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# AMD – How to Improve Outcomes and Help Prevent Blindness

**Damon Dierker, OD, FAAO**

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COPE ID 65999-PS 2 hours

## Disclosures - Damon Dierker, OD, FAAO

- Aerie - A
- Alcon - A/C/S
- Allergan - A/C/R/S
- ArcticDx - R
- Avellino Lab - A
- Azura - A
- Bio-Tissue - A/C/R/S
- Carl Zeiss Meditec - A
- Eyevance - A/C/S
- Genentech - A
- Glaukos - A/C/S
- Gyroscope - R
- Johnson & Johnson - C
- Kala - C/S
- Lumenis - C/S
- MacuHealth - S
- MacuLogix - A/C/S
- Notal Vision - A/C/S
- NovaBay - C
- Novartis - A/C/S
- Ocular Therapeutix - A/R
- Optovue - S
- Osmotica Pharmaceutical - C
- Oyster Point Pharma - A
- Quidel - A/C
- ScienceBased Health - S
- Scope - C
- Shire - A/C/S
- Sight Sciences - A/C/S
- Sun Pharma - A/S
- Tarsus - A/R
- TearLab - C/S

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R - Research  
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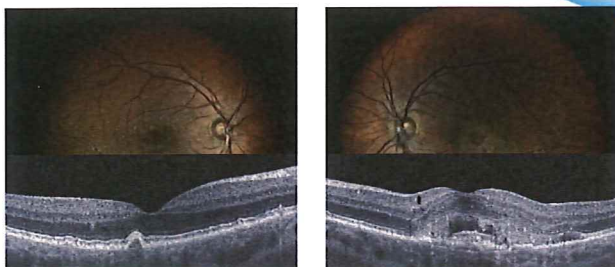
**Do you manage AMD patients on a weekly basis in your practice?**

Yes  
No

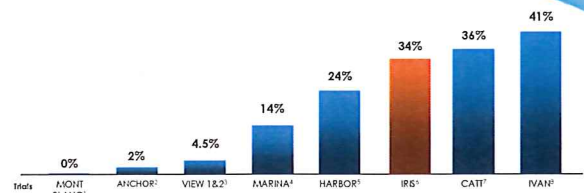
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## New Patient – Cataract Consult



## Proportion of patients with 20/40 at Wet AMD dx



Regardless of clinical trials or the real world, the majority of patients start with poor visual acuity (20/63-20/125).<sup>1-8</sup>

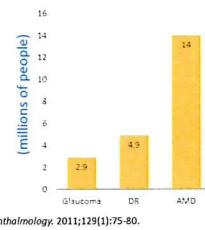
## Lecture Goals

- Review best practices in diagnosis and classification of AMD
- Understand how new technology allows for AMD detection at earlier stages
- Review evidence to support supplement use in all stages of AMD
- Present OCT strategies to detect disease progression
- Improve the care of your AMD patients and reduce the risk of blindness!

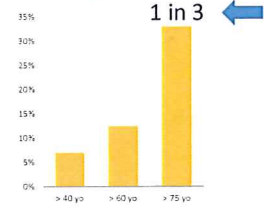


## AMD affects 14 million people in U.S.

Prevalence of Major Eye Disease in U.S.



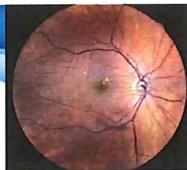
AMD Prevalence by Age in U.S.



Klein R, et al. *Arch Ophthalmology*. 2011;129(1):75-80.  
Gupta P, et al. *Invest Ophthalmol Vis Sci*. 2016 May; 57(6): 2577-2585.

### JAMA Ophthalmology | Original Investigation Prevalence of Undiagnosed Age-Related Macular Degeneration in Primary Eye Care

David C. Neely MD, Nevin J. Bray MD, Corina E. Hastings MPH, Mark E. Clark BS, Gerald McGwin Jr, PhD, Cynthia Owsley PhD



- Published in *JAMA Ophthalmology* in 2017
- 1288 eyes (644 adults  $\geq$  age 60)
- Most recent comprehensive dilated examination did not indicate a diagnosis of AMD
- Color photos were reviewed by masked, trained graders who determined the presence or absence of AMD findings

**25% of "normal" patients had findings c/w AMD**

**Almost 1/3rd of missed AMD eyes had large drusen**

Neely DC, et al. *JAMA Ophthalmol*. 2017;135(6):570-5.

## AMD Risk Factors

### Established

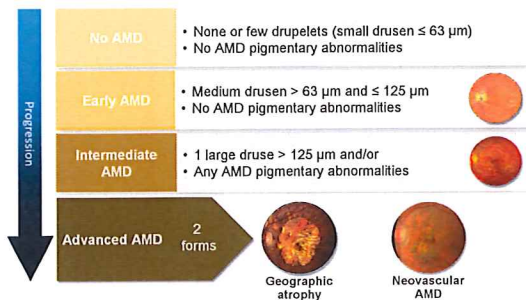
- Age
- Family history
- Smoking
- Nutrition



### Putative

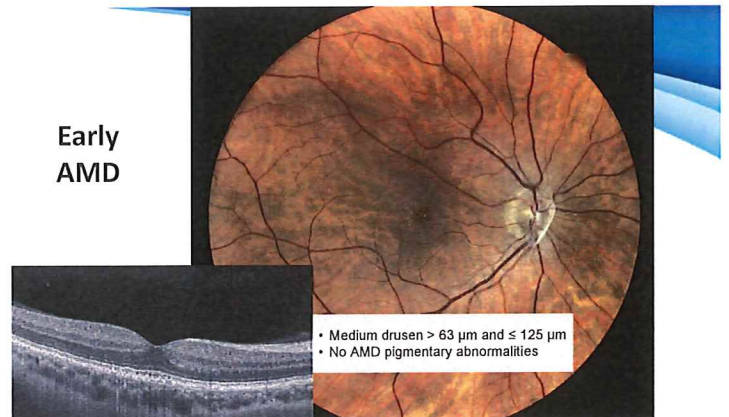
- Light exposure
- Obesity
- Cardiovascular disease
- Low macular pigment levels
- Diabetes

## The Beckman Committee Classifies AMD Into 4 Stages



Ferris FL, et al. *Ophthalmology*. 2013;120(4):844-851.

### Early AMD



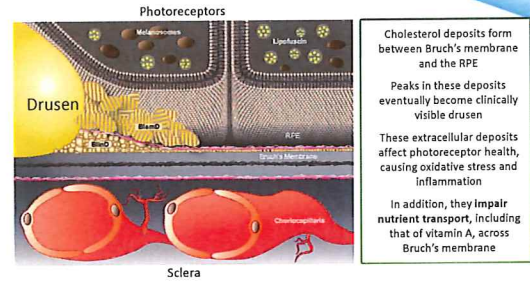


## What is the earliest symptom of AMD?

- Poor reading vision
- Decreased color perception
- Poor night vision
- Metamorphopsia

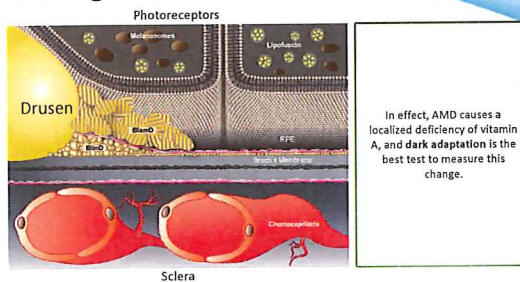
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## AMD Pathogenesis – The Oil Slick



Curcio CA, Johnson M. Structure, function, and pathology of Bruch's membrane. In: Ryan SJ, et al, eds. *Retina*, Vol 1, Part 2: Basic Science and Translation to Therapy, 5th ed. London: Elsevier; 2013:466-481.

## AMD Pathogenesis – The Oil Slick

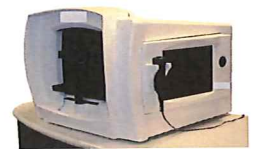


Curcio CA, Johnson M. Structure, function, and pathology of Bruch's membrane. In: Ryan SJ, et al, eds. *Retina*, Vol 1, Part 2: Basic Science and Translation to Therapy, 5th ed. London: Elsevier; 2013:466-481.

