AMD from A to Z: 2025 Edition

COPE# 97356-TD

Timothy W. Earley, O.D.

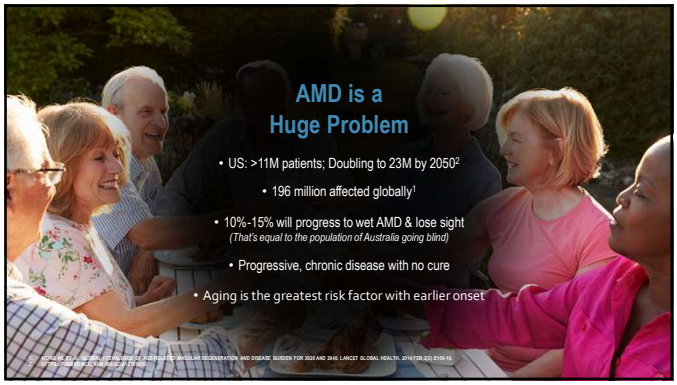
Regional Eye Associates - Cumberland, MD

Drtimearley@gmail.com

Disclosures:

Dr. Earley is a Paid Consultant and Key Opinion Leader (KOL) for Alcon Vision Care, Notal Vision, MacuHealth, Lumithera (pending) and LKC Technologies. He also serves on their Speakers Bureau.

1



2

A Brief History of AMD Diagnosis and Management

- I graduated from PCO in 1998 – no dry treatment; focal laser for wet
- I was trained to monitor dry disease, dispense Amsler, discuss UV protection
- PDT (PhotoDynamic Therapy) approved in 1999 – treatment for wet AMD
- AREDS findings released 2001 – intermediate dry or worse; role of supplements
- First OCT in 1996; OCT-2 in 2000; Stratus OCT in 2006
- First anti-VEGF in 2005 (off-label), first on-label use in 2006
- AREDS2 – began in 2006; results in 2013 – safer/more effective supplements
- Use of PHP for the detection of metamorphopsia in dry to wet conversion (2009)
- Discovery of Dark Adaptation as earliest biomarker for AMD (ALSTAR 2016)

3

And the Innovations Continue…

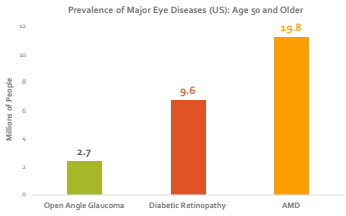
- Use of Anti-VEGf medications that are longer-lasting
- Introduction of Home-Based Testing for conversion from Dry to Wet AMD
- FDA approval for the use of injectables to treat Geographic Atrophy (GA)
- Use in Europe of photobiomodulation to treat early and intermediate AMD – Approved in U.S. by FDA in November 2024
- Oral medications in FDA clinial trial show promise
- MANY OF THE NEW THERAPIES ARE LIKELY TO BE OPTOMETRY DRIVEN!

4

Leading Cause of Legal Blindness in the US *

Do you diagnose AMD as often as DR and POAG combined in your practice?

Clinical AMD **is more prevalent** than glaucoma and diabetic retinopathy combined



5

We Miss Visible Disease With Typical Standard of Care

JAMA Ophthalmology | Original Investigation

Prevalence of Undiagnosed Age-Related Macular Degeneration in Primary Eye Care

David C. Neely, MD; Kevin J. Bray, MD; Carrie E. Huisingh, MPH; Mark E. Clark, BS; Gerald McGwin Jr, PhD; Cynthia Owsley, PhD

1288 eyes from 644 people
- Mean age of 69.4
- 36% male
- 64% female

- ✓ **25%** of "normal patients" had findings consistent with AMD
- ✓ **30%** of missed AMD eyes had large drusen (Intermediate AMD)
- ✓ MDs and ODs miss AMD diagnosis equally

6

As Clinicians, it is Frustrating That Our Patients are Still Presenting for Anti-VEGF Treatment Having Already Suffered Irreversible Vision Loss

Mean VA at diagnosis of nAMD in the 1st eye:

Mean VA at diagnosis of nAMD in the 2nd eye:

SOURCES: CERVANTES-CASTAÑEDA RA, ET AL. EYE (LOND). 2008;22(6):777-781. | OLSEN TW, ET AL. OPHTHALMOLOGY. 2004;111(2):250-255. | WO, ET AL. OPHTHALMIC SURG LASERS IMAGING RETINA. 2020;51:633-639.

7

sources: AMD, age-related macular degeneration. Ferris FL, et al. Ophthalmology. 2013;120(5):844-851.

The Beckman Classification

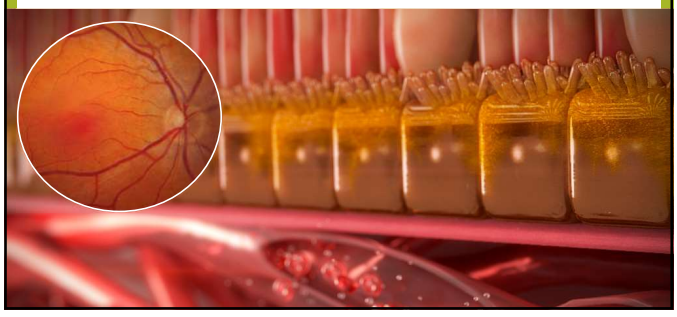
4 Stages of AMD

PROGRESSION

No AMD		No drusen or small drusen ≤ 63 µm No AMD pigmentary abnormalities
Early AMD		Medium drusen > 63 µm and ≤ 125 µm No AMD pigmentary abnormalities
Intermediate AMD		1 large druse > 125 µm and/or Any AMD pigmentary abnormalities
Advanced AMD	 	**2 forms:** Geographic Atrophy and Neovascular AMD

