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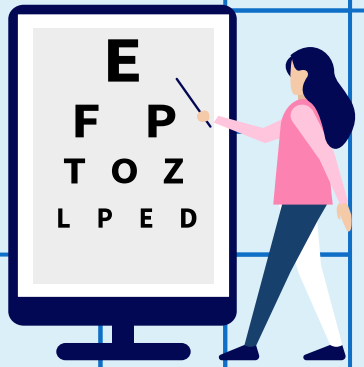
Early Intervention Strategies for Dry AMD & Presbyopia

vision expo



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Grantor Statement

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- Apellis
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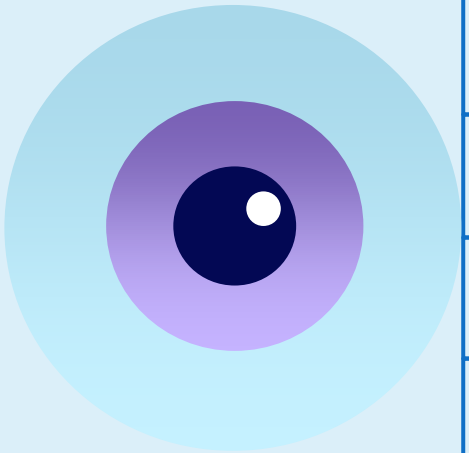


Learning Objectives

- Summarize the prevalence of early-stage presbyopia and the incidence and risk factors for the development of intermediate dry AMD and GA and the impact on functional and anatomical outcomes (Knowledge)
- Compare the mechanisms of action for current and emerging pharmaceutical treatments of early-stage presbyopia based on published clinical trial data and real-world reports, and identify ideal patient candidates for the treatment options (Knowledge, Competence, Performance)
- Integrate multimodal diagnostic strategies, including OCT-A, for early diagnosis and classification of dry AMD/GA (Competence, Performance)
- Assess safety and efficacy data for new and emerging intermediate dry AMD and GA treatments, including complement inhibition and multiwavelength photobiomodulation, understand the importance of earlier intervention, and initiate early collaborative management with retina specialists who are utilizing these therapies (Knowledge, Competence, performance)

Program Overview

Welcome + Introduction | Steven Ferrucci (5 Minutes)

Dry AMD/GA
Epidemiology & Risk Factors
Diagnostic Strategies, Management & Treatment Advances
(20 Minutes)

- Steven Ferrucci
- Mary Beth Yackey

Presbyopia
Epidemiology & Impact, Management & Treatment Advances
(20 minutes)

- Selena McGee
- Josh Davidson

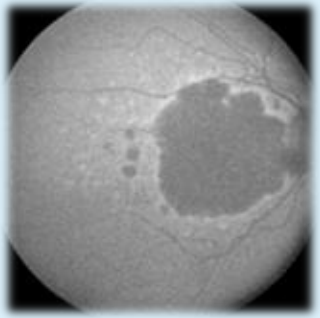
Key Takeaways and Q&A | Steven Ferrucci (5 Minutes)

Epidemiology & Risk Factors

Dry AMD & GA

Steven Ferrucci, OD, FAAO

AMD and GA Prevalence



- AMD is a degenerative disorder of the macula
- Most common cause of irreversible vision loss globally
- Classified as:
  - Early
  - Intermediate
  - advanced non-neovascular (dry) AMD
  - advanced neovascular (wet) AMD

~ 80% of people with AMD have the dry form

- Dry AMD characterized by progressive degeneration of the macula
  - Advanced dry form leads to atrophic scars and, ultimately, geographic atrophy (GA)
- ~ 1 million people in the United States have GA in at least 1 eye
- Prevalence of GA in Medicare populations greatest among patients aged ≥75 years and individuals classified as White race
- 2021 estimates: 28.0% of Medicare patients with GA also have wet AMD

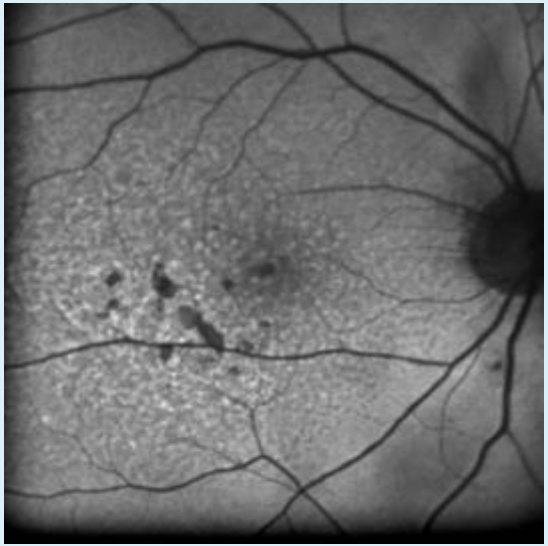
Schultz NM, et al. Global Burden of Dry Age-Related Macular Degeneration: A Targeted Literature Review. Clin Ther. 2021;43(10):1792-1818.
Saundankar V, et al. Annual prevalence of geographic atrophy and wet age-related macular degeneration among Medicare Advantage enrollees in a US health plan. J Managed Care Specialty Pharmacy. 2025;31(1):

AMD and GA Risk Factors for Progression

- Phenotypic risk factors -- drusen and pigment abnormalities -- important for predicting disease progression
- Demographic, environmental, genetic and molecular risk factors more valuable at earlier disease stages

Patients more likely to develop AMD if they:

- eat a diet high in saturated fat
- are overweight
- smoke cigarettes
- have hypertension (high blood pressure)
- have a family history of AMD
- >50 years old



Heesterbeek TJ, et al. Risk factors for progression of age-related macular degeneration. Ophthalmic Physiol Opt. 2020;40(2):140-170.
AAO. Understanding Macular Degeneration. Updated November 25, 2025. https://www.aao.org/eye-health/diseases/amd-macular-degeneration. Accessed March 5, 2026.

Quality of Life Affected By Dry AMD and GA

Sports

- Less exercise
- Less engagement with friends

Household Chores

- Less social interactions, unsure of a clean house

Personal Hygiene

Too much effort to prepare for outing; social isolation

Reading

- Loss of reading as a hobby

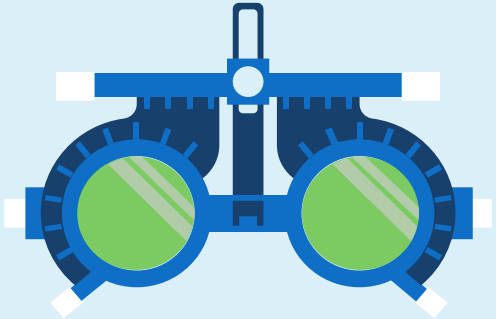
Transportation

- Isolation from family and friends
- Reliance on others

Need for Aids

- Need to always carry magnifier

Chamberlain CX, et al. Impact of Dry Age-Related Macular Degeneration on Daily Activities and Quality of Life: Interview Findings From Patients and Caregivers Relative to a General Population. Clin Ophthalmol. 2025;19:599-615.

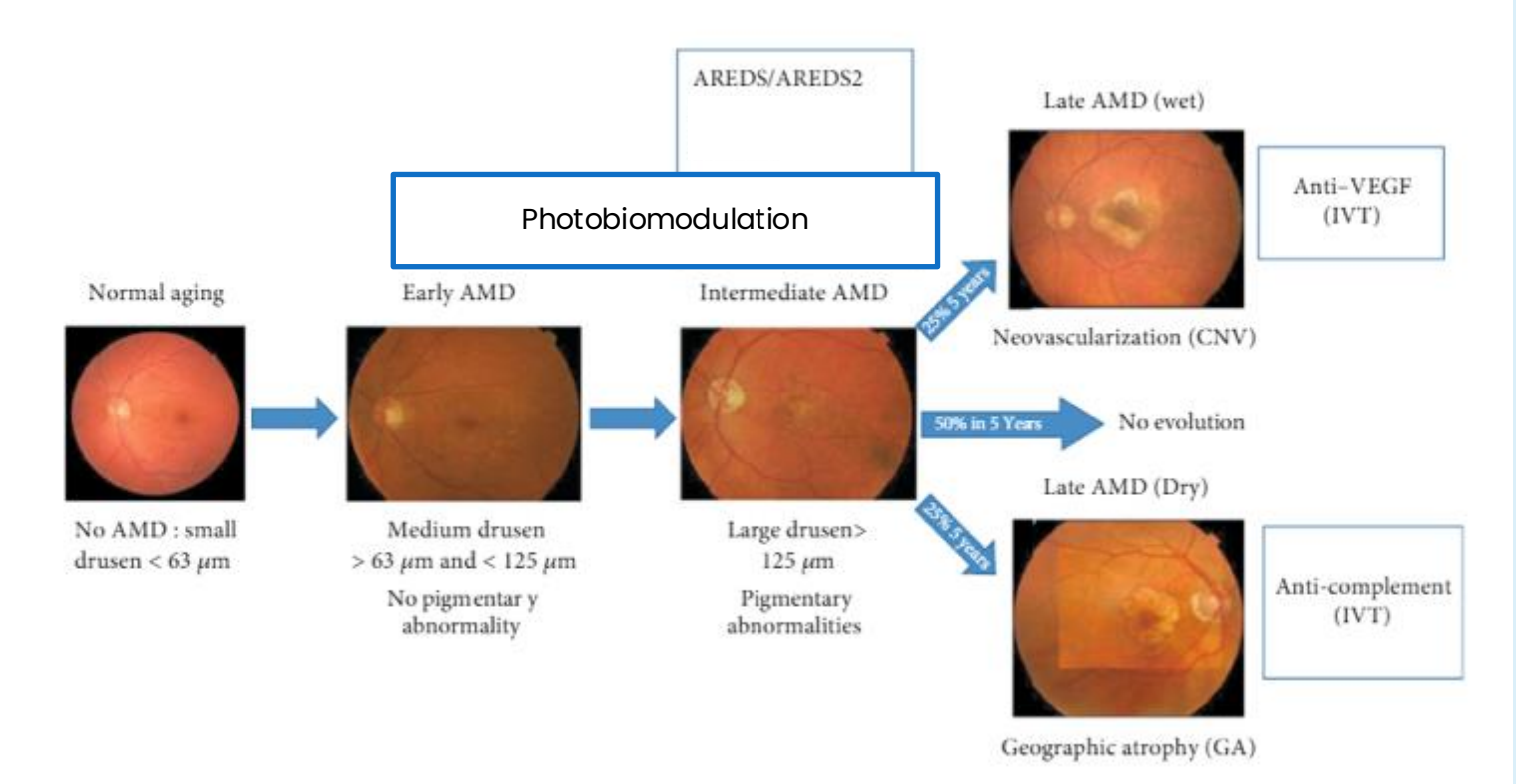


Diagnostic & Monitoring Strategies

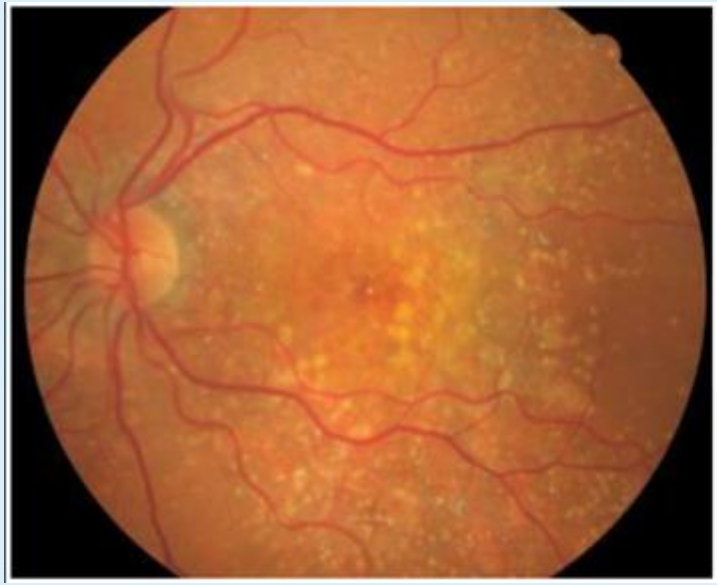
Dry AMD/GA

Mary Beth Yackey, OD

Age Related Macular Degeneration Stages



Drusen: First Clinical Feature of AMD
What is drusen?



