New Approaches in Age-Related Macular Degeneration and Geographic Atrophy

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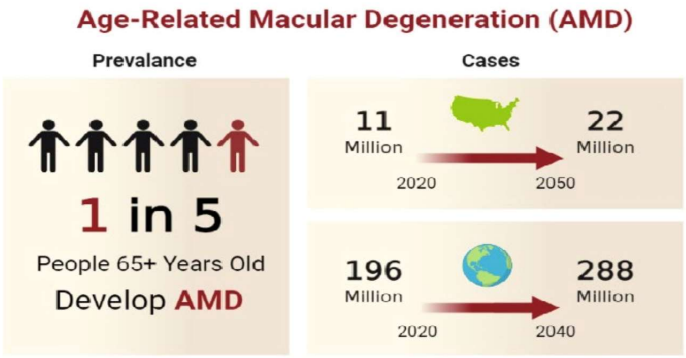
Prevalence and Impact

- In 2004, an estimation of 1.75 million people have advanced age-related macular degeneration (AMD) in at least one eye in the United States
- Prevalence of AMD in the United States is estimated to increase to 22 million by 2050
- AMD is responsible for 46% of cases of severe visual loss in persons over age of 40 in the U.S.

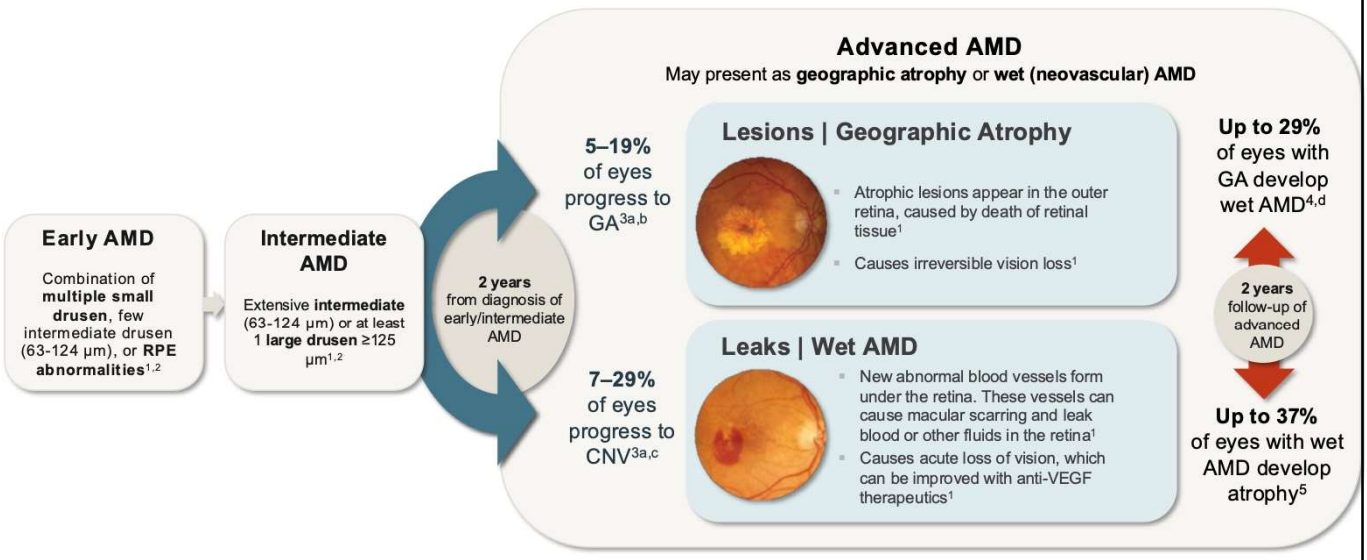


Risk Factors for AMD

- Age
- Cigarette smoking
- Cardiovascular disease
- Obesity
- Systemic hypertension and hypercholesterolemia

- Dietary: high fat intake/no green leafy vegetables (mediterranean diet 41% reduced risk of advanced AMD)
- Genetic: Complement Factor H (CFH) and ARMS2 (homozygous for the Y402H risk allele of CFH possess a 7.4 fold increased risk of AMD)
- Data regarding omega-3 polyunsaturated fatty acids, degree of sunlight exposure and levels of ocular melanin are conflicting

Clinical Course of AMD



Color fundus images of geographic atrophy and neovascular AMD used with permission from Theodore Leng, MD.
[a] From a retrospective cohort analysis (N=40,543) of a multicenter electronic medical records database from the United Kingdom to estimate rates for progression to GA or neovascular AMD. [b] By fellow eye status: early or intermediate AMD, 4.6%; CNV, 10.0%; GA, 18.6%; both GA/CNV, 16.6%. [c] By fellow eye status: early or intermediate AMD, 7.1%; CNV, 29.3%; GA, 13.87%; both GA/CNV, 23.3%. [d] By fellow eye status: GA, 11.4% if nonsubfoveal GA in study eye, 10.2% if subfoveal GA in study eye; nAMD, 29.3% if nonsubfoveal GA in study eye, 26.0% if subfoveal GA in study eye. 1. Fleckenstein M et al. *Nat Rev Dis Primers.* 2021;7(1):31. 2. Holz FG et al. *Ophthalmology.* 2014 May;121(5):1079-1091. 3. Chakravarthy U et al. *Ophthalmol Retina.* 2020;4(7):662-672. 4. Rahimy E. et al., *Ophthalmol Sci.* 2023;3:100318. 5. Gillies MC et al. *Ophthalmology.* 2020;127(2):198-210. AMD, age-related macular degeneration; CNV, choroidal neovascularization; GA, geographic atrophy; RPE, retinal pigment epithelium.

SL4

AMD Classification

AREDS Categories	
No AMD	None or a few small drusen ≤ 63 µm, no AMD pigmentary abnormalities
Early AMD (category 2)	Small drusen (<63), Medium drusen 63-124 µm, and/or minimal pigmentary abnormalities
Intermediate AMD (category 3)	Extensive mediums (63-124) or 1 or more large drusen ≥125 µm
Advanced AMD (category 4)	Geographic atrophy or neovascular AMD

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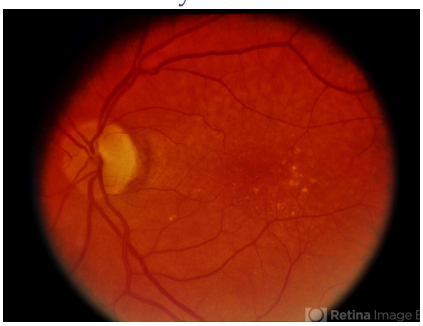
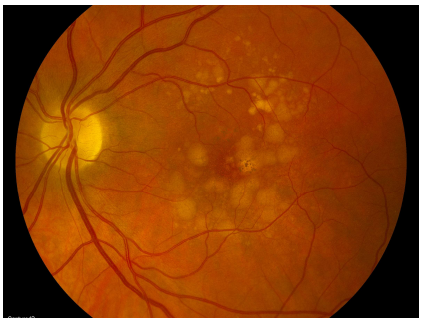
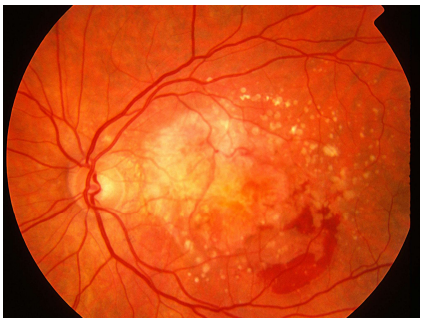
Early AMD



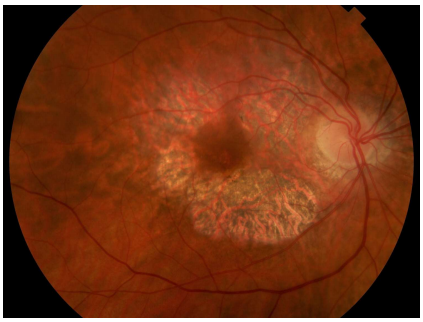
Intermediate AMD

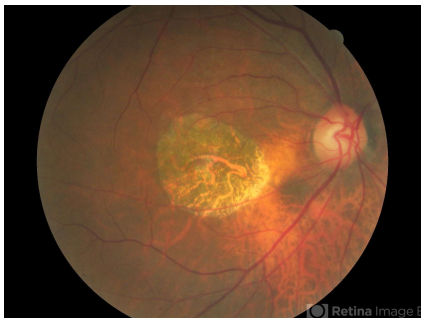


Advanced Exudative AMD

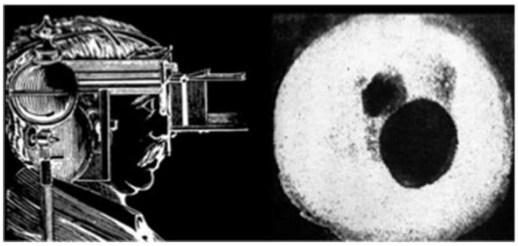


Advanced Non-Exudative AMD w/o fovea and w/ fovea





Imaging Options



- Optical Coherence Tomography (OCT) - defines the cross-sectional architecture of the retina. Detecting subretinal and intraretinal fluid and degree of thickening. SD-OCT and swept-source OCT
- Color Fundus Photography- can be used as a baseline for landmarks
- Fluorescein Angiography- detect the presence and determine the type, size and location of choroidal neovascularization. Risks involved: pain, tissue infiltration, allergic reactions including anaphylaxis.
- OCT-Angiography- provides noninvasive evaluation of the retinal and choroidal vasculature
- Fundus Autofluorescence- detect geographic atrophy and quantify lipofuscin in the RPE

Normal OCT

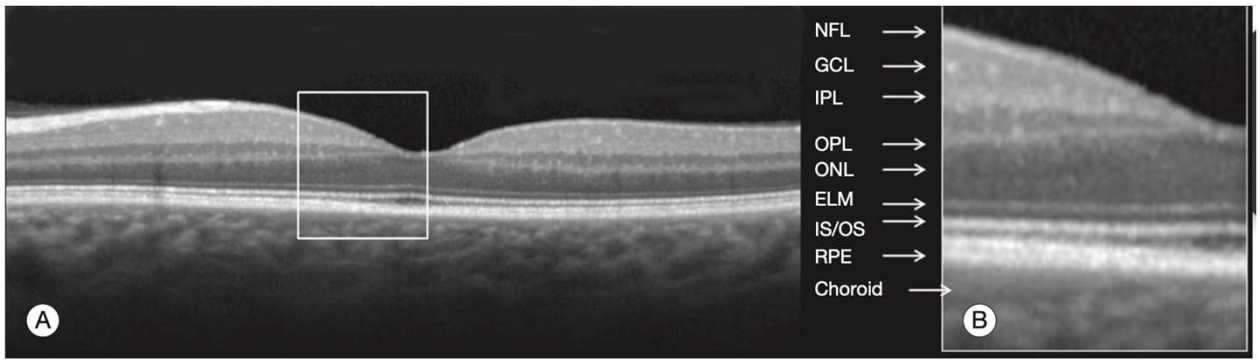
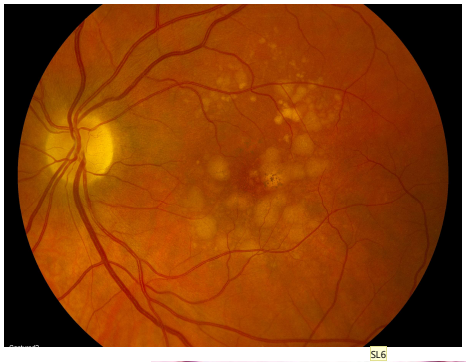


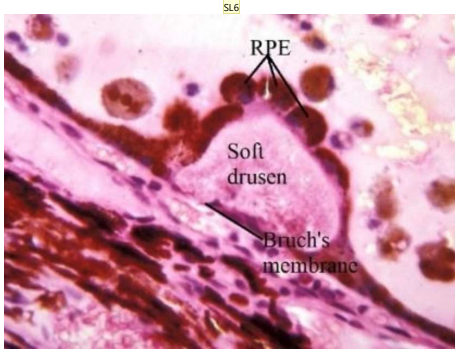
Fig. 3.7 Spectral domain optical coherence tomography (Spectralis, Heidelberg) image of a normal individual. The multilayered retinal architecture can be observed and each retinal layer can be identified. NFL, nerve fiber layer; GCL, ganglion cell layer; IPL, inner plexiform layer; OPL, outer plexiform layer; ONL, outer nuclear layer; ELM, external limiting membrane; IS/OS, junction of the inner and outer segments of the photoreceptors; RPE, retinal pigment epithelium.