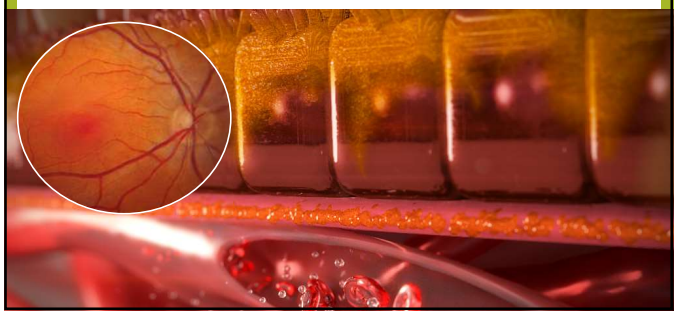
8

Healthy Choriocapillaris, Bruch's, RPE, and Photoreceptors



9

Cholesterol Barrier Deposited Along Bruch's and RPE

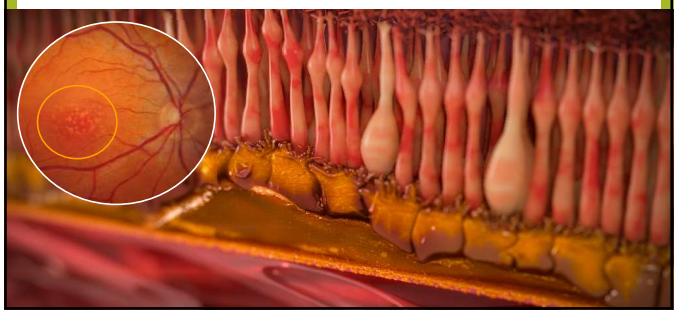


10

RPE Secretes Even More Cholesterol and Degenerates

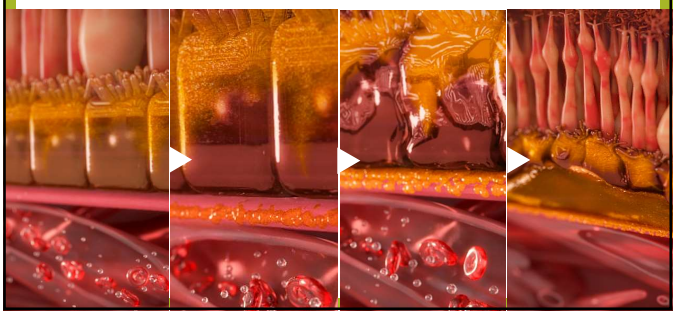
11

Visibly Evident Drusen on Fundus Evaluation



12

Disease Process of AMD Starts Below the RPE!



13

Impaired Dark Adaptation is Earliest Biomarker of AMD

RESEARCH SHOWS:
Impaired dark adaptation identifies subclinical AMD
at least three years before
it can be seen with imaging, OCT or clinical exam.

UAB ALSTAR Study

Prospective Study of Subclinical AMD

- Sample consisted of 325 adult's w/o clinically detectable AMD
- At baseline, 24% of the subjects exhibited impaired dark adaptation
- AMD status determined at 3-year follow-up visit

sources: Owsley, C et al. Ophthalmology. 2016;123(2):344-351.

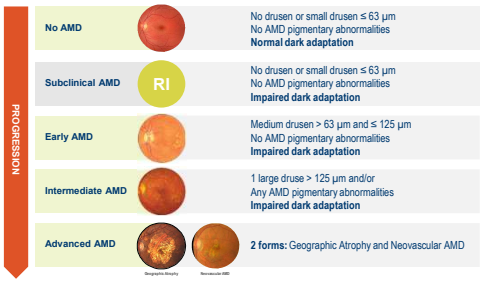
14

What IS Dark Adaptometry?

- Dark Adaptometry is the time it takes for the macular ROD photoreceptors to recover from a bleaching event.
- The photoreceptors that are bleached are slightly superior to the fovea centralis (this allows for normal fixation during testing)
- A normal adult macula will recover from a bleaching event in 6.5 minutes or less!
- If the adaptation time is greater than 6.5 minutes, this indicates a reduces macular pigment function; the lack of pigment leads to an outsize dose of light hitting the photoreceptors causing a delayed adaptation time
- The RODS are tested (not the cones) because they outnumber the cones and are active in scotopic conditions (patients with poor macular pigment will describe difficulty driving at night)

15

This Leads to a More Comprehensive AMD Classification System: Structure + FUNCTION!



16

Dark Adaptometry Validated in Multi-Site Study

JOHNS HOPKINS UNIVERSITY

VERI TAS HARVARD

PENNSTATE HERSHEY College of Medicine

High Sensitivity
Correctly identified
90.6%
of confirmed AMD cases

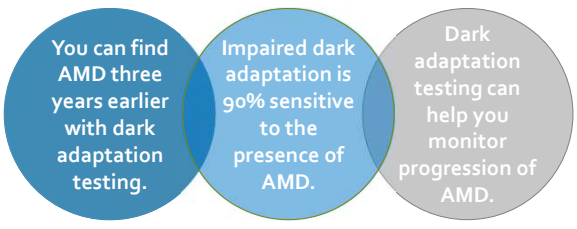
High Specificity
Correctly identified
90.5%
of confirmed normal cases

High Accuracy
90.6%
overall

sources: Jackson GR, et al. Invest Ophthalmol Vis Sci. 2014;55(3):1427-1431.

17

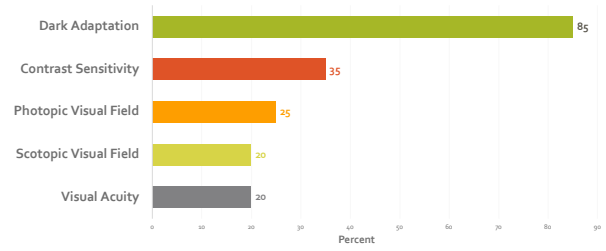
Using Dark Adaptometry in Clinical Practice Allows for Enhanced Confidence When Managing All Stages of AMD



maculogix

18

Comparing Diagnostic Sensitivity for Identifying AMD



SOURCES: OWSLEY C, HUISINGH C, CLARK ME, ET AL. COMPARISON OF VISUAL FUNCTION IN OLDER EYES IN THE EARLIEST STAGES OF AGE-RELATED MACULAR DEGENERATION TO THOSE IN NORMAL MACULAR HEALTH. J OPHTHALMIC VIS RES. 2015 AUG 13;10:(3):PUB ANEAD OF PRINT]

19

Goldman-Weekers Dark Adaptometer

- Manual dark adaptometer
- High patient burden
- Expert technician required
- Used in academic clinics for research and retinal degeneration diagnosis

20

Roland Consult Dark Adaptometer

- Automated dark adaptometer
- Interfaces with external computer
- No automated analysis

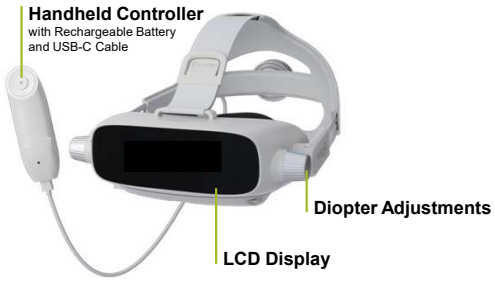
21

First Automated Dark Adaptometer Available for Clinical Use

- ✓ Easy to administer
- ✓ Low patient burden
- ✓ Reimbursable (CPT 92284)
- ✓ Objective output (Rod Intercept)
- ✓ Rapid & Extended Tests
- ✓ FDA 510(k) Cleared & CE Mark

22

Head-Mounted Dark Adaptometer Now Available for Clinical Use



23

Wearable Diagnostic Testing: Here to Stay!!

