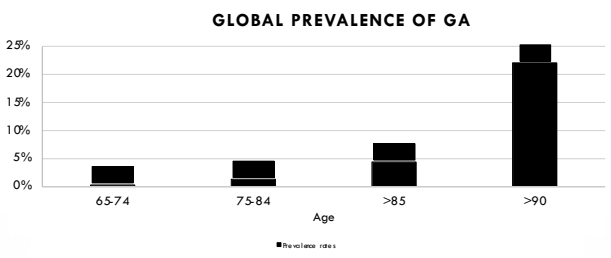
## HOT TOPICS IN RETINA!


- STEVEN FERRUCCI OD
  - CHIEF, OPTOMETRY SEPULVEDA VA
  - PROFESSOR, SCCO
- MARK DUNBAR, OD, FAAO
  - BASCOM PALMER EYE INSTITUTE


1

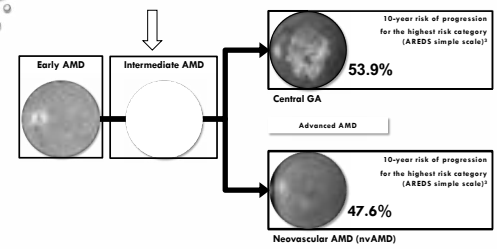
## GA CURRENTLY AFFECTS >5 MILLION PEOPLE WORLDWIDE




RUDNICKA A, ET AL. OPHTHALMOLOGY, 2012;119:571–80. 2. WONG ET AL, LANCET GLOB HEALTH 2014;2:E106–16.

2

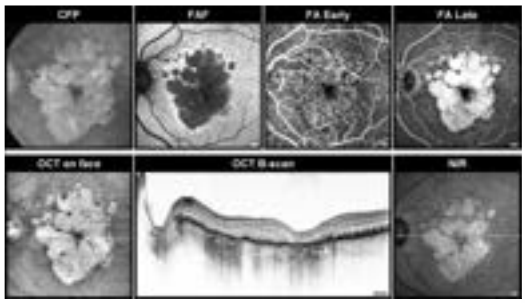
## STAGING OF AMD




AMD, age-related macular degeneration; AREDS, Age-related Eye Disease Study; GA, geographic atrophy; nvAMD, neovascular AMD.
1. Eye Diseases Prevalence Research Group. Arch Ophthalmol. 2004;122(4):477-485. 2. Ferris FL, et al. Ophthalmology. 2013;120(4):844-851. 3. Chew EY, et al. JAMA Ophthalmol. 2014;132(3):272-277. 4. Age-Related Study Disease Study Research Group. Arch Ophthalmol. 2005;123(11):1570-1574.

3

## MULTIMODAL IMAGING OF GA



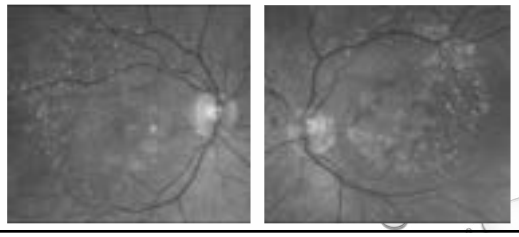

Reprinted with permission from Fleckenstein M, et al. The progression of geographic atrophy secondary to age-related macular degeneration. Ophthalmology. 2018;125(3):369-390. Copyright 2017 by the American Academy of Ophthalmology.

CFP, color fundus photography; FA, fluorescein angiography; FAF, fundus autofluorescence; NIR, near-infrared reflectance.

4

## GA IMAGING- COLOR FUNDUS PHOTOGRAPHY (CFP)

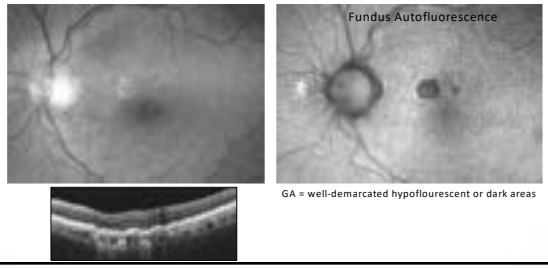
- A sharply demarcated, usually circular zone of partial or complete RPE depigmentation, typically with exposure of underlying large choroidal blood vessels
- **Less sensitive in detecting early GA** and NOT an ideal way track enlargement over time



5

## GA IMAGING - FUNDUS AUTOFLUORESCENCE (FAF)

**ONE OF THE PRIMARY METHODS USED TO DETECT & MONITOR GA LESIONS (SUPERIOR FOR EARLY GA DETECTION COMPARED TO CFP)!!!**




GA = well-demarcated hypoflourescent or dark areas

6

## GA IMAGING - FUNDUS AUTOFLUORESCENCE (FAF)

**ONE OF THE PRIMARY METHODS USED TO DETECT, MONITOR, AND QUANTIFY GA LESIONS!!!**

7

## GA IMAGING - OCT ANGIOGRAPHY (OCTA) IMAGING OF GA

Highlights loss of the choriocapillaris!!! (allows for visualization of the deep/larger choroidal vessels)

8

## GEOGRAPHIC ATROPHY FEATURES ON OCT

Zone of RPE loss/attenuation & overlying PR degeneration ≥ 250µm in diameter

**HYPER-TRANSMISSION**

9

## OCT En-Face ANALYSIS (Sub-RPE Slab) - GA

**GA area enlarges over time**

**Distance to center of fovea**

10

## PROGRESSION

**FASTER PROGRESSION!!!**

| | | |
|---|---|---|
| Central | Extrafoveal | |
| Monofocal | Multifocal | |
| Smaller lesions | Larger lesions | |

AREDS2 Report #16: Progression of GA in ARMD

**Bilateral GA**

Keenan TD, et al. AREDS2 Research Group. Progression of GA in ARMD: AREDS2 Report #16. Ophthalmology 2018
Heesterbeek M, et al. The progression of GA secondary to ARMD. Ophthalmology. 2018

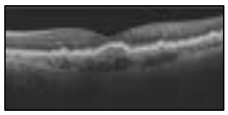
11

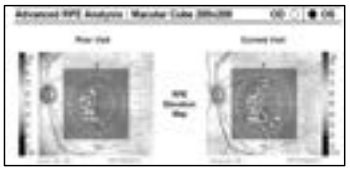
## OCT BIOMARKERS MAY HELP PREDICT CONVERSION TO GA OR WET AMD

12

## OCT BIOMARKERS MAY HELP PREDICT CONVERSION TO GA OR WET AMD

- DRUSEN VOLUME
- INCREASED DRUSEN HEIGHT
- ABNORMAL THINNING OF THE RPE LAYER

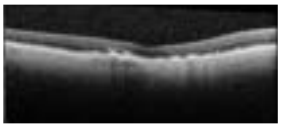


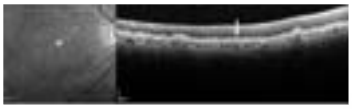


13

## OCT BIOMARKERS MAY HELP PREDICT CONVERSION TO GA OR WET AMD

- HYPER-REFLECTIVE FOCI (HRF)
- RETUCULAR PSEUDO DRUSEN
- HYPER-TRANSMISSION DEFECTS
- OCT-REFLECTIVE DRUSEN SUBSTRUCTURES





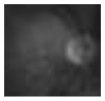
*Life* **2022**, *12*, 34. https://doi.org/10.3390/life12010034 https://www.mdpi.com/journal/life

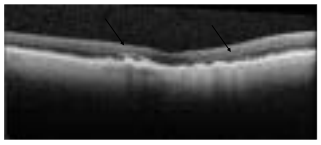
14

## OCT BIOMARKERS MAY HELP PREDICT CONVERSION TO GA OR WET AMD

HYPER-REFLECTIVE FOCI (HRF)

- EXTRACELLULAR PIGMENT GRANULES AND OUTER SEGMENT DEBRIS (OUTER HRF)
- MAY ALSO REPRESENT DISPLACEMENT AND CLUMPING OF DEGENERATED RPE CELLS
- AREDS2 STUDY: **PATIENTS WITH HRF HAD 5 X INCREASED RISK OF PROGRESSION TO GA AT 2 YEARS VS. CONTROLS**



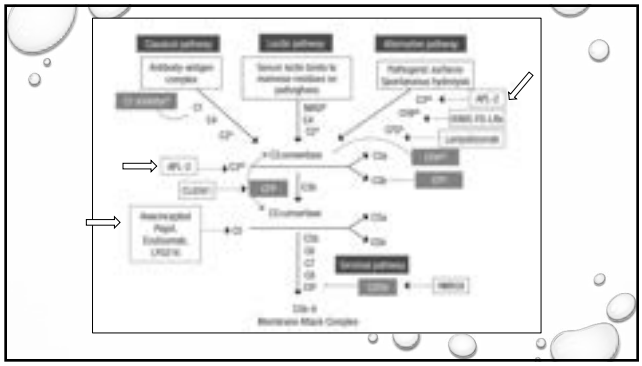


15

## GEOGRAPHIC ATROPHY

- LESIONS GROW WITH TIME, AT VARIOUS RATES
  - LARGER LESIONS, MULTI-FOCAL LESIONS, EXTRAFOVEAL LESIONS GROW FASTER
- TREATMENT GEARED AT DECREASE IN LESION GROWTH
- GROWTH ASSOCIATED WITH OVER-ACTIVATION OF COMPLEMENT SYSTEM
  - VARIOUS TARGETS BEING INVESTIGATED: C3, C5

16



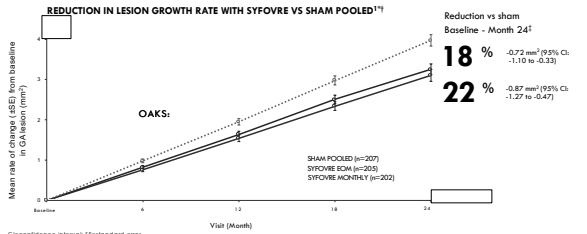
17

## SYFOVRE™

- PEGCETACOPLAN
- FDA APPROVED FEB 17, 2023
- FIRST FDA APPROVED MED FOR TREATMENT OF GA
- 15 MG (0.1 ML OF 150 MG/ML) ADMINISTERED BY INTRAVITREAL INJECTION TO AFFECTED EYE ONCE EVERY 25 TO 60 DAYS