Filho, Carlos. Optical Coherence Tomography, Editors: Ryan, Stephen et al. Retina (5th Edition). W.B. Saunders. 2013. Page 86

Drusen

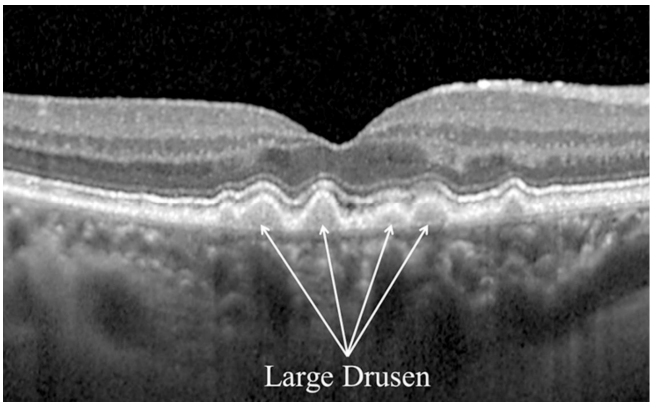
- Focal yellow or white deposits of extracellular material between the RPE and Bruch's membrane
- Diffuse thickening of the inner aspect of Bruch's membrane
- Hallmark sign of non-neovascular AMD

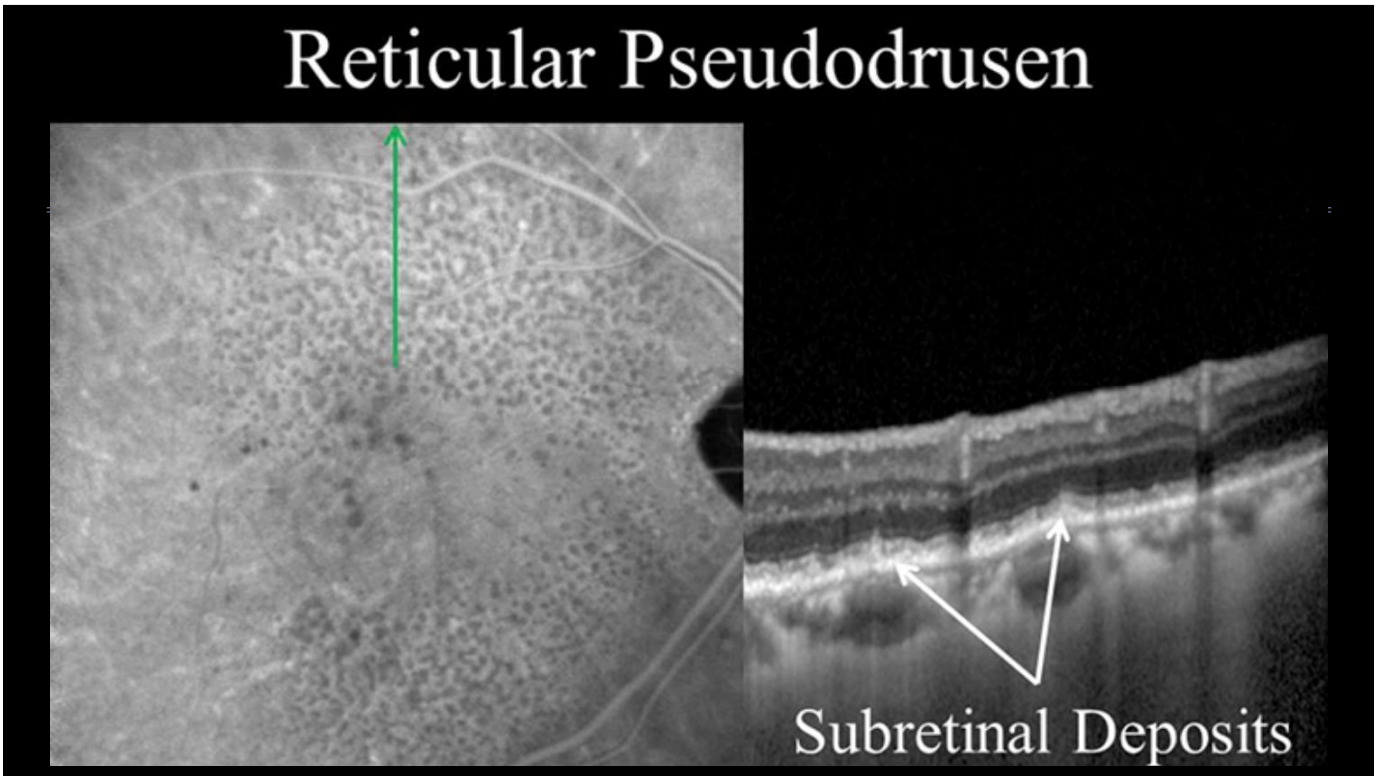


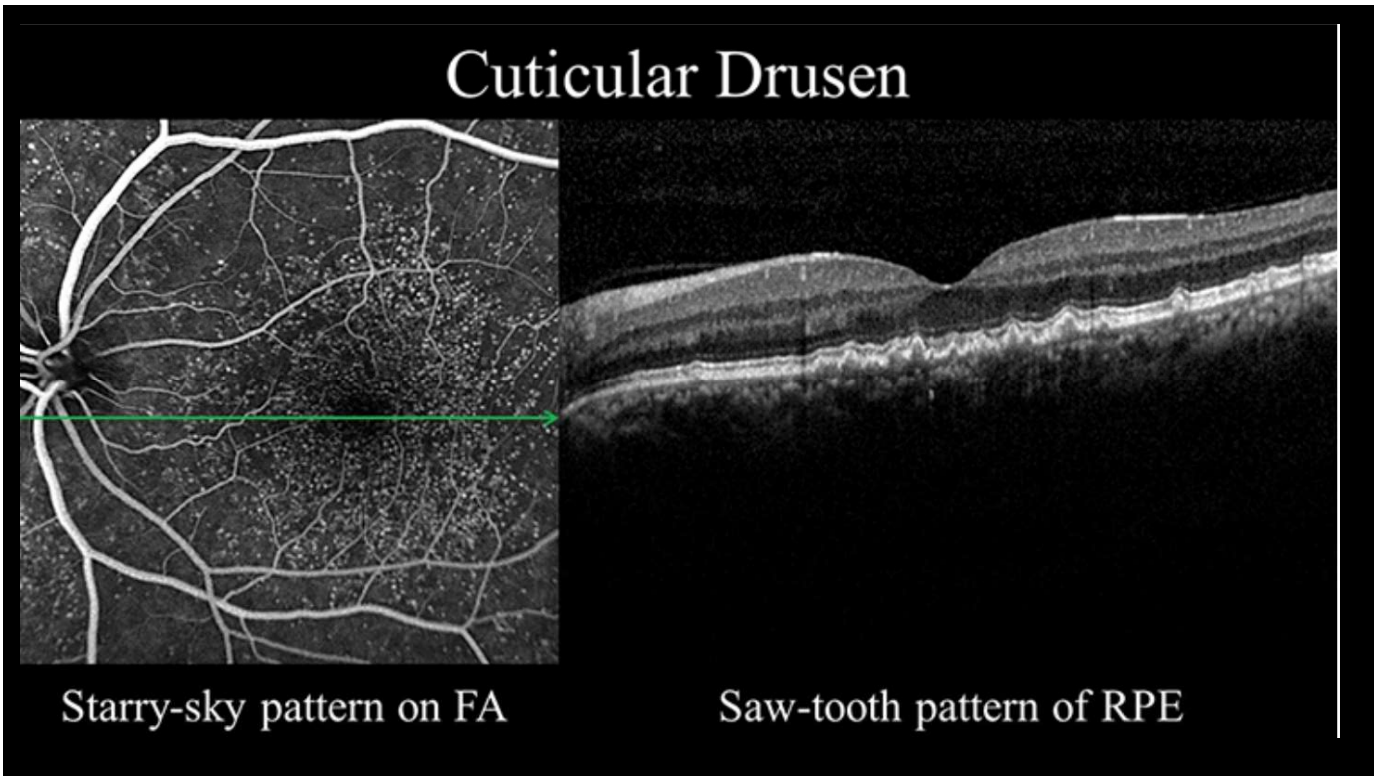


Different Types of Drusen

- Hard Drusen- yellow-white deposits with distinct borders at the level of Bruch's membrane
- Soft Drusen- larger yellow-white dome-shaped mounds of deposits with indistinct borders under the RPE
- Basal laminar/cuticular (sawtooth)- yellow-white punctate accumulations under the RPE. Gives a "stars in the sky" appearance on FA. Spheroid or triangular shape on OCT
- Reticular pseudodrusen (sub retinal drusenoid deposits above the RPE)- light gray accumulations ABOVE the RPE on OCT **High risk for advanced AMD development**

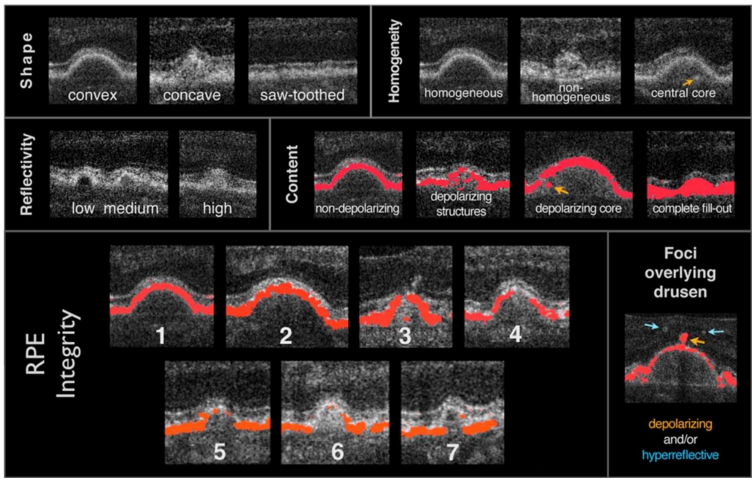






Drusen Phenotypes/High Risk Features

- Homogenous, uniform, medium reflectivity less risk of advanced AMD
- Hyper and hypo or non-uniform=high risk
- Hyperreflective foci=high risk. Represent RPE compromise