- Head-Mounted VR-style Diagnostic Testing Offers Advantages Over Traditional Larger-Footprint Devices
  - Frees Up Our Technicians
  - Does Not Confine Testing to a Pretest Room
  - Easy to Adjust/Customize for a Comfortable Experience
  - Consistency of Testing with AI

24

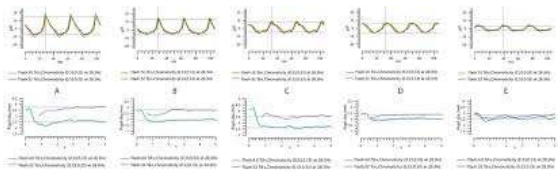
Standard of Care Comparison: Two Multifactorial Diseases

	GLAUCOMA		AMD
Structure	 Cup-to-Disc Ratio	▶	 Drusen
Function	 Visual Field	▶	 Dark Adaptation
Risk	Intraocular Pressure (IOP) Corneal Thickness Demographics and Family History	▶	Macular Pigment Optical Density (MPOD) Contrast Sensitivity Genetic Testing Demographics, Family History, Lifestyle

25

ANOTHER RECENT OBJECTIVE, FUNCTIONAL TEST OF RETINAL HEALTH…

26

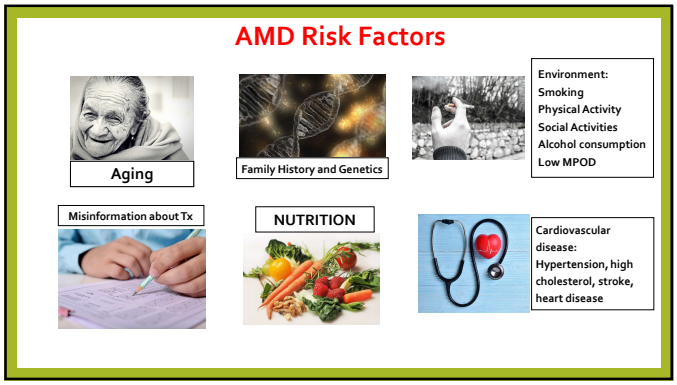


IN CHRONIC RETINAL/MACULAR/ONH DISEASE, THE SPEED OF A LIGHT SIGNAL AND THE STRENGTH OF THE SIGNAL ARE REDUCED BY DEAD/DYING CELLS

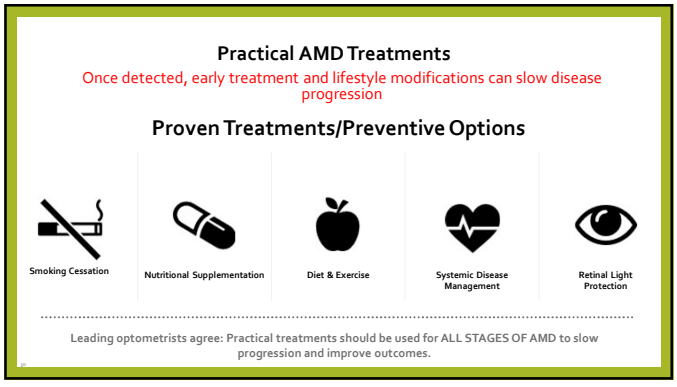
27


Clinically Useful Objective Measure of Retinal Function:
• Hand-held
• Portable
• Tech-driven
• Clinical Utility High; Several disease states can be managed
• Low patient burden; well-tolerated
• Used when subjective testing is not reliable

28


AMD Risk Factors
Aging
Family History and Genetics
Environment:
Smoking
Physical Activity
Social Activities
Alcohol consumption
Low MPOD
Misinformation about Tx
NUTRITION
Cardiovascular disease:
Hypertension, high cholesterol, stroke, heart disease

29


Practical AMD Treatments
Once detected, early treatment and lifestyle modifications can slow disease progression
Proven Treatments/Preventive Options
Smoking Cessation
Nutritional Supplementation
Diet & Exercise
Systemic Disease Management
Retinal Light Protection
Leading optometrists agree: Practical treatments should be used for ALL STAGES OF AMD to slow progression and improve outcomes.

30

Once Detected, Early Treatment Can Slow Disease Progression
Smoking Cessation is the First Step

SMOKING IS THE LARGEST MODIFIABLE RISK FACTOR FOR AMD.

Current smokers carry a **2.5 to 4.8 times** higher risk than non-smokers for late AMD[1].

However…

90% of patients with AMD were not advised to stop smoking[2]

<50% of smokers know that smoking may contribute to blindness[3]

References: 1. Chakravarthy U et al. Cigarette smoking and age-related macular degeneration in the EUREYE Study. Ophthalmology. 2007;114(6):1157-1163.
2. Caban-Martinez AJ et al. Age-related macular degeneration and smoking cessation advice by eye care providers. Prev Chronic Dis. 2011;8(6):A147.
3. Handa S et al. Awareness of blindness and other smoking-related diseases ... in eye patients. Eye. 2011;25(9):1175-1176.

maculogix

31

Devolution

We live in an era of nutrient-deficient foods

1953
1 Bowl of Spinach

has the same nutrional content as..

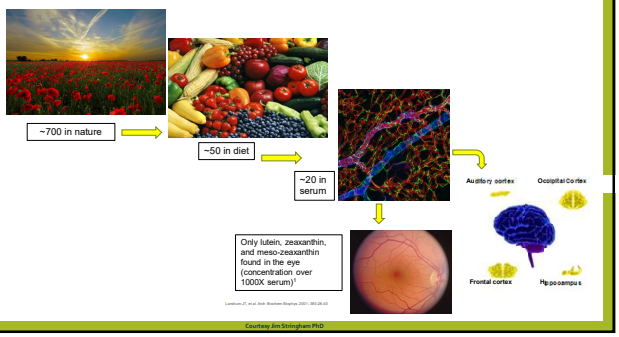
2000
43 Bowls of Spinach
84% **less** in nutrition according to USDA data

Ref: United States Department of Agriculture

32

33

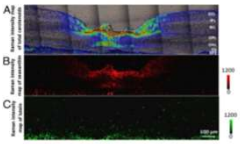
Carotenoids



Courtesy Jim Stringham PhD

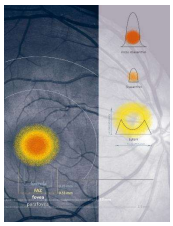
34

Distribution of Macular Carotenoids



Distributions of meso-zeaxanthin, zeaxanthin and lutein in a human retinal section

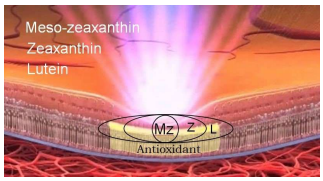
Imaging lutein and zeaxanthins in the human retina with confocal resonance Raman microscopy
Weiqing Liu, Evan W. Georgas, Gregory T. Rogonzo, Aruna Gorusupudia, Arunkumar, Rangasamthana, Yu-Yen Chanpa, Linjia Shia, Jeanne M. Fredericka, and Paul S. Bernsteina.



