida Atlantic University, Charles E. Schmidt School of Medicine, Boca Raton, FL, USA. [6]New England Retina Consultants, Springfield, MA, USA. [7]Division of Ophthalmology, Tel Aviv Sourasky Medical Center, Tel Aviv University, Tel Aviv, Israel. [8]Retina Vitreous Associates Medical Group, Los Angeles, CA, USA. [9]Wills Eye Hospital, Philadelphia, PA, USA. [10]Retina Consultants of Texas; Retina Consultants of America; Blanton Eye Institute, Houston Methodist Hospital, Houston, TX, USA. [11]Department of Ophthalmology, Duke University, Durham, NC, USA. [12]Iveric Bio, Parsippany, NJ, USA.

The Retina Society 55th Annual Scientific Meeting, Pasadena, CA
November 2 – 5, 2022

MED-2200207

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

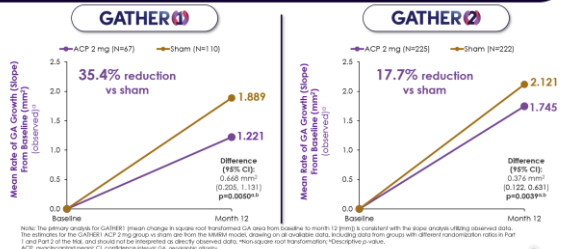
Avacincaptad pegol is a pegylated RNA aptamer designed to be a specific inhibitor of complement C5



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

GATHER1 GATHER2

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



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

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

1. IZERVAY™ (avacincaptad pegol intravitreal solution) Prescribing Information. IVERIC bio, Inc., Parsippany, NJ 07054.

New Data on Zeaxanthin


Ophthalmol Ther
https://doi.org/10.1007/s40123-023-00742-9

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 · Melissa M. Brown · Dennis Gierhart · R. Joseph Oik

Received: March 20, 2023 / Accepted: May 22, 2023
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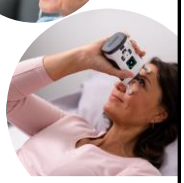
ABSTRACT

Introduction: Oral administration of zeaxanthin (Zx) 20 mg daily in patients with unilateral neovascular age-related macular degeneration (nAMD) treated with triple therapy (photodynamic therapy/intravitreal bevacizumab/intravitreal dexamethasone) reduced fellow-eye 2-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.
Methods: Consecutive, unilateral nAMD

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

#3 New IOP, VF and MPOD devices

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

iCare HOME2 and HOME
Measurement guidance before the measurement

iCare HOME2

Smart light guide enables **active positioning guidance** for the patient. The light rings help find the correct measurement distance.

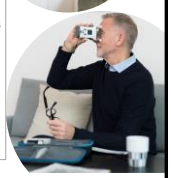
- Solid red light means the device is not level and cannot take a measurement
- Visible **blue light ring** indicates that the probe is too far from the eye
- When the patient sees a symmetrical green light ring, the device is positioned in correct angle

iCare HOME

Probe base light to help level the tonometer

- 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

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

Wearable Devices for VF

Radiusxr
Olleyes
M&S Technologies

tvst
Glaucoma

Validation of a Wearable Virtual Reality Perimeter for Glaucoma Staging, The NOVA Trial: Novel Virtual Reality Field Assessment

Chris Bradley[1], Iqbal Ike K. Ahmed[2,3], Thomas W. Samuelson[4], Michael Chaglasian[5], Howard Barnebey[6,7], Nathan Radcliffe[8], and Jason Bacharach[4]

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Keywords: visual field; glaucoma; virtual reality

Citation: Bradley C, Ahmed IIK, Samuelson TW, Chaglasian M, Barnebey H, Radcliffe N, Bacharach J. Validation of a wearable virtual reality perimeter for glaucoma staging, the NOVA trial: Novel virtual reality field assessment. Transl Vis Sci Technol. 2024;13(3):15. https://doi.org/10.1167/tvst.13.3.15

Purpose: Compare estimated sensitivities of SITA-Standard to the RATA-Standard algorithm of the Radius virtual reality perimeter (VRP), and measure concordance in glaucoma staging.

Methods: One hundred adult glaucoma patients—half with suspect or mild glaucoma, and half with moderate or severe—from five clinics performed four 24-2 visual field tests during a single visit, two with the Humphrey Field Analyzer (HFA) and two with Radius, in randomized order: HRHR or RHRH. Only one eye was tested per participant. We used the Wilcoxon rank-sum test with Bonferroni correction to compare distributions of estimated sensitivities across all 54 test locations over the 15 to 40 dB measurement range of the Radius. Weighted kappa measured concordance in glaucoma staging between two masked glaucoma experts using Medicare definitions of severity.

Results: A total of 62 OD and 38 OS eyes were tested. Estimated sensitivities for SITA-Standard and RATA-Standard were not significantly different for OD, but were for OS—likely because of SITA-Standard OD and OS being significantly different in our sample, but not for RATA-Standard. Low agreement was observed between 15 to 22 dB. Concordance in glaucoma staging was high for both graders: kappa = 0.91 and kappa = 0.93. Average test duration was 298 seconds for RATA-Standard and 341 seconds for SITA-Standard. The correlation in mean deviation was 0.84.

Study on Effect of Nutrition on Computer Symptoms

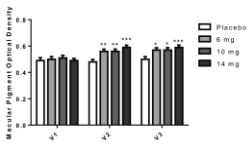
- 360 participants
- Randomized to 4 groups that utilized 1 of four nutritional formulations for 90 days
- Measurements were taken at baseline, 45 days later and 90 days later
  - 1 – Placebo
  - 2 - 6 mg Lutein, 1.2mg Zeaxanthin, 75mg chrysanthemum extract, 75mg goji berry extract, 100mg black current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

Results

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

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)



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

ELM – Eye Lipid Mobilizer (Not Yet Available)

https://www.eyedetec.com/

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*=.03)
    - Change from baseline in Meibomian Gland Score was also significantly higher with 1.0% AZR vs control (*P*=.03)