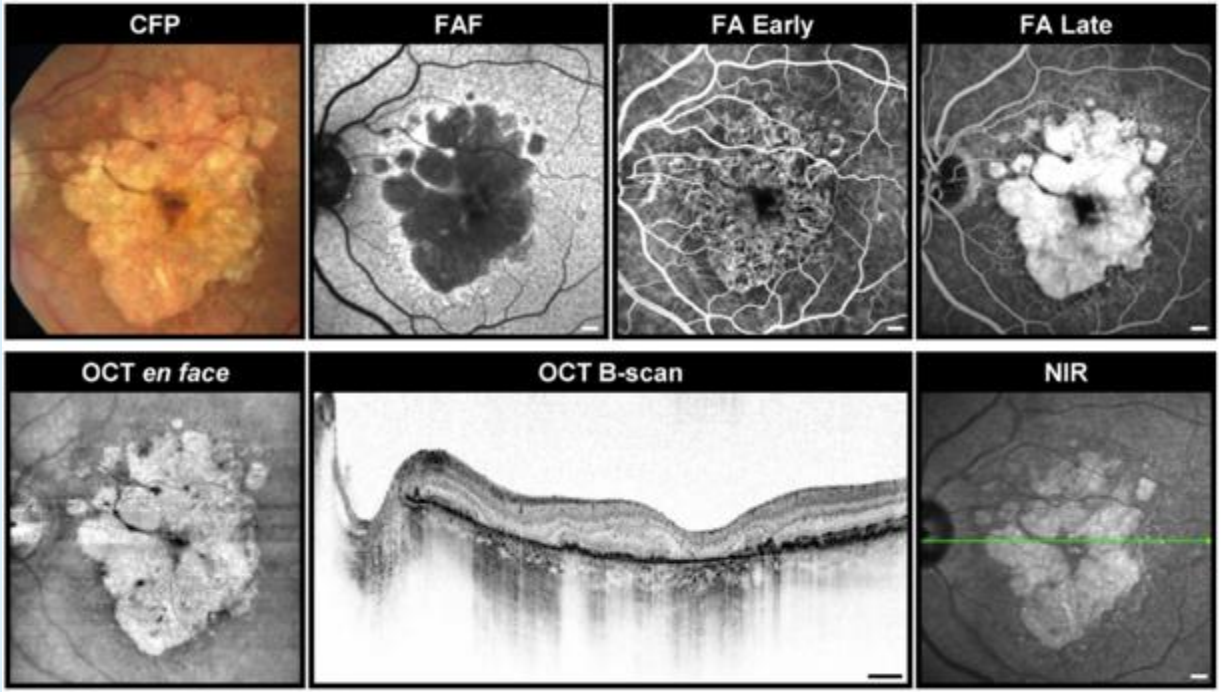
- RPE secretions are a major source of drusen[2]
- 40% of drusen content is lipid[2]
- Other components include[1]
  - Lipofuscin, albumin, apolipoprotein E, immunoglobulins, vitronectin and amyloid-P component
  - Complement factors C1q, C3, C5, and C5b–9

Image courtesy of http://retinagallery.com

Ambati J, et al. Nat Rev Immunol. 2013;13(6):438-451.
Wang L et al. PLoS One. 2010;5(4):e10329.

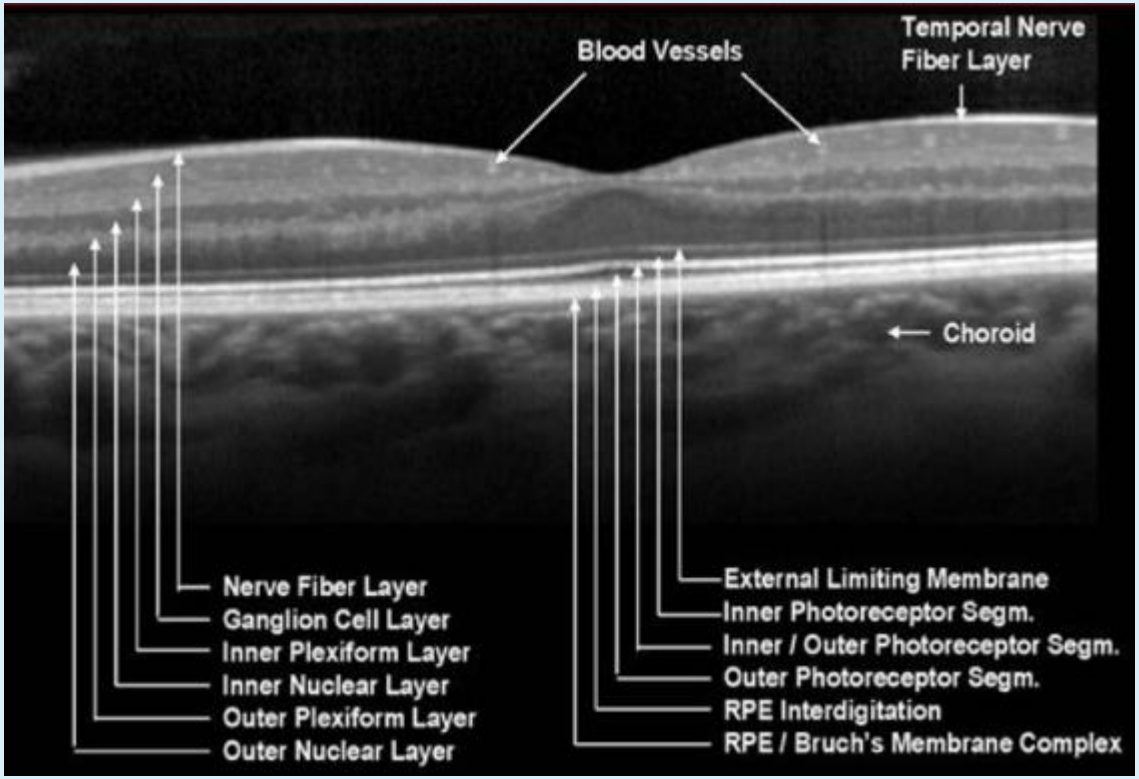
Multimodal Imaging for Early Detection and Monitoring of AMD

- Multimodal imaging enables earlier detection of changes and better management of dry AMD progression



Courtesy of Fleckenstein et al.

Optical Coherence Tomography (OCT)



The OCT provides cross-sectional imaging of retinal layers with micrometer resolution

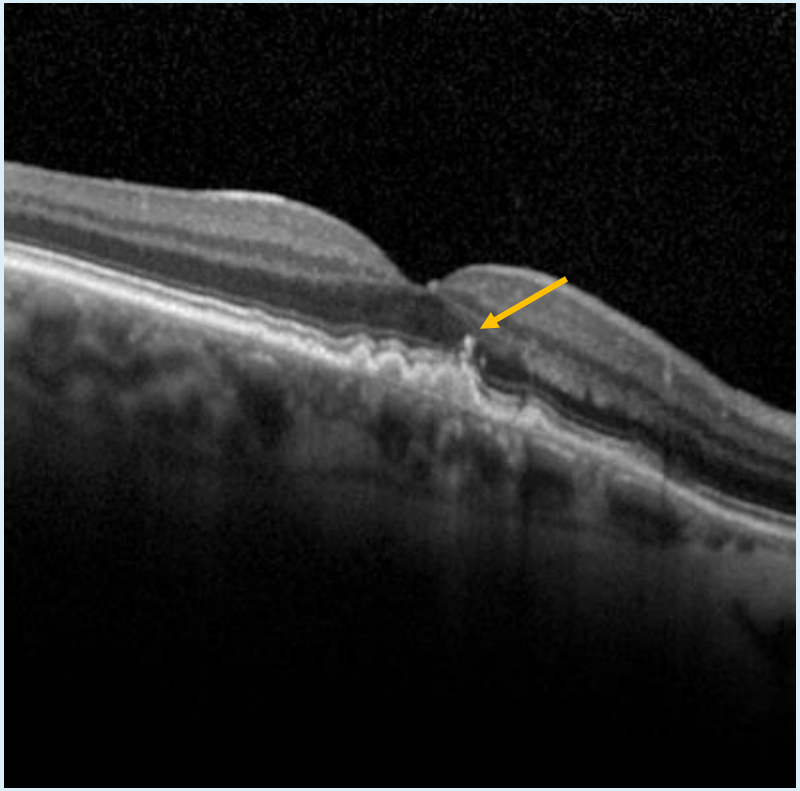
www.torontoeyeclinic.ca/optical-coherence-tomography-oct/.

OCT: Biomarkers for GA Progression in AMD

- In addition to drusen and pigment changes in the fundus, we have learned of many other risk factors for developing GA in AMD
- Defined biomarkers and nomenclature in GA
- SD-OCT helps to identify and differentiate the atrophy as it progresses

Vallino V, et al. Structural OCT and OCT angiography biomarkers associated with the development and progression of geographic atrophy in AMD. Graefes Arch Clin Exp Ophthalmol. 2024;262(11):3421-3436.

Hyperreflective Foci

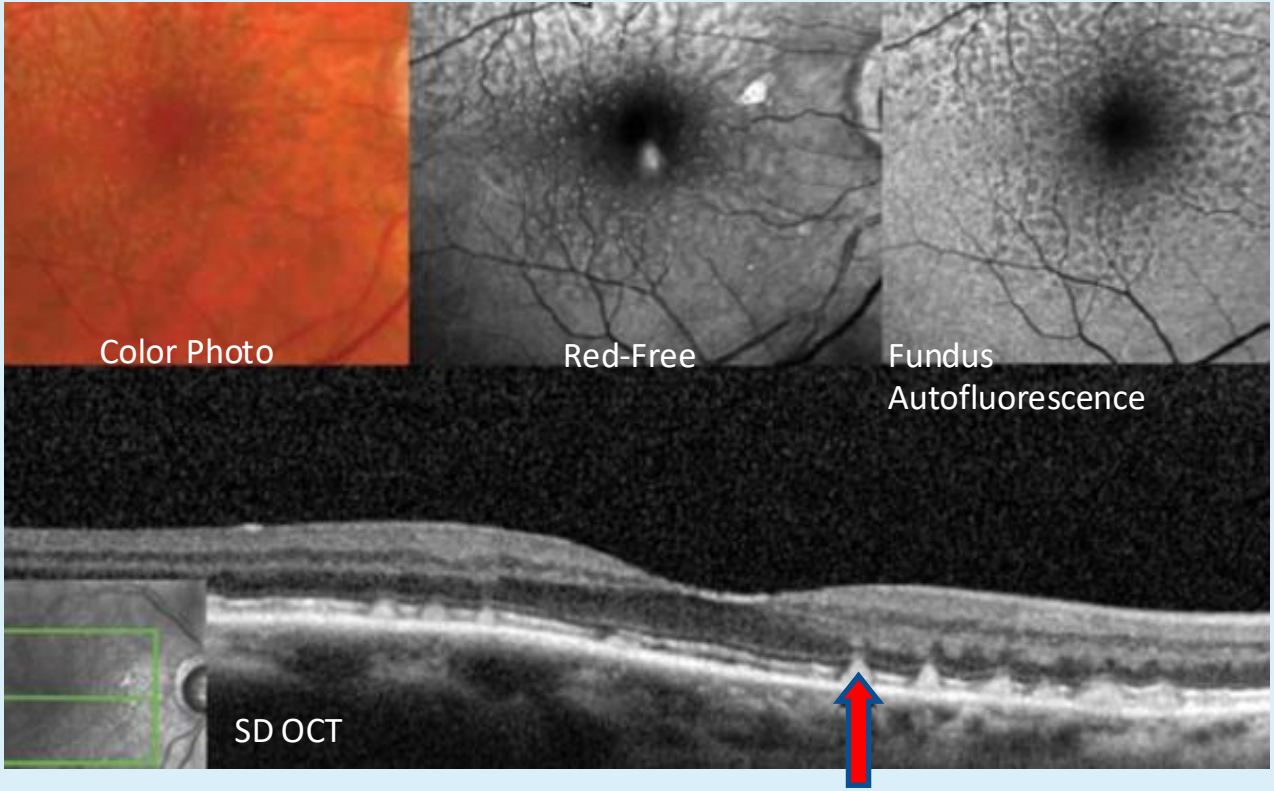


- Punctate intraretinal lesions
- Often at drusen apex
- Likely represent pigment granules
- Original in outer retina and migrate inward with time
- 5x more likely to form GA within 2 years

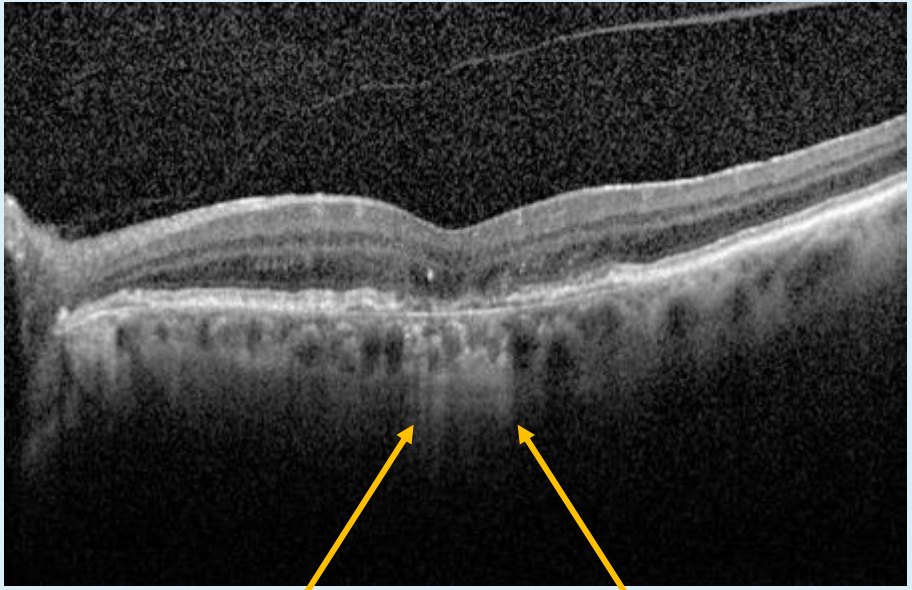
Mat Nor MN, et al. Retinal Hyperreflective Foci Are Biomarkers of Ocular Disease: A Scoping Review With Evidence From Humansand Insights From Animal Models. J Ophthalmol. 2025;2025

Subretinal Drusen Deposits (SDD)

- AKA reticular pseudodrusen
- Difficult to distinguish from true drusen on color photography
- SD-OCT allows us to see the location as deposits in the subretinal space above RPE
- Early stage: granular hyperreflective deposit below EZ
- Progression is noted when material accumulates into small mounds that break the EZ
- FAF: target shape with hypo- or isoautofluorescent surround; Collectively forms reticular pattern



SDDs = 2-6 x higher risk for GA



Hypertransmission defects signify a high risk towards nascent GA

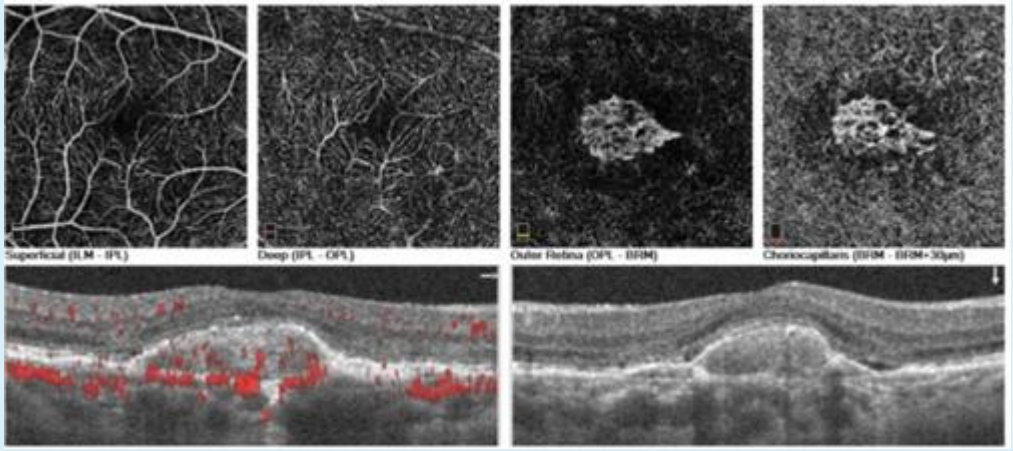
Hypertransmission Defects

- Increased hyperreflectivity in the choroid as a result of RPE disruption
- The overlying RPE may “appear” intact and unaltered, however hypertransmission defects indicate loss of integrity of the RPE

Shi Y et al. Ophthalmol Retina. 2021;5(12):1214-1225.
Laiginhas R, et al. Am J Ophthalmol. 2022;237:58-70.