35

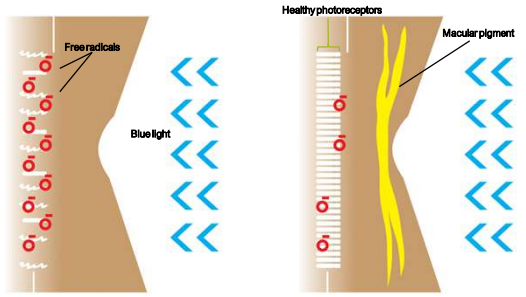
The Macula: Powerful Yet Vulnerable

- Extremely high metabolic rate
- Many free radicals to quench
- Accounts for 90% of conscious visual processing
- Provides central vision



36

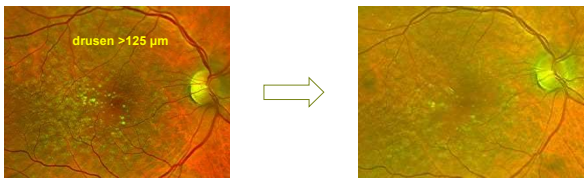
MPOD: Oxidation / inflammation feedback inhibited



37

Late Exposure to Supplementation Can Make a Difference Too: Reduction of drusen in AMD

Case: 67 YOWM, L, Z, MZ x 12 months – OD
(courtesy Gary Morgan)



9/22/17 10/18/18

38

Role of Oxidative Stress in Disease

Free Radicals Caused By:

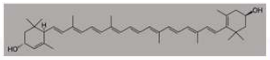
- Cellular Metabolism
- The Environment
- Lifestyle & Choices

39

Reduced by Antioxidants

- There are many antioxidants in our diet Vitamins C, E, Zinc, Lutein, Zeaxanthin and Meso-Zeaxanthin to name a few…
- Antioxidants donate / accept electrons to stabilize singlet oxygen
- Only 3 antioxidants present IN THE MACULAR PIGMENT: Lutein, Zeaxanthin, Meso-Zeaxanthin

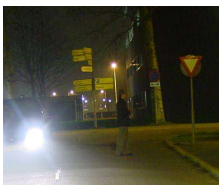
Chemical structure of lutein



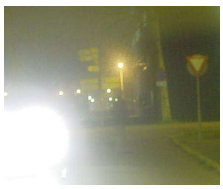
40

High vs. Low MPOD: Glare Disability Reduced

High MPOD



Low MPOD

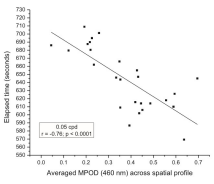


Stringham & Hammond. *Optom Vision Sci.* 2008;85:82-88; Hammond et al. Invest Ophthalmol Vis Sci. 2014;55(12):8583-9.; Nolan et al. (2016); Stringham et al. (2016)

41

Dark Adaptation Speed

Suggests increased visual cycle efficiency promoted by macular carotenoids



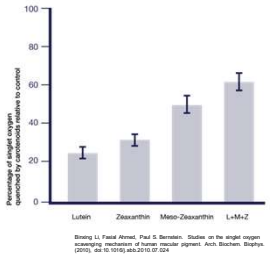
from Stringham et al. 2015

*also Stringham & Hammond, 2008; Hammond et al. 1998; Patryas et al. 2013; Hammond et al. 2014; Stringham et al. 2016

42

The Triple Carotenoid Formula

- The macular carotenoids are all exceptional antioxidants
- MZ has the highest antioxidant capacity, followed by Z, and L
- Synergistic effect of the 3 carotenoids together



Bin-ing Li, Faisal Ahmed, Paul S. Bernstein. Studies on the singlet oxygen scavenging mechanism of human macular pigment. Arch. Biochem. Biophys. (2010). doi:10.1016/j.abb.2010.07.024

43

CREST AMD (Trial 2)

Funded by the European Research Council (ERC) €1,482,342 over 5 years; Grant No. 281096

Objective

To study the effects of nutritional supplementation with the macular carotenoids on visual performance in normal subjects with early age-related macular degeneration

Design

24-month, double-blind, head to head randomized clinical.

Subjects were randomly assigned to consume 10mg lutein, **10mg *meso*-zeaxanthin,** 2mg zeaxanthin, 500mg vitamin C, 400 IU vitamin E, **25mg zinc**, 2mg copper (i.e. **Group 1**; n = 75) or 10mg lutein, 2mg zeaxanthin, 500mg vitamin C, 400 IU vitamin E, **25mg zinc**, 2mg copper (i.e. Group 2; n = 75).

Study visits were performed at baseline, 6- and 12-, 18- and 24-months.

Primary outcome measure (POM)

Change in contrast sensitivity at 6cpd

44

Results

**All data not listed

Variable	Group 1* N	Group 1* Baseline Mean	Group 1* Baseline SD	Group 1* 24 Months Mean	Group 1* 24 Months SD	Group 2‡ N	Group 2‡ Baseline Mean	Group 2‡ Baseline SD	Group 2‡ 24 Months Mean	Group 2‡ 24 Months SD	Time Effect Sig.	Time × Group Interaction Sig.
Vision												
Best corrected visual acuity, VAR	46	101.22	5.16	100.91	5.80	51	100.78	5.08	101.31	5.20	0.746	0.253
Letter contrast sensitivity, LogCS												
1.2 cpd	46	1.79	0.17	1.89	0.20	51	1.86	0.14	1.91	0.16	<0.0005	0.058
2.4 cpd	46	1.78	0.22	1.86	0.22	51	1.85	0.16	1.91	0.18	<0.0005	0.582
6 cpd, POM	46	1.53	0.24	1.57	0.29	51	1.58	0.18	1.61	0.23	0.013	0.881
9.6 cpd	46	1.29	0.28	1.31	0.30	51	1.36	0.21	1.38	0.26	0.154	0.925
15.15 cpd	46	0.92	0.33	0.95	0.34	51	0.96	0.27	1.01	0.33	0.082	0.747
Mesopic contrast sensitivity, LogCS												
1.5 cpd	46	1.55	0.22	1.62	0.24	51	1.63	0.21	1.70	0.23	0.007	0.982
3 cpd	46	1.63	0.24	1.76	0.27	51	1.69	0.18	1.84	0.27	<0.0005	0.525
6 cpd	46	1.25	0.35	1.48	0.45	51	1.34	0.34	1.49	0.42	<0.0005	0.228
12 cpd	46	0.81	0.29	0.94	0.36	51	0.87	0.28	0.96	0.35	0.002	0.605
18 cpd	46	0.33	0.13	0.39	0.23	51	0.31	0.08	0.41	0.25	<0.0005	0.369
Photopic contrast sensitivity, LogCS												
1.5 cpd	46	1.47	0.19	1.60	0.23	51	1.53	0.16	1.64	0.21	<0.0005	0.862
3 cpd	46	1.75	0.23	1.84	0.23	51	1.82	0.18	1.91	0.21	<0.0005	0.986
6 cpd	46	1.63	0.28	1.74	0.39	51	1.70	0.29	1.81	0.34	<0.0005	0.934
12 cpd	46	1.25	0.37	1.34	0.43	51	1.30	0.33	1.34	0.37	0.015	0.468
18 cpd	46	0.56	0.36	0.71	0.44	51	0.65	0.34	0.69	0.36	0.008	0.174

75% (24 of 32) of vision related measures (e.g. contrast sensitivity, glare disability, photo stress recovery) exhibited significant improvements