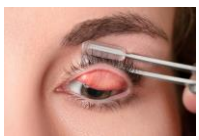
Gupta PK et al. Clin Ophthalmol. 2021;15:4389-4404. https://pmc.ncbi.nlm.nih.gov/articles/PMC8563265/ https://clinicaltrials.gov/ct2/show/NCT03652051?term=azr-md-001&draw=2&rank=4

Miebo (perfluorohexyloctane)

- **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*<.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*<.001 for both)

Tauber J et al. Cornea. 2021;40(9):1132-1140. https://ascrs.confex.com/ascrs/22am/meetingapp.cgi/Paper/81754 https://ir.bausch.com/news-releases/2021/09-30-2021-115908076

Meiverter





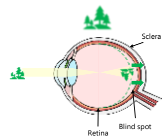
SleepTite SleepRite™

www.eyesleeptite.com

Myopia develops when normal eye growth regulation is disrupted

Time outdoors prevents shortage of dopamine, a key regulator of eye growth

Anatomy of the eye



Once started, normal glasses alone are unable to break this cycle

Blurry vision → Altered retinal processing → Dopamine shortage → Scleral remodeling → Axial elongation

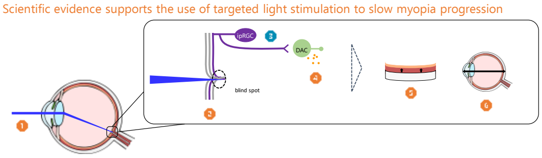
Opportunity to break the cycle of progression

Time outdoors → Melanopsin (photopigment) → Dopamine release

Dopamine is a key regulator of eye growth

MyopiaX® regulates the eye's innate growth mechanisms with blue light

Scientific evidence supports the use of targeted light stimulation to slow myopia progression



1. MyopiaX delivers a blue light to the blind spot
2. Blue light activates melanopsin at the blind spot — *Schilling et al. (2020)*
3. Melanopsin-expressing ipRGCs signal to DACs — *Amorim de Sousa et al. (2021)*, *Schilling et al. (2022)*
4. DACs increase dopamine release — *Schilling et al. (2023)*
5. elevated dopamine triggers ChT increase — *Chakraborty et al. (2024, abstract)*
6. increased ChT supports reduced axial length — *Chakraborty et al. (2024, abstract)*

45

MyopiaX® is a groundbreaking approach to manage progression of myopia

Targetedcontrol of progression through a novel mechanism and acceptance by children/parents

MyopiaX® delivers the blue light stimulus alongside a game app run on a standard smartphone

Safe
- Positive safety profile: light stimulus is targeted and low-intensity. No safety signals in ongoing pediatric clinical study

Customizable and engaging for children
- Supports individualized medical settings and games designed for children

Accessible
- Compatibility with consumer electronics reduces barriers to access

MyopiaX-1 first-in-human clinical trial of MyopiaX has achieved its 6-month readout and is scheduled to complete in September 2024

46

Compounding Pharmacies

Not a Long-term Solution for Kids

SYDNEXIS Formulation Matters

Eye & Contact Lens — Science and Clinical Practice

2023

Compounded 0.01% Atropine—What's in the Bottle?

Analyzed samples obtained from compounding pharmacies

Results:
- Shelf life ranged from 7 - 175 days
- pH range from 5.5 - 7.8
- 25% samples <90% concentration stated on bottle
- **27% of products <u>did not</u> include preservatives!**

Compounded LDA Challenges:
- Higher pH results in an unstable product
- Lack of regulation, no FDA oversight
- Nobody knows what's in the bottle (no product label, is it preserved?)
- Inconsistent product quality. Variability of products concerning for all stakeholders
- Not tested for safety or efficacy in a clinical trial (in kids)
- Compounded prescriptions are a liability for HCP once an approved product exists

47

The FDA Survey of Compounded Drug Products

Quality standards and active ingredient(s) were less than expected

SYDNEXIS Formulation Matters

Key Take Aways:

"Ten (34%) of the 29 sampled products failed one or more standard quality tests performed."

"Products analyzed contained less of the active ingredient(s) than expected (as described in the product's label). The average percent of declared potency for these nine products was calculated from the original and repeat analyses for each sample, with a range of 59 percent to 89 percent of expected potency."

"The analytical testing failure rate for **commercially produced samples** has been **less than 2 percent**. When compared to this failure rate, the percentage of sampled **compounded products** failing analytical testing in this survey (i.e., **34 percent**) was higher than expected."

48 Confidential

Who and What is SYDNEXIS?

The Company

Founded in 2014, Sydnexis Inc. is a privately held biopharmaceutical company based in San Diego. Sydnexis is currently evaluating its patented eyedrop formulation, SYD-101, in a Phase III pivotal trial to decrease myopia progression in children

The Mission

Sydnexis was founded with the goal of developing a proprietary, stable, accurate, comfortable and safe topical eyedrop to treat the progression of myopia in children and minimize the risk of co-morbidities.

Sydnexis has the Premium Low Dose Atropine Product

Backed by the Largest Pharmaceutical Treatment Study Ever Done in Myopia

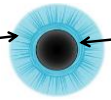
SYD-101 Low Dose Atropine and the STAR Study

Robust Clinical Trial Design

- 852 pediatric patients; the largest prospective study for a myopia pharmacologic treatment ever conducted
- Single, pivotal, Phase 3 study
- Primary endpoint readout summer 2024

MOAs of Different Miotics In Development For Presbyopia

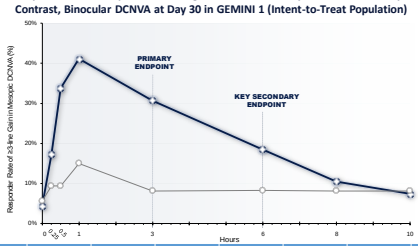
Iris Dilator Muscle Inhibition
0.75% phentolamine
0.1% brimonidine



Iris Sphincter Muscle Activation

- 0.4% pilocarpine
- 1.25% pilocarpine
- Low-dose pilocarpine
- 2% pilocarpine
- 2% aceclidine
- 2.75% carbachol + 0.1% brimonidine

Proportion of Participants Achieving 3-Lines or More Improvement in Mesopic, High Contrast, Binocular DCNVA at Day 30 in GEMINI 1 (Intent-to-Treat Population)