18

## SYFOVRE ACHIEVED CONTINUOUS REDUCTIONS IN LESION GROWTH RATE THROUGH MONTH 24[1,2] (OAKS)



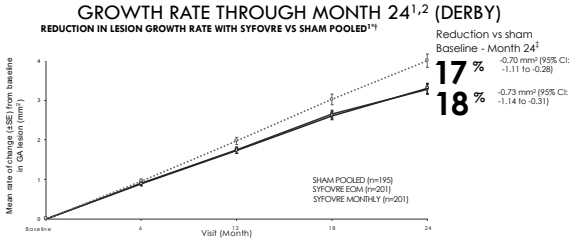

CI=confidence interval; SE=standard error.
*Based on a mixed effects model for repeated measures assuming a piecewise linear trend in time with knots at Month 6, Month 12, and Month 18.[1]
†SHAM EOM and SHAM Monthly were pooled for analysis.[2]
‡Slope for baseline to Month 24 is an average of slope of baseline to Month 6, Month 6 to Month 12, Month 12 to Month 18, and Month 18 to Month 24.[1]

1. SYFOVRE (pegcetacoplan injection) [package insert]. Waltham, MA: Apellis Pharmaceuticals, Inc; 2023. 2. Data on file. Apellis Pharmaceuticals, Inc.

19

19

## SYFOVRE ACHIEVED CONTINUOUS REDUCTIONS IN LESION GROWTH RATE THROUGH MONTH 24[1,2] (DERBY)




*Based on a mixed effects model for repeated measures assuming a piecewise linear trend in time with knots at Month 6, Month 12, and Month 18.[1]
†SHAM EOM and SHAM Monthly were pooled for analysis.[2]
‡Slope for baseline to Month 24 is an average of slope of baseline to Month 6, Month 6 to Month 12, Month 12 to Month 18, and Month 18 to Month 24.[1]

1. SYFOVRE (pegcetacoplan injection) [package insert]. Waltham, MA: Apellis Pharmaceuticals, Inc; 2023. 2. Data on file. Apellis Pharmaceuticals, Inc.

20

20

**OAKS and DERBY Combined:**

## Adverse Reactions in Study Eye Reported in ≥2% of Patients Treated With SYFOVRE Through Month 24

| | SYFOVRE MONTHLY (n=419) | SYFOVRE EOM (n=420) | SHAM POOLED (n=417) |
|---|---|---|---|
| Ocular discomfort* | 13% | 10% | 11% |
| Neovascular AMD* | 12% | 7% | 3% |
| Vitreous floaters | 10% | 7% | 1% |
| Conjunctival hemorrhage | 8% | 8% | 4% |
| Vitreous detachment | 4% | 6% | 3% |
| Retinal hemorrhage | 4% | 5% | 3% |
| Punctate keratitis* | 5% | 3% | <1% |
| Posterior capsule opacification | 4% | 4% | 3% |
| Intraocular inflammation* | 4% | 2% | <1% |
| Intraocular pressure increased | 2% | 3% | <1% |

- 839 patients were exposed to SYFOVRE
- Endophthalmitis, retinal detachment, hyphema and retinal tears were reported in <1% of patients
- Optic ischemic neuropathy was reported in 1.7% of patients treated monthly, 0.2% of patients treated every other month and 0.0% of patients assigned to sham
- Deaths were reported in 6.7% of patients treated monthly, 3.6% of patients treated every other month, and 3.8% of patients assigned to sham. The rates and causes of death were consistent with the elderly study population

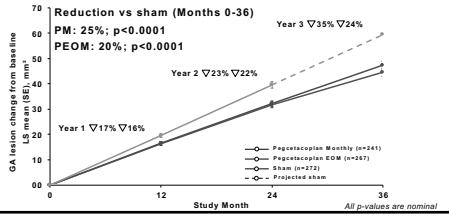
*The following reported items were combined:
- **Ocular discomfort** included: eye pain, eye irritation, foreign body sensation in eyes, ocular discomfort, abnormal sensation in eye
- **Neovascular age-related macular degeneration included**: exudative age-related macular degeneration, choroidal neovascularization
- **Punctate keratitis** included: punctate keratitis, keratitis
- **Intraocular inflammation** included: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, anterior chamber flare

SYFOVRE (pegcetacoplan injection) [package insert]. Waltham, MA: Apellis Pharmaceuticals, Inc; 2023.

21

21

## GALE TOTAL POPULATION (NONSUBFOVEAL + SUBFOVEAL): REDUCTIONS IN GA GROWTH FOLLOWING 36 MONTHS OF **CONTINUOUS** PEGCETACOPLAN INCREASED OVER TIME



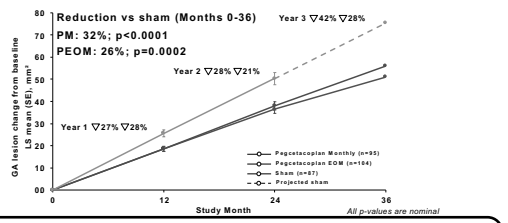

**1.49 mm² (PM) & 1.21 mm² (PEOM) of Retinal Tissue Preserved Over 36 Months**

LS means estimated from a piecewise linear mixed-effects model that evaluated mean rate of change in GA area between pegcetacoplan arms and sham arm from baseline to Month 36, with knots at Months 12 and 24 allowing for the slope to be linear over each of the 12-month segments but to differ between segments (piecewise slope analysis). Mean rate of change of hypothetical sham from Month 24 to Month 36 was estimated from the mean rate of change in each period from Month 0 to Month 24. The modified full analysis set was used for the analysis, defined as patients who are in OAKS/DERBY antecedent study's ITT set, have not been enrolled in APL2-103, and received ≥1 injection of pegcetacoplan in GALE. Projected sham is shown with a dashed line. Data shown for patients who continued into the GALE trial after OAKS & DERBY. **EOM**, every other month; **GA**, geographic atrophy; **ITT**, intent to treat; **LS**, least-squares; **PEOM**, pegcetacoplan every other month; **PM**, pegcetacoplan monthly; **SE**, standard error.

22

22

## GALE NONSUBFOVEAL SUBGROUP (N=286 EYES): REDUCTIONS IN GA GROWTH WITH 36 MONTHS OF **CONTINUOUS** PEGCETACOPLAN




**2.44 mm² (PM) & 1.94 mm² (PEOM) of Retinal Tissue Preserved Over 36 Months**

LS means estimated from a piecewise linear mixed-effects model that evaluated mean rate of change in GA area between pegcetacoplan arms and sham arm from baseline to Month 36, with knots at Months 12 and 24 allowing for the slope to be linear over each of the 12-month segments but to differ between segments (piecewise slope analysis). Mean rate of change of hypothetical sham from Month 24 to Month 36 was estimated from the mean rate of change in each period from Month 0 to Month 24. The modified full analysis set was used for the analysis, defined as patients who are in OAKS/DERBY antecedent study's ITT set, have not been enrolled in APL2-103, and received ≥1 injection of pegcetacoplan in GALE. Projected sham is shown with a dashed line. Data shown for patients who continued into the GALE trial after OAKS & DERBY. **EOM**, every other month; **GA**, geographic atrophy; **ITT**, intent to treat; **LS**, least-squares; **PEOM**, pegcetacoplan every other month; **PM**, pegcetacoplan monthly; **SE**, standard error.

23

23

## IZERVAY™

- AVACINCAPTAD PEGOL (ACP)
- FDA APPROVED AUGUST 5, 2023
- APPROVED FOR THE TREATMENT OF GA SECONDARY TO AMD
- 2 MG MONTHLY INJECTIONS

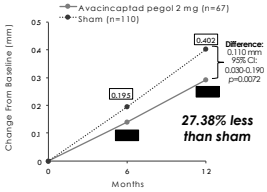
24

24

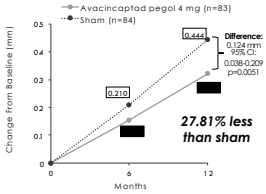
## AVACINCAPTAD PEGOL SIGNIFICANTLY REDUCED THE MEAN GA GROWTH RATE OVER 12 MONTHS COMPARED WITH SHAM[1]

GATHER1 PRIMARY END POINT (SQUARE ROOT TRANSFORMATION)

**Avacincaptad pegol 2 mg vs sham[1,2]**




**Avacincaptad pegol 4 mg vs sham[1,2]**

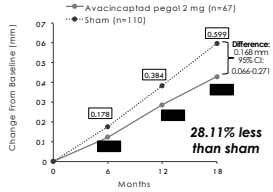



Note: Based on LS means from MRM; for ITT population. Hochberg procedure was used for significance testing. These LS means are estimates from the MRM, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data.
**1.** Jaffe GJ, et al. Ophthalmology. 2021;128:576-586. **2.** Data on file. IVERIC Bio.

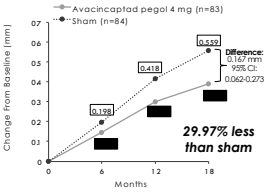
25

## CONTINUOUS TREATMENT EFFECT AND SEPARATION FROM SHAM OBSERVED OVER 18 MONTHS (SQUARE ROOT TRANSFORMATION)

**Avacincaptad pegol 2 mg vs sham**




**Avacincaptad pegol 4 mg vs sham**




Note: Based on LS means from MRM; for ITT population. Hochberg procedure was used for significance testing; prespecified and descriptive analysis. These LS means are estimates of the MRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data.
CI: confidence interval; GA, geographic atrophy; ITT, intent-to-treat; LS, least square; MRM, mixed-regression model.
Data on file. IVERIC Bio.