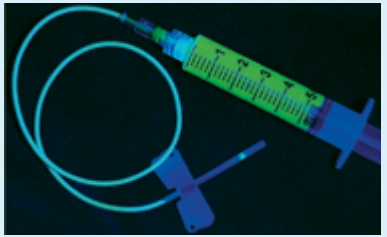
OCT-Angiography (OCT-A)

- Using reflected light off of red blood cells (RBCs)
- Retina is stationary, RBCs are moving
  - Image same spot at multiple intervals using en-face imaging
  - Calculate the difference between OCT signal
  - Layer by layer identification is obtained by slicing and projecting slabs from 3D OCT-A data
    - Better than fluorescein



amdbook.org/node/509

Fluorescein Angiography (FANG)



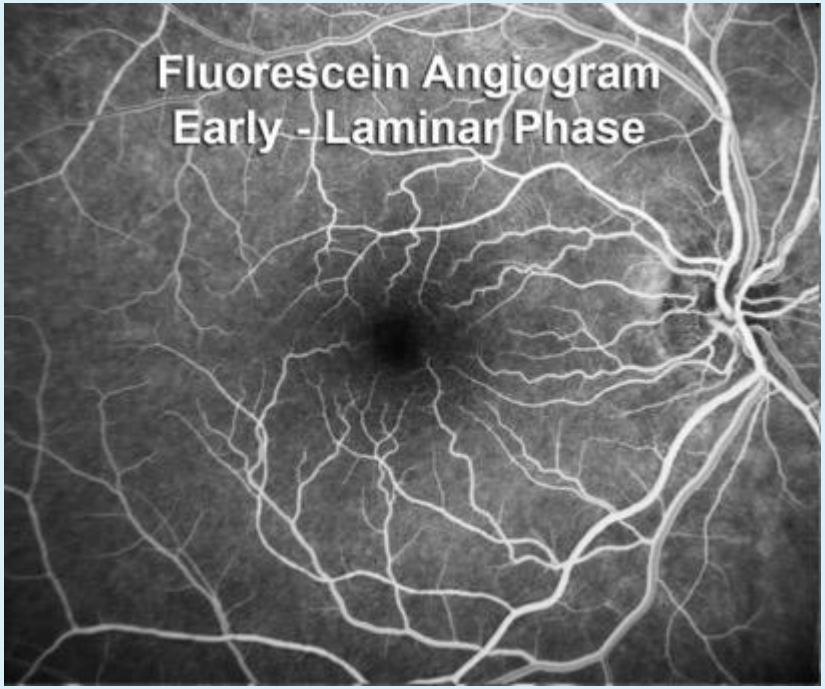


Image courtesy of Retina Vitreous Associates of Florida.

- Fluorescein sodium is injected into the arm → systemic circulation
  - Illuminates the retina with blue-green light
  - Photographs of the emitted fluorescent green light are captured over time
- Used to examine the circulation of the retina and choroid

OCT-A vs FANG

OCT-A

- Non-invasive
- Generally limited to posterior pole
  - New machines with widefield capability
- Shows ALL capillary plexi
  - Helpful in many disease processes
  - Great for Type 1 CNVM (sub RPE)
- Threshold for motion detection may miss or overcall flow
  - Microaneurysms
  - Polyps

FANG

- Invasive, possible allergy to fluorescein
- Widefield capability
- Poor identification of deep capillary layers
- Important for uveitis
  - Demonstration of vascular leakage
- Identifies microaneurysms and polyps

Fundus Autoflourescence (FAF)

- Does not require injection of fluorescein dye in order to image the retina
  - Uses fluorescent properties of lipofuscin within the retinal pigment epithelium (RPE)
- Lipofuscin, a byproduct of lysosymal breakdown of photoreceptor outer segments
  - Composed of bisretinoids (A2E, A2PE, isoA2E, A2DHP-PE)
  - Bisretinoids absorb blue light and emit yellow-green light due to the chemical makeup of the lipofuscin
- A detector is then used to record the emission signals and create an image that acts as a density map of lipofuscin
  - Brighter areas represent regions of increased lipofuscin density (damaged photoreceptors)
  - Dark areas show photoreceptor death

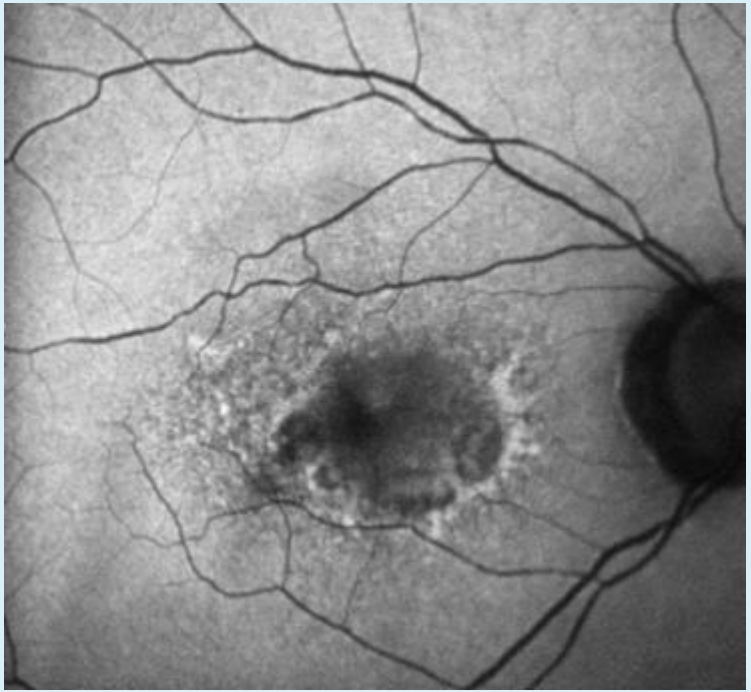
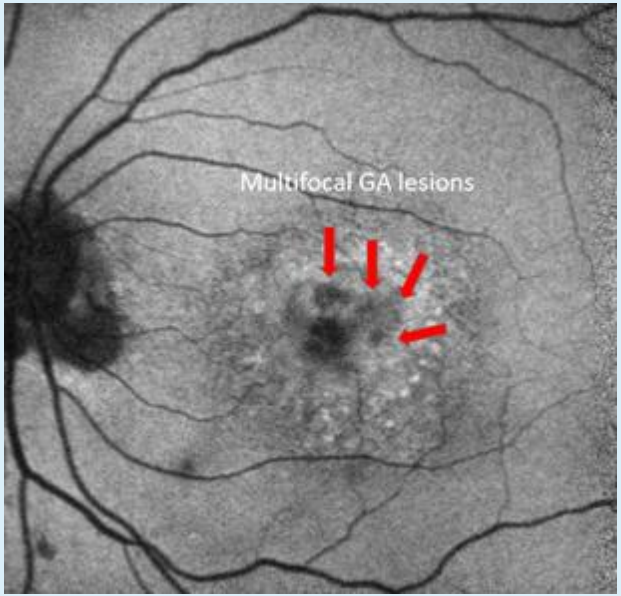


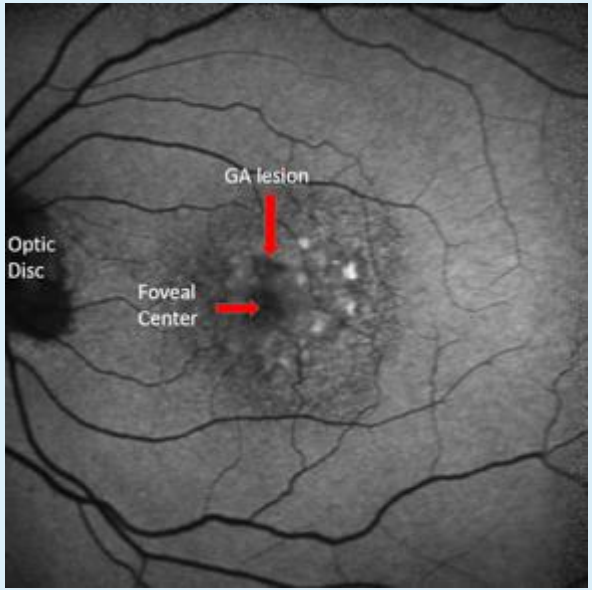
Image courtesy of Mary Beth Yackey, OD

Curcio CA, et al. Fundus Autofluorescence Variation in Geographic Atrophy of Age-Related Macular Degeneration: A Clinicopathologic Correlation. IOVS. 2025; 66:49.

FAF to Monitor GA Progression

- Analyze the progression patterns of GA, focusing on the key stages at which optometric intervention can alter patient outcomes
  - Fundus Autofluorescence:
    - Multifocal lesions grow quicker than monofocal lesions

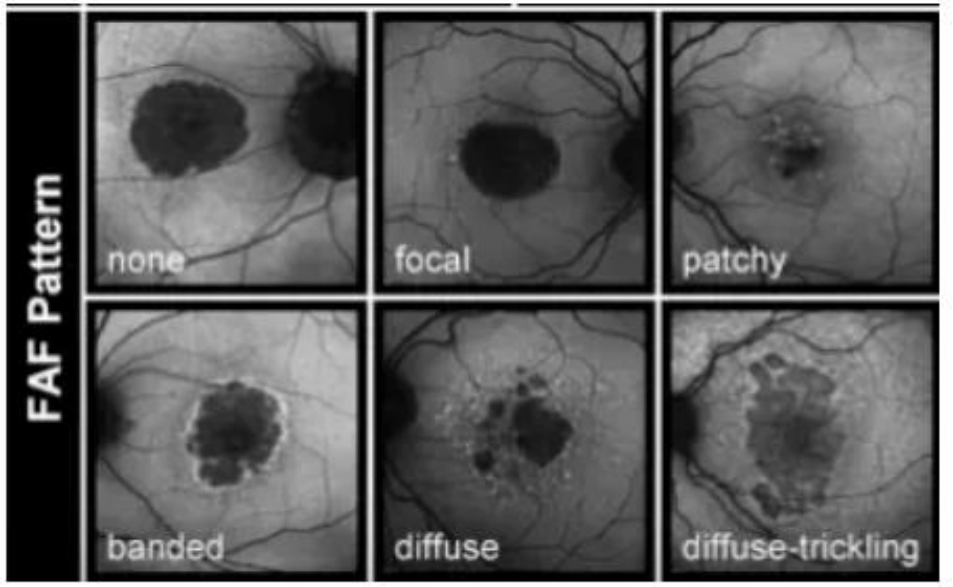




Images courtesy of Mary Beth Yackey, OD

Disease Progression and Management for GA

- Banded or diffuse patterns show greater progression of GA than those with focal patterns or no pattern



Courtesy of Fleckenstein et al.