Mesopic illumination was defined as 10-11 lux, measured at the target

Timepoint	Hour 0	Hour 0.25	Hour 0.5	Hour 1	Hour 3	Hour 6	Hour 8	Hour 10
VUITY (%)	4.3	17.7	34.8	41.6	30.7	18.4	10.6	7.5
Vehicle (%)	5.9	9.8	9.8	15.7	8.1	8.8	8.5	8.6
Difference (95% CI)	-1.5 (-6.4, 3.3)	7.9 (0.3, 15.5)	25.0 (16.2, 33.8)	25.9 (16.4, 35.5)	22.5 (14.3, 30.8)	9.7 (2.3, 17.0)	2.1 (-4.4, 8.5)	-1.1 (-7.1, 5.0)

VUITY™ [package insert]. North Chicago, IL: Allergan, an AbbVie Company, USA

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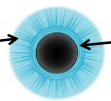
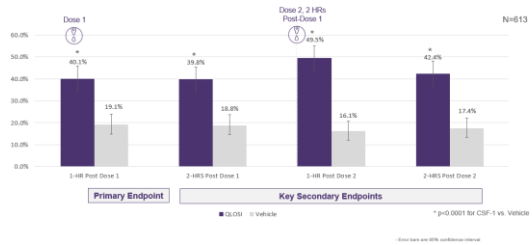


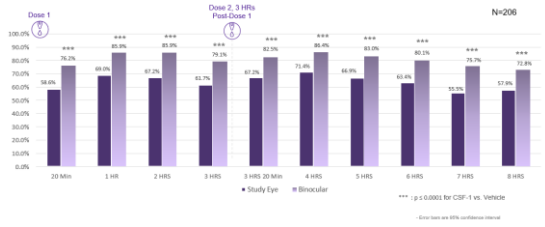
QLOSI™ ACHIEVED ALL PRIMARY & KEY SECONDARY ENDPOINTS

POOLED DAY 8 – PROPORTION OF PARTICIPANTS ACHIEVING ≥ 3-LINE IMPROVEMENT DCNVA, AND NO LOSS OF 1-LINE OR MORE IN DISTANCE VISUAL ACUITY (STUDY EYE)



Binocular Summation Contributes to Higher Achievement of DCNVA vs Study Eye Alone

POOLED DAY 15 – PROPORTION OF QLOSI™ PARTICIPANTS ACHIEVING DCNVA 20/40 OR BETTER IN STUDY EYE VERSUS BINOCULAR VISION WITH BASELINE BINOCULAR SUBJECTS 20/40 OR BETTER REMOVED



MOAs of Different Miotics In Development For Presbyopia

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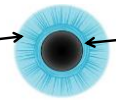

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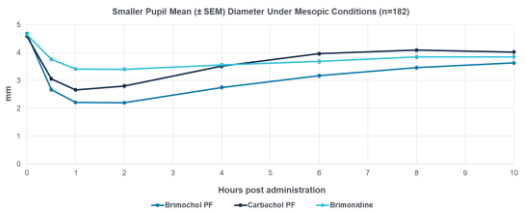
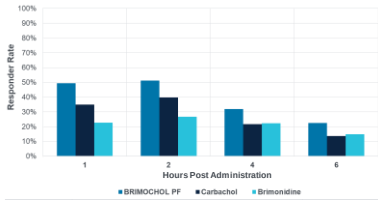
BRIMOCHOL™ PF Significantly Superior to Carbachol & Brimonidine in Pupil Diameter Reduction: 30mins to Hour 10

- **All Differences Between BRIMOCHOL™ PF and Monotherapies Highly Significant (p<0.001) at All Timepoints**
- **Gradual offset of BRIMOCHOL™ PF miosis balances near vision improvement with minimizing night-time vision risks**



US FDA Primary Endpoint Met at Hours 1, 2, 4, and 6

Primary for US FDA: Proportion of Subjects with a ≥15 ETDRS Letter Gain from Pre-dose Baseline in BUCNVA without a ≥5 ETDRS Letter Loss in BUCDVA under Mesopic Conditions (n=182)



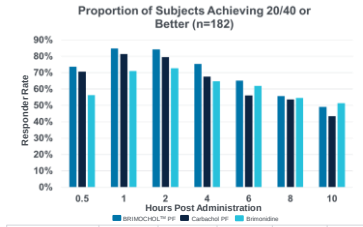
P-values	Hr1	Hr2	Hr4	Hr6
vs. Carbachol	<0.001	0.008	0.012	0.006
vs. Brimonidine	<0.001	<0.001	0.022	0.039

BRIMOCHOL™ PF superior to Carbachol and Brimonidine at multiple timepoints – 1,2,4 and 6 hours

BRIMOCHOL™ PF has higher peak efficacy and longer duration than only marketed product

BRIMOCHOL™ PF is being evaluated against vehicle as part of ongoing Phase 3 Program – evaluating 8+ hour performance

Percent of Subjects Achieving 20/40 or Better in BUCNVA



P-values	Hr0.5	Hr1	Hr2	Hr4	Hr6
vs. Carbachol	0.443	p=0.129	p=0.036	p=0.276	p=0.020
vs. Brimonidine	<0.001	p<0.001	p<0.001	p=0.006	p=0.313

Approximately 50% of subjects have improved from moderate to mild presbyopia out to hour 10 with **BRIMOCHOL™ PF**

BRIMOCHOL™ PF outperforms Carbachol PF and Brimonidine PF arms out to **8 hours**

Near Visual Acuity of 20/40 is adequate for most near vision tasks[1]

1. McDonald MB et al. Ophthalmol Ther 2022;11(1):1-11.

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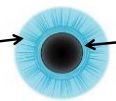

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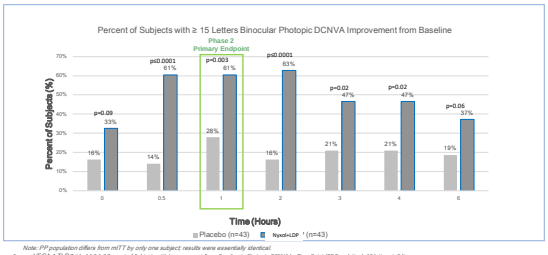
Met Primary & Secondary Endpoints

61% Patients had ≥ 15 Letter Near Gain with Fast Onset & Durable Responses



Note: PP population differs from mITT by only one subject; results were essentially identical.