## 2014-2019: Measuring Dark Adaptation

- AdaptDx - MacuLogix
- Automated dark adaptometer
- Simple, objective tool to measure dark adaptation as earliest functional correlate of AMD
- Two clinical protocols
  - Rapid test (<6.5 minutes)
  - Extended test

CPT 92284



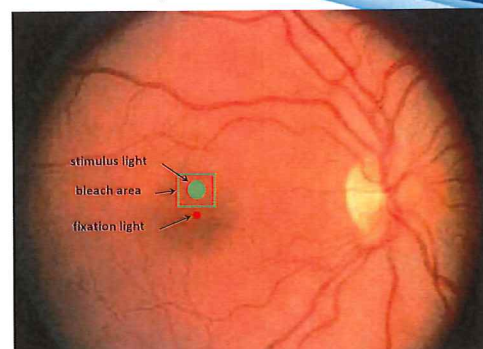
## 2020: Measuring Dark Adaptation

- AdaptDx Pro - MacuLogix
- Automated dark adaptometer
- Simple, objective tool to measure dark adaptation as earliest functional correlate of AMD
- Two clinical protocols
  - Rapid test (<6.5 minutes)
  - Extended test

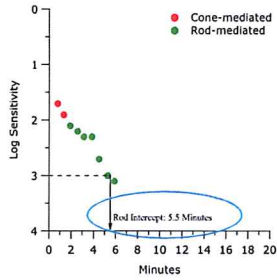
CPT 92284



## Automated dark adaptation testing



## Dark Adaptation – Normal Patient



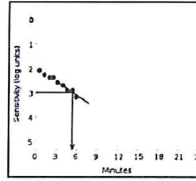
The rod intercept provides a uniform, objective parameter for characterizing dark adaptation speed.

Jackson GR, et al. *Vision Res.* 1999;39(23):3975-3982.  
Leibrock CS, et al. *Eye (Lond).* 1998;12(pt 3b):S11-S20.

## Dark Adaptation Test Results

DOB: 08-06-1957; Age: 57; Patient ID: 485922

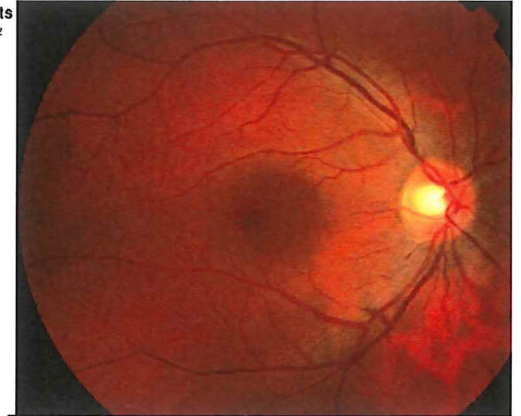
Test Eye: Right  
Test Date: 11-24-2014  
Protocol: Rapid Test  
Pupil Size: 7.00  
Spherical Correction: 4.00  
Cylindrical Correction: 0.00 @ 180°



Rod Intercept is 5.40 minutes.

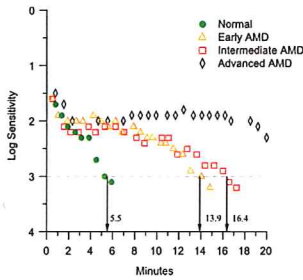
Fixation error rate: 0%.

Comments: none



## Dark Adaptation Impairment in AMD

Dark adaptation worsens as AMD progresses



Jackson et al. (2014) *IOVS* 55:1427.

## AdaptDx Diagnostic Study

Rod Intercept <6.5 = normal  
Rod Intercept >6.5 = AMD



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

### High Sensitivity:

- Correctly identified 90.6% of confirmed AMD cases

### High Specificity:

- Correctly identified 90.5% of confirmed normal cases

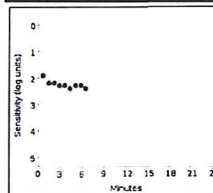
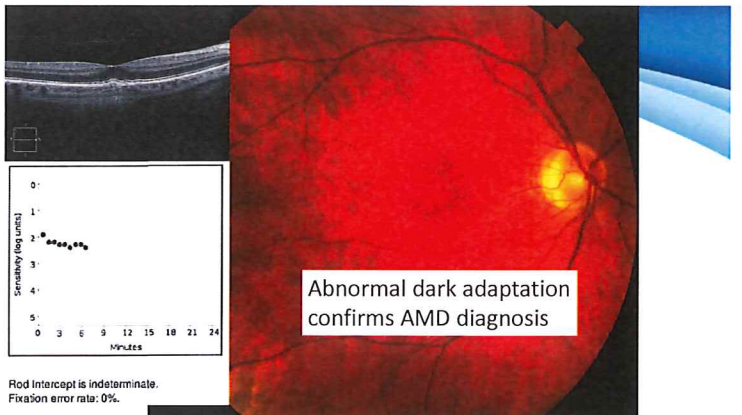
### High Accuracy:

- 90.6% overall accuracy

## How accurate are retina specialists in making the diagnosis of AMD?

- 100% - retina specialists are always right **A**
- 80% - pretty good but not great **B**
- 50% - it's a coin flip **C**

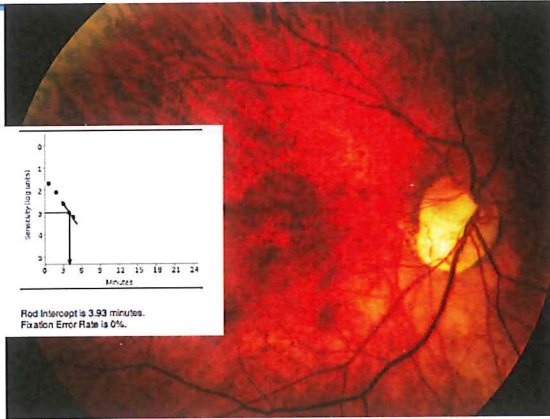
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Abnormal dark adaptation confirms AMD diagnosis

Rod Intercept is indeterminate.  
Fixation error rate: 0%.

Normal dark adaptation rules out AMD



## Better Outcomes Start with Early Detection

**UAB**  
**ALSTAR Study**

Impaired dark adaptation identifies subclinical AMD at least **three years** before it can be seen with imaging or clinical exam.

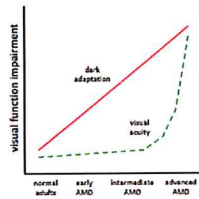
### Prospective Study of Subclinical AMD

Sample consisted of 325 adults without clinically detectable AMD. At baseline, 24% of the subjects exhibited impaired dark adaptation. AMD status determined at 3-year follow-up visit.

Owsley et al. *Ophthalmology*. 2016;123(2):344-351.

## Dark Adaptometry – Who to test?

- Clinical findings of early to intermediate AMD
- Clinical findings that kind of look like AMD
- Patients with symptoms of poor night vision
- Patients with known risk factors for AMD
  - Age  $\geq$  50
  - Caucasians
  - Family history
  - Smokers
  - Overweight
  - HTN/ $\uparrow$ cholesterol



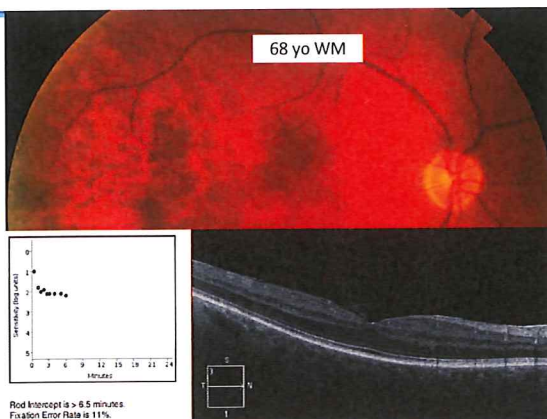
EYE SURGEONS  
of INDIANA

## Case Example

- 68 yo WM returns for annual diabetic eye exam
- Smokes  $\frac{1}{2}$  ppd, no family history of AMD
- When asked, states night vision is “not great”
- Rare drusen noted in past but no diagnosis of AMD
- BCVA 20/20 OD, OS
- SL exam: 1+ NS cataract OU

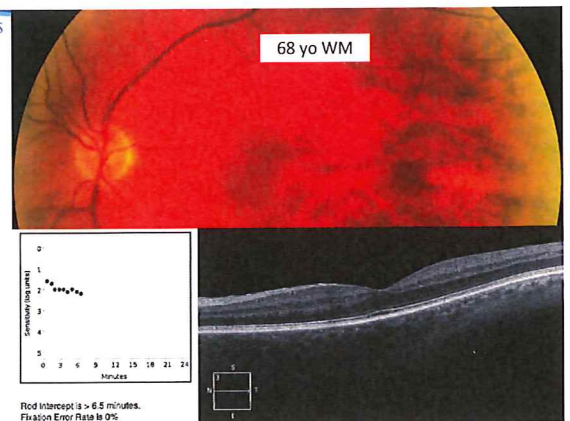
EYE SURGEONS  
of INDIANA

Abnormal Dark Adaptation  
RI>6.5 minutes



EYE SURGEONS  
of INDIANA

Abnormal Dark Adaptation  
RI>6.5 minutes



## Would you diagnose this patient w/ AMD?

Yes - definitely

No - why are we even talking about AMD in this patient?