The larger the geographic lesion, the quicker the growth

Lesion growth may affect the vision, even before the fovea is affected by GA

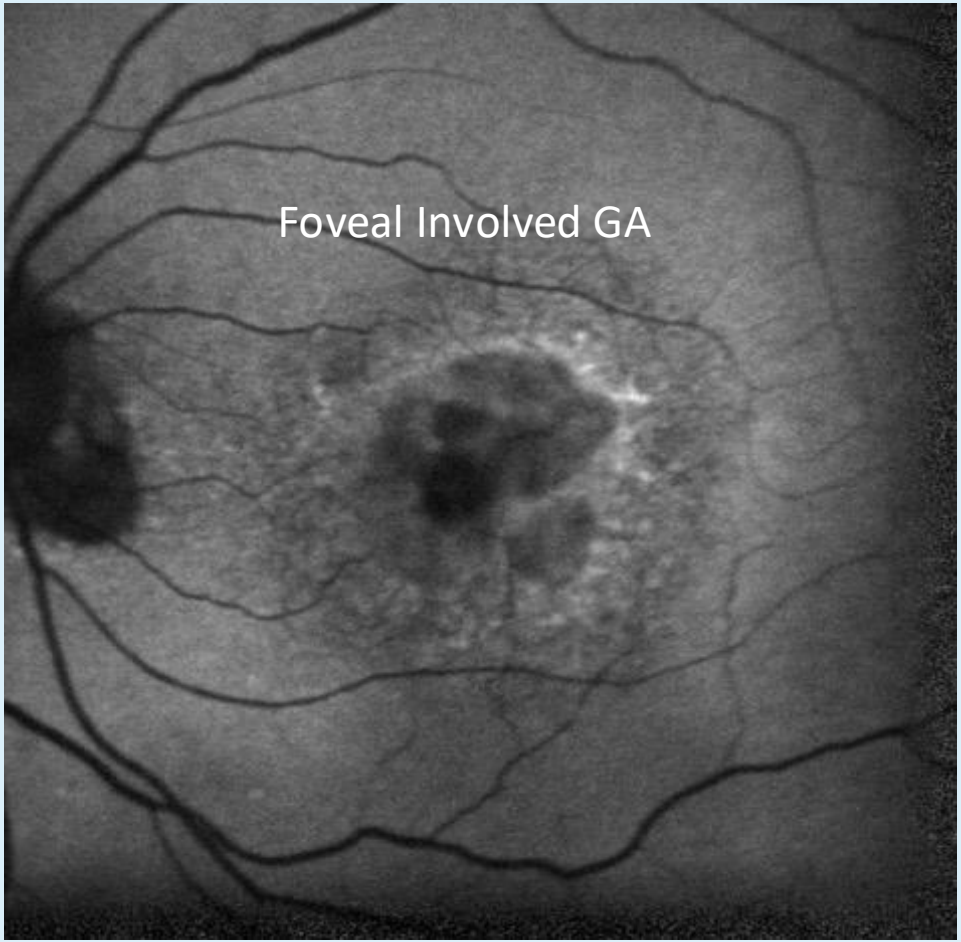


Image courtesy of Mary Beth Yackey, OD

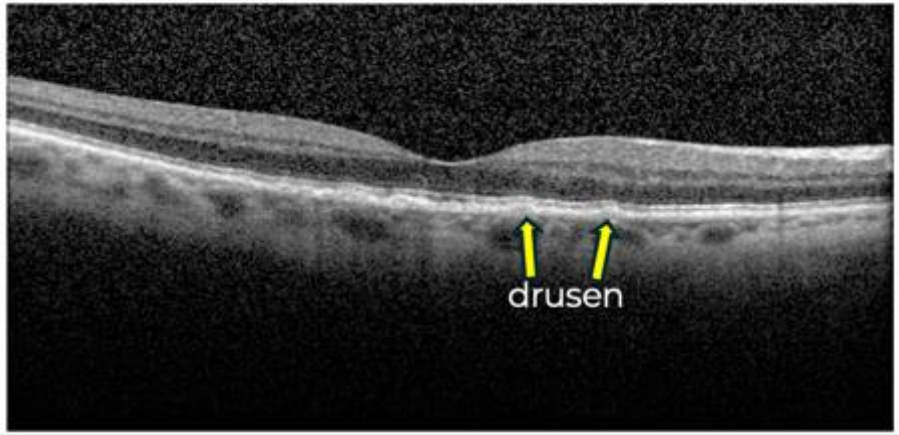
Bakri SJ, et al. Geographic atrophy: Mechanism of disease, pathophysiology, and role of the complement system. J Manag Care Spec Pharm. 2023;29(5-a Suppl):S2-S11.

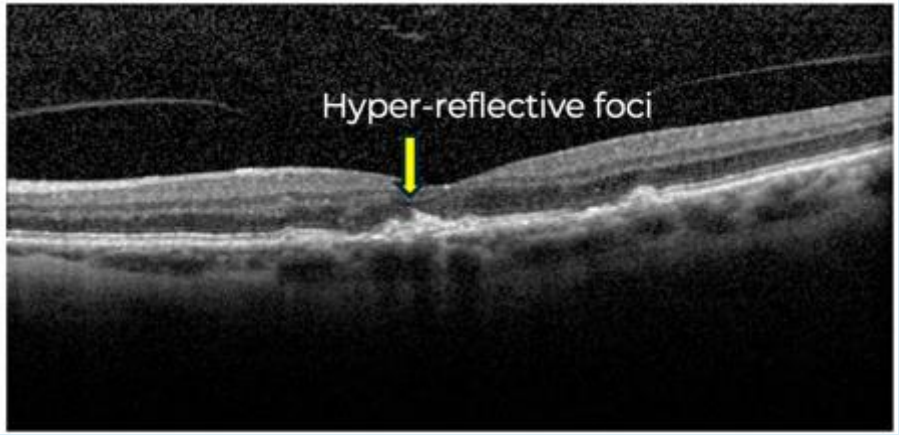
Case Study

- 72-year-old man
- CC: The 72-year-old White male presents for an evaluation of age-related macular degeneration (AMD) in the right and left eyes. The patient was referred from his local Optometrist. Patient states that he is having difficulties reading small print. The patient thinks he is seeing distortion in the left eye and describes it as wavy lines. The patient denies flashes, floaters, pain or redness in either eye.
- Systemic health is positive for Systemic HTN, Arthritis, Thyroid Disease
- Family Medical History: +Macular Degeneration (mother and father), Stroke (father), Thyroid disease (mother)
- POHx: S/P Phaco/PCIOL OU x 2 years ago; +PVD OD

March 22, 2022

- OD: 20/20 J1
- OS: 20/20 J2

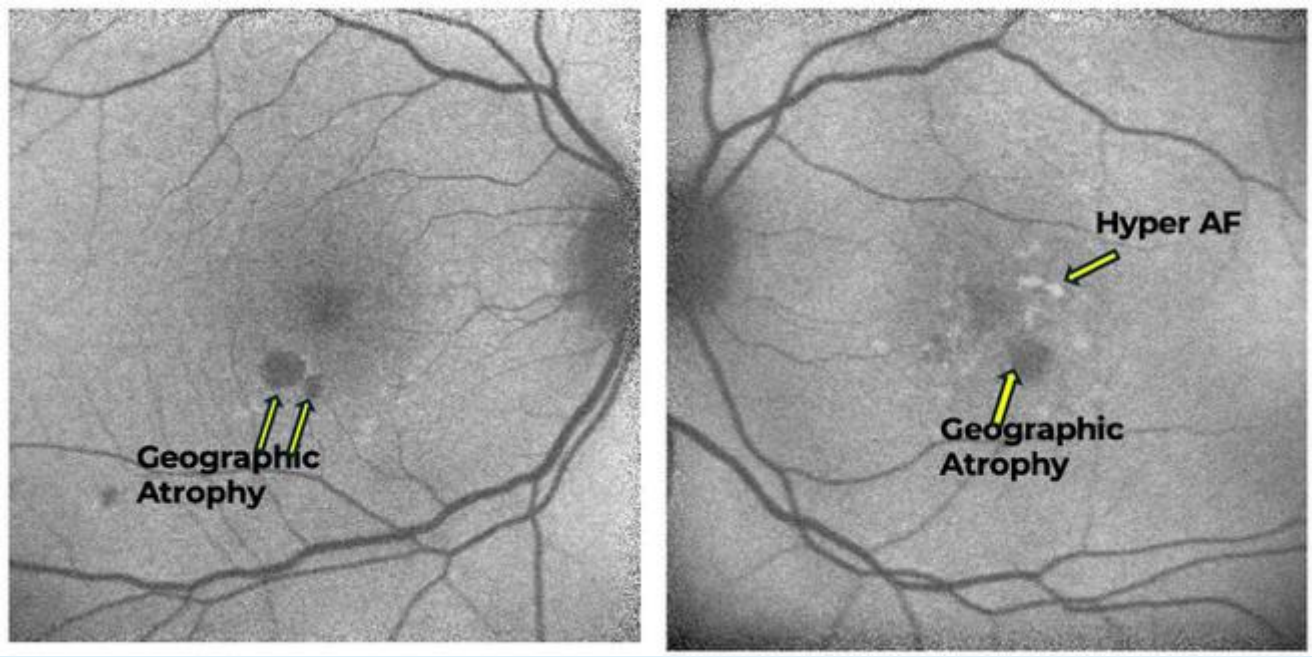




Images courtesy of Mary Beth Yackey, OD

March 22, 2022

- OD: 20/20 J1
- OS: 20/20 J2



Images courtesy of Mary Beth Yackey, OD

Case Study: Update

March 22, 2022

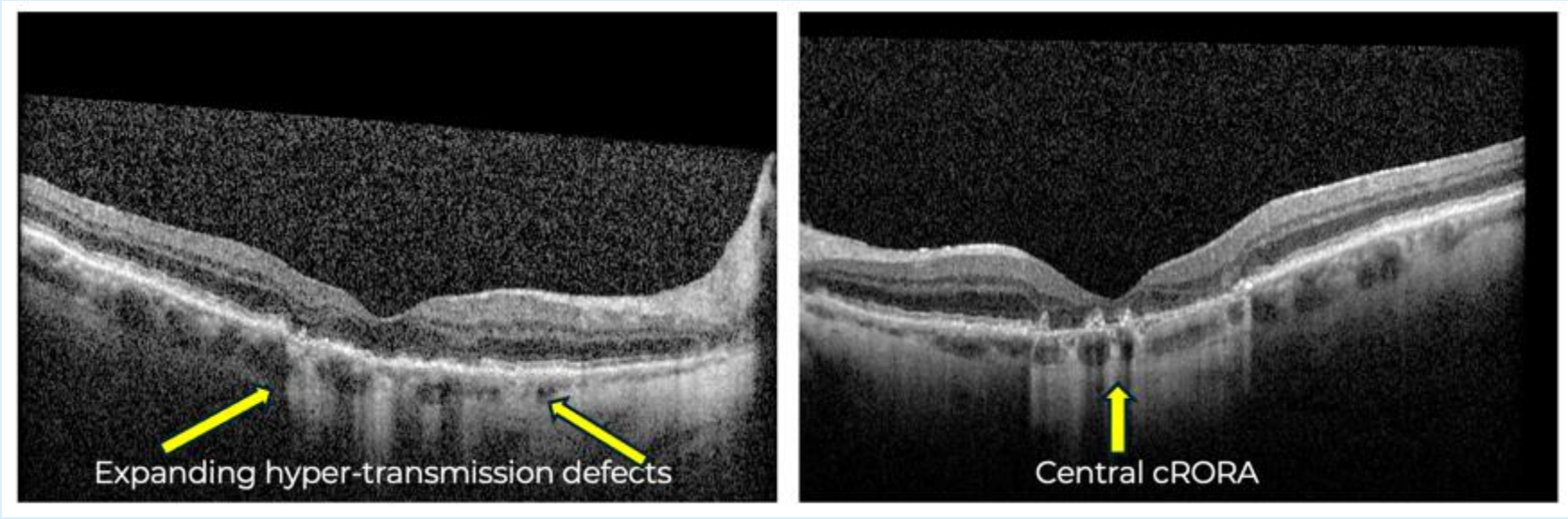
- Patient is instructed to continue to take AREDS2, monitor vision with Amsler Grid, and call with any new distortion or changes.

July 26, 2023:

- The patient presents with worsening distortion and vision changes in both eyes (OS>OD)
- The patient's insurance was not covering GA treatment at this time
- The doctors were not able to give out sample drug Patient was instructed to follow up in 6 months with hopes that his insurance would be able to cover treatment

January 26, 2024

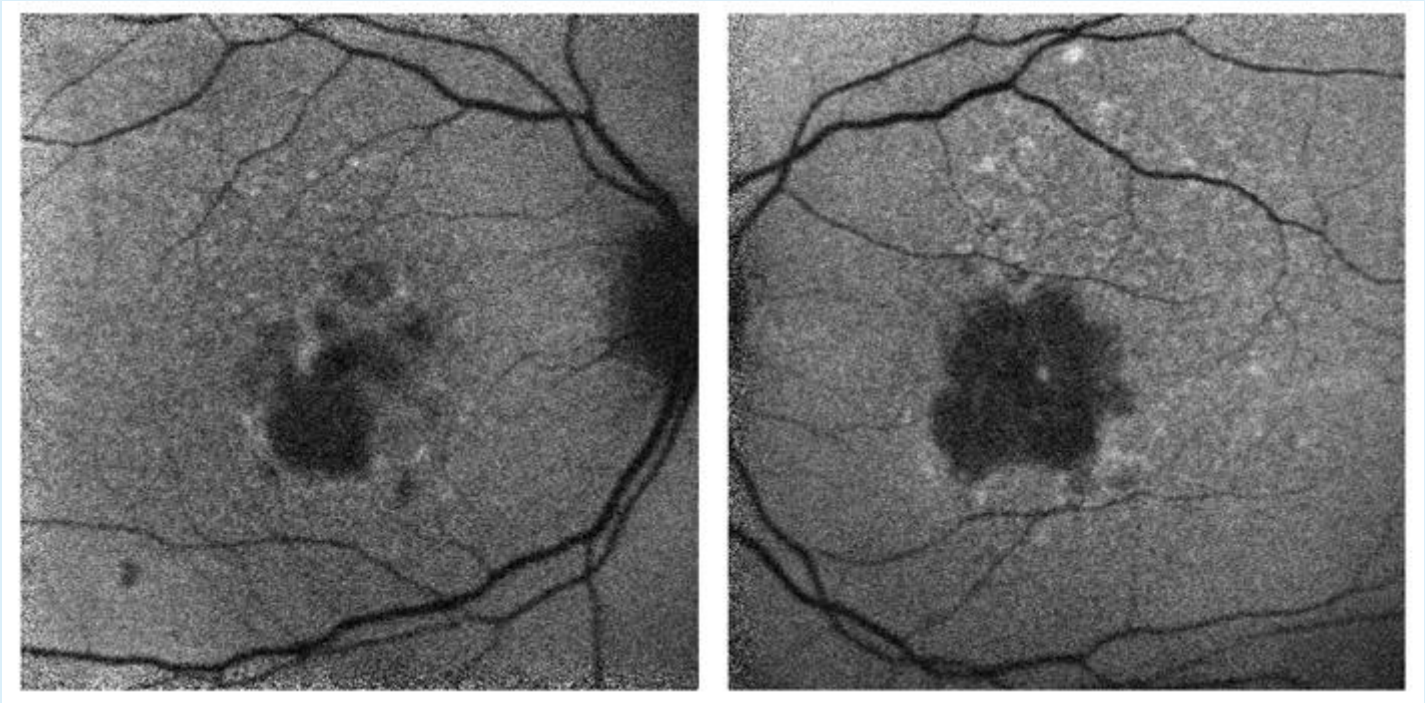
- OD: 20/30 J7
- OS: CF7’(@D) 20/400 (@N)