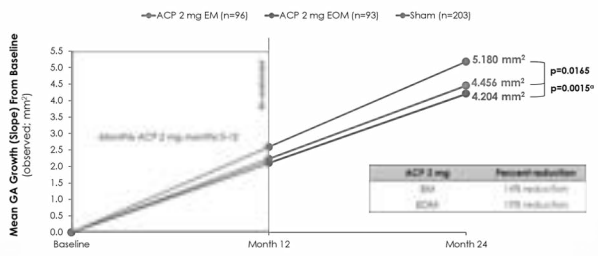
26

## OCULAR TEAES ≥2% IN STUDY EYE

| | 12 Months[1,2,a] | | 12 Months[2] | |
|---|---|---|---|---|
| **Ocular TEAEs, n (%)** | [redacted] | [redacted] | [redacted] | [redacted] |
| Conjunctival hemorrhage | 10 (14.9) | 13 (11.8) | 27 (12.0) | 17 (7.7) |
| Punctate keratitis | 4 (6.0) | 8 (7.3) | 11 (4.9) | 14 (6.3) |
| Conjunctival hyperemia | 3 (4.5) | 4 (3.6) | 12 (5.3) | 13 (5.9) |
| Choroidal neovascularization | **6 (9.0)** | 3 (2.7) | **15 (6.7)** | 9 (4.1) |
| Dry eye | 0 | 2 (1.8) | 8 (3.6) | 8 (3.6) |
| Eye pain | 2 (3.0) | 3 (2.7) | 9 (4.0) | 6 (2.7) |
| Vitreous detachment | 2 (3.0) | 5 (4.5) | 7 (3.1) | 6 (2.7) |
| Visual acuity reduced | 2 (3.0) | 4 (3.6) | 3 (1.3) | 5 (2.3) |
| Vision blurred | 1 (1.5) | 2 (1.8) | 6 (2.7) | 2 (0.9) |
| Visual impairment | 0 | 0 | 6 (2.7) | 2 (0.9) |
| Intraocular pressure increased | **4 (6.0)** | 1 (0.9) | **21 (9.3)** | 2 (0.9) |
| Vitreous floaters | 1 (1.5) | 1 (0.9) | 6 (2.7) | 1 (0.5) |
| Visual acuity reduced transiently | --- | --- | 6 (2.7) | 1 (0.5) |
| Blepharitis | 0 | 1 (0.9) | 6 (2.7) | 0 |
| Ocular hypertension | --- | --- | 5 (2.2) | 0 |

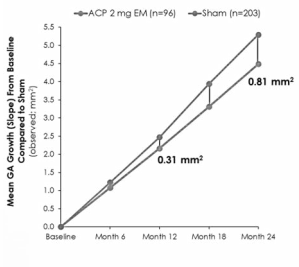
27

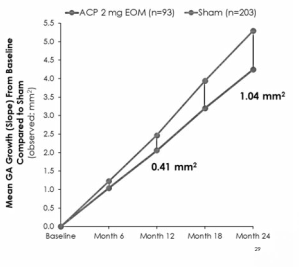
## ACP REDUCED GA GROWTH WHEN DOSED EM AND EOM VS SHAM




28

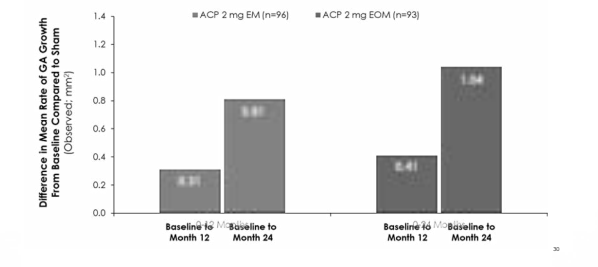
## EARLY TREATMENT EFFECT OBSERVED BY 6 MONTHS AND INCREASED OVER TIME THROUGH 2 YEARS




29

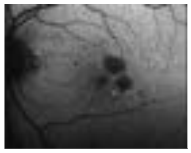
## TREATMENT EFFECT VS SHAM MORE THAN DOUBLED WITH ACP 2 MG EM AND EOM OVER 2 YEARS COMPARED TO THE TREATMENT EFFECT OVER 1 YEAR

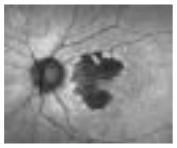



30

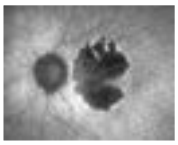
## WHEN TO REFER?

- ANY GA THAT IS **THREATENING** CENTRAL VISUAL FUNCTION
- ANY GA THAT IS BEGINNING TO INVOLVE THE FOVEA
  - LIKELY ALREADY HAVING REDUCED VA
- LARGE EXTRAFOVEAL LESIONS





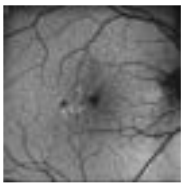
Progression to subfoveal involvement 18 mo

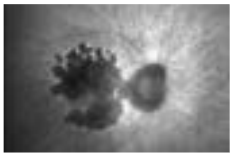


31

## WHEN TO REFER?

- EXTRAFOVEAL LESIONS THAT ARE NOT A THREAT TO CENTRAL VA?
- CENTRAL GA LESIONS THAT HAVE ALREADY HAVE SIG LOSS OF VISUAL FUNCTION?





32

## Valeda® Light Delivery System

**VALEDA OVERVIEW**

- Valeda treatment delivery very similar to many ophthalmology office diagnostic and treatment devices
- Implementation support available from LumiThera Customer Success Team
- Treatment is simple to learn and easy to train for operators
- No pupil dilation required
- Nine (9) flexible treatment sessions delivered over 3–4 weeks
- 2-3 treatment cycles per annum

33

## Photobiomodulation (PBM) Approach

PBM uses low-level light to stimulate cells to restore energy production and improve cellular health

| Valeda Wavelengths (nm) | Cellular Targets | Secondary Effects |
|---|---|---|
| 590 | Stimulates CCO activity, increases nitric oxide (NO) synthesis, inhibits VEGF expression | Vasodilation, Improves local $O_2$ and nutrient delivery, VEGF reduction |
| 660 | Promotes $O_2$ binding to CCO active $Cu_A/Fe_{a3}$ site | Upregulates Electron Transport Pathway, Increases energy (ATP), Reduces Inflammation and cell death |
| 850 | Drives electron transfer at $Cu_A$ site of CCO | Upregulates Electron Transport Pathway, Increases energy (ATP), Reduces Inflammation and cell death |

PHOTONS ARE ABSORBED BY PHOTOACCEPTORS IN THE TARGETED TISSUE MITOCHONDRIAL PROTEIN, CYTOCHROME C OXIDASE (CCO) TO RESTORE ENERGY PRODUCTION

SUSTAINED CELLULAR CHANGES ALSO OCCUR THROUGH ACTIVATION OF TRANSCRIPTION FACTORS

*Wong-Riley MTT, et al. J Biol Chem. 2005; 280: 4761-71; Ball KA, et al. J Photochem Photobiol B Biol, 2012; 102: 182-91.*

**Valeda wavelengths were selected based on their cellular targets and importance in AMD**

34

## FDA AUTHORIZES BREAKTHROUGH VALEDA THERAPEUTIC FOR DRY AMD TO IMPROVE VISION (NOVEMBER 04, 2024)

**Valeda Light Delivery System**

- Five successful clinical studies
- US LIGHTSITE III pivotal trial data met BCVA primary endpoint
- Data from two-year LIGHTSITE III trial used to support Valeda FDA submission
- First FDA authorized therapy for Dry AMD Patients to improve vision
- CE marked: Available in Europe and other countries
- Non–invasive, safe therapy for patients

35

## First FDA treatment for Dry AMD Patients to Improve Vision

**Indications for Use:**

The Valeda Light Delivery System is intended to provide improved visual acuity in patients with best corrected visual acuity (BCVA) of 20/32 through 20/70 and who have dry age-related macular degeneration (AMD) characterized by:

- The presence of at least 3 medium drusen (> 63 µm and 125 µm in diameter), or large drusen (> 125 µm in diameter), or non-central geographic atrophy, AND
- The absence of neovascular maculopathy or center-involving geographic atrophy

After about two years, the Valeda Light Delivery System treatment provides improved mean visual acuity of approximately one line of visual acuity (ETDRS) compared to those not receiving the treatment.

36

## LIGHTSITE III: US PIVOTAL 24-MONTH STUDY

The LIGHTSITE III study was an FDA, IDE-approved, prospective, double-masked, randomized, sham-controlled, parallel group, multi-center study to assess the safety and efficacy of photobiomodulation (PBM) in subjects with dry age-related macular degeneration (AMD)

37

## LIGHTSITE III: SAFETY SUMMARY

- Similar frequencies of adverse events (AE) (Sham, 25.5%; PBM, 25.8%) and ocular-specific AEs (Sham, 20.0%; PBM, 22.6%) observed between treatment groups
- Three subjects had ocular-specific AEs considered related to the procedure: punctate keratitis (Sham; n = 2; 3.6%), visual perseveration (after image) (Sham; n = 1; 1.8%), and application site warmth (PBM; n = 1; 1.1%). No ocular-specific AEs led to study discontinuation.
- Seven (7.5%) ocular-specific serious adverse events (SAE) of nAMD were reported in the PBM group and three (5.5%) ocular-specific SAEs (2 nAMD, 1 cystoid macular edema) were reported in the Sham group. No SAEs were considered associated to the treatment by the primary investigator.
- Severity of AEs reported were mostly mild/moderate in both treatment groups
- No signs of phototoxicity
- No adverse effect on color vision or perimetry

38

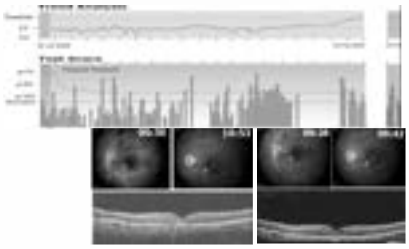
## LIGHTSITE III: STUDY SUMMARY

**LIGHTSITE III study results show significant effect on clinical and anatomical outcomes that support vision improvement and disease modifying effects**