45

The Importance of Meso-Zeaxanthin

Of the 3 macular carotenoids, **MZ is the most powerful antioxidant**, found in the center of the fovea – where oxidative stress is highest

Estimated that 15 - 20% of population has impaired conversion of Lutein into Meso-Zeaxanthin[1]

Triple Carotenoid formula demonstrated to augment the entire MP spatial profile; a high lutein-only formula was unable to rebuild the central region[2]

References: 1. MOST. **2.** Nolan et al. 2012 (Atypical Dip Study)

46

Carotenoids + Omega-3s = Synergy

- L, Z, MZ and Omega 3s accumulate in SAME areas of the body: the retina, the brain and vascular tissues
- L, Z, and MZ protect DHA from oxidation and promote optimal function
- Speed of visual/cognitive processing is enhanced[1,2]
- Cleaner neural processing realized (enhanced signal-to-noise ratio)[3,4]

1. J Stringham, et al. Macular Carotenoid Supplementation Improves Visual Performance, Sleep Quality, and Adverse Physical Symptoms in Those with High Screen Time Exposure, *Foods*, 2017.
2. J Stringham ,et al Contrast Sensitivity and Lateral Inhibition are enhanced with macular carotenoid supplementation, *Visual Psychophysics and Physiological Optics*, 2012.
3. Nolan, et al. Enrichment of macular pigment enhances contrast sensitivity in subjects free from retinal disease: Central Retinal Enrichment Supplementation Trials – Report 1. *Retina*, 2016.
4. N Stringham, et al. Effects of macular xanthophyll supplementation on brain-derived neurotrophic factor, pro-inflammatory cytokines, and cognitive performance, *Physiology & Behavior*, 2019.

47

SOURCE OF OMEGA-3 FA ALSO IMPORTANT:

LOOK FOR THESE:

- Open sea/Wild caught fish
- Smaller Fish (fewer toxins)
- Re-esterified triglyceride supplements
- The purer, the better (more distillations/less "fish burp")
- 75% DHA/EPA in equal concentrations is ideal

AVOID THESE:

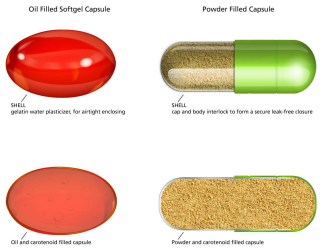
- Farm-raised fish
- Larger fish (tend to accumulate more toxins/heavy metals)
- Ethyl Ester-based supplements
- Read the labels and do the math – some supplements have very little DHA/EPA

48

Formulation and Manufacturing Matter

Some forms of encapsulation are extremely vulnerable to oxidation & light exposure

- A recent study found that of 46 supplements tested, 61% did not meet the amount claimed on the label for carotenoid content

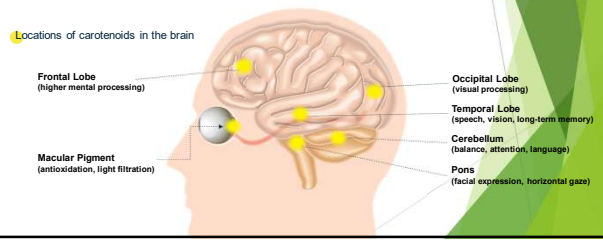


https://www.ctvnews.ca/health/many-supplements-for-vision-loss-do-not-achieve-their-label-claim-researcher-says-1.5468929

49

Support Cognitive Function

Carotenoid deposition in the brain improves visual processing and overall cognitive function measures.

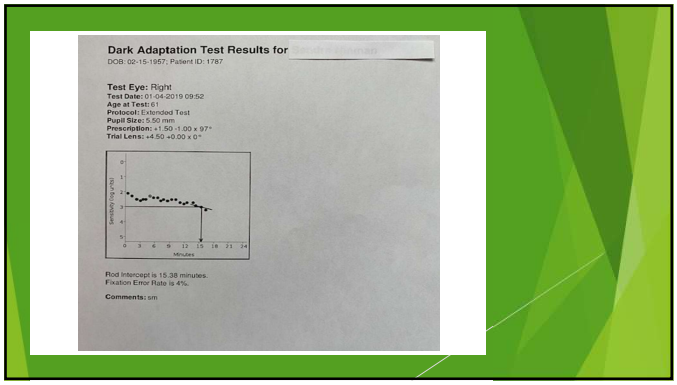


50

Case Study

- 63 year-old female with history of Rheumatoid Arthritis
- On Plaquenil 200mg PO 3-4x/week
- Family Hx of AMD; pt. never a smoker
- BCVA 20/20, OU but patient reports "I try not to drive at night; I feel very light sensitive and it's getting worse"
- SLE/fundus photography of macula shows no foveal reflex with subtle areas of RPE changes but no drusen or focal atrophy

51

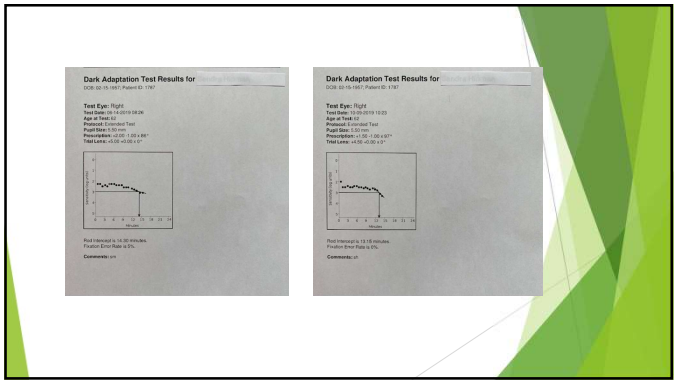


52

Prescribed Carotenoid Supplementation

- Discussed with patient the potential for RPE damage from her high-risk medication as well as her risk for AMD (reduced night vision and family history)
- Prescribed triple-carotenoid supplement containing
  - Zeaxanthin
  - Lutein
  - Meso-Zeaxanthin

53

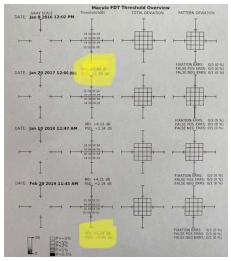


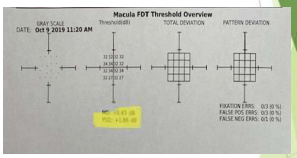
54

- **Rod Intercept time improved in same eye (OD):**
  - January 2019: 15.38 minutes (4% fixation error rate)
  - June 2019: 14.30 minutes (5% fixation error rate)
  - October 2019: 13.15 minutes (0% fixation error rate)

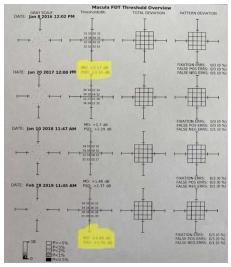
In this case, RI was not the only improvement we have found……

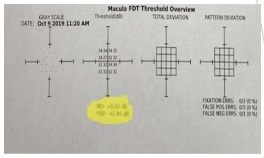
55





56



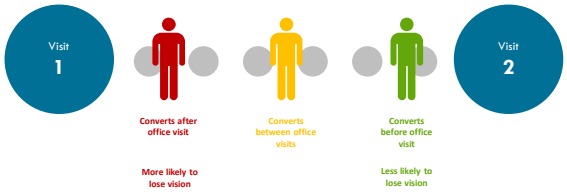


57

SWITCHING GEARS… HOW DO WE MANAGE HIGH-RISK DRY AMD??