Source: VEGA-1 TLR Table 14.2.1.2 Percent of Subjects with Improvement From Baseline in Photopic DCNVA by Time Point (PP Population). 15 letters ≈ 3 lines.

MOAs of Different Miotics In Development For Presbyopia

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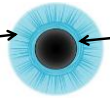

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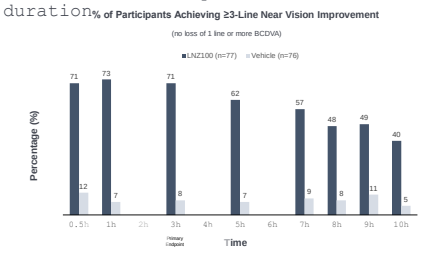
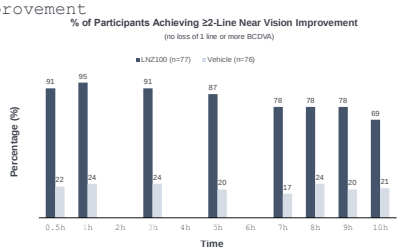
- 2.75% carbachol + 0.1% brimonidine

LNZ100 achieved rapid onset and 10 hours duration



CLARITY 2, day 1 results, full analysis set. Near visual acuity was assessed at 40cm using Monocular BCDVA (best-corrected distance visual acuity)

Nearly all participants (95%) achieved a ≥2-Line improvement



CLARITY 2, day 1 results, full analysis set. Near visual acuity was assessed at 40cm using Monocular BCDVA (best-corrected distance visual acuity)

Do Miotics Have a Chance?

- The emmetropic presbyope
- Low myope/astigmatism
- Caution on the hyperope
- Contact lens wearer

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

Cyclosporine 0.09%

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

Klarity-C Drops PF

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

Verkazia

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

Cyclosporine 0.1%

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

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

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% concentraton
  - non-preserved sterile unit dose vials
- It is a lymphocyte functioning antigen-1 (LFA-1) antagonist

Tyrvaya

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

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

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

Study Design

Randomized Controlled Trial of Patients with Dry Eye Disease & Positive MMP-9 via POC Testing (n=88)

Device rinse with 15mL of irrigating solution n=46

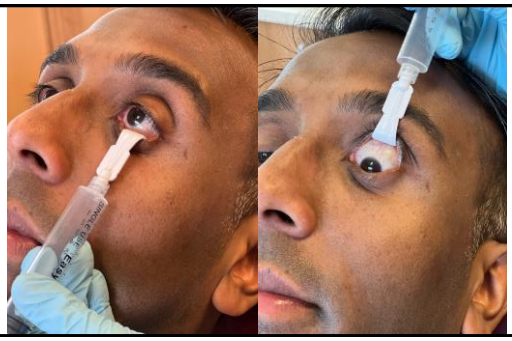
Standard rinse with 15mL of irrigating solution n=42

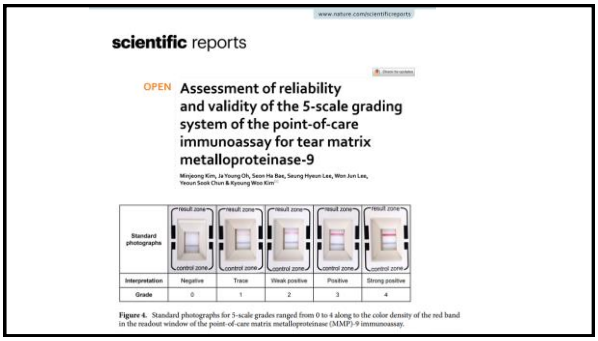
Three Hours Post-Rinse
Primary Endpoint: Change in MMP-9 POC Testing
Secondary Endpoint: Percentage of patients negative MMP-9

1 week & 4-12 weeks Post-Rinse
Exploratory EPs: Percentage of patients negative MMP-9 in Device Arm; Results of CDES-Q*

Irrigating Eyelid Retractor

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



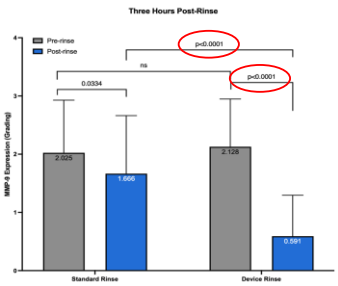


scientific reports

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

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 matrix metalloproteinase (MMP)-9 immunoassay.

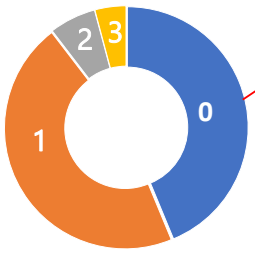
Results—Primary Endpoint



Paired t-test: decreased MMP-9 expression in both standard and device groups with greater attenuation in the device rinse group.

Two-way ANOVA: decreased MMP-9 expression in device group compared to standard ($p<0.0001$).

Results—Secondary Endpoint



44% of patients converted to negative

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.

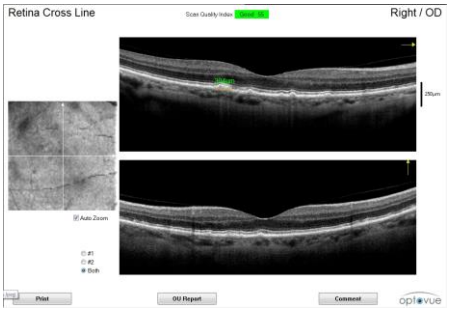
Further work on the durability of these findings is ongoing.