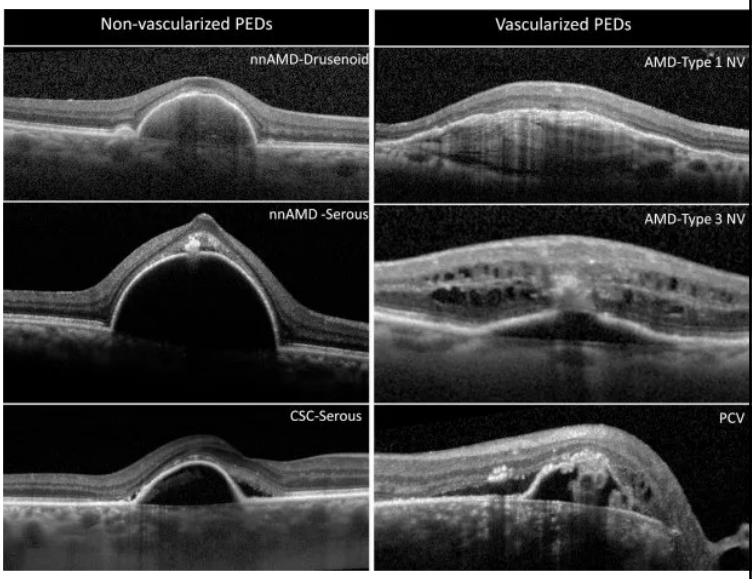


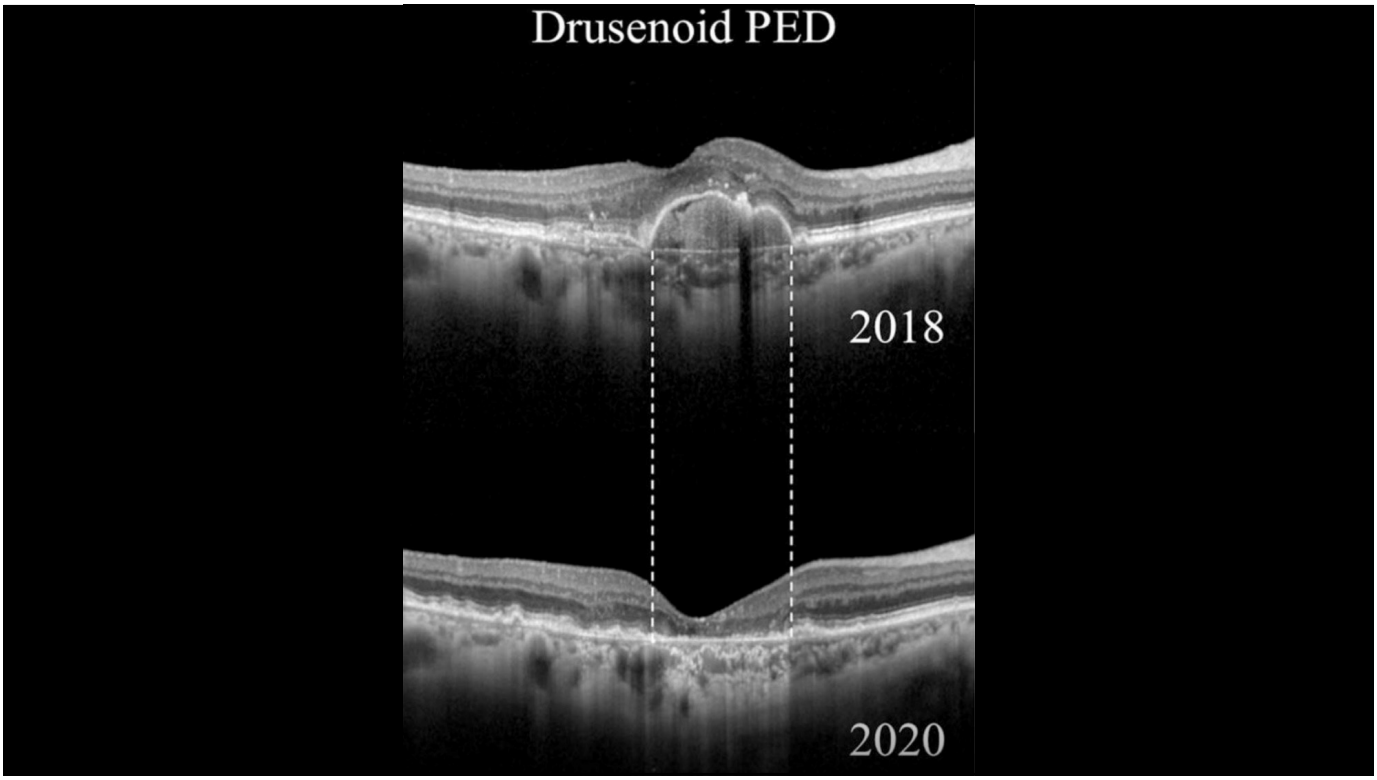
Schlanitz F, Baumann B, Sacu S, *et al. Br J Ophthalmol* 2019;**103**:227–232.

Pigment Epithelial Detachment (PED)

- Separation of RPE from the underlying Bruch's membrane (drusenoid, serous, vascularized)
- Drusenoid PED-well circumscribed yellow elevations of RPE, 350 µm in size
- Serous PED-clear or yellow-orange circular elevations of RPE. Occur commonly in central serous chorioretinopathy. In AMD, typically associated with neovascular AMD
- PEDs are found in 62% of eyes with advanced AMD*

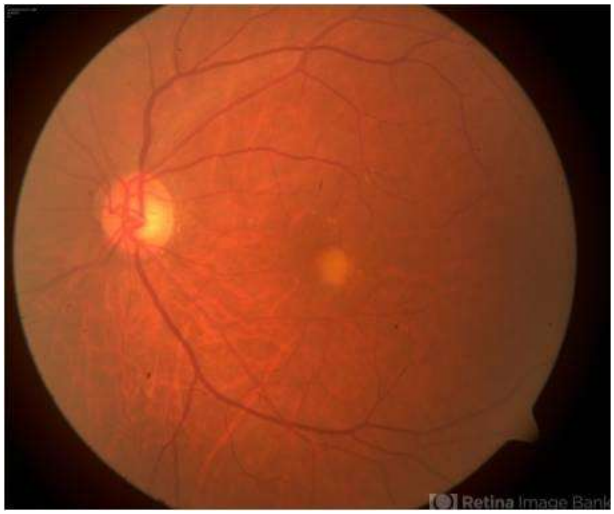
*Coscas F, Coscas G, Souied E, Tick S, Soubrane G. Optical coherence tomography identification of occult choroidal neovascularization in age-related macular degeneration. Am J Ophthalmol. 2007;144:592-599.





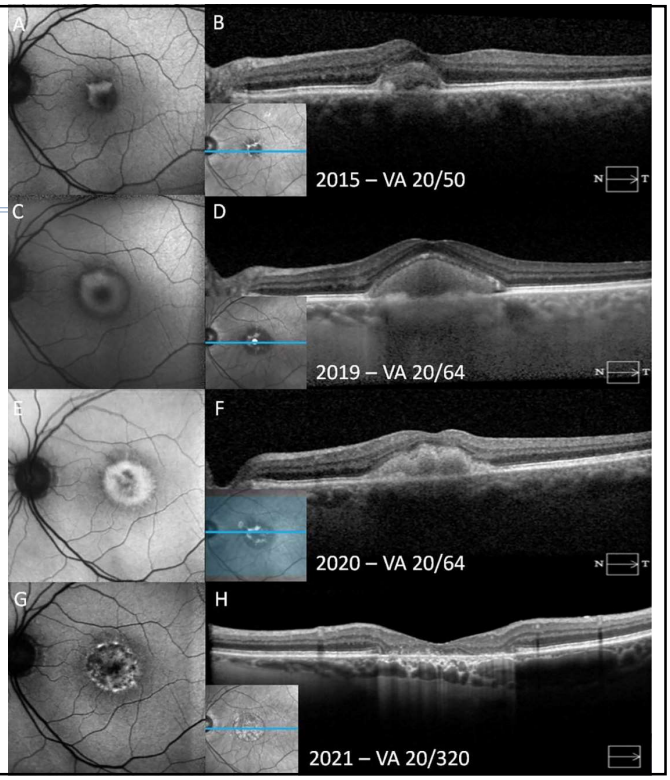
Acquired Vitelliform Lesions

- Accumulations of yellow material in the sub retinal space
- Hyperautofluorescence on autofluorescence
- Material contains lipofuscin, melanofuscin granules in macrophages, and extracellular material derived from outer segment discs
- Due to RPE dysfunction
- SD-OCT, the vitelliform lesion corresponds to the dome shaped subretinal hyper reflective material (SHRM) between RPE and ellipsoid zone



Natural Course of Acquired Vitelliform Lesions

- Highly variable
- Varying degrees of RPE attenuation/loss, thinning of outer nuclear layer
- 4 stages: Vitelliform, pseudohypopyon, vitelliruptive, atrophic



Nipp GE, Lee T, Sarici K, Malek G and Hadziahmetovic M (2023) Adult-onset foveomacular vitelliform dystrophy: epidemiology, pathophysiology, imaging, and prognosis. Front. Ophthalmol. 3:1237788. doi: 10.3389/fopht.2023.1237788