Start the presentation to see live content. For screen share software, share the entire screen. Get help at [poller.com/app](http://poller.com/app)

## What should we do in this case?

Diagnose this patient with AMD and counsel them regarding their condition

## What can we do about early AMD?

Start the presentation to see live content. For screen share software, share the entire screen. Get help at [poller.com/app](http://poller.com/app)



## Risk Reduction Strategies – Early AMD

- Smoking cessation
- Diet
- Nutritional supplements
- HTN/cholesterol control
- Exercise/weight control
- UV/blue light protection

## DON'T SMOKE EVER AGAIN!

- Smoking and AMD
  - Depletes serum antioxidants
  - Decreases macular pigment density
  - Increases risk of progression to advanced AMD
- Discuss strategies for quitting, consider referral

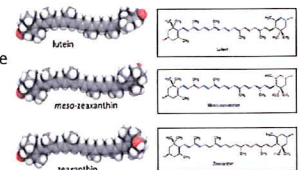


**Age-Related Macular Degeneration and Smoking Cessation Advice by Eye Care Providers: A Pilot Study**

*Helping these patients to stop smoking is the most powerful thing we can do to reduce risk of vision loss*

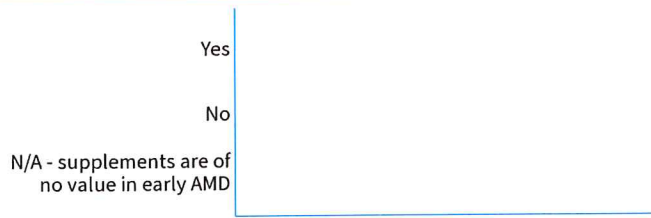
## Macular Carotenoids and AMD

- Lutein, zeaxanthin, meso-zeaxanthin
- Dietary carotenoids and AMD
  - Green leafy vegetables (spinach, kale)
  - AREDS showed benefit w/ ↑ dietary intake
    - ↓ Risk of wet AMD and geographic atrophy
    - Drusen progression slowed
- Supplemental carotenoids and AMD
  - Improve visual function
  - Improve macular pigment density
  - Reduce risk of AMD progression



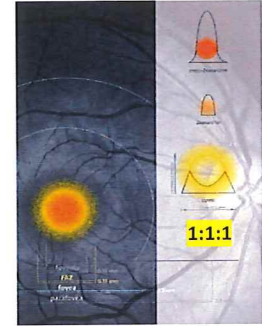
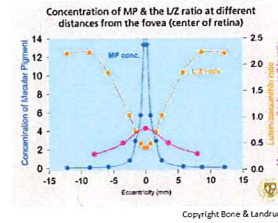
AREDS Report No. 22. *Arch Ophthalmol.* 2007;125(9):1225-1232.  
 Akufu XO et al. *Invest Ophthalmol Vis Sci.* 2017;58:5347-5360.

## Do you prescribe supplements for early AMD?



Start the presentation to see live content. For screen share software, share the entire screen. Get help at [poller.com/help](https://poller.com/help)

## DISTRIBUTION OF CAROTENOIDS IN THE MACULA

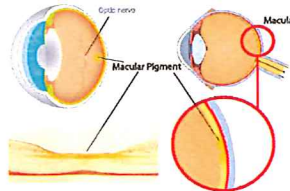


## FUNCTIONS OF MACULAR PIGMENT

*Antioxidant*

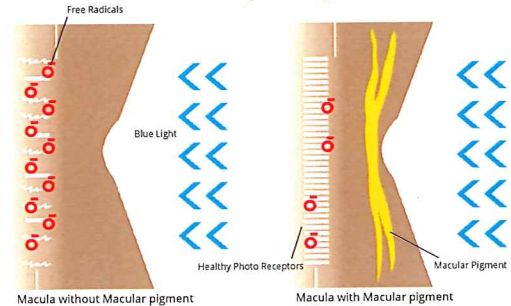
*Anti-inflammatory*

*Filters short wavelength blue light*



Khachik F et al. *Invest Ophthalmol Vis Sci.* 1997;38(9):1802-11.  
 Suk-Yee Li et al. *Invest Ophthalmol Vis Sci.* 2012;53(10):5976-5984.  
 Hammond BR Jr et al. *Invest Ophthalmol Vis Sci.* 1998;39(2):397-406.

## SHORT-WAVELENGTH (BLUE) LIGHT FILTRATION



## SOURCES OF MACULAR CAROTENOIDS



A field turns from orange to green as harvesters pick marigold flowers in Mexico.

Is Meso-Zeaxanthin necessary?



# MESO-ZEAXANTHIN OCULAR SUPPLEMENTATION (MOST) TRIALS



## MOST TRIALS: EXPLORATORY STUDIES



**2010** This study reported increases in serum concentrations of MZ and L following supplementation with all three macular carotenoids (in a MZ:LZ [mg] ratio of 10:10:2) and a significant increase in MP, after two weeks of supplementation.

**2011** Subjects supplemented with all three macular carotenoids (in a MZ:LZ [mg] ratio of 10:10:2) exhibited significant increases in serum concentrations of these carotenoids and a subsequent increase in central MP. Pathology analysis suggested no adverse clinical implications of consuming these carotenoids.

**2012** The formulation containing all three macular carotenoids (in a MZ:LZ [mg] ratio of 10:10:2) was the most efficacious in terms of achieving the highest combined concentration of the three MP constituent carotenoids in serum, thereby potentially optimizing the bioavailability of these compounds for capture by the target tissue (retina).

**2014** Serum MZ response is positively related to MP following supplementation in AMD subjects, and a formulation containing equal amounts of L and MZ (10 mg of each) appears to result in a greater augmentation of MP across the measured spatial profile, when compared with formulations lacking MZ.

## MOST TRIALS: CLINICAL STUDIES

**2012**

**Normal**

These results suggest that supplementation with all three macular carotenoids potentially offered advantages over preparations lacking MZ, both in terms of MP response and visual performance enhancement in subjects free of retinal disease.

**2014**

**AMD**

Augmentation of the MP across its spatial profile and enhancements in contrast sensitivity were best achieved after supplementation with a formulation containing high dose of MZ in combination with L and Z (in a MZ:LZ [mg] ratio of 10:10:2). The safety of consumption of this formulation was confirmed following extensive clinical pathology analysis.

## MOST TRIALS: CLINICAL STUDIES

**2015**

**10:10:2**

This final report from MOST found that the inclusion of MZ in a supplement formulation confers benefits in terms of MP augmentation and in terms of enhanced contrast sensitivity in subjects with early AMD.

## MESO-ZEAXANTHIN - REBUILDING CENTRAL DIPS

**2012**

Typical central peak of MP can be realized in subjects with atypical spatial profiles, following supplementation with a preparation containing all three macular carotenoids, but not with a supplement lacking MZ.

Group 1: High L group (L = 20 mg/day, Z = 2 mg/day).  
 Group 2: Combined Carotenoid group (MZ = 10 mg/day, L = 10 mg/day, Z = 2 mg/day).  
 Group 3: High MZ group (MZ = 10 mg/day, L = 3 mg/day, Z = 2 mg/day).

## CREST NORMAL- TRIAL 1 - SUMMARY



### Objective:

To study the effects of nutritional supplementation with the macular carotenoids on visual performance in normal subjects with low central MP (<0.56 ODU).



### Design:

1-year, placebo-controlled, double-blind, intervention study with the active intervention: 10 mg lutein, 10 mg meso-zeaxanthin, 2 mg zeaxanthin versus placebo

### Result:

Compared to placebo, statistically significant improvements from baseline contrast sensitivity were detected at 6 cycles per degree (primary outcome measure).

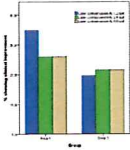
Creation: Nolan JM, Power R, Stringham J, et al. Enhancement of macular pigment enhances contrast sensitivity in subjects free of retinal disease: central retinal external supplementation trials - report 1. *Int J Ophthalmol* 2014; 7(3): 3129-3439. DOI:10.1167/14.19.20

**CREST AMD - TRIAL 2 - SUMMARY**



**Objective:**

To evaluate the impact of supplemental macular carotenoids (with and without meso-zeaxanthin [MZ]) in combination with co-antioxidants on visual function in patients with non-advanced age-related macular degeneration (AMD).