Images courtesy of Mary Beth Yackey, OD

January 26, 2024

- OD: 20/30 J7
- OS: CF7’(@D) 20/400 (@N)



Images courtesy of Mary Beth Yackey, OD

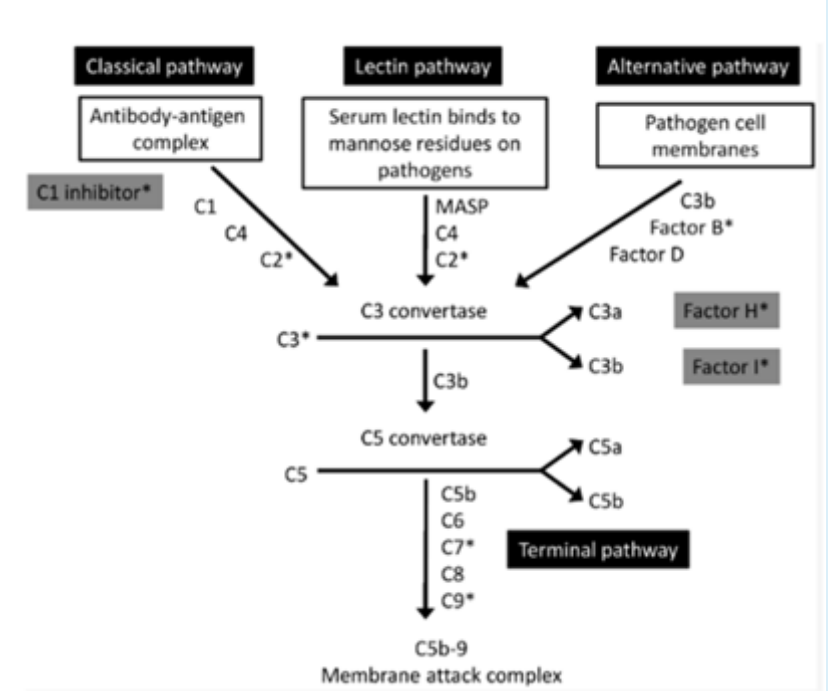
Case Study: Treatment Options Re-Discussed

- More options now available and the patient's insurance will cover both FDA-approved GA drugs
- Discussed risks and benefits reviewed with patient
- Patient received first treatment with pegcetacoplan in the right eye on February 5, 2024, with one of our retina specialists
- Patient will continue with AREDS2 and Amsler grid monitoring

Complement Therapy in GA

What is the complement system?

- The complement system normally plays a pivotal role in the immune system's defense against pathogens and abnormal cells
- In patients with GA secondary to AMD, increased levels of complement activity have been found in the lesion and the area just outside of it
- This overactivation of the complement system accelerates cell damage outside of the lesion, increasing the risk of GA lesion growth



Bakri SJ, et al. Geographic atrophy: Mechanism of disease, pathophysiology, and role of the complement system. J Manag Care Spec Pharm. 2023;29(5-a Suppl):S2-S11.

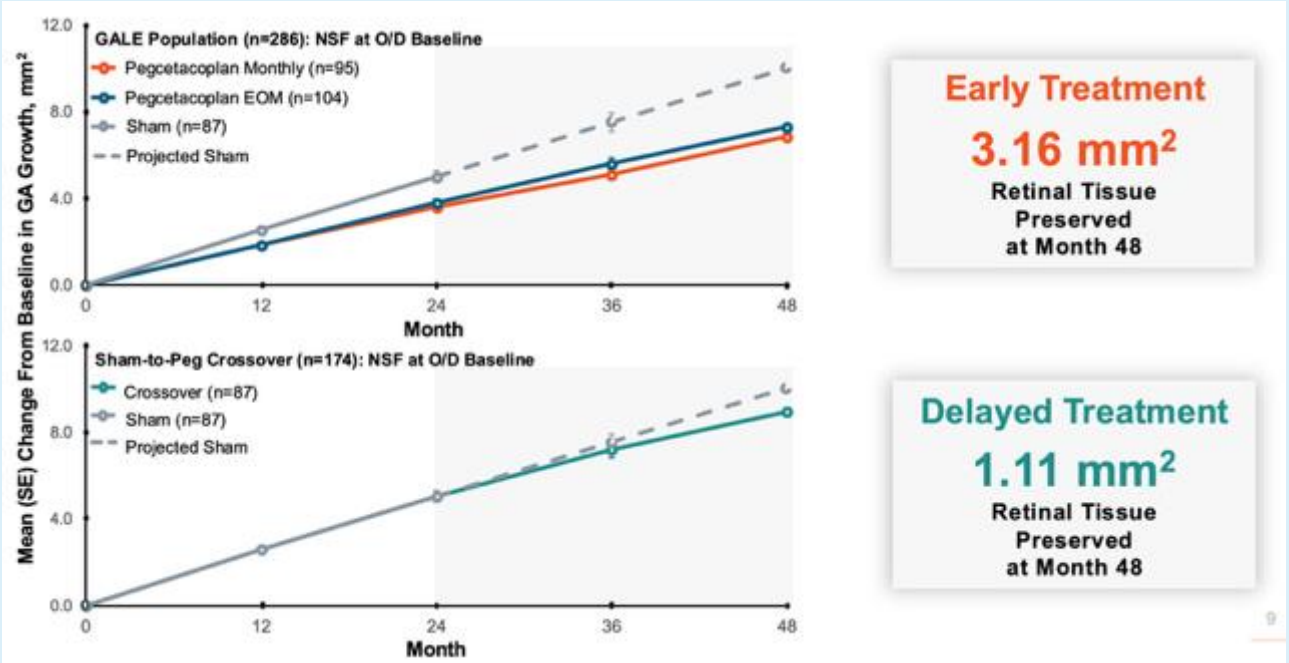
Pegcetacoplan | 48-month Results: OAKS, DERBY and GALE Open-label Extension

- Inhibits the C3 cleavage; stops downstream progression of complement cascade
- Continuous pegcetacoplan treatment significantly preserves retinal tissue, with greater effectiveness in years 3 and 4 compared to the initial 2 years
- Delayed treatment results in markedly less retinal tissue preservation, emphasizing the importance of early intervention for optimal outcomes
- Early-treated patients experience a 35% risk reduction in vision loss, particularly in critical central vision loci
- Safety profile of pegcetacoplan consistent with previous studies, supported by real-world data from more than 700,000 injections

Apellis. Syfovre Prescribing Information. https://pi.apellis.com/files/PI_SYFOVRE.pdf. Updated July 2025. Accessed September 4, 2025.
Goldberg RA. https://www.ophthalmologytimes.com/view/asrs-2025-48-month-results-from-oaks-derby-and-gale-open-label-extension. Updated August 12, 2025. Accessed March 5, 2026.

Pegcetacoplan | 48-month Results: OAKS, DERBY and GALE Open-label Extension

- Earlier treatment leads to more tissue preserved



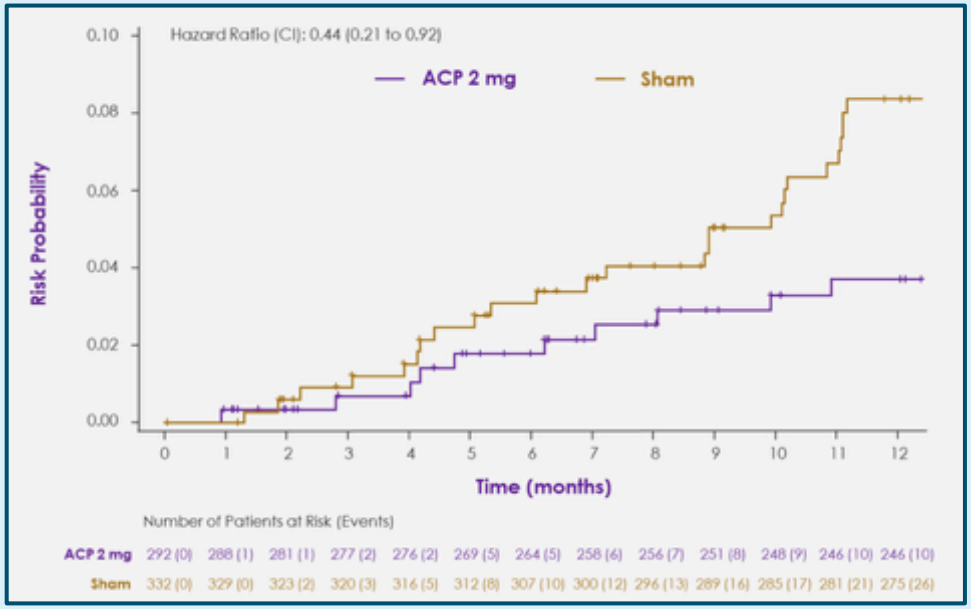
Goldberg RA. https://www.ophthalmologytimes.com/view/asrs-2025-48-month-results-from-oaks-derby-and-gale-open-label-extension. Updated August 12, 2025. Accessed March 5, 2026.

Avacincaptad Pegal
GATHER1 and GATHER2

- Preserves proinflammatory and anti-inflammatory effects of C3a and opsonization by C3b
- Prevents the proinflammatory effects of C5a and cell lysis/death and damage on RPE cells by MAC (C5b-9)
- GATHER 2: met the primary objective to significantly slow GA growth compared to sham at 24 months
- Results suggest that avacincaptad pegol might slow disease progression and potentially change the trajectory of disease for patients with GA

Astellas. Izervay Prescribing Information. https://www.astellas.com/us/system/files/izervay_pi.pdf. Updated March 2025. Accessed September 4, 2025.
Khanani AM, et al; GATHER2 trial investigators. Efficacy and safety of avacincaptad pegol in patients with geographic atrophy (GATHER2): 12-month results from a randomised, double-masked, phase 3 trial. Lancet. 2023;402(10411):1449-1458.

Avacincaptad Pegal
GATHER1 and GATHER2



Post-hoc analysis showed that ACP treatment resulted in overall 59% risk reduction in rate of vision loss compared to sham treatment at 12 months[a]

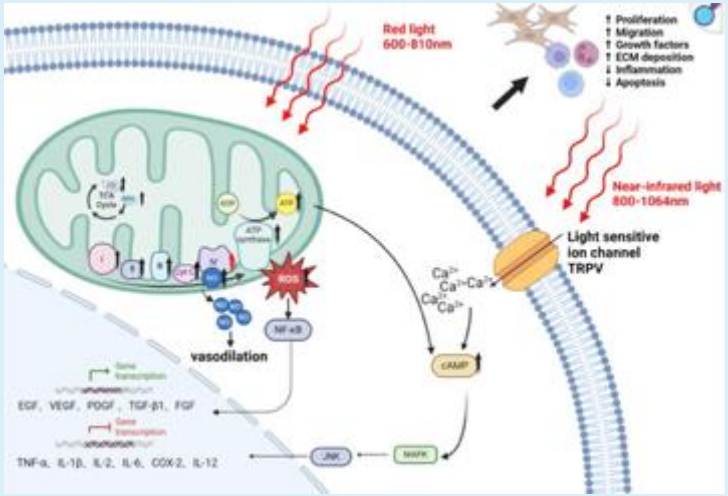
[a]Defined as ≥15-letter loss in BCVA from baseline measured at any 2 consecutive visits up to 12 months.
CI, confidence interval

Danzig C, et al. Ophthalmol Retina. Available online: https://www.sciencedirect.com/science/article/pii/S2468653024002240?via%3Dihub

Panel Discussion

- How are the latest generation of complement therapy treatments changing the way we communicate with patients with dry AMD about their disease?
- How do the currently available complement therapy treatments differ?
- How can optometrists best identify ophthalmologists who are utilizing complement therapy?

Multiwavelength Photobiomodulation: A new approach for dry AMD



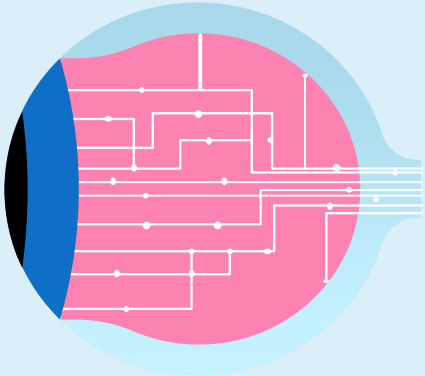
LIGHTSITE III Trial

- Patients with dry AMD were given either multiwavelength photobiomodulation or sham treatments over 24 months
- Met BCVA primary endpoint
- Patients who received photobiomodulation experienced VA gains of 6.3 letters at month 21
- Patients who received photobiomodulation had significantly decreased odds of going on to develop GA

Boyer D, et al. LIGHTSITE III: 13-Month Efficacy and Safety Evaluation of Multiwavelength Photobiomodulation in Nonexudative (Dry) Age-Related Macular Degeneration Using the Lumithera Valeda Light Delivery System. Retina. 2024;44(3):487-497.