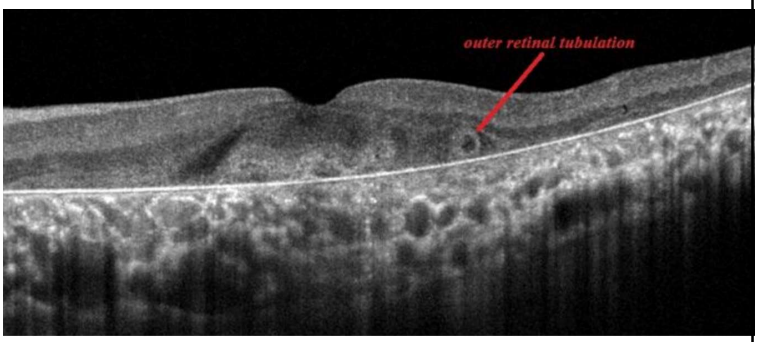
	1. Vitelliform	2. Pseudohypopyon	3. Vitelliruptive	4. Atrophic
Color Fundus Photography	"Egg-yolk" appearance Lesion is yellowish-white, rounded, regular in shape, centered on fovea (3)	Unchanged as compared to vitelliform stage (43)	"Scrambled egg" appearance Yellowish lesion appears to break apart, is less regular in shape (43)	Visible choroidal blood vessels Pale fundus (44)
Fundus Autofluorescence	Entire lesion is hyperautofluorescent (13)	Hyperautofluorescent inferior half, hypoautofluorescent superior half (45)	Hypoauto-fluorescent (45, 46)	Hypoauto-fluorscent (45, 46)
Fluorescein Angiography	Non-fluorescent central spot in lesion Hyperfluorescent spoked ring around lesion (3, 10, 13, 47)	Less hyperfluorescent "Stars-in-the-sky" appearance (48)	Persistent hyper-fluorescence "Stars-in-the-sky" appearance (48)	Late-stage hyperfluorescence of atrophic area (44)
Spectral Domain Optical Coherence Tomography	Intralesional cuticular Drusen at RPE/Bruch's membrane complex is common Subretinal drusenoid deposits Disruption of the ellipsoid zone			
	Dome-shaped homogeneous SHRM (10, 16, 43)	Two zones of the vitelliform lesion (43). * Upper zone is hyporeflective with a few clumps of SHRM * Lower zone features homogenous SHRM Normal overlying retina * Intraretinal pseudocysts may be present	Fragmented vitelliform lesion with mix of hyper- and hyporeflective spaces with overlying photoreceptor loss (16) As lesion progresses, SHRM may "clump" and resolve along RPE layer (43).	Widespread loss of photoreceptor layers and RPE atrophy. Corresponds with cRORA definition (44)
Optical Coherence Tomography Angiography	Increased subfoveal choroidal thickness, particularly as compared to AMD patients			
	Reduced blood flow in superficial and deep choroid plexus in areas corresponding to lesion (19, 49, 50) Reduction in apparent choriocapillaris vessel density (19, 49, 51, 52)	Reduced blood flow in superficial and deep choroid plexus in areas corresponding to lesion (19, 49, 50) Reduction in apparent choriocapillaris vessel density (19, 49, 51, 52)	Increased choriocapillaris vessel density (19)	Increased choriocapillaris vessel density (19)

SHRM, subretinal hyperreflective material; cRORA, complete retinal pigmental epithelium and outer retinal atrophy; AMD, age-related macular degeneration.

Nipp GE, Lee T, Sarici K, Malek G and Hadziahmetovic M (2023) Adult-onset foveomacular vitelliform dystrophy: epidemiology, pathophysiology, imaging, and prognosis.

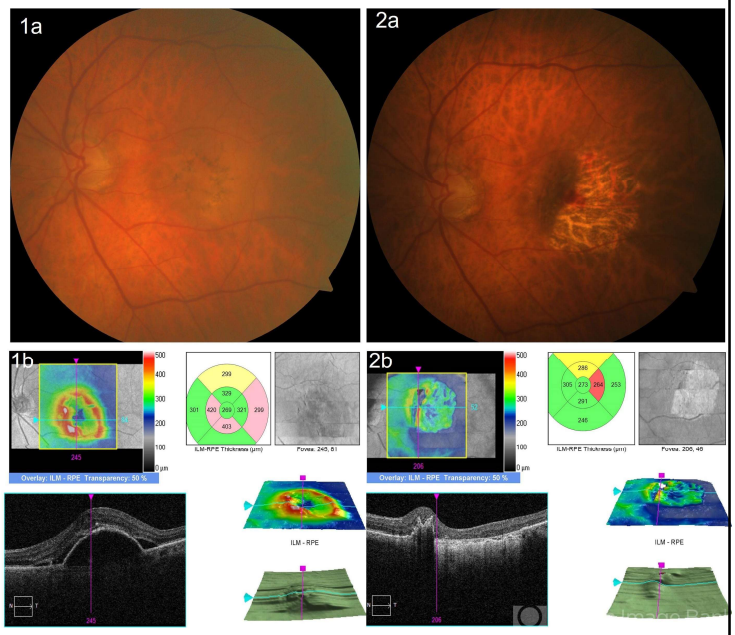
Outer Retinal Tubulation (ORT)

- Distinct OCT finding of thick hyper-reflective band surrounding a hypo reflective cavity located within the ONL
- Common in advanced AMD
- Overlying areas of degenerate or absent RPE
- Can be mistaken for cystic fluid



RPE Tear

- Fairly common occurrence in PED associated with type 1 (occult) CNV
- CNV can spontaneously contract after treatment putting traction on RPE
- RPE scrolls and retracts



Geographic Atrophy (GA)

- Early classifications used CFP to define GA as sharply delineated round areas of depigmentation with increased visibility of choriodal vessels of at least 175 µm
- Denotes areas of RPE and choriocapillaris loss
- The definition is being revised to include SD-OCT and fundus autofluorescence
- Areas of RPE loss appear hypoautofluorescent and show a margin of hyperautofluorescence that indicate cells at risk
- GA may be preceded by reticular pseudodrusen or may follow regression of large drusen, PED, or acquired vitilleform lesion

Imaging Geographic Atrophy (GA)

A: Color fundus photography

B: Fundus autofluorescence

C-D: Fluorescein angiography (over course of exam)

E-F: Optical coherence tomography

G: Near-infrared reflectance

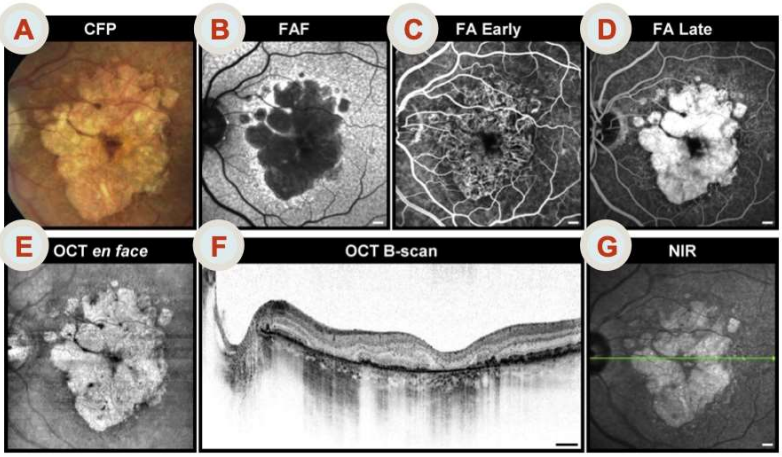
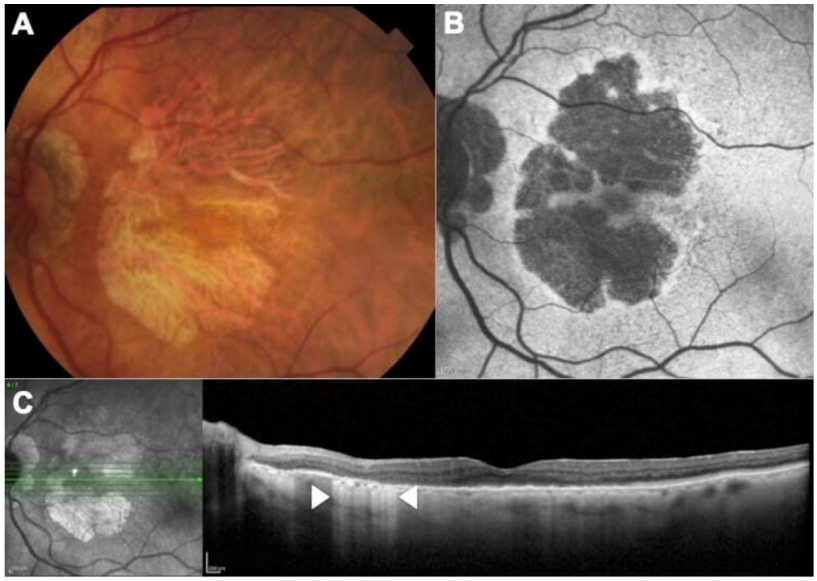


Figure 1 from Fleckenstein M et al. Ophthalmology. 2018;125(3):369-390.

1. Fleckenstein M et al. *Ophthalmology*. 2018;125(3):369-390. CFP, color fundus photography; FA, fluorescein angiography; FAF, fundus autofluorescence; GA, geographic atrophy; NIR, near-infrared reflectance; OCT, optical coherence tomography.

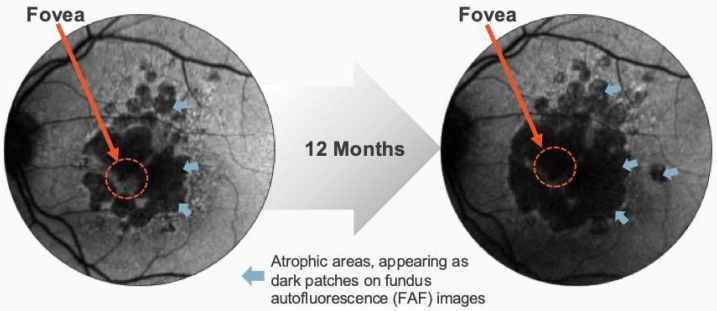
- CFP: Areas of RPE hypopigmentation with sharply demarcated border and visible choroidal vasculature
- Autofluorescence: hypoautofluorescence due to loss of RPE cells with ring of hyperautofluorescence surrounding atrophic regions
- SD-OCT: marked choroidal hyper-transmission in the area of outer retinal and RPE atrophy



Su, D. Geographic Atrophy Treatments In the Pipeline 2022 https://www.ophthalmologyadvisor.com/slideshow/retina-vitreous/potential-therapies-for-geographic-atrophy-in-amd/

Geographic Atrophy Progression

- Atrophic regions within the retinal pigment epithelium typically begin in the perifoveal region and expand to involve the fovea[1]
- Mean GA lesion growth rates range from 0.53 to 2.6 mm^2/year (median ≈1.78 mm^2/year) across studies of GA[1]
- The median time from first diagnosis of GA to central GA was 2.5 years in a large, prospective study of persons with AMD[2]