- LIGHTSITE III met the primary efficacy endpoint with a statistically significant improvement in BCVA in the PBM versus the Sham group
- Eyes with worse BCVA at baseline showed larger magnitude gains in BCVA
- Increased rate of > 5, 10, and 15 letter BCVA gains following PBM compared to BCVA loss in the Sham group
- Cox proportional analyses showed a significant reduction in the hazard ratios for BCVA vision loss and incident GA in PBM vs Sham treatment groups
- Reduced occurrence of incident GA and other exploratory markers of disease progression
- Reduced macular drusen volume
- Improved QoL in VFQ-25 Composite score and select subscales
- A favorable safety profile was observed with no signs of phototoxicity and no deterioration in other visual outcomes, including contrast sensitivity, low luminance BCVA, Radner reading, perimetry, or color vision observed

39

## FORESEE HOME



40

## At-risk Patients May Convert to Wet AMD at Any Point Between Follow-up Visits

Visit **1**

Visit **2**

| Converts after office visit | Converts between office visits | Converts before office visit |
|---|---|---|
| More likely to lose vision | | Less likely to lose vision |

**Reference:** Rauch R, et al. *Retina*. 2012;32(7):1260-1264.

41

41

## Amsler grid alone has limited ability to detect visual changes

**Accurately taking the test[1,2]**
- Fixation
- Testing distance
- Test questions
- Compliance

**Cortical completion[1]**

**Low sensitivity; subjectivity exam to exam, patient to patient[1]**

**References:** 1. Midena E, Vujosevic S. *Ophthalmic Res*. 2015;55(1):24-36. 2. Isaac DL, et al. *Arq Bras Oftalmol*. 2007;70(5):771-776. 3. Liu TY, et al. *JAMA Ophthalmol*. 2015;133(12):1355-360. 4. Wong TY, et al. *Ophthalmology*. 2008;115(1):116-126.

42

42

## ForeseeHome® product overview


**Reference:** Data on File.

43

## AREDS2-HOME STUDY

| ForeseeHome plus standard care arm | Intent to Treat (ITT) population results | Standard care arm |
|---|---|---|
| 763 participants | 1520 participants | 757 participants |
| 51 CNV events | Mean follow up 1.4 yr ± 0.6 years<br>Mean VA at entry 20/25 | 31 CNV events |
| • Routine monitoring<br>• Patient symptoms<br>• ForeseeHome | | • Routine monitoring<br>• Patient symptoms |

***Primary outcome:** Change in BCVA from baseline to CNV detection*

**Reference:** AREDS2-HOME Study Research Group. Ophthalmology. 2014;121(2):535-544.

44

## FORESEEHOME ARM

Intent to Treat (ITT)

Per Protocol 1 (PP1)

Per Protocol 2 (PP2)

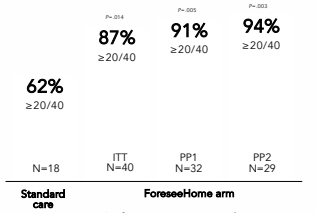
**at least 1 test throughout the study**

**≥ 2x per week (8x per month)**

**Reference:** AREDS2-HOME Study Research Group. Ophthalmology. 2014;121(2):535-544.

45

## MORE PATIENTS WHO USED FORESEEHOME MAINTAINED ≥20/40 VA




**50% MORE** patients maintained 20/40 or better when using ForeseeHome vs standard of care alone

***94% of patients maintained 20/40 at time of wet AMD diagnosis; Absolute visual acuity at time of wet AMD diagnosis is critical to visual acuity outcomes at year 1***

**Reference:** AREDS2-HOME Study Research Group. Ophthalmology. 2014;121(2):535-544.

46

## HOME OCT

- SCANLY AI POWERED HOME OCT APPROVED 5/16/24
- TWO US TRIALS OVER 500 PTS
  - SAFE AND EFFICACIOUS WAY TO VISUALIZE INTRA AND SUB-RETINAL EDEMA
  - 5,426 SCANS PERFORMED, 97% SUCCESSFUL
  - ADHERENCE OF 5.9 SCANS/WEEK
  - SELF-IMAGING TOOK 44 SECONDS ON AVERAGE

47

## HOME OCT

- Monitoring of intra- and subretinal fluid based on daily patient self-imaging
  - Easy-to-use, patient-operated device
  - Takes less than one minute per eye
  - AI algorithm analyzes images on cloud
  - Remote diagnostic clinic, provider of monitoring program, reports changes meeting physician-selected fluid volume thresholds to referring physician
  - 24/7 physician access to all data
- GREAT WAY FOR RETINA MDS TO KNOW WHEN NEXT INJECTION TRULY NEEDED

48

## IS AMD IN OUR DNA?

- **AMD IS A GENETIC DISEASE WITH KNOWN MARKERS ACCOUNTING FOR AT LEAST 70% OF THE POPULATION ATTRIBUTABLE RISK**
- **OTHER 30% IS ENVIRONMENTAL/LIFESTYLE**
- **RISK FACTORS**
  - **NON-MODIFIABLE: AGE, RACE, GENDER**
  - **MODIFIABLE: SMOKING, INCREASED BMI, POOR DIET/NUTRITION, UV EXPOSURE**

49

## HOW CAN WE USE THIS INFORMATION?

- INCREASED SURVEILLANCE FOR THOSE AT HIGHER RISK
  - SOONER/MORE FREQUENT APPOINTMENTS
  - MORE DILIGENT HOME MONITORING
- MORE DILIGENCE WITH MODIFIABLE RISK FACTORS
- CONSIDER EARLIER VITAMIN SUPPLEMENTATION
- POTENTIAL TREATMENTS IN THE FUTURE

50

## AMD RISK TESTING FOR A FULL SPECTRUM OF PATIENTS

AMDIGUARD DNA PROGRESSION ASSESSMENT

FOR PEOPLE ≥55YO WITH OR WITHOUT AMD FINDINGS

FOR PEOPLE <55YO WITH AMD FINDINGS

- ASSESSES A PATIENT'S RISK OF PROGRESSION TO ADVANCED AMD WITHIN 2, 5,10, 20 AND 30 YEARS
- DELAYING PROGRESSION TO ADVANCED AMD WITH SECONDARY PREVENTION INCLUDING AREDS VITAMINS, INCREASED SURVEILLANCE (HOME MONITORING)

AMDIGUARD DNA RISK ASSESSMENT

FOR PEOPLE <55YO WITHOUT AMD FINDINGS

- ASSESSES A PATIENT'S LIFETIME RISK OF DEVELOPING ADVANCED AMD (GA OR CNV) *ALLOWING PREVENTIVE LIFESTYLE CHANGES AT YOUNGER AGE*
- DELAYING ONSET OF DISEASE WITH PRIMARY PREVENTION INCLUDING LIFESTYLE MODIFICATIONS, SUPPLEMENTATION (I.E. NUTRITION) AND NUTRITIONAL INTERVENTION

Visible GENOMICS

PRIVATE AND CONFIDENTIAL. DO NOT SHARE.

51

## AMD GENE PANEL

- BASED ON THE LATEST IN AMD GENETICS RESEARCH
- CLINICALLY PROVEN AND CLINICALLY ACTIONABLE TO BE THE MOST IMPACTFUL VARIATIONS ON AMD PROGRESSION
- COMBINES BOTH GENETIC + NON-GENETIC MARKERS

23andMe SNPs

| Gene | SNP No. | Allele Variants | AMD Risk | Chromosome | Pathway |
|---|---|---|---|---|---|
| **ARMS2/HTRA1** (HtrA Serine Peptidase 1) | Rs10490924 (A69S) | GG | Lower Risk (Reference) | 10q26 | Immune/ inflammatory |
| | | GT | Moderate Risk | | |
| | | TT | Higher Risk | | |
| **CFH** (Complement Factor H) | Rs1061170 (Y402H) | TT | Highly Protective | 1q31 | Complement |
| | | CT | Moderately Protective | | |
| | | CC | Higher Risk (Reference) | | |
| | Rs12191305 9 (R1210C) | CC | Lower Risk (Reference) | | Complement |
| | | CT | Moderate Risk | | |
| | | TT | Higher Risk | | |
| | Rs1410996 (IVS14) | AA | Highly Protective | | Complement |
| | | GA | Moderately Protective | | |
| | | GG | Higher Risk (Reference) | | |
| **C3** (Complement Component 3) | Rs2230199 (R102G) | GG | Lower Risk (Reference) | 19p13 | Complement |
| | | GC | Moderate Risk | | |
| | | CC | Higher Risk | | |

PRIVATE AND CONFIDENTIAL. DO NOT SHARE.