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

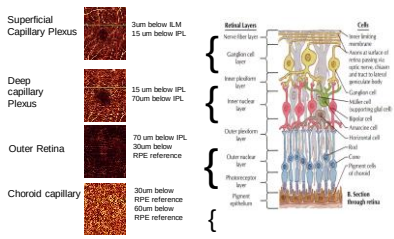
Early AMD
-Approximately >9 small drusen or <15 intermediate drusen (63-124um) or pigment abnormalities associated with AMD

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

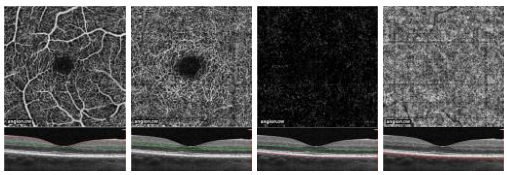
Advanced AMD
-Geographic atrophy with involvement of the macular center or non-central GA atleast 350um in size



Visualize Retinal Vasculature

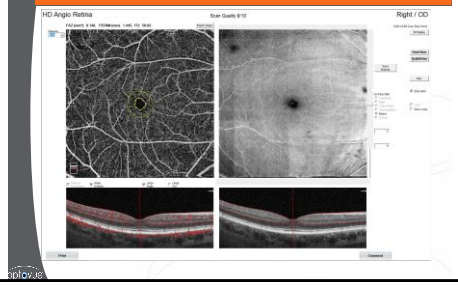


Normal Retinal Vasculature

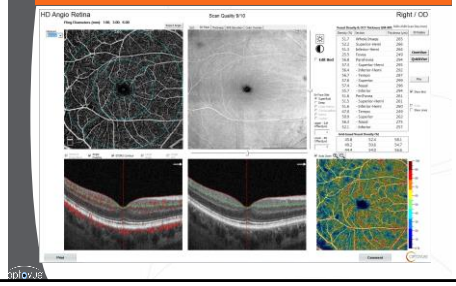


Superficial Capillary Plexus	Deep Capillary Plexus	Outer Retina	Choriocapillaris
3μm Below ILM → 15 μm Below IPL	15μm Below ILM → 70 μm Below IPL	70μm Below IPL → 30 μm Below RPE Reference	30 μm Below RPE Reference → 60 μm Below RPE Reference