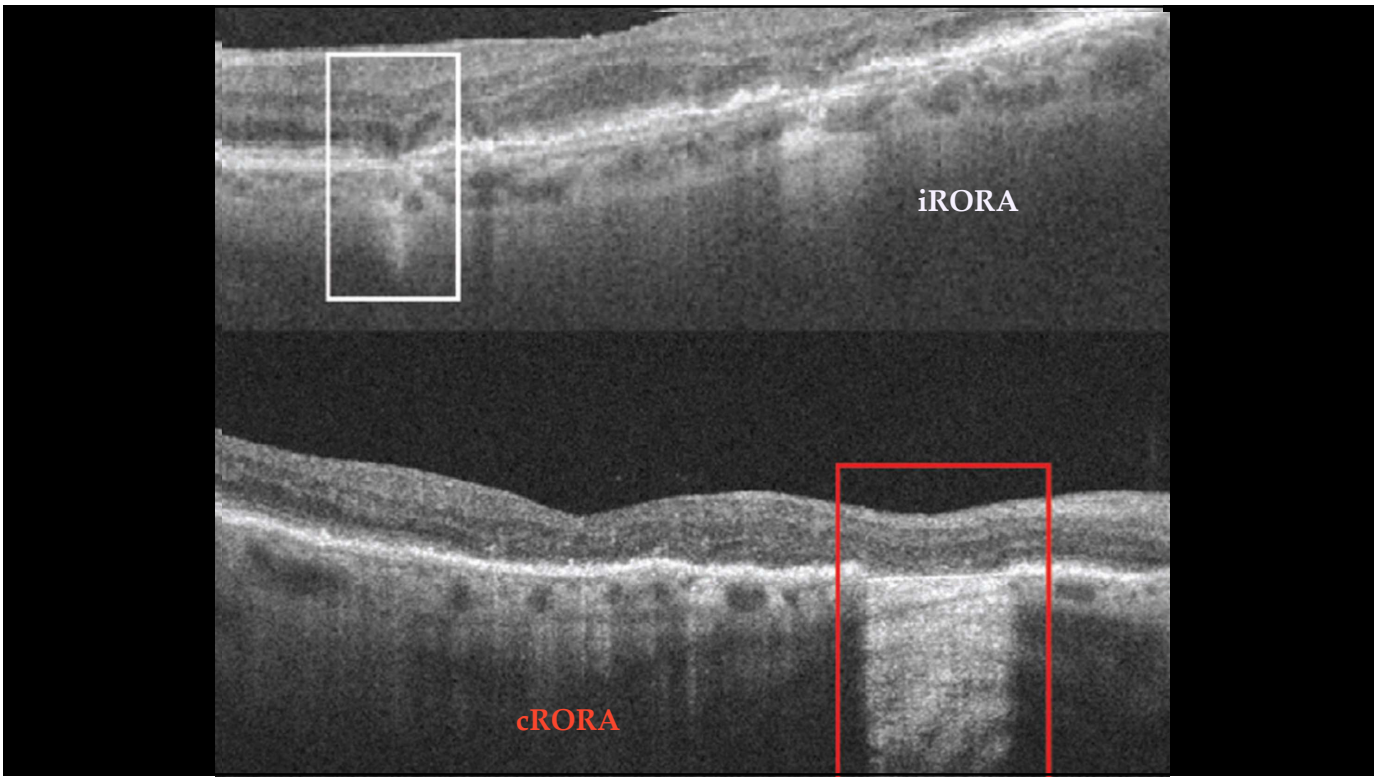


Classification of Atrophy Meeting (CAM)

- CAM defines a classification system and criteria for OCT-defined atrophy
- Recognized that photoreceptor atrophy can occur without RPE atrophy
- Provided consistent definitions for future studies

Complete RPE and outer retinal atrophy (cRORA)	• Hypertransmission region ≥250 µm • Absence of RPE ≥250 µm • Overlying photoreceptor degeneration • No RPE tear
Incomplete RPE and outer retinal atrophy (iRORA)	• Inhomogeneous hypertransmission region • Interrupted RPE • Overlying photoreceptor degeneration • No RPE tear
Complete outer retinal atrophy (cORA)	• Intact RPE • Absence of ELM, EZ, and IZ • Severe thining of the outer retina • Intermittent hypertransmission region
Incomplete outer retinal atrophy (iORA)	• Intact RPE • Continuous ELM • Intermittent EZ disruption • Absence of IZ • SDD • Detectable thinning of the outer retina • No hypertransmission region

2. Guymer, Robyn H et al. Incomplete Retinal Pigment Epithelial and Outer Retinal Atrophy in Age-Related Macular Degeneration: Classification of Atrophy Meeting Report 4. *Ophthalmology* vol. 127,3 (2020):349-409.
3. Sadda, Srinivas R et al. Consensus Definition for Atrophy Associated with Age-Related Macular Degeneration on OCT: Classification of Atrophy Report 3. *Ophthalmology* vol. 125,4 (2018): 537-548.



Non-Exudative AMD Management Options

- AREDS II supplements
- Amsler grid and/or Foresee home device
- Intravitreal injections of complement inhibitors for geographic atrophy

AREDS/AREDS II

- Early AMD- No evidence to support the use of supplements
- Intermediate AMD or advanced AMD in one eye- benefited from antioxidant vitamins with zinc and copper
- The rate of development of advanced AMD at 5 years was reduced 25% with AREDS (2001)
- AREDS II found that replacing beta-carotene with lutein and zeaxanthin improved efficacy

Foresee Home Device

- Teleconnected home based monitoring detects early vision changes
- Uses preferential hyperacuity perimetry (vernier acuity)
- Candidates are patients with intermediate non-exudative AMD OD, OS, or OU
- "SCANLY" Notal Home OCT FDA authorized

Pathophysiology of Geographic Atrophy

- Due to oxidative stress, genetic predisposition and environment there is a complement deposition between RPE and Bruch's membrane.
- Leads to a loss of complement regulation
- Overactivation of complement system is the problem
- MAC leads to apoptosis of retinal cells

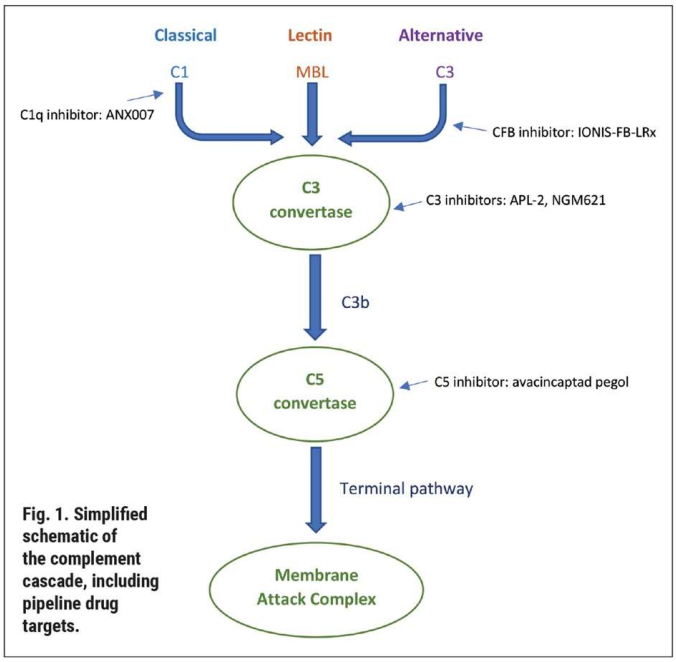


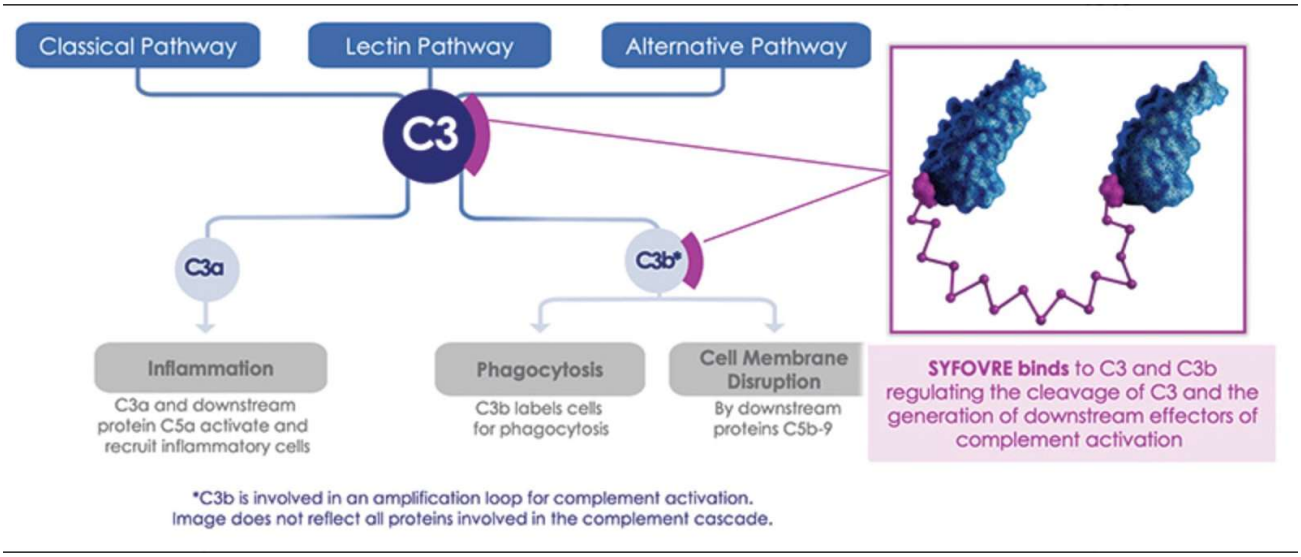
Fig. 1. Simplified schematic of the complement cascade, including pipeline drug targets.

FDA Approved Geographic Atrophy Drugs

- Syfovre-pegcetacoplan/Apellis— Targets C3
- Izervay- avacincaptad pegol/Astellas—Targets C5

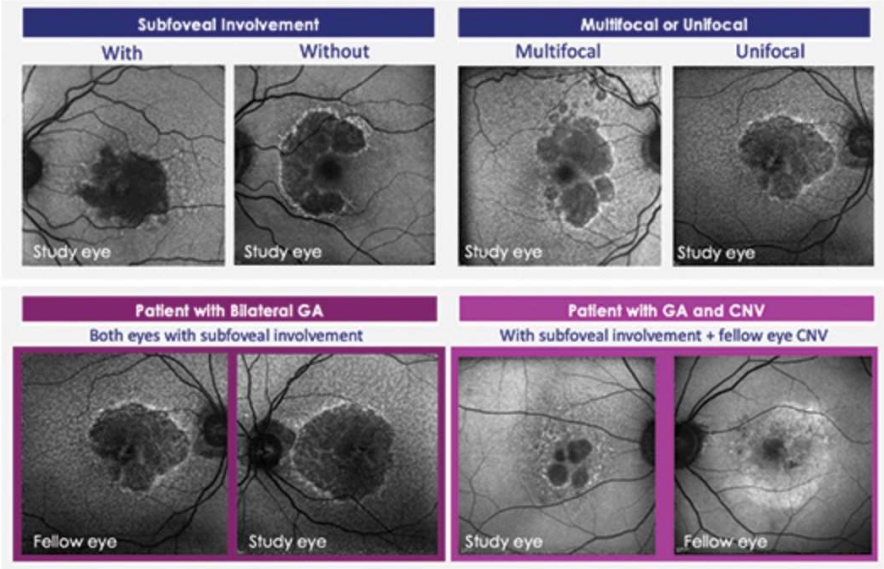
Syfovre

- 24 month OAKS and Derby studies- rate of GA lesion growth reduced compared to sham
- Studied subfoveal versus without subfoveal involvement
- Extrafoveal lesions responded better
- FDA approved on February 17, 2023
- GALE extension study