58

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



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

59

59

Amsler grid alone has limited ability to detect visual changes

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

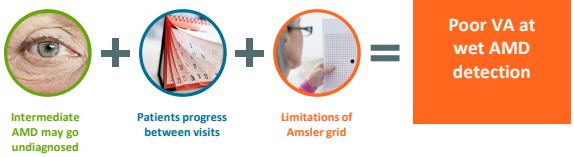
Cortical completion[1]

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):781-784. 3. Liu T, et al. *JAMA Ophthalmol*. 2013;131(3):335-341. 4. Wong TY, et al. *Ophthalmology*. 2008;115(1):116-126.

60

A Perfect Combination for Poor Visual Acuity at Wet AMD Diagnosis



Intermediate AMD may go undiagnosed

Patients progress between visits

Limitations of Amsler grid

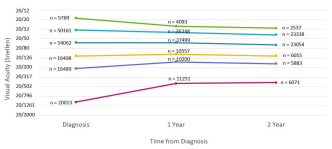
Poor VA at wet AMD detection

61

Real-world data supports clinical trial results: early diagnosis with good VA is essential to preserve functional vision with anti-VEGF therapy

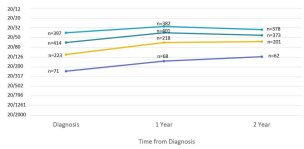
AAO IRIS® Registry Real World Data (US)[1]
January 2013 – June 2017

Mean VA at 1-year & 2-year post-diagnosis by group baseline VA

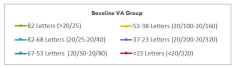


Comparison of Age-related Macular Degeneration Treatment (CATT) Trial (US)[2]

Mean VA at 1-year & 2-year



162,902 eyes diagnosed with wet AMD (153,141 patients)



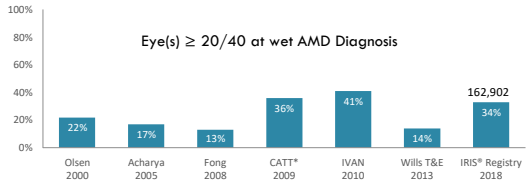
1,185 eyes diagnosed with wet AMD

References: 1. Ho AC, et al. Ophthalmic Surg Lasers Imaging Retina. 2020;51:633-639. 2. Ying GS, et al. Ophthalmology. 2015;122(12):2523-2531.

62

Clinical trial and real-world data show small proportion of patients with good VA at initiation of anti-VEGF therapy

Intermediate AMD patients who convert to wet AMD lose a substantial amount of vision before detection and treatment



Not enough diagnosed wet AMD eyes are detected early

63

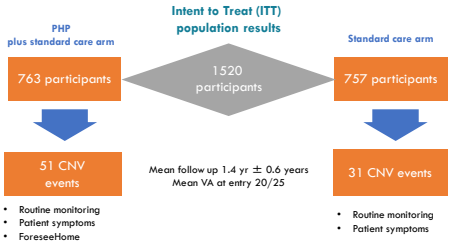
To detect wet AMD earlier we need…

More sensitive, specific disease detection

Reliable, advanced at-home monitoring

64

AREDS2-HOME Study



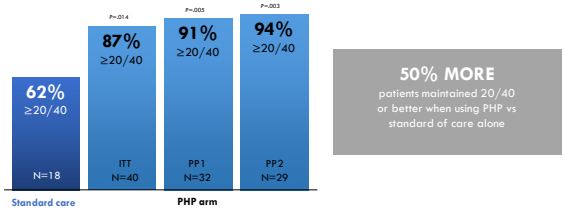
**Primary outcome:* *Change in BCVA from baseline to CNV detection*

Reference: AREDS2-HOME Study Research Group. Ophthalmology. 2016;121(2):535-544.

65

65

More patients who used PHP maintained ≥20/40 VA



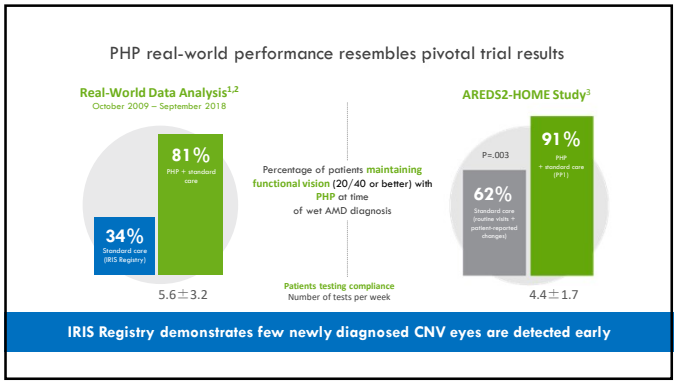
50% MORE
patients maintained 20/40 or better when using PHP vs standard of care alone

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

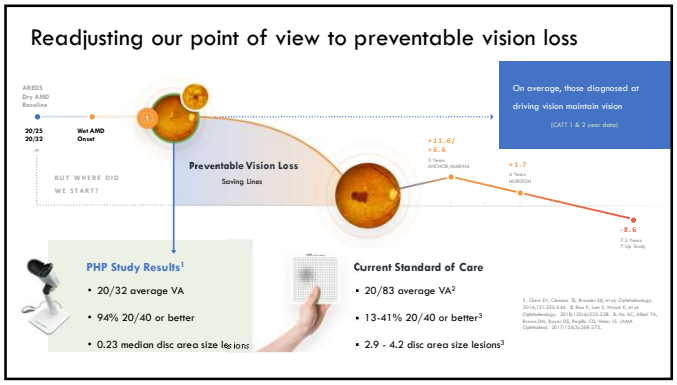
Reference: AREDS2-HOME Study Research Group. Ophthalmology. 2016;121(2):535-544.