52


53

## GENETIC TREATMENTS

- SEVERAL COMPANIES LOOKING AT GENETIC TREATMENT FOR AMD
- VIRAL VECTORS ARE USED TO INTRODUCE AN ANTI-VEGF ENCODING TRANSGENE TO ALLOW THEY EYE TO BEGIN TO SECRETE ANTI-VEGF
  - TRANSFORMS THE EYE INTO A "BIOFACTORY"
  - PRODUCES ITS OWN ANTI-VEGF SUPPLY
  - REDUCES NEED FOR EXTRINSIC INJECTIONS
- RGX-314 AND ADVM-022

54

## ANTI-VEGF AGENTS

- THE OG
  - MACUGEN (PEGAPTANIB) 2004
  - LUCENTIS (RANIBIZUMAB)2006
  - EYLEA (AFLIBERCEPT) 2011
  - BEOVU (BROLUCIZUMAB) 2019
  - AVASTIN (BEVACIZUMAB) ≈2005

55

## HIGH DOSE AFLIBERCEPT (EYLEA)

- PULSAR (AMD) AND PHOTON (DME) STUDIES
  - LOOKED AT 8 MG VS 2 MG OF EYLEA
  - DEMONSTRATED NON-INFERIOR AND CLINICALLY EQUIVALENT VISION GAINS AT 48 WEEKS WITH 8 MG AT 12 AND 16 WEEK DOSING AFTER 3 INITIAL DOSES COMPARED TO EYLEA EVERY 8 WEEKS AFTER INITIAL DOSING
- EYLEA HD FDA APPROVED 8/18/2023 FOR AMD, DME AND DR
  - RECOMMENDED DOSE 1 INJECTION EVERY 4 WEEKS FOR FIRST 3 MOS FOR ALL INDICATIONS, THEN EVERY 8-16 WEEKS (2-4 MOS) FOR AMD AND DME AND EVERY 8-12 WEEKS (2-3 MOS) FOR DR

56

## VABYSMO (FARICIMAB)

- ROCHE/GENENTECH
  - FDA APPROVED JANUARY 3, 2022 FOR AMD AND DME
- FIRST BI-PHASIC ANTIBODY FOR INTRAOCULAR USE
  - ONE ARM: VEGF-A INHIBITOR
  - OTHER ARM: ANGIOPOIETIN-2 (ANG-2)INHIBITOR
    - GROWTH FACTOR THAT PROMOTES VASCULAR DESTABILIZATION AND AND INFLAMMATION
  - DUAL INHIBITION OF VEGF AND ANG-2 HAVE PROVEN MORE EFFECTIVE THAN INHIBITING EITHER TARGET ALONE
- MULTIPLE STUDIES SHOW SIMILAR RESULTS TO MONTHLY LUCENTIS/EYLEA BUT ABLE TO OBJECT LESS FREQUENTLY, MANY PTS Q 16 WEEKS
- MAY BE FDA APPROVED FOR RVO BY END OF YEAR

57

## SUSVIMO

- PREVIOUSLY CALLED GENENTECH PORT DELIVERY SYSTEM (PDS)
  - REFILLABLE PORT PLACED UNDER CONJUNCTIVA TO ALLOW STEADY SUPPLY OF LUCENTIS
- STUDIES (LADDER, ARCHWAY) DEMONSTRATED EQUIVALENT RESULTS TO MONTHLY LUCENTIS AT 40 WEEKS
  - LARGE % OF PTS DID NOT NEED REFILL PRIOR TO 6 OR 12 MOS
- FDA APPROVED 10/1
- RECALLED 10/22
  - ISSUE WITH IMPLANTS BREAKING WHEN REFILLED
- REAPPROVED JULY 8, 2024 WITH NEW IMPLANT AND REFILL NEEDLE

58

## ANTI-VEGF BIOSIMILARS

- 2 FDA APPROVED LUCENTIS (RANIBIZUMAB) BIOSIMILARS
  - BYOOVIZ (SAMSUNG) APPROVED SEPT 2021
  - CIMERLI (COHERUS) APPROVED OCT 2022
- 3 FDA APPROVED TWO EYLEA (AFLIBERCEPT) BIOSIMILARS
  - YESAFILI (AFLIBERCEPT-JBVF) BIOCON BIOLOGICS MAY 2024
  - OPUVIZ (AFLIBERCEPT-YSZY) SAMSUNG BIOEPIS/BIOGEN MAY 2024
  - PAVBLU (AFLIBERCEPT-AYYH) AMGEN AUGUST 2024
- MANY OTHERS IN THE WORKS….

59

## DIABETIC RETINOPATHY GRADING

- DEVELOPED AS A MEANS OF CREATING A **"PROGNOSTIC STANDARD"**
  - RISK OF VISION LOSS IF NOT TREATED
- BASED ON ETDRS/DRS STUDIES THAT WERE DONE IN THE 1980'S
- UTILIZES FUNDUS PHOTOGRAPHY WITH A SET OF "STANDARD SLIDES"
- PHOTOGRAPHS ONLY CAPTURED IMAGES MAINLY OF THE POSTERIOR POLE BETWEEN THE ARCADES
- DOES NOT INCORPORATE CHANGES SEEN IN THE RETINA USING NEWER MODALITIES

Standard Slide 2A

Standard Slide 6A

Standard Slide 8A

60

## DIABETIC RETINAL NEURODEGENERATION (DRN)

- MAY BE A **"PRECLINICAL MANIFESTATION"** OF DIABETIC RETINAL DISEASE (DRD)
  - DEVELOPS IN THE EARLY STAGES OF DRD
- IDENTIFIED AS **PROGRESSIVE RETINAL THINNING** AND **VISUAL DYSFUNCTION** IN PATIENTS WITH DM BEFORE THE DEVELOPMENT OF DR
- EARLY RETINAL NEURODEGENERATION MAY PRECEDE VASCULAR PATHOLOGY - SUGGESTING THAT NEURONAL DAMAGE MAY CONTRIBUTE TO DISEASE PATHOGENESIS AND REPRESENT AN INDEPENDENT TARGET FOR INTERVENTION
- DRN MAY BE AN INITIAL COMPONENT - ANOTHER STAGE - OF DRD

61

## NEURODEGENERATIVE MECHANISMS

- GLUTAMATE EXCITOTOXICITY
- OXIDATIVE STRESS
- INFLAMMATION
- RENIN-ANGIOTENSIN SYSTEM ACTIVATION

62

## THE LANDSCAPE OF IMAGING MODALITIES

- WIDE-FIELD FUNDUS PHOTOGRAPHY
- SD OCT
- OCT ANGIOGRAPHY
- ADOPTIVE OPTICS
- ERG

63

## DIABETIC RETINOPATHY GRADING

- THE **TRADITIONAL END-POINT** FOR DR HAS EVOLVED:
  - LASER PRP (OR VITRECTOMY) ONCE PTS PROGRESSED TO PDR
  - FOCAL/GRID LASER ONCE THEY DEVELOPED CSME
- TO NOW ANTI-VEGF TREATMENTS
  - CI-DME
  - SEVERE NPDR AND PDR
- EARLIER INTERVENTION BEFORE PDR

64


65


66

67

WHAT IS ERG?

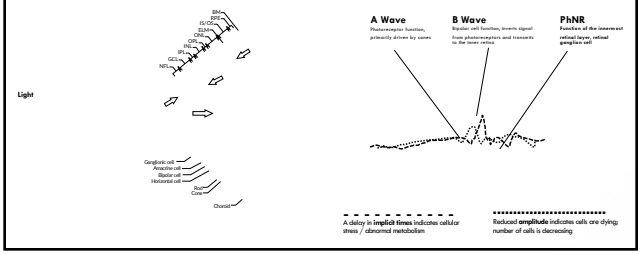
## *ELECTRORETINOGRAPHY*

ERG MEASURES THE ELECTRICAL RESPONSES OF VARIOUS CELL TYPES IN THE RETINA, INCLUDING THE **PHOTORECEPTORS** (RODS AND CONES), **INNER RETINAL CELLS** (BIPOLAR AND AMACRINE CELLS), AND THE **GANGLION CELLS** IN RESPONSE TO A STIMULUS.

68

WHAT IS ERG?

## *THE ERG WAVEFORM*




69

## *PUPILLARY RESPONSE IS ALSO IMPACTED BY DR*

DR assessment protocol combines:

**IMPLICIT TIME (ERG)**
How long it takes the retina to respond

**AMPLITUDE (ERG)**
How strong the signal from the retina is

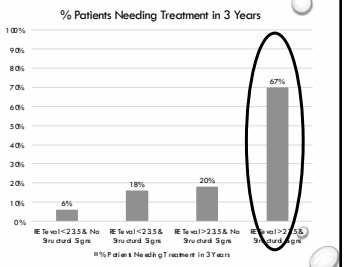
**PUPIL RESPONSE**
Change in pupil diameter–dim vs. bright

**PATIENT AGE**

70

## A Global DR Score Predicts Who Will Need Tx

- N = 237 in US
- Primary outcome: % receiving laser, IV therapy and/or vitrectomy over 3 yrs
- Clinically observable SEVERE NPDR in tandem with ERG+pupillometry score > 23.5 best predicted Tx




Brigell MG, Chiang B, Maa AY, Davis CQ. Enhancing Risk Assessment in Patients with Diabetic Retinopathy by Combining Measures of Retinal Function and Structure. *Trans Vis Sci Tech.* 2020;9(9):40-40.

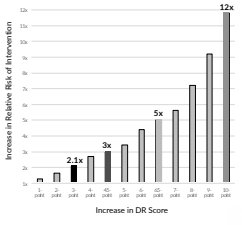
71

## *FUNCTION: ASSESS RISK*

***Each 1-point change in the DR Score increases the probability of ocular intervention over 3 years by 28%***

Higher DR Score & change over time dramatically increases risk:

- Risk of intervention more than **doubles** with a 3-point increase in DR Score (e.g. 20 to 23)
- Risk of intervention **triples** with a 4.5-point increase in DR Score (e.g. 20 to 24.5)
- Risk of intervention **increases 5x** with a 6.5-point increase in DR Score (e.g. 20 to 26.5)
- Risk of intervention **increases 12x** with a 10-point increase in DR Score (e.g. 16 to 26)



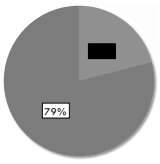

Cox proportional hazards analysis ($CI = 1.17 - 1.40$, $p < 0.0001$)

Source: Brigell MG, Chiang B, Maa AY, Davis CQ. Enhancing Risk Assessment in Patients with Diabetic Retinopathy by Combining Measures of Retinal Function and Structure. Trans Vis Sci Tech. 2020;9(9):40-40.