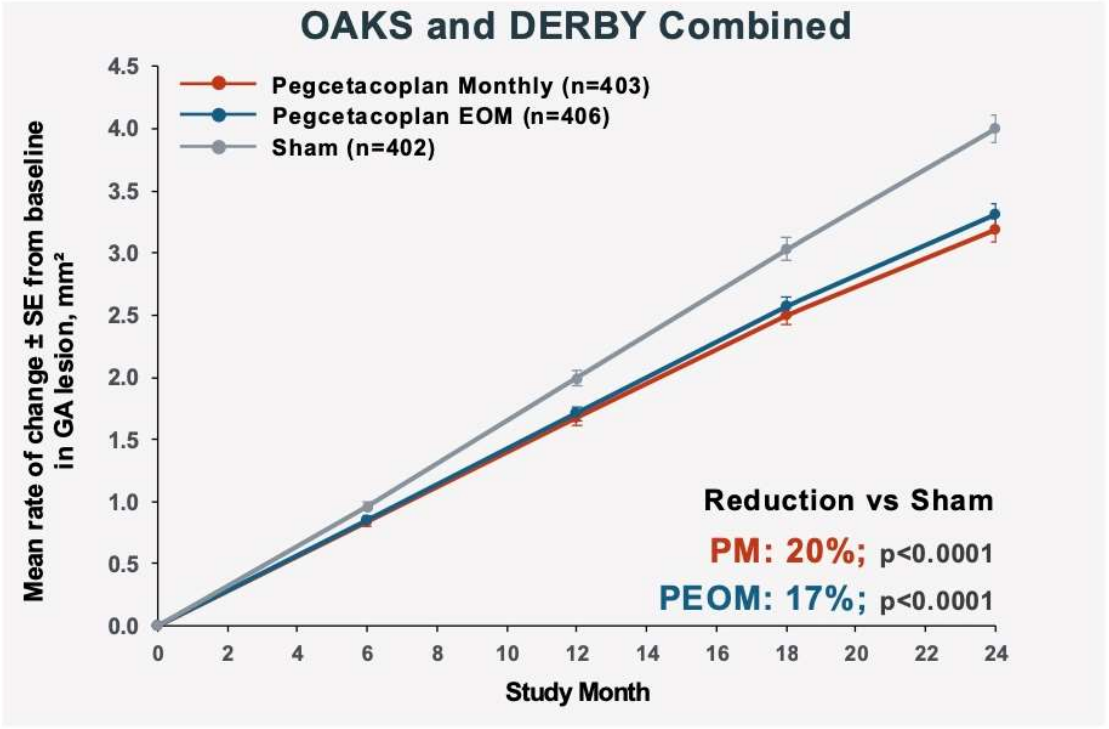
Key Inclusion Criteria

- GA lesion requirements:
  - Total size:
    - 2.5 mm^2 to 17.5 mm^2
  - With and without subfoveal lesion involvement
  - If multifocal, ≥1 focal lesion ≥1.25 mm^2 (0.5 DA)
  - Presence of perilesional hyperautofluorescence
  - **GA, CNV, or both** were permitted in the fellow eye
- Age ≥60 years
- BCVA ≥24 letters using ETDRS charts in study eye

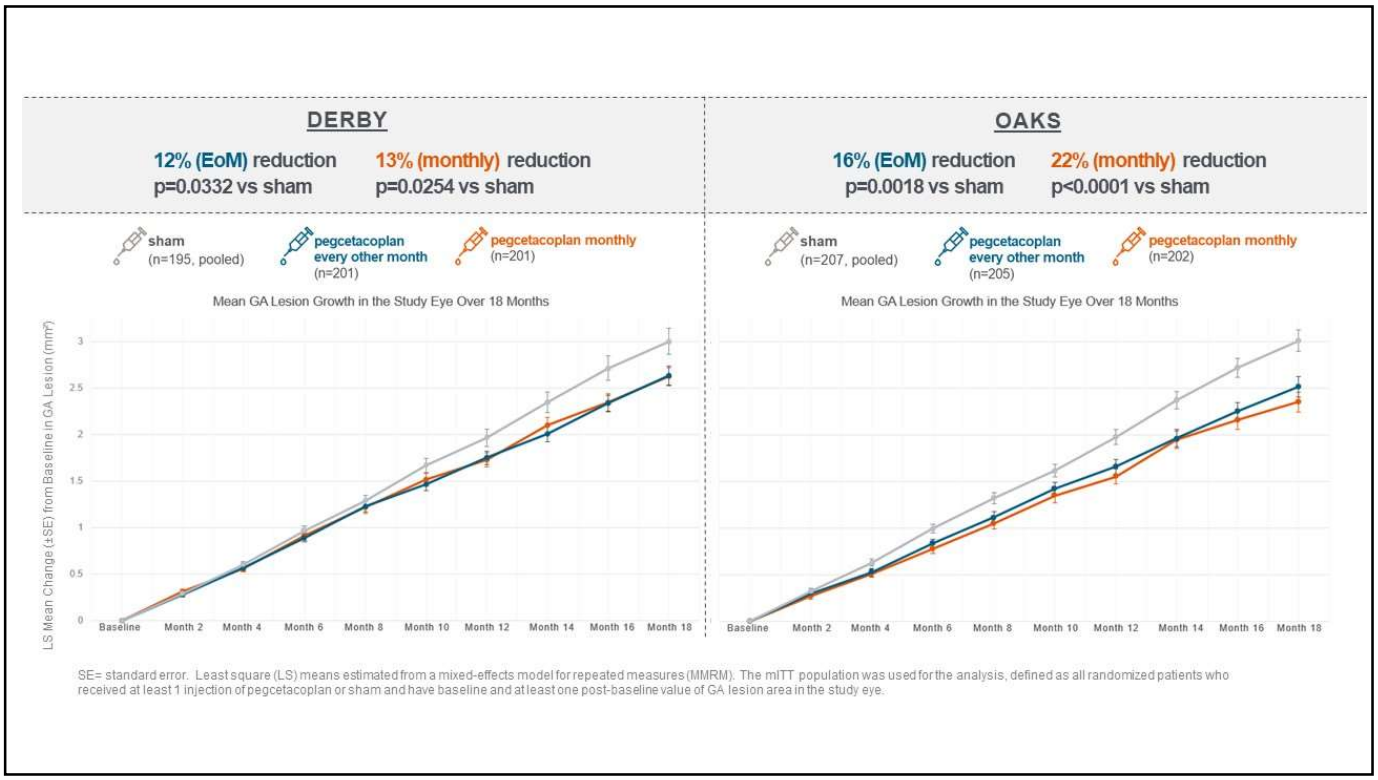


Images are for illustration purposes only.

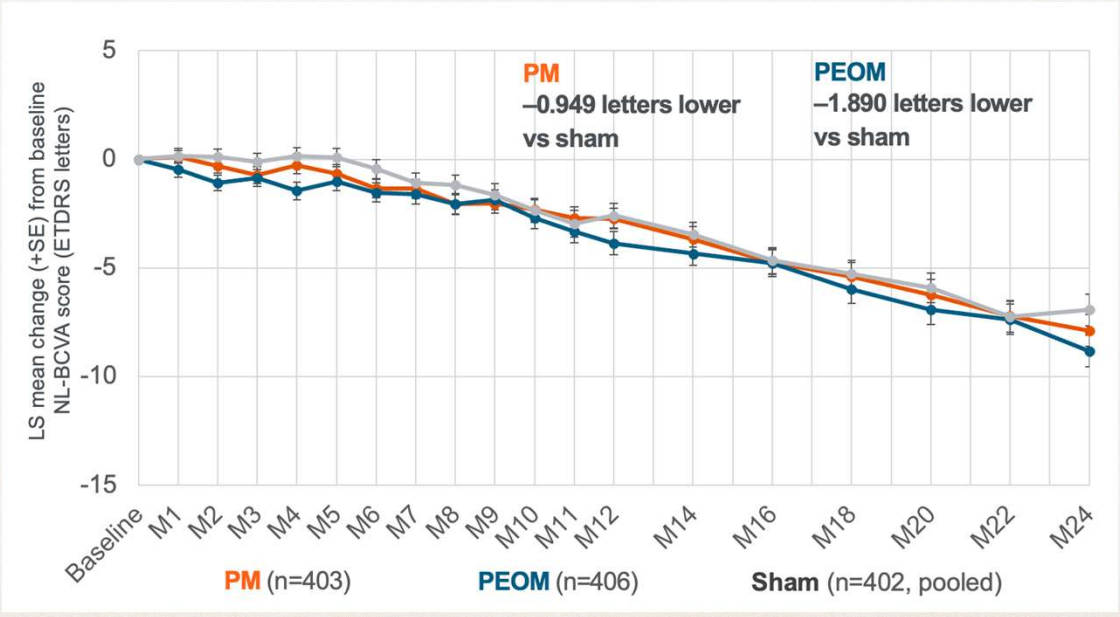
CNV=choroidal neovascularization. DA=disk area; ETDRS=Early Treatment Diabetic Retinopathy Study.



(all p-values are nominal)

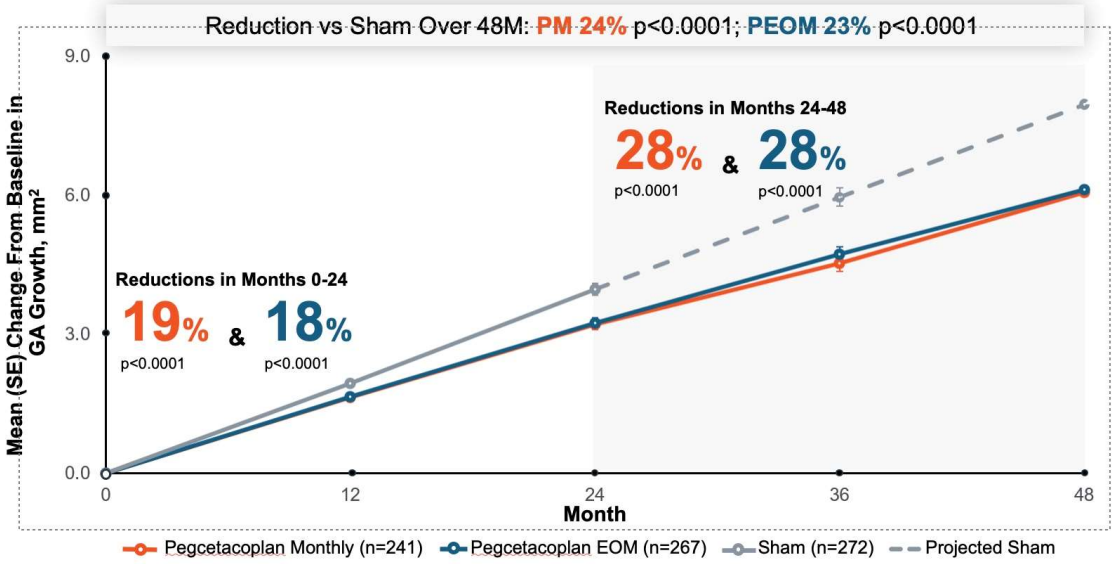


GALE Extension



Pegcetacoplan Showed Increasing Effects Over Time in a Heterogeneous GA Population Over 48 Months