**Design:**

2-year, randomized, double-blind, intervention study comparing AREDS2 low-zinc plus meso-zeaxanthin (group 1) to AREDS2 low-zinc (group 2)

**Result:**

In terms of macular pigment augmentation and visual performance, the AREDS2 intervention with the addition of meso-zeaxanthin is as efficacious as the AREDS2 formula.

Carotenoids, Madsen EO, Reay S, Peto T et al. The impact of supplemental antioxidants on visual function in non-advanced age-related macular degeneration: a randomized, randomized clinical trial. Invest Ophthalmol Vis Sci. 2017;58(5):517-526. DOI: 10.1167/iovs.16.21192

**Is Meso-Zeaxanthin necessary?**

**YES**

**Omega 3 Fatty Acids and AMD**

- Dietary Omega 3s
  - Blue Mountains Eye Study – 1 serving/week protective
  - Women’s Health Study – 1 serving/week protective
  - AREDS showed reduced AMD incidence and progression risk in those w/ highest dietary intake
- Supplemental Omega 3s
  - AREDS2 showed no benefit
  - NAT 2 – High serum DHA levels assoc. w/ ↓ CNV risk



Christen et al. Arch Ophthalmol. 2011;129(7):921-929  
Chua B et al. Arch Ophthalmol. 2006;124:981-986  
Souled et al. Ophthalmology. 2013;120(8):1619-31.

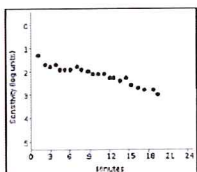


**Early AMD – Sample F/U protocol**

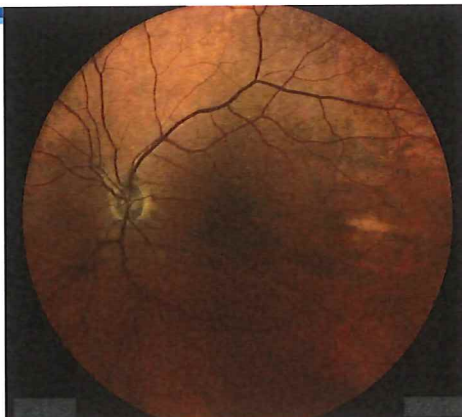
- Baseline
  - Dilated exam
  - Dark adaptation rapid test OD
  - Color photos
- F/U 1-4 weeks
  - Dark adaptation extended test OS (undilated)
  - Macula OCT (undilated)
  - Risk reduction recommendations including triple carotenoid supplement
- F/U 6-12 months
  - Dilated exam
  - Special testing (photos, OCT, dark adaptation) as indicated



Test Eye: Left  
Test Date: 03-11-2019 19:26  
Age at Test: 72  
Protocol: Extended Test  
Pupil Size: 8.00 mm  
Prescription: -2.00 +2.50 x 95°  
Trial Lens: +1.00 +2.50 x 95°

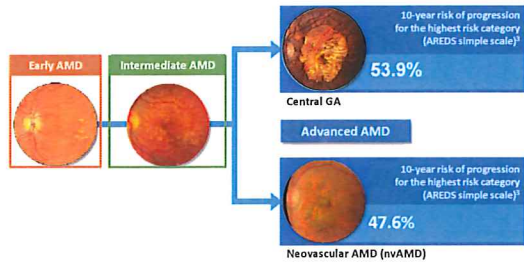


Rod Intercept is > 20.0 minutes.  
Fixation Error Rate is 0%.



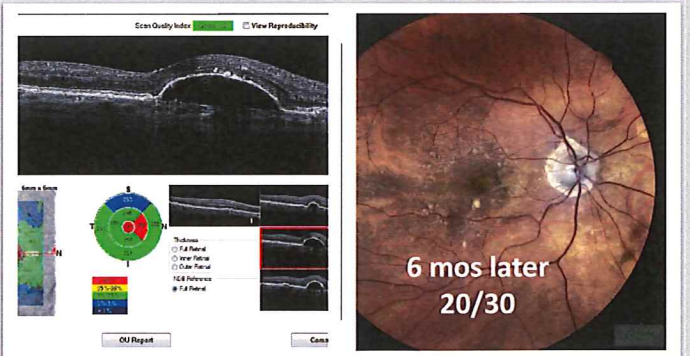
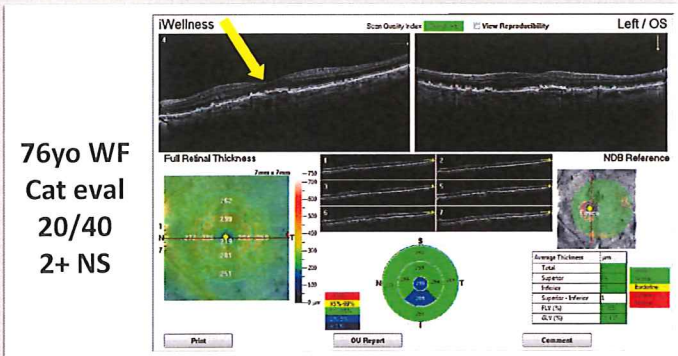
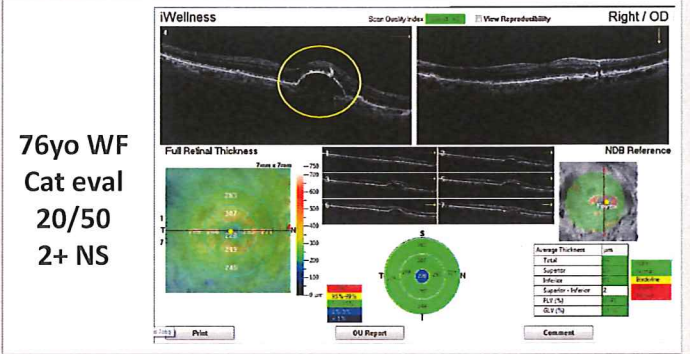
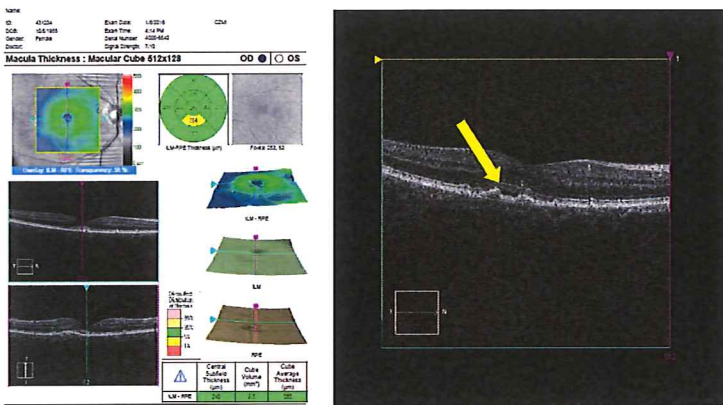
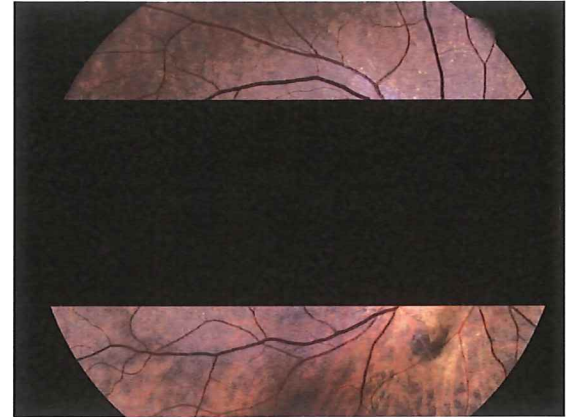
**Q&A**