72

DIABETIC RETINOPATHY

## *NEWEST STUDY SHOWS THE DR SCORE WAS THE STRONGEST PREDICTOR OF PROGRESSION TO VTC*




**Patients with a DR Score of 26.9 or higher had a 79% chance of progressing to needing treatment in less than 1 year.**

- Longitudinal prospective study published in *Ophthalmology Science*, the journal of the American Academy of Ophthalmology
- 48 weeks (~11 months)
- 74 patients with moderate to severe NPDR tested with ERG
- Evaluated 56 parameters at multiple US sites from 4 testing modalities:
  - RET*eval* DR Assessment (ERG + pupillometry)
  - Color fundus photography (FP)
  - OCT angiography (OCT-A)
  - Ultra-widefield fluorescein angiography (UWF-FA)

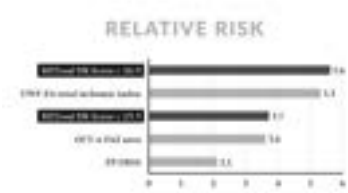
*Davis, C. Quentin et al. Predicting Progression to Vision-Threatening Complications in Diabetic Retinopathy. Ophthalmology Science, online June 17, 2025, 100859*

73

DIABETIC RETINOPATHY

## *STUDY SHOWS THE DR SCORE WAS THE STRONGEST PREDICTOR OF PROGRESSION TO VTC*

**RET*eval* DR Score was the strongest predictor of progression to vision-threatening complications!**




*Davis, C. Quentin et al. Predicting Progression to Vision-Threatening Complications in Diabetic Retinopathy. Ophthalmology Science, online June 17, 2025, 100859*

74

DIABETIC RETINOPATHY

## *WHY THE DR SCORE MATTERS*

- **ENABLES RISK STRATIFICATION** TO IDENTIFY PATIENTS WHO NEED CLOSE MONITORING OR EARLY REFERRAL, EVEN WHEN STRUCTURAL IMAGING APPEARS STABLE.
- ALLOWS TARGETED REFERRALS AND/OR RESOURCE PRIORITIZATION, **REDUCING OVERTREATMENT AND MISSED PROGRESSION.**
- CREATES POTENTIAL TO IMPROVE DR STAGING SYSTEMS AND **SUPPORT VALUE-BASED CARE MODELS.**

75

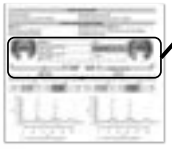
DIABETIC RETINOPATHY

## *HOW TO USE THE DR SCORE IN PRACTICE → INTERPRETATION GUIDE*

**PATIENT TEST CONDITIONS**
Test is always done un-dilated. Patient is diabetic with suspected retinopathy or diabetic with existing retinopathy.

**PROTOCOL**
DR Assessment

**RESULTS**
If the **Operator-selected limit** is marked red with text **Outside limits,** the patient is at risk to develop vision threatening DR within the coming 36 months.



***Predicting DR progression***

**DR SCORE <23.5:**
Patient is much less likely to progress to needing treatment in the next few years

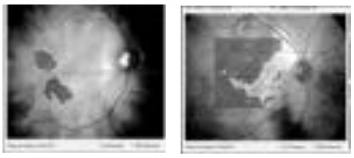
DR SCORE ≥23.5:
High chance of requiring treatment in next 3 years

DR SCORE ≥26.9:
Patient is 79% likely to progress to needing treatment in less than 1 year

76

- **OLD DEFINITIONS BEING REPLACED WITH NEWE**
  - **CENTER INVOLVED**
  - **NON-CENTER INVOLVED**
  - **OCT BEST WAY TO EVALUATE RETINA FO**
- **DME RESPONSIBLE FOR MORE CASES OF MODERATE VISUAL LOSS IN PTS WITH TYPE 2 DM THAN DR**
- **NEW TREATMENTS**

CSME
1. RT within 500 microns (1/3 DD) from FAZ
2. Hard exudates with associated thickening 500 microns from FAZ
3. RT > 1DD in area any part of which is within 1DD from FAZ



77

## PROTOCOL V

- 702 PTS WITH CI-DME WITH VA 20/25 OR BETTER
- 3 TREATMENT GROUPS
  - EYLEA
  - FML
  - OBSERVATION
- AT END OF 2 YEARS, RATE OF LOSS OF 5 LETTERS OR MORE SIMILAR IN ALL 3 GROUPS
- AVG ACUITY IN ALL 3 GROUPS WAS 20/20
- BOTTOM LINE: PTS WITH CI-DME AND GOOD VA CAN BE OBSERVED

78

## OPTOMED AURORA AEYE

- FIRST FDA CLEARED HANDHELD AI FUNDUS CAMERA
- USES AI TO ASSESS LEVEL OF DR
  - REFERRABLE DR DETECTED
  - NO REFERRABLE DR DETECTED
  - OVER 90% SPECIFIC AND SENSITIVE
  - 99% IMAGEABILITY
  - RESULTS IN UNDER 90 SECONDS

79

## AI OPTICS SENTINEL CAMERA

- FDA APPROVED JAN 29, 2025
- HANDHELD DIGITAL IMAGING SYSTEM
- HAS AI CAPABILITIES BUT NOT YET APPROVED

80

## FLOATERS

81

## WOULD YOU RECOMMEND SURGICAL INTERVENTION FOR PATIENTS WITH INTRACTABLE SYMPTOMS OF FLOATERS?

82

## THE BURDON OF FLOATERS

**RETROSPECTIVE STUDY BASCOM PALMER EYE INSTITUTE 2008-2011**

- 7.2% OF PATIENTS REFERRED TO A RETINAL SPECIALIST HAD FLOATERS
- 5TH MOST COMMON DIAGNOSIS OVER THAT TIME
  - > 60 YO 3RD MOST COMMON DX
- VITRECTOMY: VERY SUCCESSFUL, TECHNICALLY SIMPLE, WITH LOW SIDE-EFFECT PROFILE
  - RISK OF CATARACT, ERM, AND RETINAL TEARS/DETACHMENTS

83

## IMPORTANT CONSIDERATIONS IN PATIENTS WITH FLOATERS

ARE THEY ACUTE OR CHRONIC?

- ACUTE FLOATERS – OFTEN FROM PVD
  - USUALLY RESOLVE
- CHRONIC FLOATERS THAT IMPACT DAILY ACTIVITIES

84

## REASONS FOR SURGERY FOR FLOATERS

SYMPTOMS THAT IMPACT THE QUALITY OF LIFE

- UNABLE TO READ CONTINUOUSLY
- UNABLE TO SAFELY DRIVE A CAR
  - THE FLOATERS/CLOUD MOVES IN FRONT OF THEIR VISION AND THEY NEARLY HAVE TO PULL OVER FOR FEAR OF HAVING AN ACCIDENT
- AFFECTS ABILITY TO PERFORM YOUR JOB

85

## THE IDEAL CANDIDATE FOR TREATMENT OF FLOATERS

- SYMPTOMATIC
- PSEUDOPHAKIC
- PVD

The **NOT** Ideal Candidate for Treatment of Floaters

- Young
- Phakic
- Attached vitreous
- High myope

86

## LASER VITREOLYSIS FOR FLOATERS

- DONE WITH A YAG
- HIGHLY VARIABLE RESULTS
- COMPLICATIONS:
  - CATARACT (HITTING THE LENS)
  - POSTERIOR CAPSULE TEARS
  - RETINAL BURNS
  - FOVEAL BURNS
  - CHOROIDAL RUPTURE
  - CHOROIDAL HEMORRHAGES
  - RETINAL TEAR

87

**Long-Term Follow-Up of Efficacy and Safety of YAG Vitreolysis for Symptomatic Weiss Ring Floaters**

[redacted]

- 35 OF 52 PATIENTS RANDOMIZED TO YAG VITREOLYSIS OR CONTROL FOLLOWED FOR 2.3 YEARS
- 50% FELT THEIR SYMPTOMS WERE SIGNIFICANTLY OR COMPLETELY BETTER AT 6 MONTHS
  - ~60% OVERALL IMPROVEMENT IN SYMPTOMS
- 3 PATIENTS DEVELOPED RETINAL TEARS AFTER 6 MONTHS (NOT SYMPTOMATIC)

Ophthalmic Surg Lasers Imaging Retina 2020

88

## VITRECTOMY 2023

- SMALLER-GAUGE INSTRUMENTS (25 OR 27) COMPARED WITH THE 20-GAUGE NEEDLES USED LESS THAN 15 YEARS AG
- SMALLER VITRECTOMY INSTRUMENTS ALLOW FOR SUTURELESS PROCEDURES
  - SMALLER SCLEROTOMY
  - TROCARS ALLOW FOR SMALL, THIN-WALL CANNULA
- LESS INFLAMMATION
- FEWER COMPLICATIONS
- MUCH GREATER SUCCESS RATE

89

## RISK FACTORS FOR VITRECTOMY

- CATARACT
- RETINAL TEAR OR DETACHMENT
- ERM/MACULAR PUCKER
- MACULAR EDEMA
- ENDOPHTHALMITIS

90

## INDUCE A PVD….OR NOT

- RISK OF DEVELOPING A RETINAL TEAR BY INDUCING PVD
- REDUCED RISK/TIME OF DEVELOPING CATARACT WITH PARTIAL VITRECTOMY

91

## BASCOM PALMER VITRECTOMY FOR FLOATERS STUDY

- RETROSPECTIVE CHART REVIEW
- PPV FOR SYMPTOMATIC PRIMARY VITREOUS FLOATERS
- **150 PATIENTS** EVALUATED BETWEEN 1/1/2012– 1/1/2023
- AGE OF ONSET 66/67
- GENDER: 65 FEMALE, 85 MALE
- **# OF EYES: 208**
- SYMPTOMS DURATION **12.3 MO ± 8 MO**
- 74% PSEUDOPHAKIA

Ocular Disease
- 4 eyes treated tears
- 2 asteroid hyalosis
- 5 eyes glaucoma
- 10 high myopia
- 10 eyes refractive surgery

92

## COMPLICATIONS

| Post Op Complications | # Eyes | Mean Time of Dx following Surgery |
|---|---|---|
| Cataract | 18 (53%) | 9.13 ± 6 months |
| Steroid induced Increase in IOP | 10 (4.8%) | 1 moth |
| Vit Heme | 8 (3.9%) | 4 ± 4 days |
| Retinal Detachment | 7 (3.4%) | 20 ± 37 months |
| Symptomatic CME | 4 (1.9%) | 16.8 ± months |
| ERM | 3 (1.4%) | 15 ± months |
| Endophthalmitis | 1 (0.5%) | 1 day |
| Hyphema | 1 (0.5%) | 1 day |
| Symptomatic floats | 1 (0.5) | 6 months |