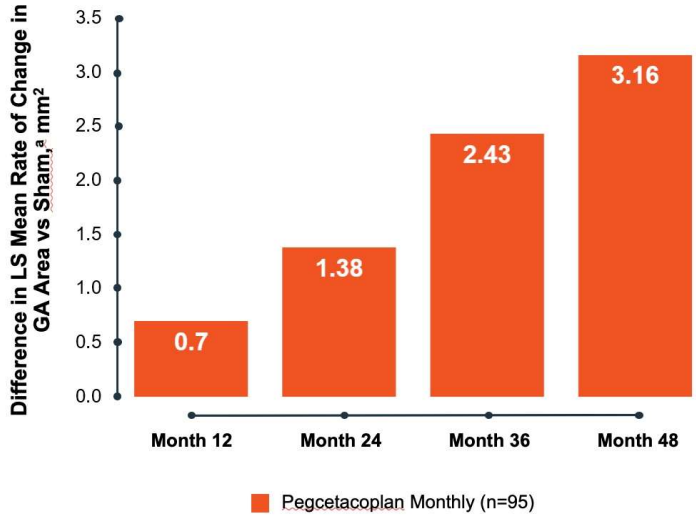
Overall **GALE** Population (N=780): NSF and SF



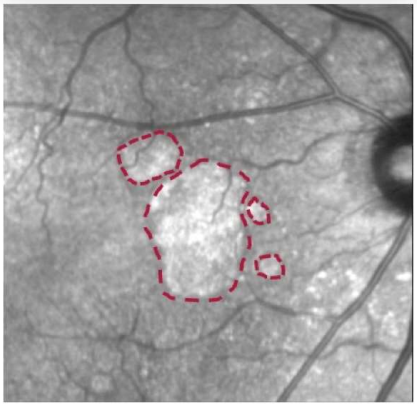
All p-values are nominal. Mean rate of change in GA lesion area between pegcetacoplan group and sham group from antecedent study baseline to Month 48, with knots at Months 12, 24, 36 allowing for the slope to be linear over each of the 12-month segments but to differ between segments using piecewise slope analysis. Mean rate of change of projected sham from Month 24 to Month 36 and Month 36 to 48 was estimated from the mean rate of change in each 6-month period from Month 0 to Month 24 in the sham group. The modified full analysis set was used for the analysis, defined as patients who were in the OAKS or DERBY antecedent study's ITT set, had not been enrolled in the phase 1b APL2-103 study, and received ≥1 injection of pegcetacoplan in GALE. ITT, intent to treat; LS, least squares; SE, standard error. *Post hoc analysis.

First Time Data on GALE 24 Months: 48 Months of Treatment Preserves 1.5 Disc Areas

Nonsubfoveal (n=286)



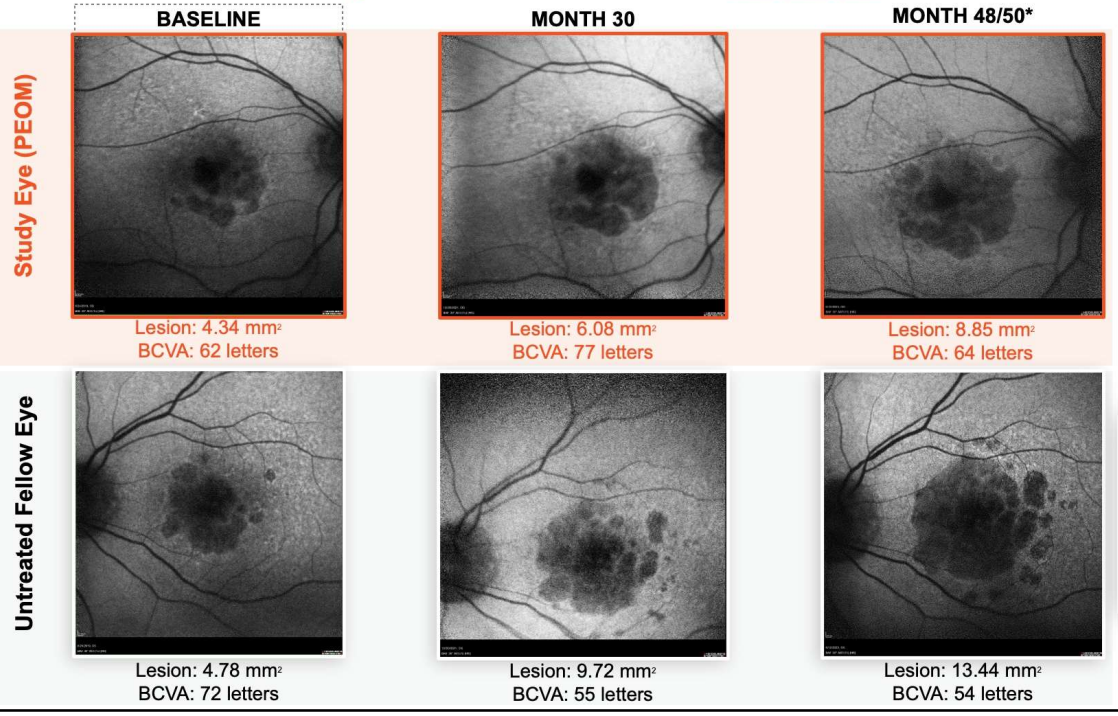
What is 3.16 mm²?



1 DA ~2.5 mm²
1 Foveal Area ~1.77 mm²

[a]Difference in mean rates of change in GA area vs pooled sham up to Month 24, and vs projected sham at Months 36 and 48. Data shown for patients who continued into the GALE study after OAKS and DERBY. Projected sham during Months 24–48 was estimated from the mean rate of change in each period in Months 0–24. EOM, every other month; GA, geographic atrophy; LS, least squares.

GALE Patient Case: 85 y/o Female with Bilateral Subfoveal GA



~2X greater growth in untreated eye

Safety Profile in GALE 24M: Consistent with OAKS/DERBY

GALE[a] Months 24-48	PM to PM (n=250)	SM to PM (n=129)	PEOM to PEOM (n=268)	SEOM to PEOM (n=143)
AEs in study eye reported in ≥2% of patients, %				
Exudative AMD[a]	13.9%	8.1%	4.8%	6.5%
Intraocular pressure increased	8.8%	8.5%	7.5%	2.8%
Vitreous floaters	6.4%	10.9%	3.0%	7.0%
Conjunctival hemorrhage	5.2%	10.1%	3.4%	6.3%
Ocular discomfort[a]	5.6%	7.0%	3.7%	7.0%
Cataract	7.2%	4.7%	3.4%	4.9%
Retinal hemorrhage	5.2%	5.4%	2.6%	2.1%
AEs of interest in study eye, patient (%) events				
Infectious endophthalmitis	3 (1.2%)	1 (0.8%)	1 (0.4%)	0
Intraocular inflammation[a]	12 (4.8%)	6 (4.7%)	3 (1.1%)	2 (1.4%)
Ischemic optic neuropathy	1 (0.4%)	0	0	1 (0.7%)

- Rates from OAKS, DERBY & GALE Months 0-48:
  - Infectious endophthalmitis: 0.04% per injection
  - ION: 0.04% per injection
  - IOI[a]: 0.26% per injection
- **No study events of occlusive or non-occlusive retinitis or vasculitis**

[a]Safety population, consisting of all enrolled patients who received at least 1 pegcetacoplan or sham injection and analyzed according to the actual treatment received. The following terms were combined: Ocular discomfort included: eye pain, eye irritation, foreign body sensation in eyes, ocular discomfort, abnormal sensation in eye. Exudative age-related macular degeneration included: exudative age-related macular degeneration, choroidal neovascularization. Intraocular inflammation included: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, anterior chamber flare.
Table 14.3.1.1.2.1, Table 14.3.1.1.5.1, Table 14.3.1.1.14.1.1 [APL2-GA-305 Month 12 Report] and Table 14.3.1.2.1 [Integrated APL2-303, APL2-304, APL2-GA-305 Month 48 Report]

Retinal Vasculitis Reports

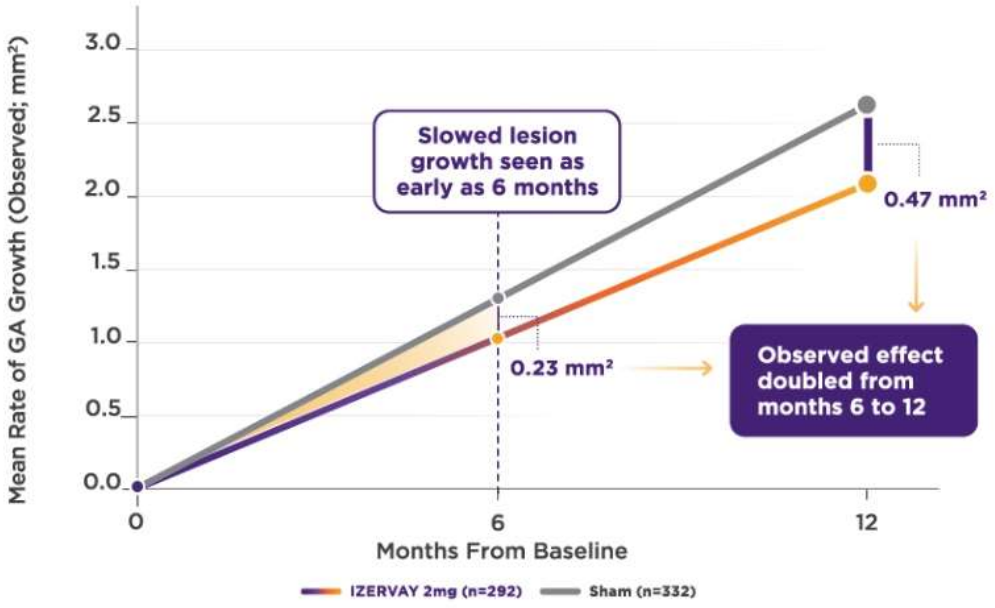
- 12,000 injections were given in Derby/Oaks with no cases of vasculitis
- Upon introduction in the real world, there were rare and sporadic reports of vasculitis post Syfovre injection
- Appelis issued a field correction of changing a 19g filter needle to draw up medication
- All adverse events were reported after first injection

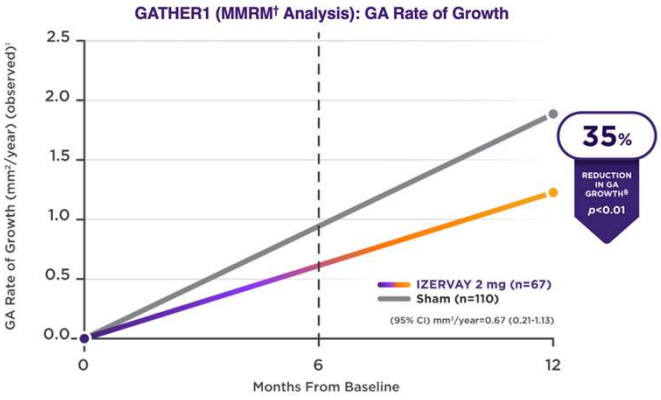
Injection Month	Classification	Days to Visual Symptoms	Pre-Event VA	VA at Event	Most Recent Reported VA	Visual Outcome
May	Suspected Non-Occlusive vasculitis	10	20/70 (OD) 20/100 (OS)	CF (OD); 20/800 (OS)	20/60 (OD) 20/80 (OS)	Return to baseline vision
May	Occlusive Vasculitis	18	20/150	20/150	20/150	Return to baseline vision
June	Non-Occlusive Vasculitis	14	20/60	20/200	20/50	Return to baseline vision
April	Occlusive Vasculitis	11	20/200	20/400	20/400	Partial recovery*
May	Non-Occlusive Vasculitis	12	OD: 20/30 OS: 20/30	20/200 OU	20/70 OU	Partial recovery
May	Occlusive Vasculitis	15	20/30	20/400	20/100	Partial recovery
August	Suspected Occlusive Vasculitis	11	20/50	20/350	20/250	Partial recovery (ongoing)
April	Occlusive Vasculitis	10	20/40	HM	LP	Visual impairment
June	Non-Occlusive Vasculitis	8	20/150	HM	LP	Visual impairment
June	Occlusive Vasculitis	10	20/100	20/400	LP**	Visual impairment