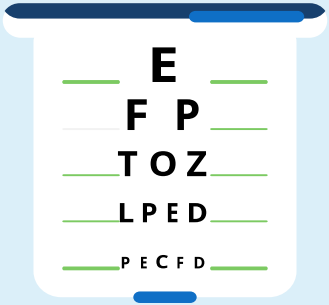
Lifestyle Modifications

Dry AMD & GA



Steven Ferrucci, OD, FAAO

Strategies for Individualized Care Plans



- Medical Management
  - Regular Monitoring
    - Schedule routine eye exams with optometrist (and retina specialist if needed) to track disease progression
  - FDA-Approved Therapies
    - Discuss complement inhibitors
  - Nutritional Supplements: ** AREDS2 **
  - Comorbidity Management
    - Address other health conditions that may exacerbate vision loss (diabetes, systemic hypertension, cholesterol)
- Lifestyle Modifications
  - Smoking Cessation
  - Dietary Changes: Rich in leafy greens, antioxidants and fish
  - UV Protection

Kaiser PK, et al. BMJ Open Ophth 2023;8:e001395.
Mayo Clinic. Geographic Atrophy. Updated May 17, 2025. Accessed September 4, 2025
Keenan TDL, et al. Ophthalmology. 2025;132(1):14-29.

Major AREDS/AREDS2 Findings

- ✓ Taking AREDS or AREDS2 supplements reduces the risk of progression from intermediate to advanced AMD by about 25%
- ✓ AREDS and AREDS2 supplements do not prevent AMD onset
- ✓ AREDS and AREDS2 supplements do not have an effect on cataract
- ✓ Omega-3 fatty acid supplements do not have an effect on cataract or AMD
- ✓ Current and former smokers should take the AREDS2 formula and avoid the AREDS formula with beta-carotene because of the increased risk of lung cancer

Commercially available formulas based on AREDS/AREDS2

Nutrient	AREDS formula*	AREDS2 formula
Vitamin C	500 mg	500 mg
Vitamin E	400 IU	400 IU
Beta-carotene	15 mg	-
Copper (cupric oxide)**	2 mg	2 mg
Lutein	-	10 mg
Zeaxanthin	-	2 mg
Zinc	80 mg	80 mg

*Not recommended for current or former smokers
**Added to avoid zinc-related copper deficiency
mg = milligrams; IU = international units

NIH. AREDS/AREDS2 Clinical Trials. Updated October 22, 2025. https://www.nei.nih.gov/eye-health-information/clinical-trials/age-related-eye-disease-studies-aredsareds2/about-areds-and-areds2. Accessed March 6, 2026.

Vision Aids and Rehabilitation

- **Low Vision Aids**: Introduce magnifiers, screen readers, or electronic devices to assist with daily tasks
- **Occupational Therapy**: Work with specialists to adapt home and work environments for safety and independence
- **Orientation and Mobility Training**: Teach navigation techniques for patients with significant central vision loss

Kaiser PK, et al. BMJ Open Ophth 2023;8:e001395.
Mayo Clinic. Geographic Atrophy. Updated May 17, 2025. Accessed September 4, 2025
Keenan TDL, et al. Ophthalmology. 2025;132(1):14-29.

Prevalence and Impact

Presbyopia

Selina McGee, OD, FAAO

Presbyopia

Prevalence:

Global: 1.8 billion

Age of onset: 40-45 years

Presbyopes are changing:

- Population growing
- Incomes and education rising
- Life expectancy increasing
- Working longer
- Near vision increasingly important

Markoulli M, et al. BCLA CLEAR Presbyopia: Epidemiology and impact. Cont Lens Anterior Eye. 2024;47(4):102157.

Presbyopia Impact

- Uncorrected presbyopia leads to substantial productivity losses, estimated at more than USD $25 billion worldwide
- Gender differences prominent in specific populations
- Systematic research showed that women experience presbyopia earlier than men and are less likely to utilize corrective services in low-income settings
- Some studies suggest earlier onset in women, possibly due to hormonal and vocational disparities
- Eye care providers must be vigilant in assessing patients during routine examinations for nuanced alterations in near-vision capabilities, especially in low-light conditions or during prolonged reading activities
- Early recognition fosters preparedness rather than surprise, enabling smoother transitions to appropriate corrective strategies for patients

Frick KD, et al. The Global Burden of Potential Productivity Loss from Uncorrected Presbyopia. Ophthalmology. 2015;122(8):1706-10.
Katz JA, et al.Presbyopia - A Review of Current Treatment Options and Emerging Therapies. Clin Ophthalmol. 2021;15:2167-2178.
Hickenbotham A, et al. Meta-analysis of sex differences in presbyopia. Invest Ophthalmol Vis Sci. 2012;53(6):3215-20.

The Digital Demand Problem

The Fundamental Mismatch

- Human ocular biology hasn't changed, but visual demand has grown exponentially

Modern Visual Landscape

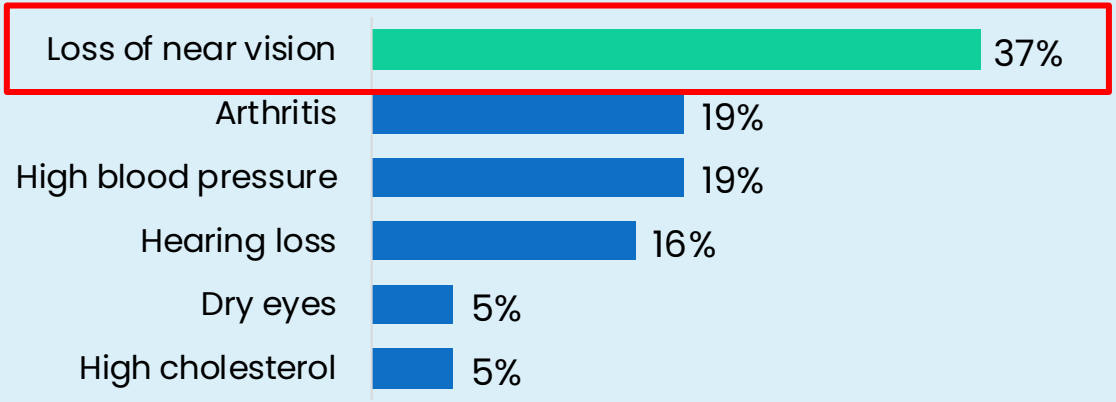
- Nearly 60% of Americans use digital devices for ≥5 hours each day
- 70% of Americans use ≥ 2 devices at a time
- 90% of patients do not talk with their eye care provider about digital device usage

The Vision Council. Eyes Overexposed: The Digital Device Dilemma; 2016 Digital Eye Strain Report; 2016.

Presbyopia Impacts Quality of Life

- Functionality
- Aesthetic
- Falls / Hip Fractures, Head Injuries
- Psychological
- Mental Health
- Productivity/ Occupation

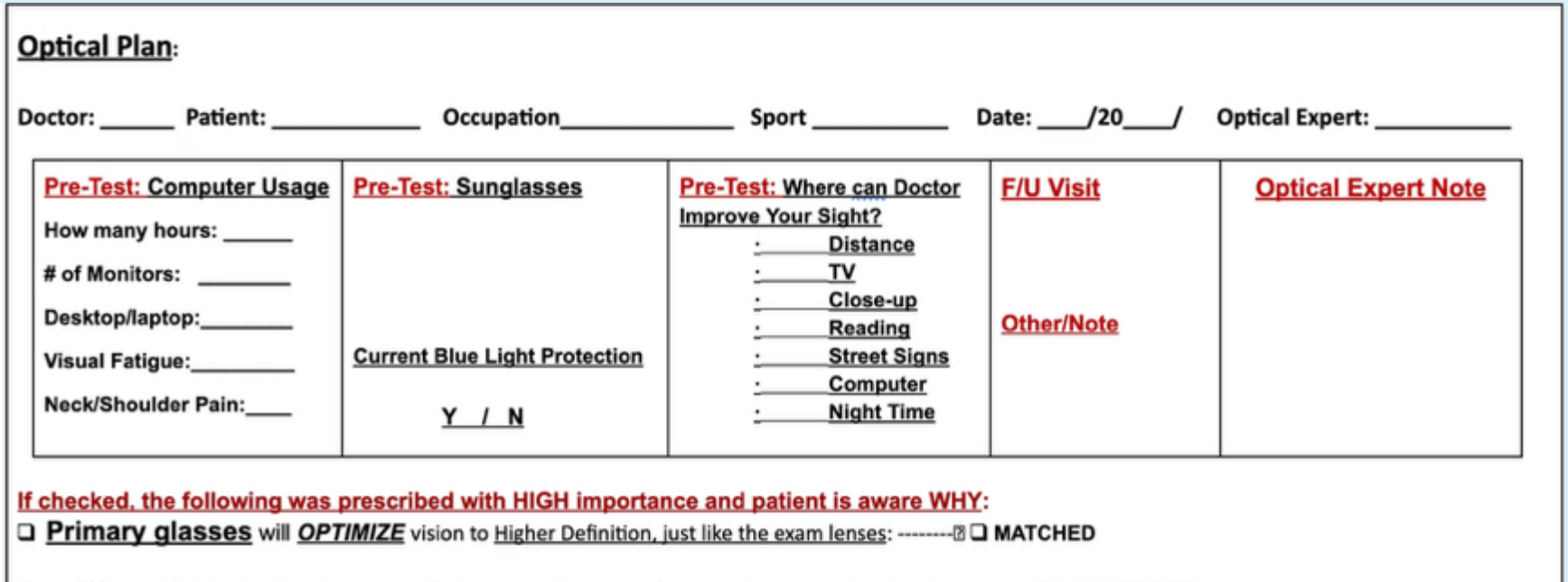
Loss of Near Vision ranks as having the most significant impact on quality of life compared to other age-related ailments



Burke Healthcare Research. April 2020, n = 1,000 presbyopes

Lifestyle Impact Assessment

- Work environment
  - Screen time, reading demands, lighting conditions
- Leisure activities
  - Reading, sports, driving, outdoor activities
- Daily schedule
  - When vision needs are most critical
- Device usage
  - Smartphones, tablets, computers, viewing distances



Optical Plan:

Doctor: _____ Patient: _____ Occupation_____ Sport _____ Date: ____/20____/ Optical Expert: _____

Pre-Test: Computer Usage	Pre-Test: Sunglasses	Pre-Test: Where can Doctor Improve Your Sight?	F/U Visit	Optical Expert Note
How many hours: _____ # of Monitors: _____ Desktop/laptop:_____ Visual Fatigue:_____ Neck/Shoulder Pain:____	Current Blue Light Protection Y / N	· Distance · TV · Close-up · Reading · Street Signs · Computer · Night Time	Other/Note	

If checked, the following was prescribed with HIGH importance and patient is aware WHY:

❑ **Primary glasses** will ***OPTIMIZE*** vision to Higher Definition, just like the exam lenses: --------❑ ❑ MATCHED

Traditional Presbyopia Solutions

OPTICAL

- Glasses
  - Negative impact on self confidence
  - Inconvenient
  - Fogging

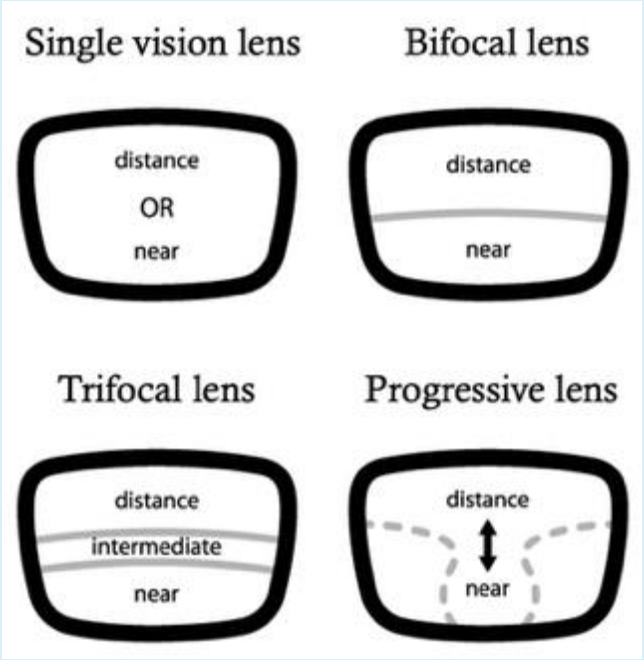


Image credit: www.bettervisionguide.com

Traditional Presbyopia Solutions

OPTICAL

- Contact Lenses
  - Inconvenient
  - CL-related dry eye
  - Compliance issues

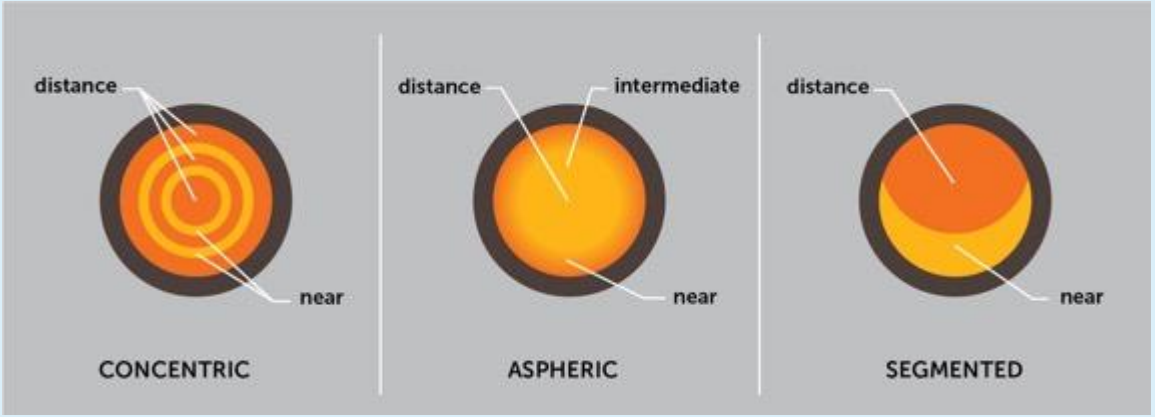


Image credit: skyvisioncenters.com

Presbyopia Pharmaceutical Treatments:

- Presbyopia drops reduce pupil size temporarily
- Assess pupil size before prescribing presbyopia drops
- Monitor side effects, particularly in low-light conditions
- Counsel patients on getting the most out of their presbyopia drops

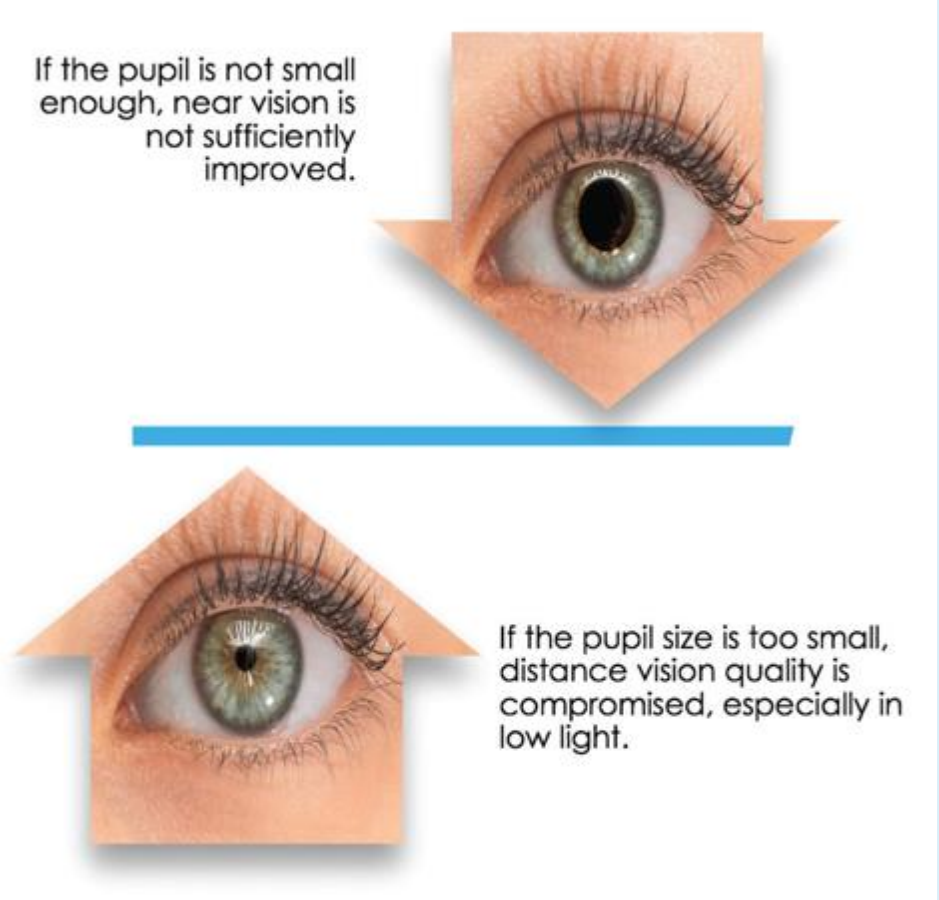
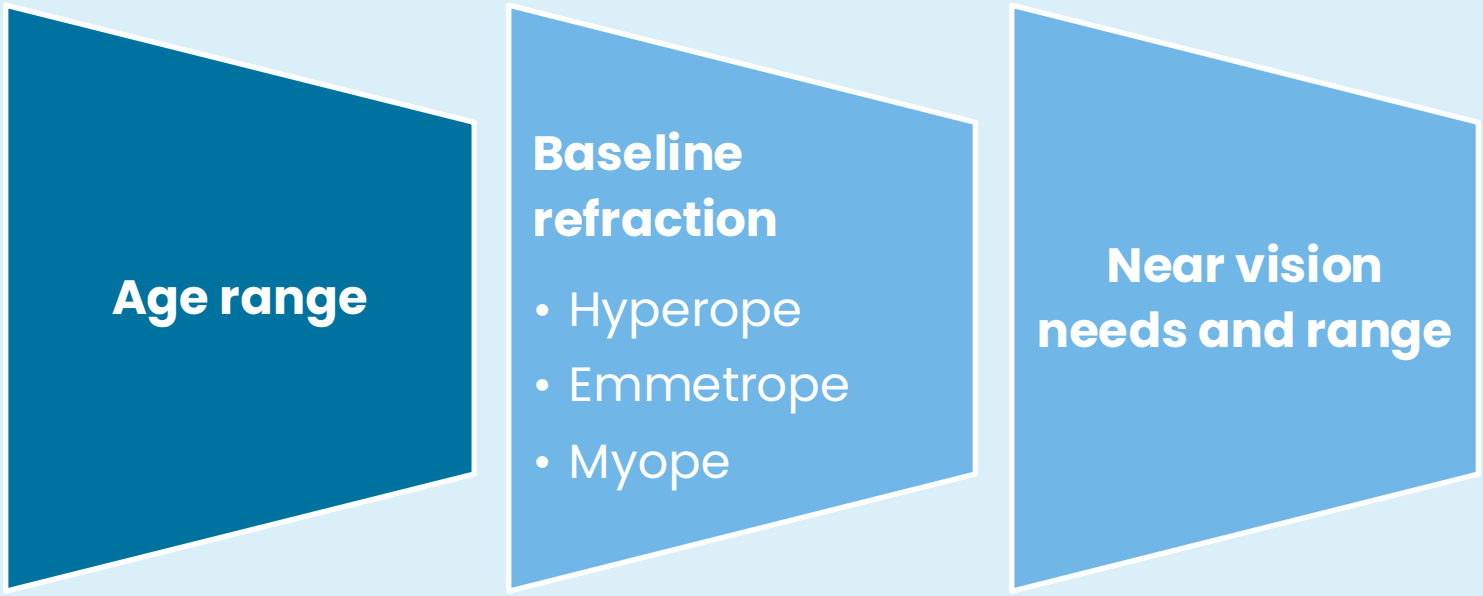


Image Credit: Presbyopia Management: Exploring Options for Today's Patient. (2021) Cataract & Refractive Surgery Today.

Who is the Ideal Patient?



Patient-Specific Characteristics to Consider

- Profession
- Hobbies
- Eye color
- Prior eye surgeries
- Contact lens wear
- Monovision

Patient Expectations

Key Considerations for Topical Presbyopia Treatments

Maximize duration of effect
What percentage of patients will be using this habitually vs situationally?

Minimize onset time
How do you gauge what onset time is important to your patients?

Limit reduction of distance and night vision
How do you discuss night vision expectations with your patients?

Minimize adverse events
How do you counsel patients about side effects?

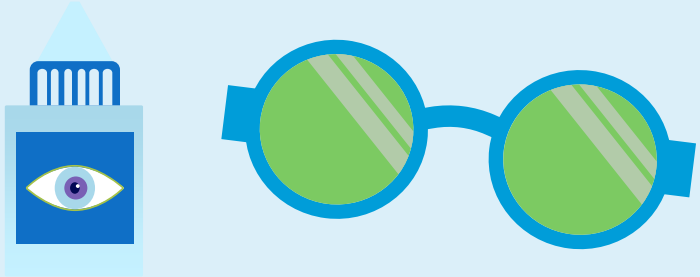
Minimize impact on ocular surface health
How important is ocular surface health when considering these topical presbyopia treatments?

Maximize drop administration comfort to increase compliance
How does drop administration comfort affect patient compliance?

Patient selection pearls for presbyopia drops. Review of Ophthalmology .https://www.reviewofophthalmology.com/article/patient-selection-pearls-for-presbyopia-drops#:~:text=Patient%20hesitation%20most%20often%20centers,Epitropoulos%20says. Updated January 13, 2026. Accessed March 5, 2026.

Management & Treatment Advances

Presbyopia



Joshua Davidson, OD, FAAO, FSLS

Case Study: A 52-Year-Old Elite Female Triathlete

- A 52-year-old elite female triathlete
- Former Louisiana Iron Man representative who demanded a correction solution as rigorous as her training regimen
- **Her Goal:** Effortless access to her watch, heart rate monitor, and bike dials — no reading glasses, no mid-race interruptions
- Manifest Refraction:
  - OD: +0.50 | OS: +0.50
  - Binocular Add: +2.00
- Current Correction:
  - Multifocal CLs (+0.75 distance, medium add) — bilateral

Case Study: New Options

The Challenge:

- Patient had exhausted every contact lens combination available
- Sought what she called her "millionth opinion”
- Specifically seeking a practice with the latest options
- She had never heard of pharmacologic presbyopia correction
- When presented with the option, she was visibly emotional — equal parts frustrated with prior providers and relieved by the new possibility

Clinical Pearl:
Even highly motivated, well-informed patients may be entirely unaware of pharmacologic presbyopia options.
Proactively introducing drops can change the clinical conversation — and the outcome.

Presbyopia Pharmaceutical Treatments

Agent	Composition	MOA	Status
Aceclidine			
Vizz (Lenz)	1.75% aceclidine	Pupil modulation	US FDA-Approved July 2025
Carbachol			
Yuvezzi (Tenpoint)	2.75% carbachol + 0.1% brimonidine	Combination of pupil modulation and ciliary body contraction	FDA–Approved January 2026
Phentolamine			
MR-141 (Opus Genetics/Viatris)	0.75% phentolamine	Combination of pupil modulation and ciliary body contraction	Phase 3 trial completed; not yet submitted to FDA
Pilocarpine			
Qlosi (Orasis)	0.4% pilocarpine	Pupil modulation	US FDA-approved 2023; commercially available April 2025
Vuity (AbbVie)	1.25% pilocarpine	Pupil modulation	US FDA-approved 2021

Table adapted from: Dell SJ. (2 Pharmacologic treatments for presbyopia. (2024). Cataract & Refractive Surgery Today. Retrieved from https://crstoday.com/articles/july-2024/pharmacologic-treatments-for-presbyopia.
Ophthalmology Times. https://www.ophthalmologytimes.com/view/the-emerging-era-of-presbyopia-correcting-eye-drops-what-s-next-. Updated August 20, 2025. Accessed August 29, 2025.
FDA Approves Yuvezzi, First Dual-Agent Eye Drop for Presbyopia. https://eyewire.news/news/fda-approves-yuvezzi-first-dual-agent-eye-drop-for-presbyopia?c4src=article:infinite-scroll. Updated January 26, 2026. Accessed March 5, 2026.

Carbachol and Brimonidine (fixed combination)

- Dosing: once daily
- Preservative Free
- BRIO-I and BRIO-II Trials: two pivotal phase 3 trials (N = 811)

Most common (>5%) treatment-related AEs with up to 12 months exposure

System Organ Class Preferred Term	Carbachol + Brimonidine (N=358)	Carbachol (N=121)	Vehicle (N=159)
Eye irritation	50 (14.0)	22 (18.2)	1 (0.6)
Eye pain	24 (6.7)	5 (4.1)	0
Visual impairment	23 (6.4)	3 (2.5)	1 (0.6)
Headache	56 (15.6)	8 (6.6)	1 (0.6)

Clinical Trial Vanguard. Brio-II Phase 3 Study Shows Positive Topline Data for Brimochol PF in Presbyopia Treatment. http://www.businesswire.com/news/home/20250109824922/en/Tenpoint-Therapeutics-Announces-Positive-Topline-Data-from-Phase-3-Pivotal-Study-BRIO-II-of-BRIMOCHOL%E2%84%A2-PF-for-the-Treatment-of-Presbyopia. Updated Januayr 10, 2025. Accessed August 29, 2025.
Eyewrire News. https://eyewire.news/news/visus-therapeutics-presents-topline-clinical-data-from-phase-3-pivotal-brio-i-trial-of-brimochol-pf-for-the-treatment-of-presbyopia-at-eyecelerator-at-ascrs-2023?c4src=article:infinite-scroll. Updated May 4, 2024. Accessed August 29, 2025.
https://eyewire.news/news/visus-therapeutics-presents-topline-clinical-data-from-phase-3-pivotal-brio-i-trial-of-brimochol-pf-for-the-treatment-of-presbyopia-at-eyecelerator-at-ascrs-2023?c4src=article:infinite-scroll
Optometry Times. https://www.optometrytimes.com/view/tenpoint-therapeutics-announces-positive-topline-results-from-phase-3-pivotal-trial-brio-ii-assessing-brimochol-pf-for-the-treatment-of-presbyopia. Updated January 9, 2025. Accessed August 29, 2025.

Carbachol and Brimonidine
Phase 3 Clinical Trial Highlights

- Mesopic lighting conditions used to isolate pharmacodynamic effect from lighting and minimize visibility

Key Outcomes

- Patients had clinically and statistically significant improvement in near visual acuity across several endpoints
- 6x greater improvement in reading performance
- Vision increased by 1 to 3 letters
- 83% rate effectiveness as “good/excellent”
- 72% rate duration as “just right”
- Well-tolerated

Tenpoint Therapeutics, BRIO-I CSR.
Tenpoint Therapeutics, BRIO-II CSR.