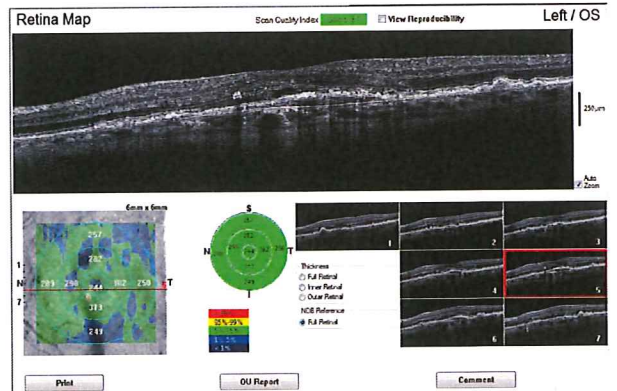
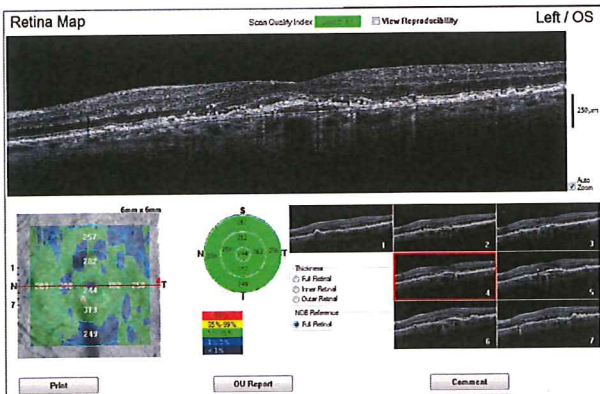
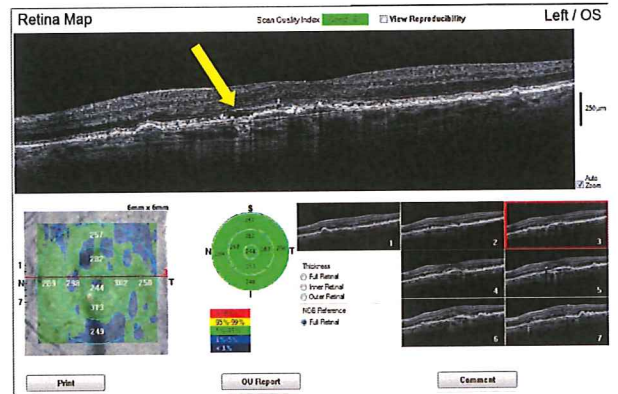
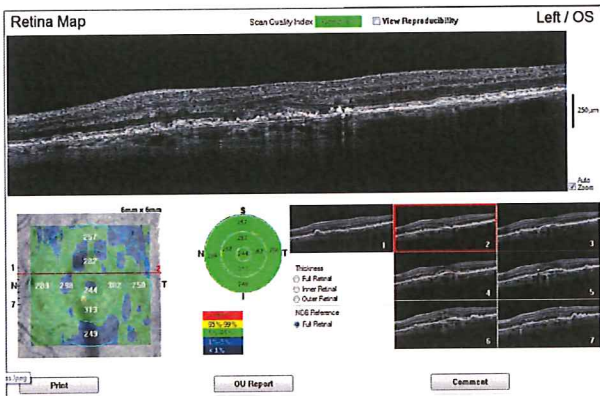
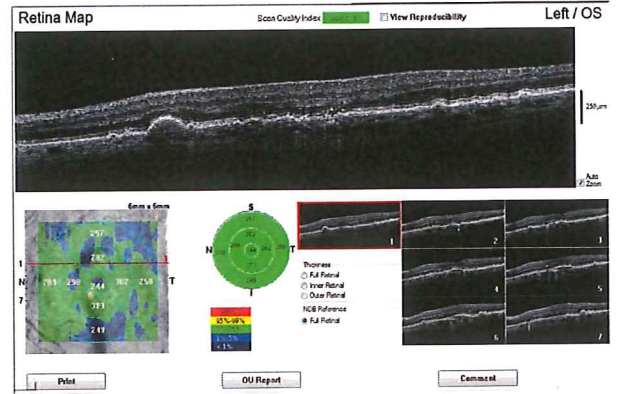
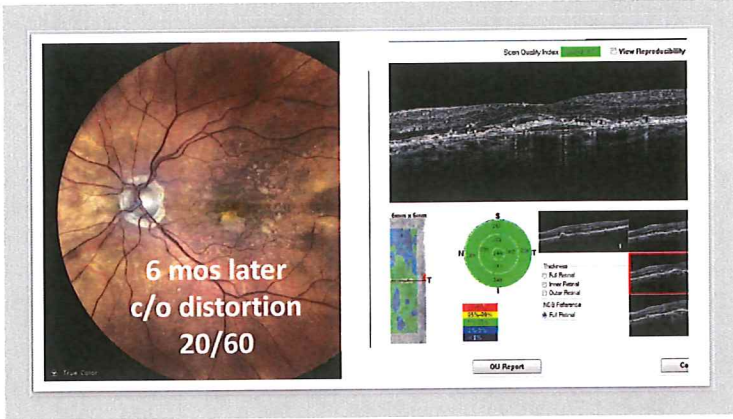
AMD Is the Leading Cause of Blindness for Caucasians in the US<sup>1</sup>

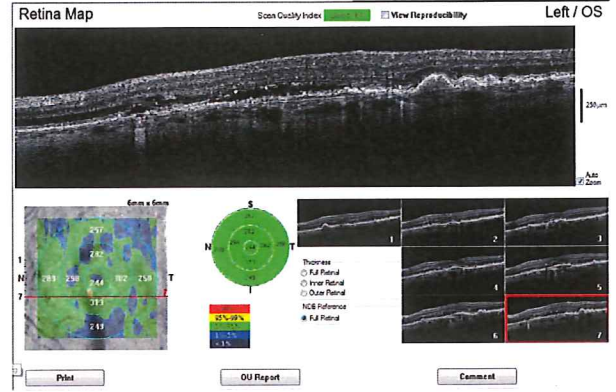
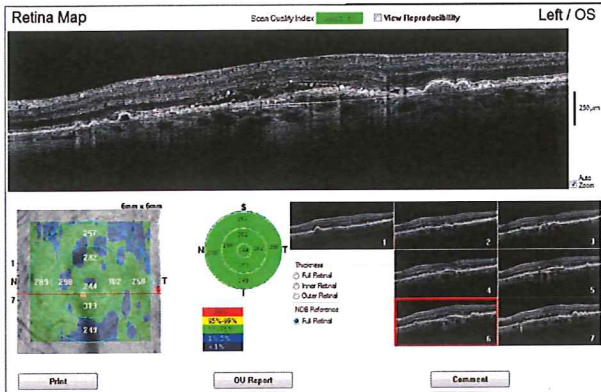


Eye Diseases Prevalence Research Group. *Arch Ophthalmol.* 2004;122(4):477-485  
 Ferris FL, et al. *Ophthalmology.* 2013;120(4):844-851.  
 Chew EY, et al. *JAMA Ophthalmol.* 2014;132(3):272-277.  
 Age-Related Study Disease Study Research Group. *Arch Ophthalmol.* 2005;123(11):1570-1574.

Advanced  
AMD  
CNV







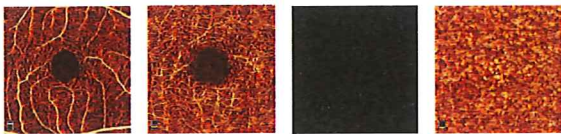
## A New Approach to Visualizing Blood Flow

### Patient Benefits

- Reduces patient burden to allow more frequent imaging
- Avoid potential side-effects of fluorescein injection

### Clinical Benefits

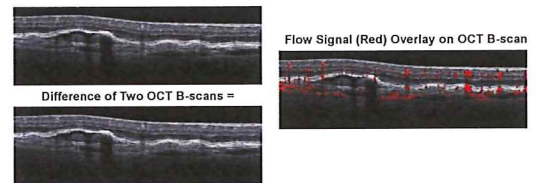
- Faster than a dye-based procedure
- Ultra-high resolution imaging of retinal microvasculature
- 3D visualization: segments retinal vasculature into individual layers



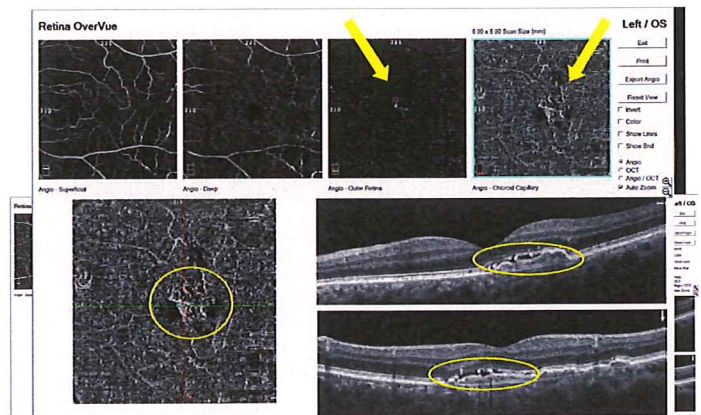
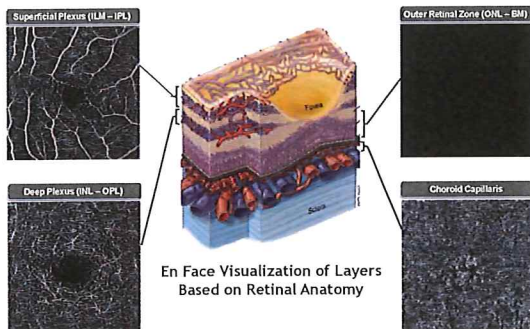
## Principles of AngioVue OCTA