93

## RATE OF COMPLICATIONS FOR VITRECTOMY FOR VITREOUS FLOATERS IS "LOW"

NEEDS TO BE DISCUSSED WITH THE PATIENT

- RRD: 7 EYES (3.4%)
- VH: 7 EYES (3.4%): ALL CLEARED
- OTHER
  - ENDOPHTHALMITIS 1 EYE
  - REDO SURGERY 1 EYE

94

ARVO Annual Meeting Abstract | June 2013

## Long-term Safety of Vitrectomy for Patients with Floaters

- 66 EYES IN 52 PATIENTS (AGE = 63 ± 12 YEARS) WERE INCLUDED
- 36/66 **(54.5%)** EYES WERE **PHAKIC**
- AVERAGE DURATION OF COPING WAS 30 MONTHS
- ETIOLOGY OF FLOATERS WAS **PVD IN 44/66 (67%)**, MYOPIA IN 19/66 (28%), ASTEROID HYALOSIS IN 8/66 (12%)
- RETINOPEXY FOR RETINAL BREAKS OCCURRING AT THE TIME OF PVD WAS PERFORMED IN 16 EYES (36% OF ALL EYES WITH PVD; 24% OF ALL EYES). A **MINIMUM OF 3 MONTHS PRIOR TO VITRECTOMY**
- **22 EYES WITHOUT PVD: PVD NOT INDUCED AND VITREOUS REMAINED INTACT PERIPHERALLY.**
- MAIN OUTCOME: INCIDENCE OF RET TEARS/DETACHMENTS AND CATARACT REQUIRING SURGERY

95

ARVO Annual Meeting Abstract | June 2013

## Long-term Safety of Vitrectomy for Patients with Floaters

- **FLOATER SYMPTOMS RESOLVED IN 65 OF 66 EYES (98.5%)**
- NO PATIENTS (0/66; 0%) DEVELOPED RETINAL BREAKS, HEMORRHAGE, INFECTION, OR GLAUCOMA (3 MONTH – 3 YEARS)
- **NO RETINAL BREAKS/ DETACHMENTS IN THE 22 PATIENTS WITHOUT PVD PRE-OPERATIVELY (0/22 VS 9/30)**
- ONLY **7/36 (19%) PHAKIC EYES DEVELOPED CATARACTS** REQUIRING SURGERY, AN AVERAGE OF 16.5 MONTHS POST-VITRECTOMY (7/36 VS 18/36 (50%)

96

2018

Long-Term Safety and Efficacy of Limited Vitrectomy for Vision Degrading Vitreopathy Resulting from Vitreous Floaters

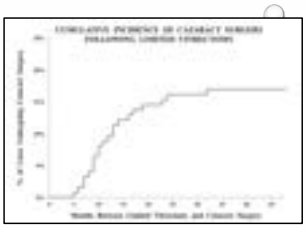
Methods 195 Eyes

Limited vitrectomy with 25-gauge instruments was performed without surgical PVD induction preserving 3 to 4 mm of retrolental vitreous in phakic eyes. Follow-up averaged 32.4 ± 23.5 months (range, 9–118 months), with 2 years or more in 144 eyes, 3 years or more in 69 eyes, 4 years or more in 51 eyes, and 5 years or more in 24 eyes.

Conclusions

Limited vitrectomy for Vision Degrading Vitreopathy decreases vitreous echodensity, improves patient well being, improves VA, and normalizes CSF. The long-term efficacy and safety profiles suggest this may be a safe and effective treatment for clinically significant vitreous floaters, warranting a prospective randomized trial.

97

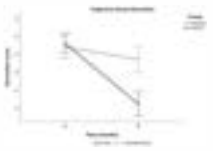


98

**Dietary Intervention With a Targeted Micronutrient Formulation Reduces the Visual Discomfort Associated With Vitreous Degeneration**

Emmanuel Ankamah, Marina Green-Gomez, Warren Roche, Eugene Ng, Ulrich Welge-Lüßen, Thomas Kaercher, and John M. Nolan

- 61 PTS FOLLOWED FOR 60 DAYS
- LESS DISCOMFORT FROM FLOATERS IN TREATED PTS FROM INITIAL VISIT TO FINAL VISIT
- LESS EFFECT OF FLOATERS ON DAILY LIFE IN TREATED PTS FROM INITIAL VISIT TO FINAL VISIT
- DECREASE IN VITREOUS OPACITES IN 20/26 (76.9%) OF TREATED PTS VS 28.6% IN PLACEBO
- INCREASE IN CONTRAST SENSITIVITY IN TREATED PTS
- OVERALL, 66.6% OF TREATED PTS EXPERIENCE AN IMPROVEMENT IN VISUAL COMFORT



99

## MACULAR HOLE SURGERY

- VITRECTOMY AND MEMBRANE PEEL
- FILLED WITH GAS WHICH DISSIPATES OVER 4-6 WEEKS
- FACE DOWN POSITIONING
  - 14 DAYS TRADITIONAL
  - NEWER STUDIES EVALUATING LESS VS NONE
- 95% SUCCESS RATE IF OPERATED WITHIN 1 YR
- RISKS
  - ENDOPHTHALMITIS: 1:1000
  - RD: 5%
  - CATARACT FORMATION: MANY PTS NEED CATARACT SURGERY WITHIN 1 YEAR OF VITRECTOMY

100

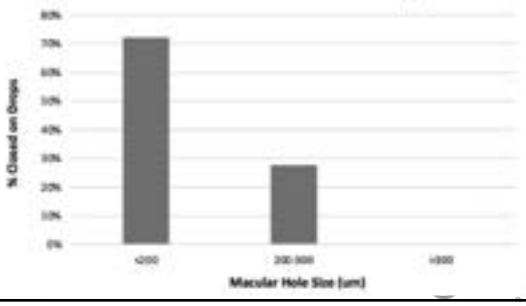
## MACULAR HOLE MEDICAL THERAPY

- 49 PTS WITH FTMH STARTED ON PF, NSAID, CAI
- 18/49 (36.7%) ACHIEVED CLOSURE WITH DROPS
  - HIGHER % IN SMALL HOLES AND THOSE WITHOUT VMT
- HOLE SIZE DIRECTLY RELATED TO CHANCE OF CLOSURE
  - EVERY 10 UM DECREASE IN SIZE INCREASED ODDS FOR CLOSURE BY 1.2X
  - BEST RESULTS LESS THAN 200UM
  - 200-300UM ≅ 25% CLOSURE
  - NO FTMH OVER 300 UM HAD CLOSURE
- AVG TIME TO CLOSURE WAS 107.2 DAYS (RANGE 20-512 DAYS)
- IF NO RESPONSE AT ALL WITHIN FIRST 1-3 MOS RESPONSE UNLIKELY AND SURGICAL CANDIDATE

Wang J, et al. Full-thickness macular hole closure with topical medical therapy. Retina 44:392.399, 2024.

101

## RATE OF FTMH CLOSURE ON MEDICAL THERAPY




102

## TAKE HOME

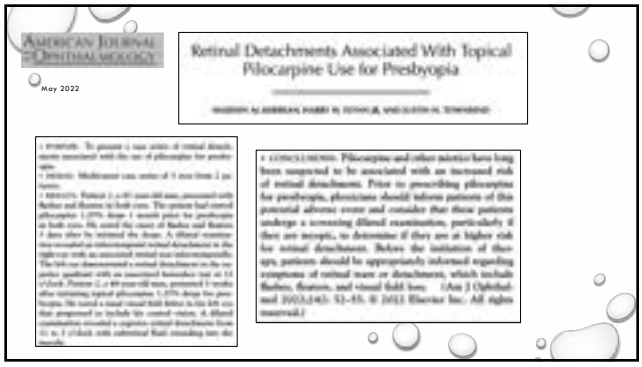
- MY TAKE HOME:
  - IF < 300 UM, TRY CONSIDER TRYING
    - PF QID
    - NSAID (VOLTAREN, ACULAR) QID
    - CAI (TRUSOPT) BID UTIL SEES RETINA
  - REFER TO RETINA 1 MOS
  - SEND OCT TO COMPARE
  - IF NO IMPROVEMENT IN 1 MOS, UNLIKELY TO HAVE CHANGE SO SURGICAL CANDIDATE
  - IF IMPROVEMENT, TRY FOR 3 MOS THEN DECIDE ON SURGERY

103

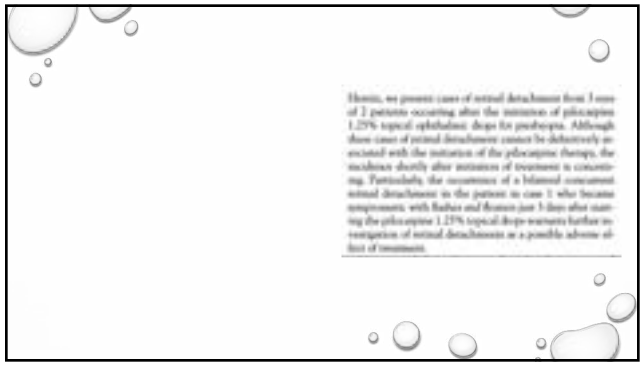
## VUITY TO TREAT PRESBYOPIA

- 1.25% PILOCARPINE
- FDA APPROVAL OCT 2021
- POSITIVE PHASE 2 PHASE 3 RESULTS, GEMINI 1 AND GEMINI 2
  - 750 PATIENTS WHO USED VUITY DAILY FOR 30 DAYS
  - **29% OF PATIENTS EXPERIENCED A ≥3 LINE INCREASE** IN DISTANCE-CORRECTED NEAR VISUAL ACUITY AT DAY 30, HOUR 3 VS 10% IN CONTROLS.
  - ADVERSE EVENTS (AE) WERE ALL MILD AND INCLUDED HEADACHES (14.1%), VISUAL IMPAIRMENT (4.3%), CONJUNCTIVAL HYPEREMIA (2.5%), VISION BLUR (2.5%), EYE IRRITATION (2.5%), EYE PAIN (2.5%), INCREASED LACRIMATION (2.5%), NAUSEA (2.5%), AND PUNCTATE KERATITIS (0.6%)
  - **NO CASES OF RETINAL TEARS, RD, MACULAR HOLES, OR VITREOMACULAR TRACTION**