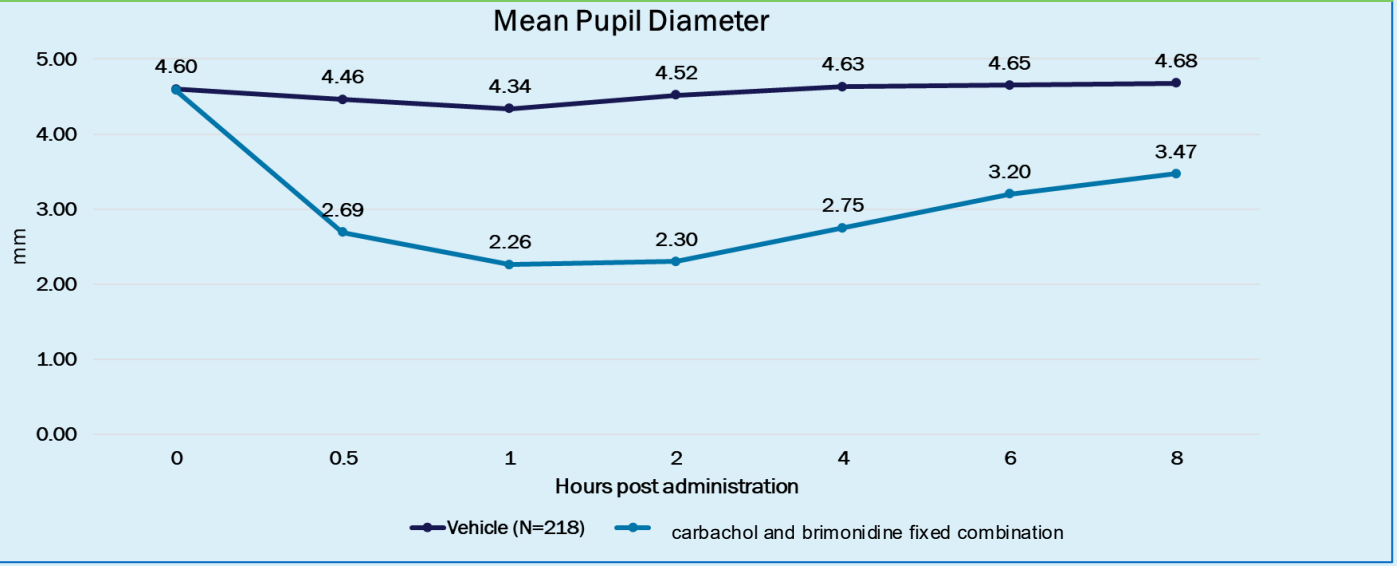
Carbachol and Brimonidine
Efficacy

- ~85% of subjects had functional near vision of 20/40 or better at 1 hour, with ~ 50% still 20/40 or better at 10 hours
- The combination demonstrated an increase in peak effect and duration over carbachol alone
- The pupil constricts within 30 minutes and then gradually returns to normal throughout the day, with no tachyphylaxis in pupil response or near vision over the 12-month study
- *This is believed to be the only company to have measured reading speed using a validated scale in its clinical trials, reporting a 39% improvement, reflecting functional gains rather than simply improvements in visual acuity*

McCabe C. .Ophthalmology Times. https://www.ophthalmologytimes.com/view/the-emerging-era-of-presbyopia-correcting-eye-drops-what-s-next-. The emerging era of presbyopia-correcting eye drops: What's next? Updated August 20, 2025. Accessed Augst 29, 2025.

Efficacy: Carbachol and Brimonidine

- Differences between carbachol and brimonidine fixed combination and vehicle highly significant (P<0.001) at all timepoints
- Within optimum pupil range for mesopic and low light conditions at most timepoints through 8 hours



1. Xu R, Thibos L, Bradley A. Effect of target luminance on optimum pupil diameter for presbyopic eyes. *Optom Vis Sci*. 2016; 93(11):1409-1419.

Aceclidine 1.75%

Dosing and Treatment-related Adverse Events

- Dosing: once daily
- Preservative Free
- CLARITY-1 and CLARITY-2 Trials (N = 466); CLARITY 3 (N = 217)

Treatment-Related AEs	Aceclidine 1.75%*
Instillation site irritation	20%
Dim vision	16%
Conjunctival hyperemia	8%
Ocular hyperemia	7%
Headache	13%

**Vehicle comparisons have not been shared*

Optometry Times. https://www.optometrytimes.com/view/fda-approved-lenz-therapeutics-vizz-for-the-treatment-of-presbyopia. Updated July 31, 2025. Accessed August 29, 2025.

Aceclidine 1.75%
Efficacy

- The company reported that 71%, 71%, and 40% of participants in the phase 3 trials achieved the FDA endpoint at 0.5 hours, 3, and 10 hours on day 1, with higher percentages achieving 2-line gains
- The drug was studied out to 6 months

LENZ Therapeutics announces positive topline data from phase 3 CLARITY presbyopia trials. News release. LENZ Therapeutics. April 3, 2024. Accessed August 29, 2025. https://ir.lenz-tx.com/news-events/press-releases/detail/11/lenz-therapeutics-announces-positive-topline-data-from-phase-3-clarity-presbyopia-trials

Pilocarpine 0.4%

Dosing and Treatment-related Adverse Events

- Dosing: once or twice daily, with second dose after 3 to 6 hours
- Preservative Free
- NEAR-1 and NEAR-2 trials (N = 613)

Treatment-Related AEs	CSF-1 n = 308; n (%)	Vehicle n = 305; n (%)
Non-Ocular		
Headache	21 (6.8%)	2 (0.7%)
Eye/facial pain	6 (1.9%)	1 (0.3%)
Nausea	4 (1.3%)	
Ocular		
Instillation site pain	18 (5.8%)	1 (0.3%)
Vision blurred	11 (3.6%)	2 (0.7%)
Conjunctival hyperemia	5 (1.6%)	1 (0.3%)
Instillation site pruritus	3 (1.0%)	1 (0.3%)
Visual impairment	3 (1.0%)	

Holland E, et al. Efficacy and Safety of CSF-1 (0.4% Pilocarpine Hydrochloride) in Presbyopia: Pooled Results of the NEAR Phase 3 Randomized, Clinical Trials. Clin Ther. 2024;46(2):104-113.

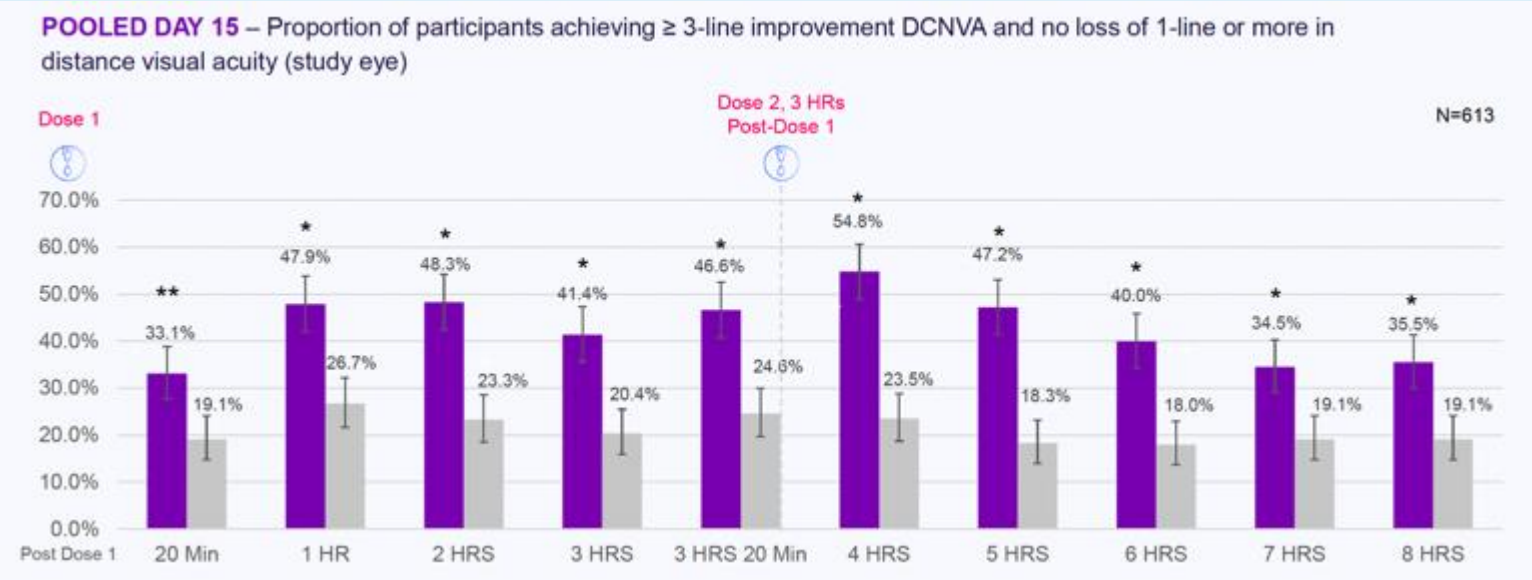
Pilocarpine 0.4%
Efficacy

Pooled Results of NEAR 3 Phase 3 Trial

- The 2-dose regimen was evaluated twice-daily drop during a 2-week period
- 40% achieved the FDA endpoint of a 3-line gain on day 8 at 1 hour post dose compared with 19% of the vehicle group, with similar results out to 4 hours
- Among those who could not achieve 20/40 near at baseline, approximately 80% had functional (20/40) near vision on day 15, with efficacy out to 8 hours.
- Lowest effective concentration of any miotic
- Effective at a minimum effective dose, possibly because of its near-neutral pH among other factors, which increases bioavailability
- Includes sodium hyaluronate and hydroxypropyl methylcellulose (lubricants for comfort)

Holland E, et al. Efficacy and Safety of CSF-1 (0.4% Pilocarpine Hydrochloride) in Presbyopia: Pooled Results of the NEAR Phase 3 Randomized, Clinical Trials. Clin Ther. 2024;46(2):104-113.

Pilocarpine 0.4%
Efficacy



Error bars are 95% confidence interval
*p<0.0001 for CSF-1vs. Vehicle
** p= 0.0002 for CSF-1vs. Vehicle

Pilocarpine 0.4% vehicle

Holland E, et al. Efficacy and Safety of CSF-1 (0.4% Pilocarpine Hydrochloride) in Presbyopia: Pooled Results of the NEAR Phase 3 Randomized, Clinical Trials. Clin Ther. 2024;46(2):104-113.

Pilocarpine 1.25%

Dosing and Treatment-Related Adverse Events

- Dosing: once or twice daily, with second dose after 3 to 6 hours
- Preservative: Benzalkonium chloride (BAK)
- GEMINI 1; GEMINI 2; VIRGO

Treatment-related AEs	GEMINI 1		GEMINI 2		VIRGO	
	Pilocarpine 1.25% group - 163, n (%)	Vehicle group - 159, n (%)	Pilocarpine 1.25% group - 212, n (%)	Vehicle group - 215, n (%)	Pilocarpine 1.25% group - 114, n (%)	Vehicle group - 116, n (%)
Headache	23 (14.11)	15 (9.43)	33 (15.57)	11 (5.12)	10 (8.77)	4 (3.45)
Blurring of vision	4 (2.5)	1 (0.6)	13 (6.13)	1 (0.47)		
Conjunctival hyperemia	4 (2.5)	4 (2.5)	15 (7.08)	11 (5.12)		
Eye irritation	4 (2.5)	1 (0.6)			114 (6.14)	0
Eye pain	4 (2.5)	1 (0.6)	12 (5.66)	3 (1.40)		

Singh M, et al. A Systematic Review and Meta-Analysis on the Efficacy and Safety of Topical Pilocarpine 1.25% in Presbyopia Treatment. J Curr Ophthalmol. 2025;36(2):111-121.

Pilocarpine 1.25%
Efficacy

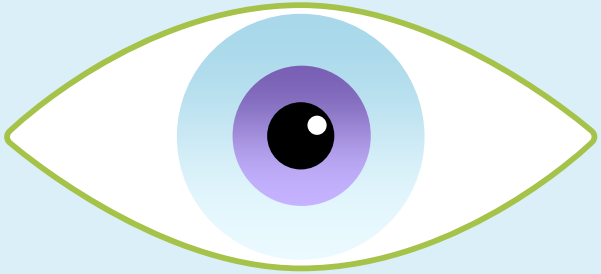
- 1.25% of pilocarpine was used either once (in the GEMINI 1 and GEMINI 2 trial) or twice daily (VIRGO trial).
- A significantly higher proportion of patients reported improvement of DCIVA and gain of ≥ 3 lines in binocular DCNVA in the pilocarpine group than the vehicle group ($P < .01$).

Why wasn't this treatment more widely adopted?

Singh M, et al. A Systematic Review and Meta-Analysis on the Efficacy and Safety of Topical Pilocarpine 1.25% in Presbyopia Treatment. J Curr Ophthalmol. 2025;36(2):111-121.

Topical Presbyopia Treatments
Things to Consider for Each Patient

1. Maximize duration of effect
2. Minimize onset time
3. Limit reduction of distance and night vision
4. Minimize adverse events
5. Minimize impact on ocular surface health
6. Maximize drop administration comfort to increase compliance



Key Take-Aways

Q&A

Steven Ferrucci, OD, FAAO

Key Take-Away Messages

- GA more common and progresses more quickly than previously thought
- Important to diagnose early!
- Newer therapeutics options shown to slow GA progression, allowing patents longer time with usable vision
- Presbyopia (like death and taxes) is inevitable!
- Several topical options now available
- Patient selection is crucial for success

Thank You for Attending!

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