66

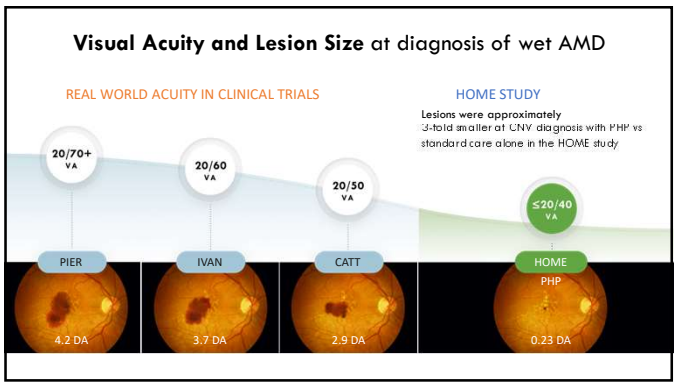
66


PHP real-world performance resembles pivotal trial results
Real-World Data Analysis[1,2]
October 2009 – September 2018
81%
PHP + standard care
34%
Standard care (IRIS Registry)
5.6±3.2
Percentage of patients maintaining functional vision (20/40 or better) with PHP at time of wet AMD diagnosis
Patients testing compliance
Number of tests per week
AREDS2-HOME Study[3]
P=.003
91%
PHP + standard care (PP1)
62%
Standard care (routine visits + patient-reported changes)
4.4±1.7
IRIS Registry demonstrates few newly diagnosed CNV eyes are detected early

67

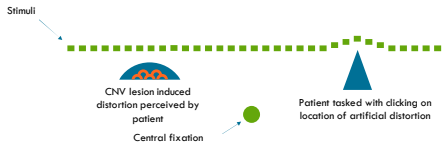

Readjusting our point of view to preventable vision loss
AREDS Dry AMD Baseline
20/25 20/32
Wet AMD Onset
BUT WHERE DID WE START?
Preventable Vision Loss
Saving Lines
On average, those diagnosed at driving vision maintain vision
(CATT 1 & 2 year data)
+11.6/ +6.6
2 Years ANCHOR/MARINA
+1.7
4 Years HORIZON
-8.6
7.3 Years 7-Up Study
PHP Study Results[1]
• 20/32 average VA
• 94% 20/40 or better
• 0.23 median disc area size lesions
Current Standard of Care
• 20/83 average VA[2]
• 13-41% 20/40 or better[3]
• 2.9 - 4.2 disc area size lesions[3]

68


Visual Acuity and Lesion Size at diagnosis of wet AMD
REAL WORLD ACUITY IN CLINICAL TRIALS
HOME STUDY
Lesions were approximately 3-fold smaller at CNV diagnosis with PHP vs standard care alone in the HOME study
20/70+ VA
20/60 VA
20/50 VA
≤20/40 VA
PIER
IVAN
CATT
HOME PHP
4.2 DA
3.7 DA
2.9 DA
0.23 DA

69

PREFERENTIAL Hyperacuity Perimetry (PHP) delivers accurate, highly sensitive, specific disease detection

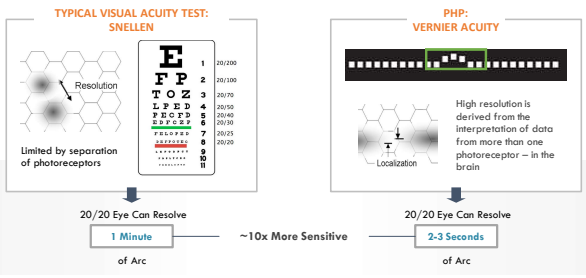


References: Data on File.

70

70

Preferential HYPERACUITY Perimetry



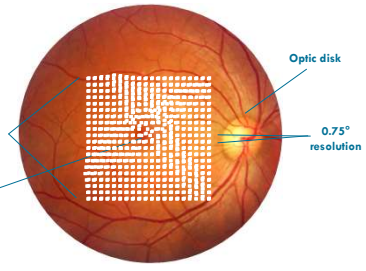
71

71

PERIMETRY: The Home PHP Test

Total of 500 data points tested 3 to 5 times each

Stimuli are presented on screen for 160 ms

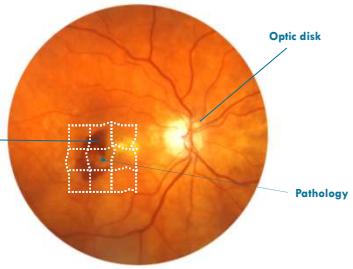


72

72

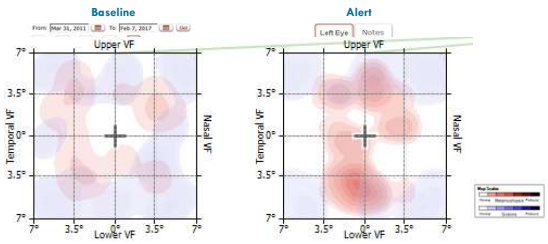
Once pathology is suspected, the area is bracketed to localize and quantify pathology

When a patient clicks on the "pathological distortion," the algorithm will present stimuli of various magnitudes over the location to determine the size and shape

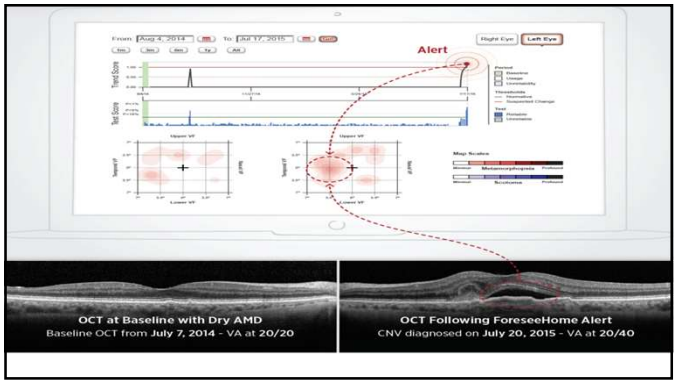


73

After pathology is quantified and localized, an Alert Metamorphopsia Map is generated



74

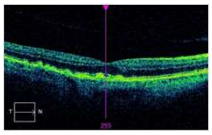


75

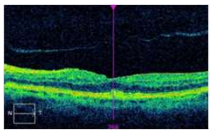
CASE 1 → Initial Exam (OU): 10/5/18

October 5, 2018:

- Patient referred for evaluation of possible age-related macular degeneration (AMD)
- VA CC 20/30^{-1} OU
- Found to have intermediate dry AMD OU
- Referred to Vision Diagnostic Clinic for Home-based PHP program OU and prescribed high-quality carotenoid supplement



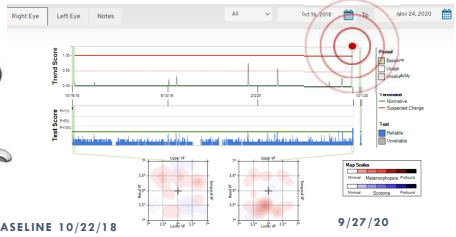
OCT OD



OCT OS

76

CASE 1 → Baseline 10/22/18: VA 20/30^{-1} (OD) prior to alert



BASELINE 10/22/18
STARTED TESTING

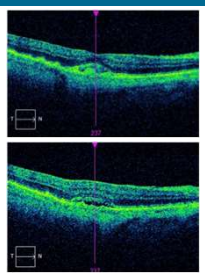
9/27/20
ALERTED

77

CASE 1 → Exam Post-Alert (OD): 10/1/20

October 1, 2020:

- Patient returned to clinic following PHP Alert on 9/27/20 OD
- VA CC 20/40^{-1} OD, 20/30^{-2} OS
- New SRF noted on OCT OD (images highlight the area of prominent fluid)
- Patient received an injection of ranibizumab 0.5 mg OD
- No prior alerts while using home-based PHP