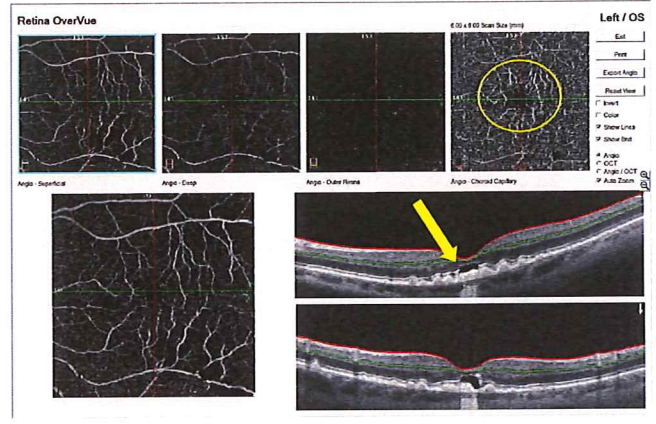
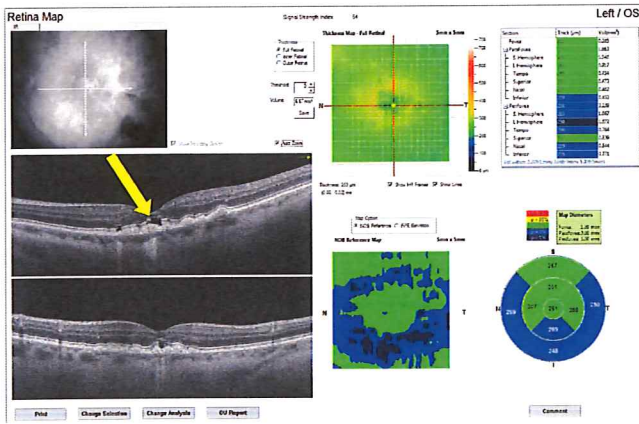
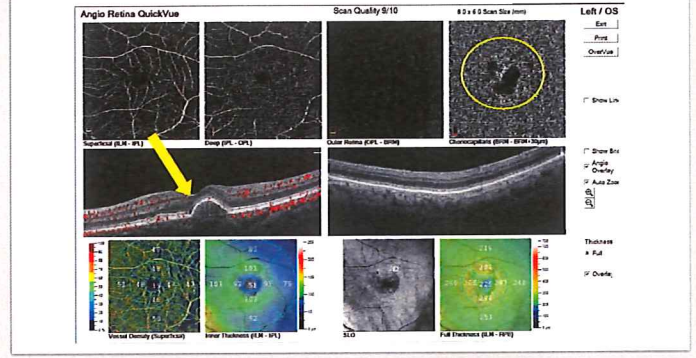
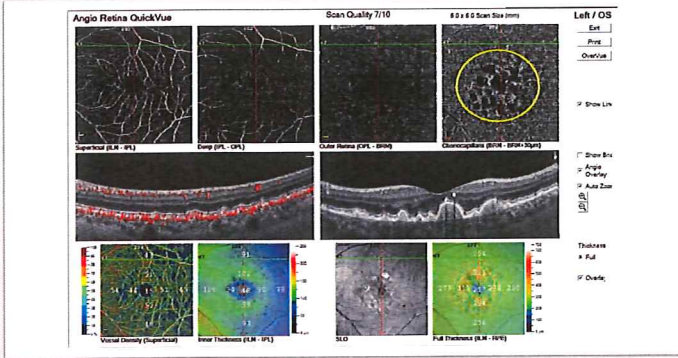
OCTA uses motion contrast to detect flow from OCT data

- Rapidly acquires multiple cross-sectional images from a single location
- Flow is the difference in signal between two sequential B-scans



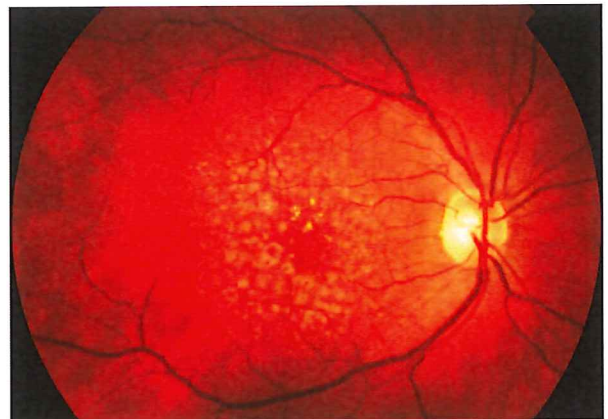
## Enface Slabs - Based on Retinal Anatomy

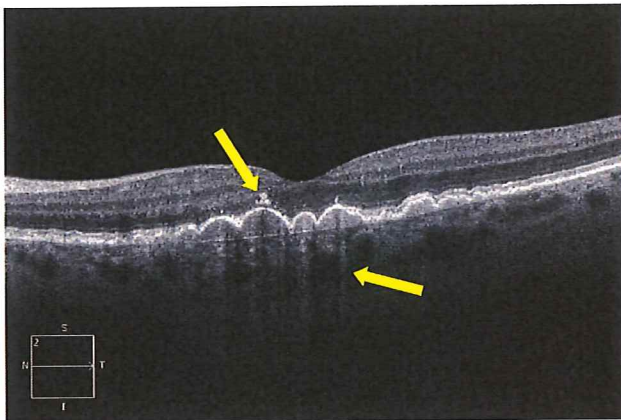
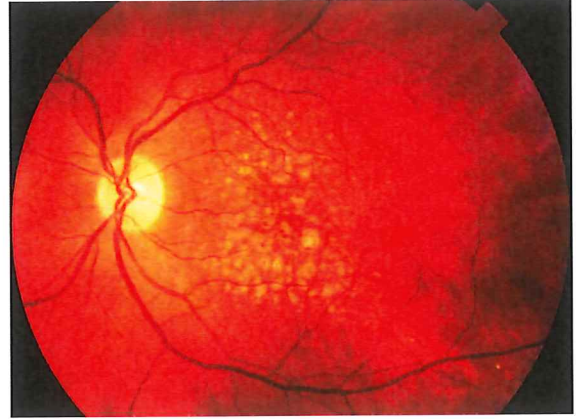
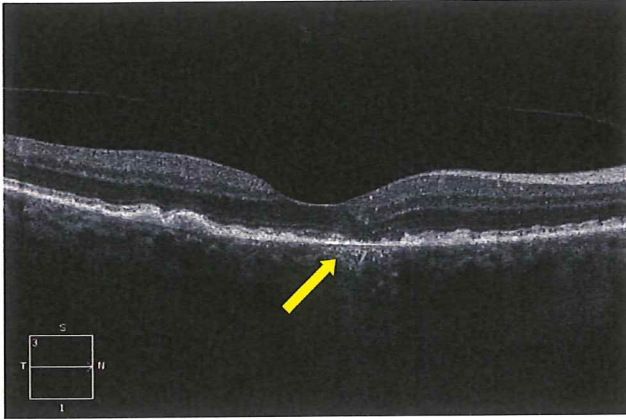




### Case Report – intermediate/advanced AMD

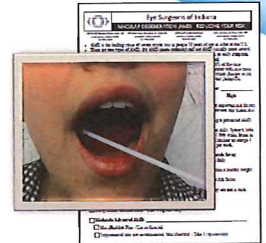
- 72 yo WF c/o vision loss OU, difficulty driving, glare
- Patient had been told they “may have early AMD”
- Visually significant cataract 20/40 BCVA OU
- Dry AMD discussed at surgical eval, OCT done
- Successful surgery w/ 20/20 BCVA OU – “my vision is perfect”
- Plan: further assessment of AMD @ final PO visit





### Risk Reduction – Intermediate AMD

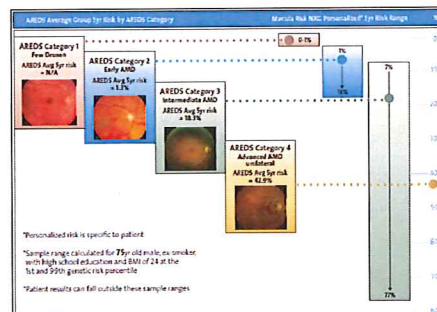
- Smoking cessation
- Diet
- Nutritional supplements
- HTN/cholesterol control
- Exercise/weight control
- UV/blue light protection



**Addition #1 - Consider genetic testing w/ Macula Risk**

### Genetic Testing Goal #1

Establish frequency of follow-up  
examinations



Genotype  
+  
Phenotype  
is more  
powerful  
than clinical  
exam alone

## Genetic Testing Goal #2

Determine if zinc  
supplementation is appropriate

## Zinc controversy

- 80 mg zinc in AREDS showed benefit in patients w/ intermediate AMD by reducing risk of progression to CNV
- Further analysis of AREDS has shown that some patients w/ a specific genotype may be harmed by 80 mg zinc (i.e. more likely to progress to wet)
- AREDS2 showed equal benefit in patients taking 80 mg vs. 25 mg zinc
- 80 mg is 700% RDA
- High-dose zinc has been linked to:
  - Urinary tract infections
  - Benign prostate hypertrophy
  - Prostate cancer
  - Alzheimer's

AREDS Report No. 8. *Arch Ophthalmol.* 2001;119:1417-1436.  
 Vavvas D et al. *PNAS.* 2018;115(4):E696-E704.  
 AREDS2 Research Group. *JAMA.* 2013;309(19):2005-2015.  
<https://ods.od.nih.gov/factsheets/Zinc-HealthProfessional/> accessed 9/1/19  
 Tolentino et al. *J Pharmacovigil.* 2016;4(1):1-5.