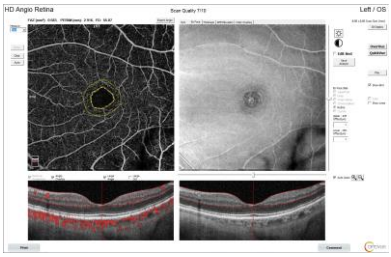
Healthy Diabetic



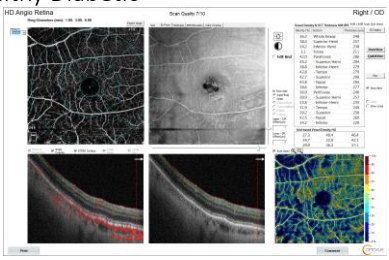
Healthy Diabetic

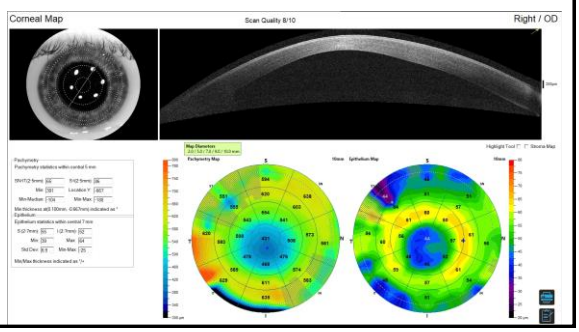


Unhealthy Diabetic

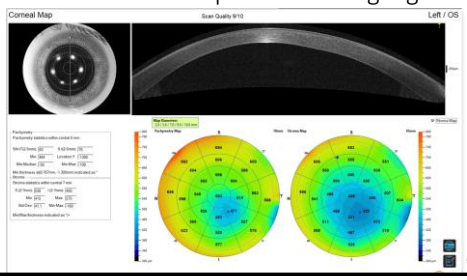


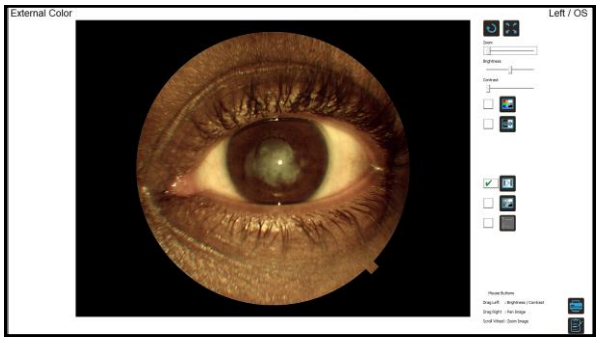
Unhealthy Diabetic



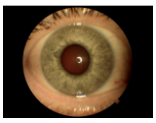


Keratoconus corneal map & stromal highlight tool

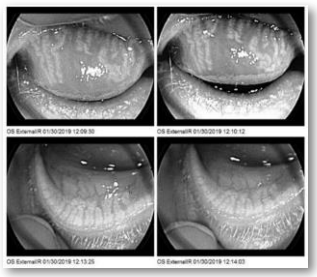




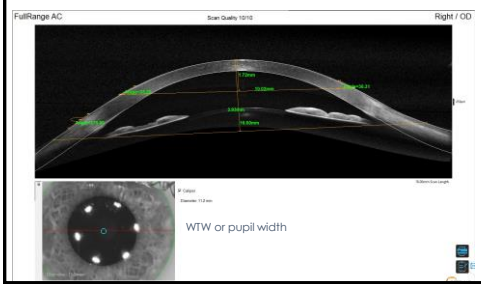
External color photography & IR


External Color Photograph


External Color Photograph with Red Reflex

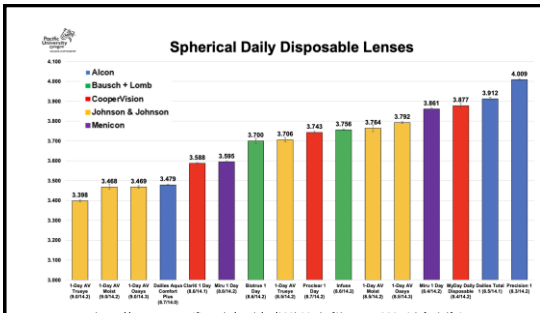


Structural measurement 16mm Chord

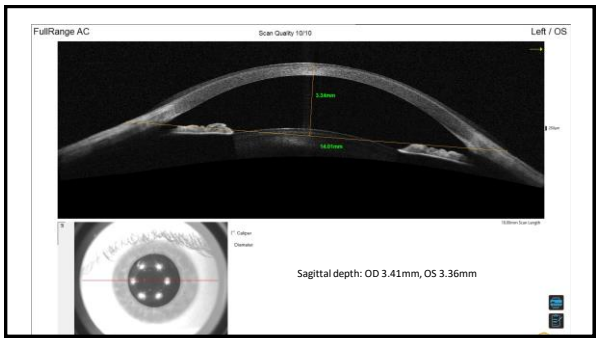


10mm Chord, 16 mm Chord with Sagittal depths 1.72mm 3.93mm

WTW or pupil width

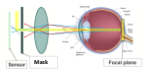


https://commons.pacificu.edu/work/ns/380b99ad-5f0b-4e77-a286-a8d1f74bdfe9



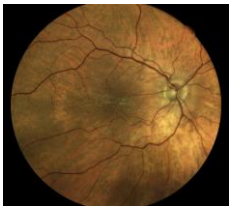
Sagittal depth: OD 3.41mm, OS 3.36mm

TrueColor Confocality

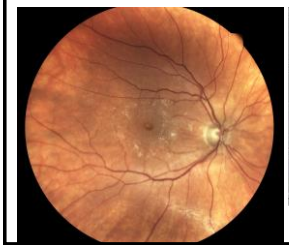


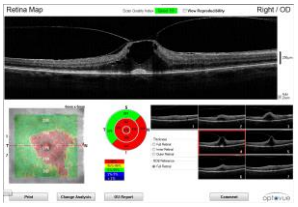
Confocal systems employ a very **thin beam** of light to scan the retina, and a **mask** that blocks the light reflected by layers that are far from the focal plane.

Differently from other Confocal systems that use monochromatic lasers, EIDON uses **white LED** illumination, thus providing **TrueColor images**.

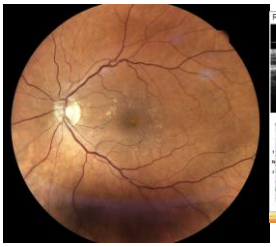


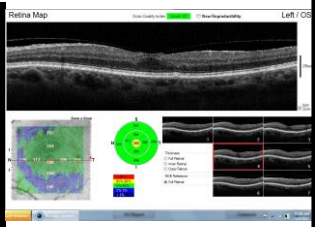
Macular findings

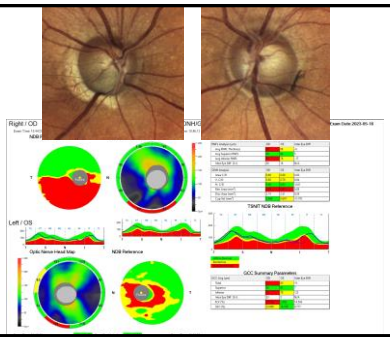




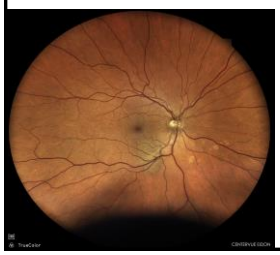
Macular findings

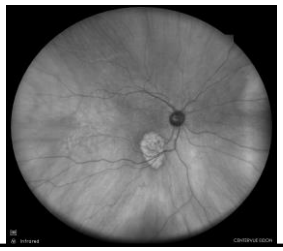






Choroidal Nevus





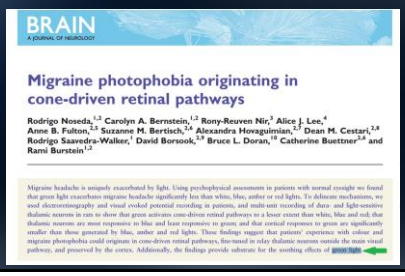
Retinoschisis change??

#9 Headache help

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.

Severe Headache & Migraine Sufferers: Breakthrough *Burstein et al*

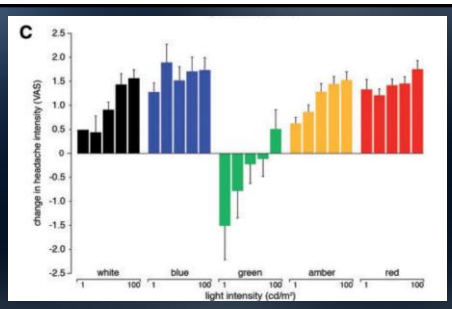


BRAIN
A JOURNAL OF NEUROLOGY

Migraine photophobia originating in cone-driven retinal pathways

Rodrigo Noseda,[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 Hovaguimian,[2,7] Dean M. Cestari,[2,8] Rodrigo Saavedra-Walker,[1] David Borsook,[2,9] Bruce L. Doran,[10] Catherine Buettner[2,8] and Rami Burstein[1,2]

Migraine headache is uniquely exacerbated by light. Using psychophysical assessments in patients with normal eyesight we found that green light exacerbates migraine headache significantly less than white, blue, amber or red lights. To delineate mechanisms, we used electroretinography and visual evoked potential recording in patients, and multi-unit recording of dura- 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; that 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 lights. These findings suggest that patients' experience with colour and migraine photophobia could originate in cone-driven retinal pathways, fine-tuned in relay thalamic neurons outside the main visual pathway, and preserved by the cortex. Additionally, the findings provide substrate for the soothing effects of green lights



Percept – MiWear Avulux

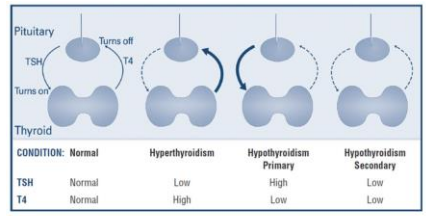
- Migraine
  - Estimated annual costs of $17 billion (U.S.)
  - Affects more than 40 million people (U.S.)
- Opportunity to help migraine sufferers live and function without optical noise