104

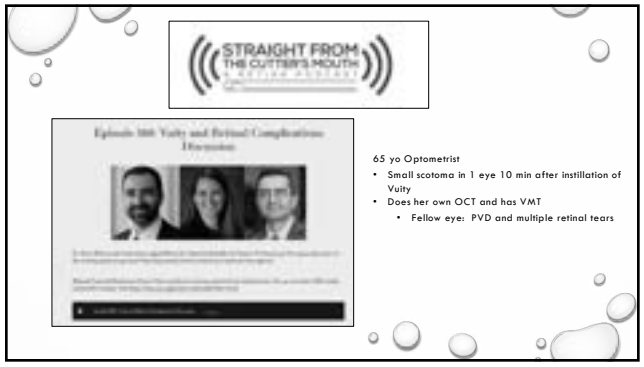



105



106


107




65 yo Optometrist
- Small scotoma in 1 eye 10 min after instillation of Vuity
- Does her own OCT and has VMT
  - Fellow eye: PVD and multiple retinal tears

108

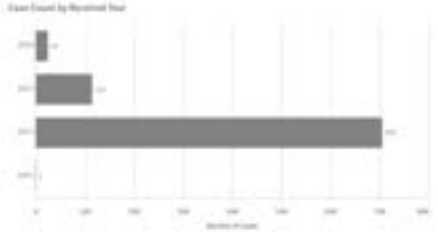
## RETINAL COMPLICATIONS ASSOCIATED WITH VUITY

- FDA ADVERSE EVENTS REPORTING SYSTEM (FAERS) DASHBOARD September 2024 (latest data)
  - 550 TOTAL CASES
  - 121 VIEWED AS SERIOUS CASES
  - 161 VISUAL IMPAIRMENT
    - 42 RETINAL DETACHMENTS
    - 25 RETINAL TEARS
    - 9 VITREOMACULAR TRACTION
    - 11 VISUAL FIELD DEFECT
    - 56 VITREOUS FLOATERS

https://fis.fda.gov/sense/app/95239e26-e0be-42d9-a960-9a5f7f1c25ee/sheet/45beeb74-30ab-46be-8267-5756582633b4/state/analysis

109

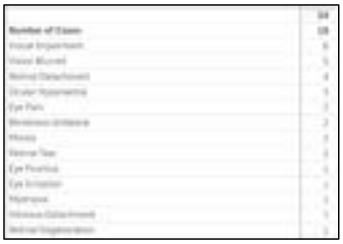
## RETINAL COMPLICATIONS ASSOCIATED WITH VUITY



110

## RETINAL COMPLICATIONS ASSOCIATED WITH VUITY

September 2024



111

## WHY RETINAL COMPLICATIONS?

- CONTRACTION OF THE CILIARY BODY
- RAPID ANTERIOR DISPLACEMENT OF THE VITREOUS
  - SHIFTING THE VITREOUS BODY FORWARD
- RESULTING IN TRACTION ON THE RETINA
- MAY PREDISPOSE SOME PATIENTS
  - LATTICE DEGENERATION AND PERIPHERAL RETINAL PATHOLOGY
  - ABNORMAL VITREOMACULAR INTERFACE

112

## RATES OBSERVED WITH VUITY DID NOT EXCEED THE NATURAL HISTORY IN THIS AGE GROUP, AND…

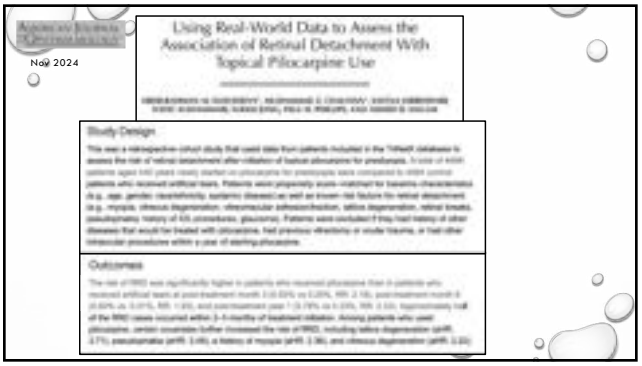
**…THEY WERE FURTHER REDUCED FOLLOWING POST-LAUNCH EDUCATION EFFORTS**

| *Indiscriminate Use Initially >25% Rxs from Non-ECPs 6 Months Post-Launch* | *Following Education by AGN and Professional Societies Rates Decreased* |
|---|---|
| • 122,000 *NEW* VUITY PRESCRIPTIONS (*JANUARY TO DECEMBER 2022*) | • 19,000 *New* VUITY Prescriptions (*January to June 2023*) |
| • FDA ADVERSE EVENTS REPORTED: 30 RDS (AS OF DECEMBER 2022 – ONLY 1 REPORTED 2H 2022) | • FDA Adverse Events reported: 2 RDs (as of June 2023) |
| • 30 REPORTS/122,000 NEW PRESCRIPTIONS = 0.025% | • 2 reports/19,000 new prescriptions = 0.011% |

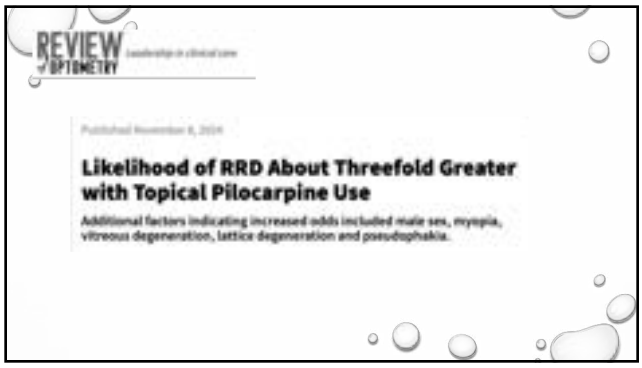
***QLOSI education initiatives will help guide ECP patient selection and calibrate expectations on RD risk relative to the most common complications ECPs (OD primarily) manage with other treatments they frequently use, i.e. contact lenses / microbial keratitis***

113

Nov 2024




114




115

## VIZZ (ACEDLIDINE 1.44%)

- LENZ THERAPEUTICS
- FDA APPROVED JULY 31, 2025 FOR PRESBYOPIA
- PUPIL SELECTIVE MIOTIC
- CILIARY SPARING
- AVAILABLE OCTOBER 2025

116

## DANEGAPTIDE

- BREYE THERAPEUTICS
- GAP JUNCTION MODIFIER
- POTENTIAL ORAL THERAPY FOR NPDR
- PHASE 1 STUDY:
  - 24 PTS WITH NPDR AND ASSOCIATED EDEMA
  - WELL TOLERATED
  - IMAGING SHOWED REDUCED RETINAL VASCULAR LEAKAGE AND "IMPROVEMENTS IN ANATOMICAL PARAMETERS"
- PHASE 2 TO BEGIN SOON

117

## TKI INHIBITORS

- TYROSINE KINASE INHIBITORS
  - SMALL MOLECULES THAT CAN ACT INTRACELLULARLY TO INHIBIT MULTIPLE PATHWAYS INVOLVED IN THE PATHOGENESIS OR RETINAL DISEASE
  - MAY BE A MORE DURABLE TREATMENT APPROACH, REDUCING TREATMENT BURDEN OVER AVNY10VEGF
  - EARLY STUDIES SHOW PROMISE
- AIV007 (AIVIVA BIOPHARMA): PHASE 1, SINGLE PERIOCULAR INJECTION FOR DME AND NAMD,
- D-4517.2 (ASHAVATTHA THERAPEUTICS): PHASE 2 TEJAS STUDY, SUBCUTANEOUS OR ORAL FOR DME AND NAMD
- EYP-1901 (EYEPOINT PHARMACEUTICALS): LUGANO ANDCLUCIA TRIALS IN AMD; VERONA IN DME
- OTX-TKI (OCULAR THERAPEUTIX): APAXLI, BIORESORBABLE INTRAVITREAL IMPLANT FOR AMD AND DR
- CLS-AX (CLEARSIDE THERAPEUTICS): SUPRACHOROIDAL INJECTION OF AXITINIB FOR NAMD
- PAN-90806 (ZHAOKE OPHTHALMOLOGY): TOPICAL KI EYE DROP FOR AMD

118

## DURAVYU

- VOROLANIB INTRAVITREAL INSERT (PREVIOUSLY EYP-1901) BY EYEPOINT PHARMACEUTICALS
- DID NOT MET ENDPOINT OF IMPROVEMENT OF AT LEAST 2 DRSS LEVELS AS OF WEEK 36
  - 12 MOS DATA STILL COMING
- DID HAVE SOME POSITIVE RESULTS
  - 86% OF PTS IN 3 MG ARM AND 80% IN 2 MG ARM WERE STABLE OR IMPROVED VS 70% CONTROL
  - 0% IN 3 MG AND 5% IN 2 MG WORSENED > 2 STEPS VS 10% IN CONTROL
  - 5% IN 3 MG AND 0% IN 2 MG IMPROVED > 2 STEPS VS 5% CONTROL
  - WELL TOLERATED WITH NO SERIOUS ADVERSE EVENTS OF ENDOPHTALMITIS

119

## NEUROTECH PHARMACEUTICALS

- ENCELTO APPROVED 3/6/2025 FIRST AND ONLY APPROVED TREATMENT FOR MAC TEL
- ENCAPSOLATED CELL THERAPY
  - A SMALL SEMI-PERMEBABLE CAPSULE SURGICALLY IMPLANTED INTO THE PATIENTS VITREOUS AND SUTURED TO THE SCLERAL WHICH ALLOWS THERAPEUTIC PROTEINS AND ESSENTIAL NUTRIENTS TO ENTER THE EYE TO TREAT CHRONIC RETINAL DISEASES
- HEADQUARTERS IN CUMBERLAND, RI
- PRICE: 200-250K!!

120