### Gene – AREDS Science – Only CNV is Relevant First four studies incorrectly included GA patients

#### First studies isolate genetic interaction w AREDS

1. AwH C. et al; CFH and ARMS2 genetic polymorphisms predict response to antioxidants and zinc in patients with age-related macular degeneration; *Ophthalmology*, November 2013
2. AwH C. et al; Treatment Response to Antioxidants and Zinc Based on CFH and ARMS2 Genetic Risk Allele Number in the Age-Related Eye Disease Study; *Ophthalmology*, January 2015

#### Measuring Progression to Geographic Atrophy (Wrong Disease) and CNV

3. Chew E. Y. et al. No Clinically Significant Association between CFH and ARMS2 Genotypes and Response to Nutritional Supplements; *Ophthalmology*, November 2014
4. Assel M. et al ; Genetic Polymorphisms of CFH and ARMS2 Do Not Predict Response to Antioxidants and Zinc in Patients with Age-Related Macular Degeneration; *Ophthalmology*, November 2017

#### All Studies 5-8 prove AREDS interaction for CNV

#### CNV - Validating Studies – Demonstrate Genetic Interaction and 'HARM' (AREDS vs. Placebo)

5. Seddon J.M. et al. Response to AREDS supplements according to genetic factors: survival analysis approach using the eye as the unit of analysis; *BIO*, July 2016
6. Vavvas D. et al; CFH and ARMS2 genetic risk influences the safety and efficacy of AREDS against progression to Wet AMD (WV); *PIAS*, January 2018;
7. Zanke B. Letter to the Editor re: Assel et al., *Ophthalmology*, May 2018

#### ASRS 2019 - Genetic Interaction with AREDS against CNV

8. Kaufman S. et al. Multiple Practice analysis of Harm with C2A0 genotype and AREDS against wet AMD.

## THE GAIN STUDY:

## GENETICS AND AREDS FORMULA INTERACTION IN NEOVASCULAR AMD

Stephen R. Kaufman, MD  
Pradeepa Yoganathan, MD FRCSC

Kent W. Small, MD  
Stephen M. Conti, MD

Deepam Rusia, MD  
Robert E. Wenz, MD

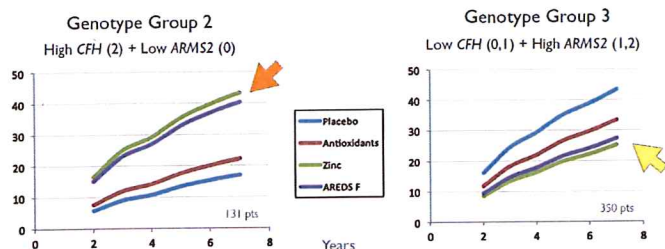
Sophia I. Pachydaki, MD  
Mark A. Gersman, MD

Fadi S. Shaya, BS      Rafal Kustrza, PhD

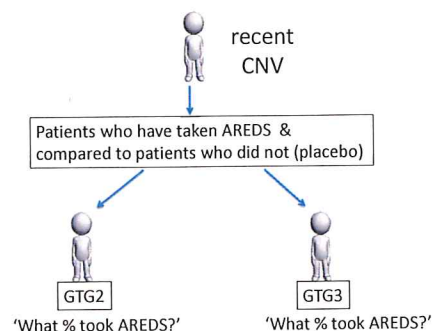
## GAIN Study: The Genetics + AREDS Formula Interaction in Neovascular AMD

## BACKGROUND

Progression rate to advanced AMD when exposed to AREDS F or Zinc vs Placebo

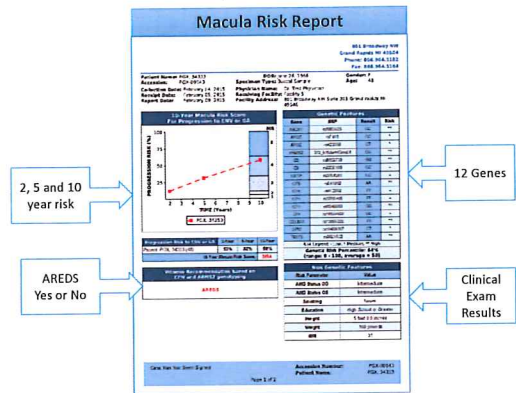
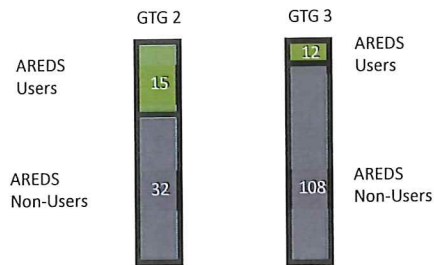


## GAIN Study: The Genetics + AREDS Formula Interaction in Neovascular AMD





The odds of AREDS Formula use in GTG 2 vs GTG 3: 4.22 (p = 0.00126)



Risk Reduction – Intermediate AMD

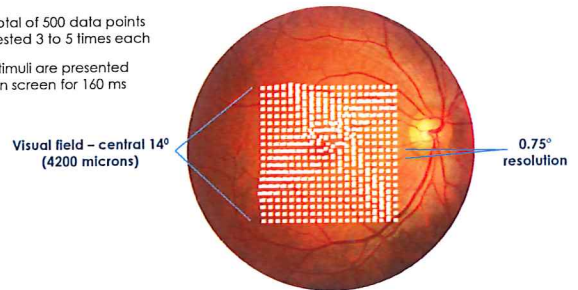
- Smoking cessation
- Diet
- Nutritional supplements
- HTN/cholesterol control
- Exercise/weight control
- UV/blue light protection



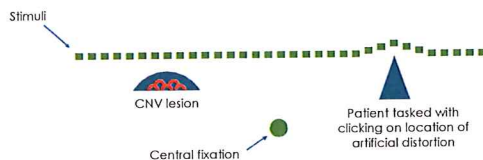
Addition #2 - Consider home monitoring

The ForeseeHome test

Total of 500 data points tested 3 to 5 times each  
Stimuli are presented on screen for 160 ms



ForeseeHome Test Procedure



When the elevation caused by CNV is larger than the Artificial Distortion, the patient will preferentially pick this spot of true distortion



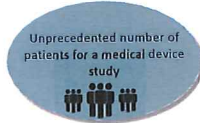
The HOME Study

## Study Methods & Demographics



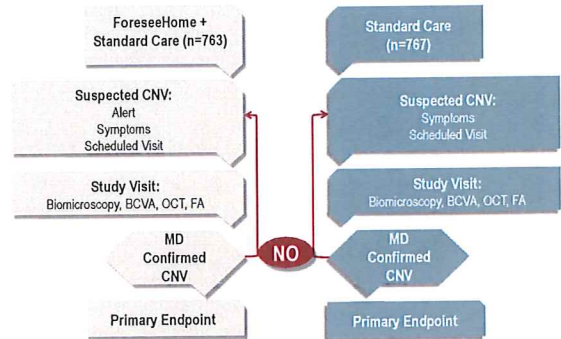
Does home monitoring with ForeseeHome (PHP) plus standard care result in earlier detection of progression to CNV when compared to standard care alone?

- Inclusion:** intermediate dry AMD eye(s)
  - ≥ 1 large druse (≥125 microns)
  - VA ≥ 20/60
  - No CNV, scarring, or central GA in the study eye(s)
- 1520 patients** enrolled from 44 AREDS2 centers



Chew EY, et al. Ophthalmology 2014;121(2):535-544.

## Study Design



Chew EY, et al. Ophthalmology 2014;121(2):535-544.