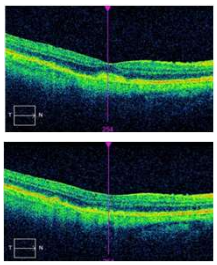
OCT OD

78

CASE 1 → Exam Post-Injection (OD): 11/3/20

November 3, 2020:

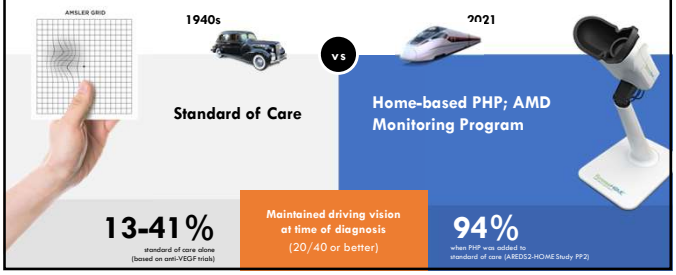
- Patient returned for follow-up after first injection OD
- VA CC $20/20^{-2}$ OD, $20/25^{-2}$ OS
- SRF resolved OD (images of the highlighted area again)
- Patient received second injection out of the planned three



OCT OD

79

At-home monitoring for conversion to wet AMD



80

Home-based PHP is appropriate for the type of patients you see every day

Unilateral or bilateral dry intermediate AMD

OR

Wet AMD in one eye and dry intermediate AMD in fellow eye

BCVA 20/60 or better

PATIENTS MUST HAVE

H35.3112	H35.3122	H35.3132
Dry intermediate Right eye	Dry intermediate Left eye	Dry intermediate Bilateral

Patients taking high-quality macular vitamins are often good candidates for Home-based PHP

81

ALOFT Study Design

Large retrospective study involving **all referred patients** from 5 clinics over 10 years

1. Retina Group of Washington
2. Virginia Eye Institute
3. Retina Associates of Kentucky
4. Wagner Macula & Retina Center
5. Elman Retina Group

2,123 patients

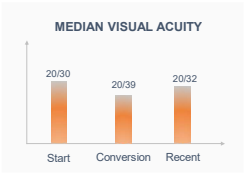
3,334 eyes

1 million+ tests | 10,000+ monitoring years

[82]

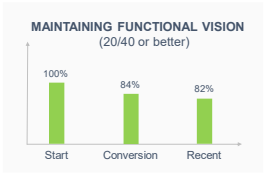
82

ALOFT Study: Visual Acuity Results



Median VA

- Start of program – 20/30
- nAMD conversion detected – 20/39
- Most recent visit – 20/32



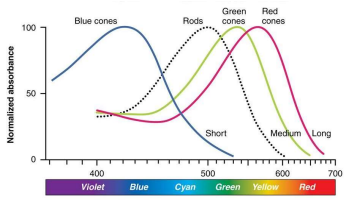
Patients at start with ≥20/40

- Maintaining 20/40 at conversion – 84%
- Maintaining 20/40 at recent visit – 82%

[83]

83

Pipeline Technologies in AMD Treatment



- Home-based OCT
- Photobiomodulation
- Treatments for GA (Geographic Atrophy) -

84

Medications for Geographic Atrophy (GA)

- **Pegcetacoplan (Syfovre)**
- Slows the progression of lesion growth in GA
- Complement C3 inhibitor
- Monthly injection reduced lesion growth by 22% (Oaks Phase 3 trial)

- **Avacincaptad pegol (Izervay)**
- Also slows progression
- Targets excessive activation of the complement system; blocks C5 protein
- Reduced lesion growth rate by 35% (Gather1 and Gather2 trials)

85

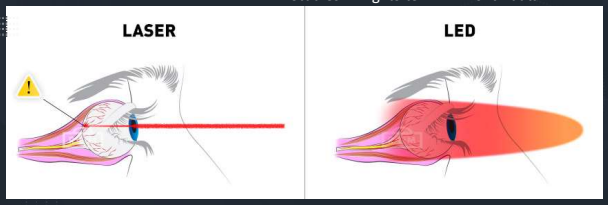
What's Next?

- It is likely that the next intravitreal medications will combine the C3 and C5 protein-inhibitors and affect the complement cascade in more than one area…

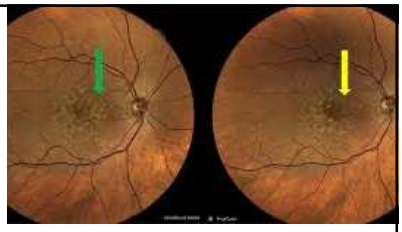
86

LASER vs. PhotoBioModulation – not the same!

- Focused Laser can be harmful
- Diffuse red and other wavelengths act on mitochondria
- Wavelengths used are critical – Approved device uses three (3) wavelengths
- Studies: – LightSite III 24-month data



87



Small Footprint Device – Uses LED light; not lasers

- Valeda Light Delivery System Approved by the FDA in November 2024 for treatment of Dry AMD

88

Uses of Photobiomodulation in Eyecare:

- Treatment is performed without optical correction
- Total treatment time for both eyes is <10 minutes/treatment
- Treatment 3x/week for 3-4 weeks
- LightSite III used three wavelengths of light; all shown to reduce inflammation and improve retinal mitochondrial function

- Fewer PBM eyes were found to progress to GA compared to the sham group:
  - 6.8% vs. 24%

89

MOST RECENT UPDATES ON VALEDA:

CHALLENGES:

- Optometric Scope of Practice
- Are we licensed to treat the retina?
- Do our liability carriers cover retinal treatments?
- Rolling out to retinal M.D. practitioners where there are few barriers

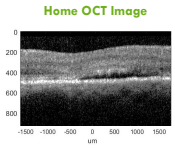
CRITERIA FOR USE:

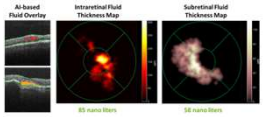
- VA between 20/32 and 20/70
- Must be dry AMD (most likely intermediate or worse)
- VA better than 20/32 or worse than 20/70 would pay "out of pocket"
- Cost to pt.: $1800 - $3000 (9 treatments)

90

Home OCT: monitoring neovascular AMD between office visits

- 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
- Device called "Scanly"



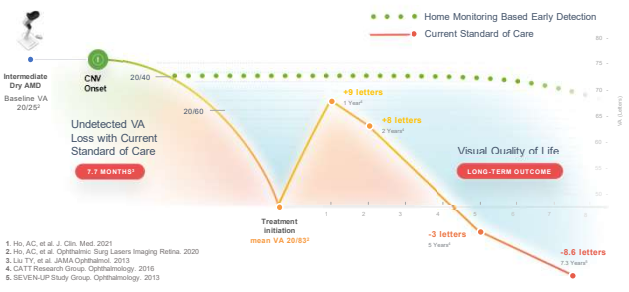


91

THANK YOU!!

92

Summary: Average nAMD Patient Journey



93