#10 New Thyroid Eye Disease Treatment

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

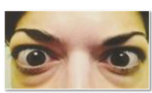
Thyroid Gland Function



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

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



From *The New England Journal of Medicine*, Terry J. Smith, Laszlo Hegedüs, Graves' disease, 375, 1553. Copyright ©2019 Massachusetts Medical Society. Reprinted with permission.[8]

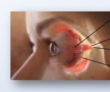
Figure is from Chapter 18 of the Thyroid section of Endotext, a free online endocrine textbook (Endotext.org). Reprinted with permission.[9]

1. Bothun ED, et al. *Clin Ophthalmol.* 2009;3:543-551. 2. Barrio-Barrio J, et al. *J Ophthalmol.* 2015;2015:249125. 3. Bartalena L, et al. *Endocr Rev.* 2000;21(2):168-199. 4. Yeatts RP. *Trans Am Ophthalmol Soc.* 2005;103:368-411. 5. Kahaly GJ, et al. *Clin Endocrinol.* 2005;63:395-402. 6. Abraham-Nordling M, et al. *Eur J Endocrinol.* 2010;163:651-657. 7. Ponto KA, et al. *Dtsch Arztebl Int.* 2009;106(17):283-289. 8. Smith TJ, Hegedüs L. *N Engl J Med.* 2016;375:1552-1565. 9. Bartalena L. Graves' disease: complications. In: Feingold KR, Anawalt B, Boyce A, et al, eds. *Endotext.* South Dartmouth, MA: MDText.com Inc;2000.

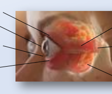
Inflammation, Tissue Expansion, and Eye Muscle Changes May Lead to the Clinical Manifestations of TED

Healthy Eye and Orbital Tissue[1]

- Eye is well protected by eyelid
- Thin periocular muscles
- Orbit contains a small amount of tissue and fat



In the Presence of TED[2]

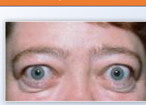


Activation of the IGF-1R/TSHR signaling complex on orbital fibroblasts triggers an inflammatory response, leading to tissue expansion and remodeling in the orbit[3-5]

1. Khazaeni LM. Merck manual professional website. https://www.merckmanuals.com/professional/eye-disorders/approach-to-the-ophthalmologic-patient/ophthalmic-anatomy?query=ophthalmic%20anatomy. Updated March, 2019. Accessed January 9, 2020. 2. Bahn RS. *N Engl J Med.* 2010;362:726-738. 3. Smith TJ, et al. *J Clin Endocrinol Metab.* 2004;89:5076-5080. 4. Smith TJ, et al. *N Engl J Med.* 2016;375(16):1552-1565. 5. Pritchard J, et al. *J Immunol.* 2003;170:6348-6354.

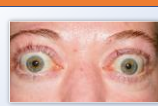
Recognizing the Signs and Symptoms of TED

Eyelid[1-3]



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

Orbital Tissue[1,3,4]



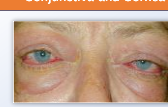
- Exophthalmos (proptosis): Occurs in 62% of patients
- Pain/deep ache
- Disfigurement

From Douglas RS, et al. *Thyroid Eye Disease.* 2015. Reprinted with permission.[5]

1. Bothun ED, et al. *Clin Ophthalmol.* 2009;3:543-551. 2. Liaboe C, et al. EyeRounds.org. https://webeye.ophth.uiowa.edu/eyeforum/tutorials/thyroid-eye-disease/. Published November 18, 2016. Accessed March 26, 2019. 3. Bartley GB, et al. *Am J Ophthalmol.* 1996;121(4):426-434. 4. Bahn RS. *N Engl J Med.* 2010;362:726-738. 5. Douglas RS, McCoy A, Gupta S. *Thyroid Eye Disease.* New York:Springer Science+Business Media;2015.

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

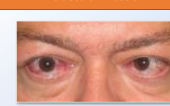
Conjunctiva and Cornea[1-3]



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

From Douglas RS, et al. *Thyroid Eye Disease.* 2015. Reprinted with permission.[4]

Extraocular Muscle[1,5]



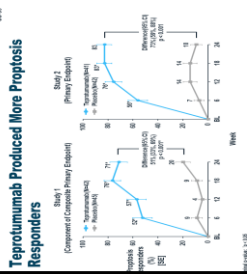
- Restricted ocular motility: Occurs in ~40% of patients
- Strabismus (misalignment of eye)
- Diplopia (double vision)
- Pain
- Retro-orbital ache
- Decreased vision and depth perception

Figure is from Chapter 18 of the Thyroid section of Endotext, a free online endocrine textbook (Endotext.org). Reprinted with permission.[6]

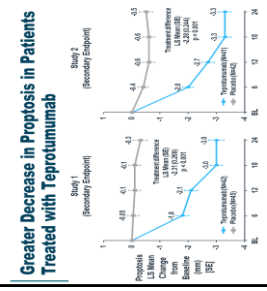
1. Bothun ED, et al. *Clin Ophthalmol.* 2009;3:543-551. 2. Bahn RS. *N Engl J Med.* 2010;362:726-738. 3. Liaboe C, et al. EyeRounds.org. https://webeye.ophth.uiowa.edu/eyeforum/tutorials/thyroid-eye-disease/. Published November 18, 2016. Accessed March 26, 2019. 4. Douglas RS, et al. *Thyroid Eye Disease.* New York: Springer Science+Business Media 2015. 5. Bartley GB, et al. *Am J Ophthalmol.* 1996;121(4):426-434. 6. Bartalena L. Graves' disease: complications. In: Feingold KR, Anawalt B, Boyce A, et al, eds. *Endotext.* South Dartmouth, MA: MDText.com Inc;2000.