## Outcome Measures

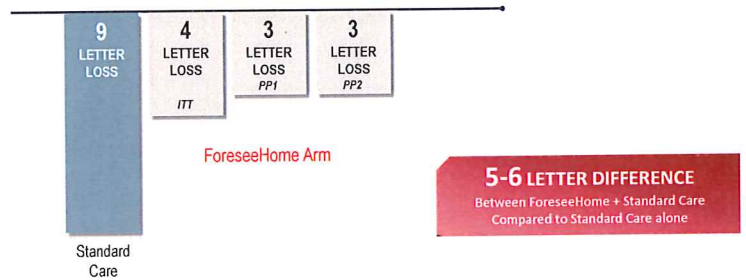


**Primary Outcome:** Visual acuity change from baseline to diagnosis of exudative CNV

- Secondary Outcomes**
  - Additional VA outcomes (i.e. proportion maintaining ≥20/40 at diagnosis)
  - Sensitivity and specificity ("First to alert" and false positive alert rate)
  - Lesion characteristics at the time of CNV diagnosis

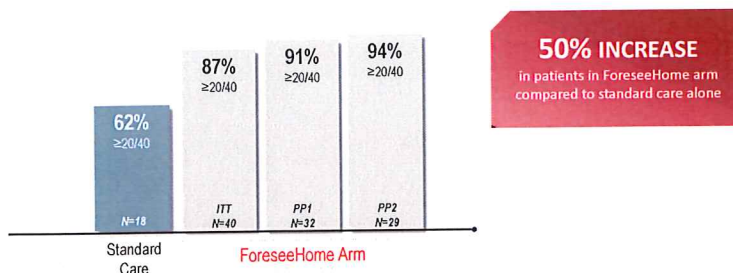
Chew EY, et al. Ophthalmology 2014;121(2):535-544.

## Change in VA Score from Baseline at CNV Detection



Chew EY, et al. Ophthalmology 2014;121(2):535-544.

## Proportion of Eyes Maintaining ≥20/40 at CNV Detection



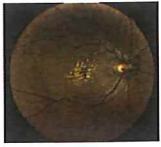
Chew EY, et al. Ophthalmology 2014;121(2):535-544.



One of the very few studies in Ophthalmology that has been stopped due to **POSITIVE EFFICACY**

### DSMC RECOMMENDATION

- On April 30, 2013, the DSMC reviewed the study results and concluded that study eyes at risk of AMD progression presented to their study sites with **SIGNIFICANTLY BETTER VISION WHEN THEIR NEOVASCULAR AMD DEVELOPMENT WAS DETECTED BY THE FORESEEHOME DEVICE** as compared to standard monitoring.
- Therefore, the DSMC **UNANIMOUSLY RECOMMENDED EARLY TERMINATION OF THE STUDY** AS THEY WERE CONFIDENT THAT THE STUDY HAD MET ITS PRIMARY OBJECTIVE; namely, demonstrating that eyes at high risk of progression to neovascular AMD can be identified with better levels of vision when they are detected by use of the home monitoring device as compared to standard methods.



**Article**  
**Real-World Performance of a Self-Operated Home Monitoring System for Early Detection of Neovascular Age-Related Macular Degeneration**

Allen C. Ho <sup>1,2</sup>, Jeffrey S. Heier <sup>2,3</sup>, Nancy M. Holkamp <sup>1</sup>, Richard A. Garfinkel <sup>1,3</sup>, Byron Ladd <sup>1</sup>, Carl C. Anh <sup>4</sup>, Rishi P. Singh <sup>1</sup>, George E. Sanborn <sup>4</sup>, Jennifer H. Jacobs <sup>4</sup>, Michael J. Elman <sup>1</sup>, Anat Loewenstein <sup>1,3,4</sup> and David A. Eichenbaum <sup>2,3</sup>

- Large scale retrospective analysis of 3.2 million tests using ForeseeHome
- Identified 306 eyes that converted to wet AMD
- Functional vision (20/40 or better) at conversion was 81%
- "The home telemonitoring system can markedly increase early detection of conversion to wet AMD"

Ho AC, Heier JS, Holkamp NM, Garfinkel RA, Ladd B, Anh CC, Singh RP, Sanborn GE, Jacobs JH, Elman MJ, Loewenstein A, Eichenbaum DA. Real-World Performance of a Self-Operated Home Monitoring System for Early Detection of Neovascular Age-Related Macular Degeneration. *J Clin Med.* 2021 Mar 25;10(7):1355.

**Intermediate AMD – Sample F/U Protocol**

- Baseline
  - Dilated exam
  - Macula OCT
  - Color photos
  - Genetic testing
- F/U 1 month
  - Macula OCT (undilated)
  - Consider dark adaptation extended test (undilated)
  - Consider home monitoring
  - Personalized risk reduction recommendations including triple carotenoid supplement +/- zinc
- F/U every 4-6 months
  - Dilated exam
  - Macula OCT every visit
  - Color photos and dark adaptation extended test as indicated

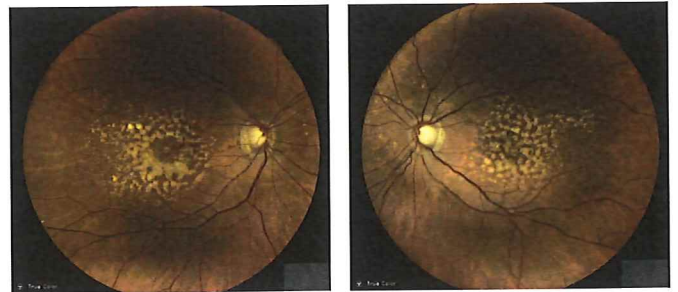
**FOR IMMEDIATE RELEASE**

**Allegro Ophthalmics Announces Positive Topline Vision Results of Phase 2 Study Evaluating Risuteganib in Patients with Intermediate Dry Age-Related Macular Degeneration**

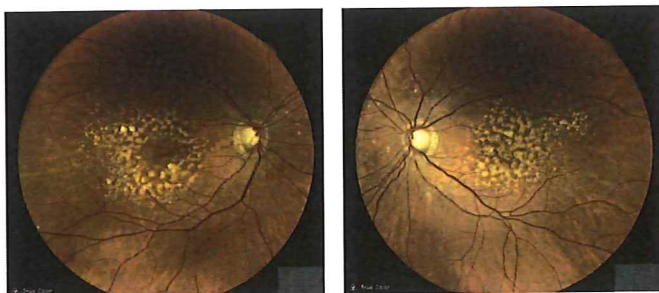
*— U.S. Phase 2 Trial Met Primary Endpoint with Statistical Significance  
 -- 48% of Patients in the Risuteganib Arm Gained ≥ 8 Letters of Vision from Baseline*

**SAN JUAN CAPISTRANO, CA — June 4, 2019 — Allegro Ophthalmics, LLC**, a privately held biopharmaceutical company focused on the development of novel anti-integrin therapies for the treatment of ocular diseases, today announced positive topline results of its U.S. Phase 2 study of risuteganib (Luminata<sup>®</sup>) for the treatment of intermediate nonexudative age-related macular degeneration (dry AMD). The clinical trial met its primary endpoint with 48 percent of patients in the risuteganib arm gaining ≥ 8 letters of vision at week 28 compared to baseline.

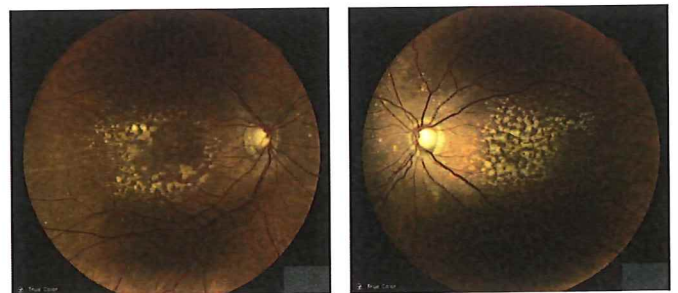
**70 yo WF – Allegro Study OD**



**70 yo WF – Allegro Study OD**

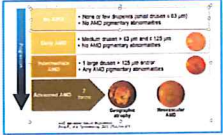


**70 yo WF – Allegro Study OD**

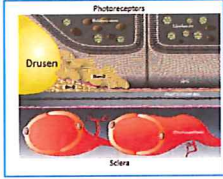




AAO National Eye Institute  
**Prevalence of Undiagnosed Age-Related Macular Degeneration in Primary Eye Care**  
Quinn, Kelly, Hill, Sear, Li, Ray, Hill, Cantello, Hough, Nishi, Sisk, C. Clark, et al. JAMA Ophthalmol 2013; 131:1005-1012



## Summary



**Eye Surgeon's Evidence**

Small text describing the evidence for AMD, including references to the National Eye Institute and the American Academy of Ophthalmology.

Thank You!

[damon.dierker@esi-in.com](mailto:damon.dierker@esi-in.com)