Treatment – Teprotumumab (Tepezza)

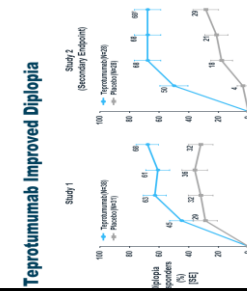
8 infusions - Treatr



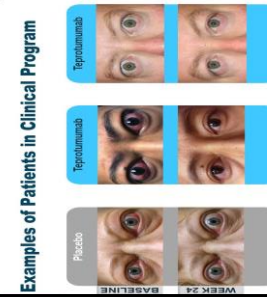
Treatment – T



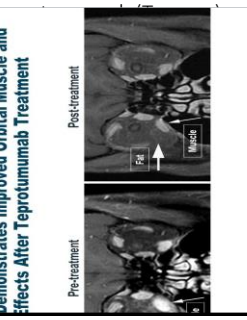
Treatment – T



Treatment –



Treatment



GlobeNewswire

Osmotica Pharmaceuticals

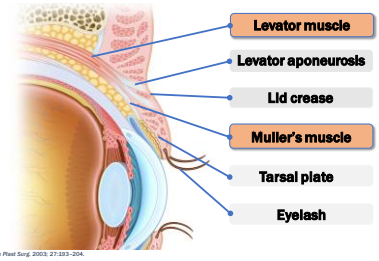
Osmotica Pharmaceuticals plc Receives FDA Approval for Upneeq™ (oxymetazoline hydrochloride ophthalmic solution), 0.1% for Acquired Blepharoptosis (Droopy Eyelid) in Adults

Email | Print Friendly | Share

Profile
Osmotica Holdings US LLC

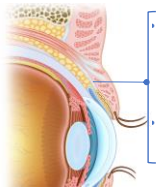
Jul 09, 2020 06:50 ET | Source: Osmotica Holdings US LLC

Lid Anatomy: Two Muscles Lift the Eyelid



Finsterer et al. *Aesth Plast Surg.* 2003; 27:193–204.

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

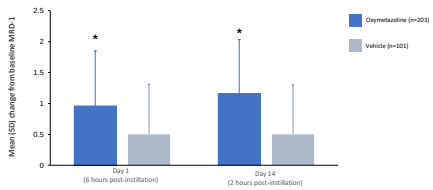


- Oxymetazoline is a potent, direct-acting **α-adrenergic receptor agonist[1,2]**
  - **≈5-fold greater affinity** for α2 receptors[3]*
- **Selectively activates α-adrenergic receptors in Müller's muscle[4]**

*Receptor binding affinity is defined via in vitro binding assays

1. Haeusler 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. Nosten LO, et al. *Clin Optom.* 2020;12:95-105. 4. Upneeq® (oxymetazoline hydrochloride ophthalmic solution), 0.1%. [Prescribing Information]. RVL Pharmaceuticals, Inc. 2020.

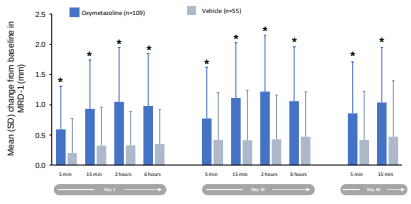
Oxymetazoline Significantly Increased Upper Eyelid Lift in Two Clinical Studies



Pooled 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, pseudoptosis or substantial dermatochalasis (redundant eyelid skin occurring within 3 mm of the upper eyelid margin), or visual field loss from any cause other than ptosis were excluded from both trials.

Slonim CB, et al. *JAMA Ophthalmol.* 2020;138(11):1168-1175.

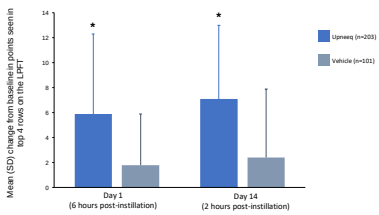
Oxymetazoline Provided a Rapid and Sustained Effect Over 42 Days



Data from 6-week, randomized, double-masked, placebo-controlled clinical trial (RVL-1201-202); p<0.05 vs. vehicle, from an ANCOVA model with treatment as a fixed factor and baseline score as a covariate.

Bacharach J, et al. *Clin Ophthalmol.* 2021:15 2743-2751

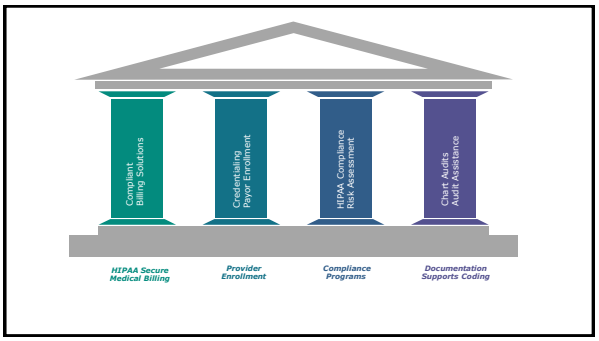
Oxymetazoline Significantly Improved Superior Visual Field Deficits

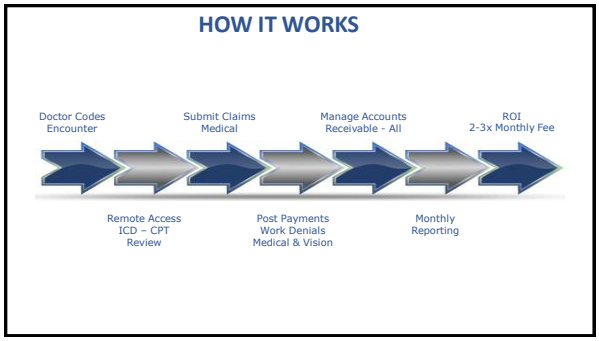


Pooled data from two 6-week, randomized, double-masked, placebo controlled clinical trials; p<0.0001 vs. vehicle, from an ANCOVA model with study and treatment as fixed factors and baseline score as a covariate.

Slonim CB, Foster S, Jaros M, et al. *JAMA Ophthalmol.* 2020;138(11):1168-1175.


#12 Billing and Coding Evolution


Compliant Billing Solutions
Credentialing Payor Enrollment
HIPAA Compliance Risk Assessment
Chart Audits Audit Assistance
HIPAA Secure Medical Billing
Provider Enrollment
Compliance Programs
Documentation Supports Coding


HOW IT WORKS
Doctor Codes Encounter
Submit Claims Medical
Manage Accounts Receivable - All
ROI 2-3x Monthly Fee
Remote Access ICD – CPT Review
Post Payments Work Denials Medical & Vision
Monthly Reporting


Thank You
mile.brujic75@gmail.com