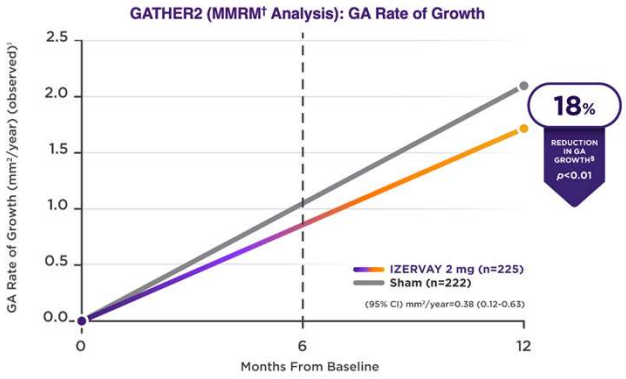
Table of events is as of August 22, 2023

Izervay-avacincaptad peg

- GATHER1/GATHER 2 studies- reduction in the rate of GA growth over 12 month period with injections given monthly versus sham
- C5 inhibitor
- Excluded foveal center involving GA

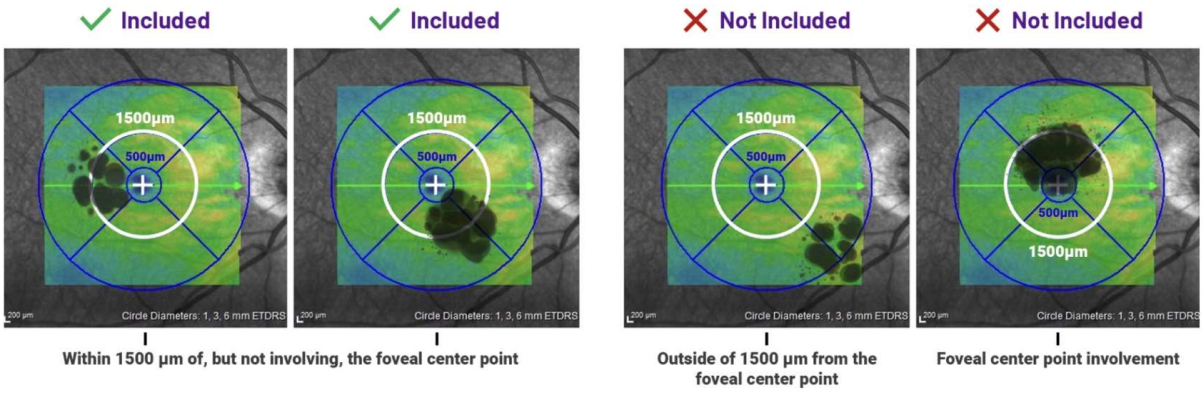






Common ocular adverse reactions (≥2%) and greater than sham in study eye through Month 12[1]	**IZERVAY** (n=292)	**Sham** (n=332)
Conjunctival hemorrhage	13%	9%
Intraocular pressure (IOP)	9%	1%
Blurred vision*	8%	5%
Choroidal neovascularization (CNV)	7%	4%
Eye pain	4%	3%
Vitreous floaters	2%	<1%
Blepharitis	2%	<1%

*Blurred vision includes visual impairment, vision blurred, visual acuity reduced, visual acuity reduced transiently.



Impact of GA on vision

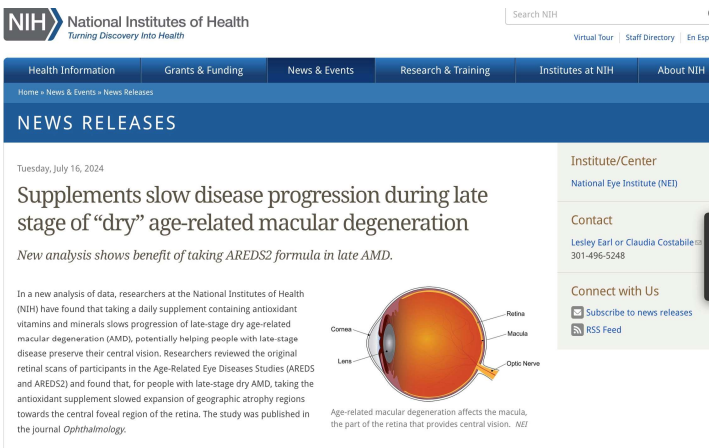
- Average time since diagnosis of GA, in as few as 2.5 years GA can lead to irreversible vision loss
- GA progression is different for each person
- Extrafoveal GA grows faster than foveal

Identifying a Good Candidate

- Extrafoveal GA is desired-goal is to preserve fovea as long as possible
- Discuss with patient in length that therapy is preventative and will not reverse geographic atrophy
- Disease will progress (not 100% effective)

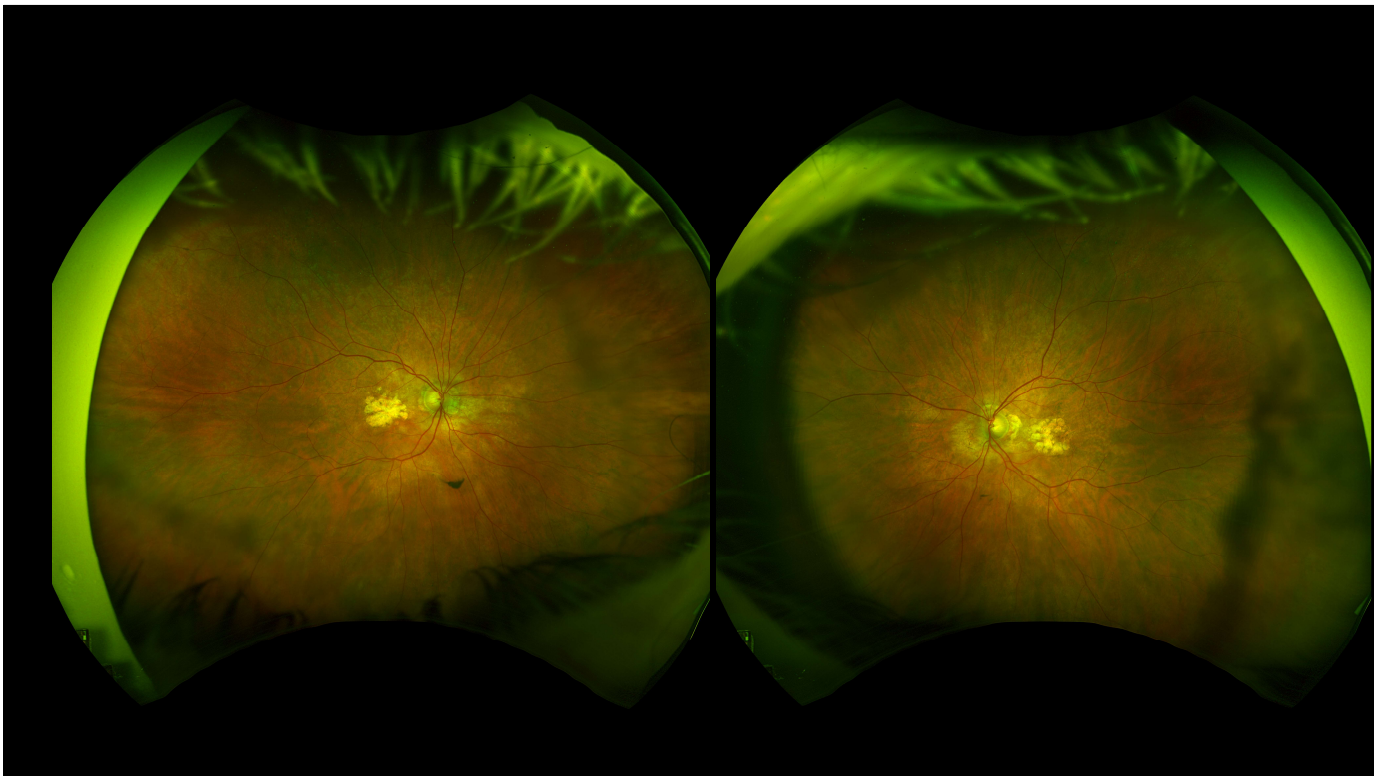
What about AREDS/AREDS II and GA?

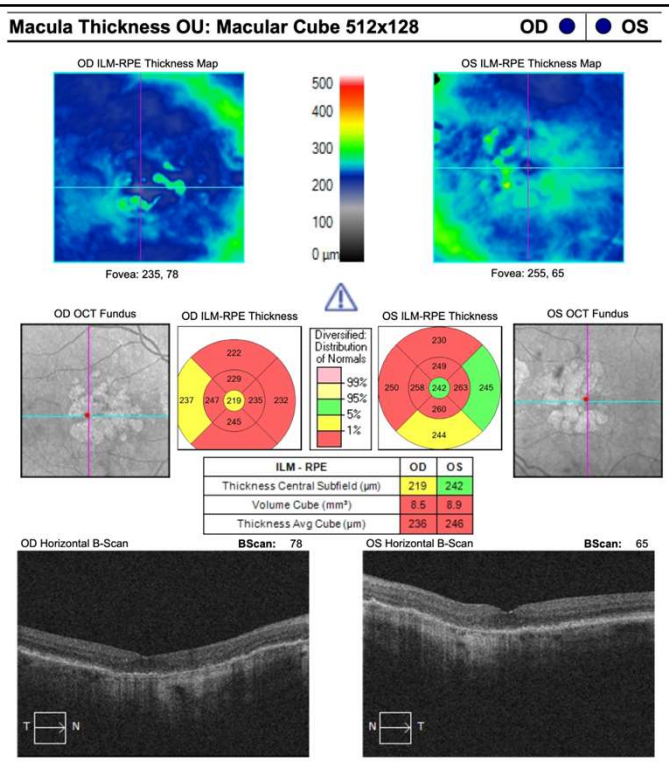
- National Institute of Health reviewed scans from late stage dry-AMD in AREDS/AREDSII
- Geographic atrophy that is far away from fovea AREDS/AREDS II slowed the progression of growth towards the fovea by 55% over 3 years
- "Foveal-sparing"

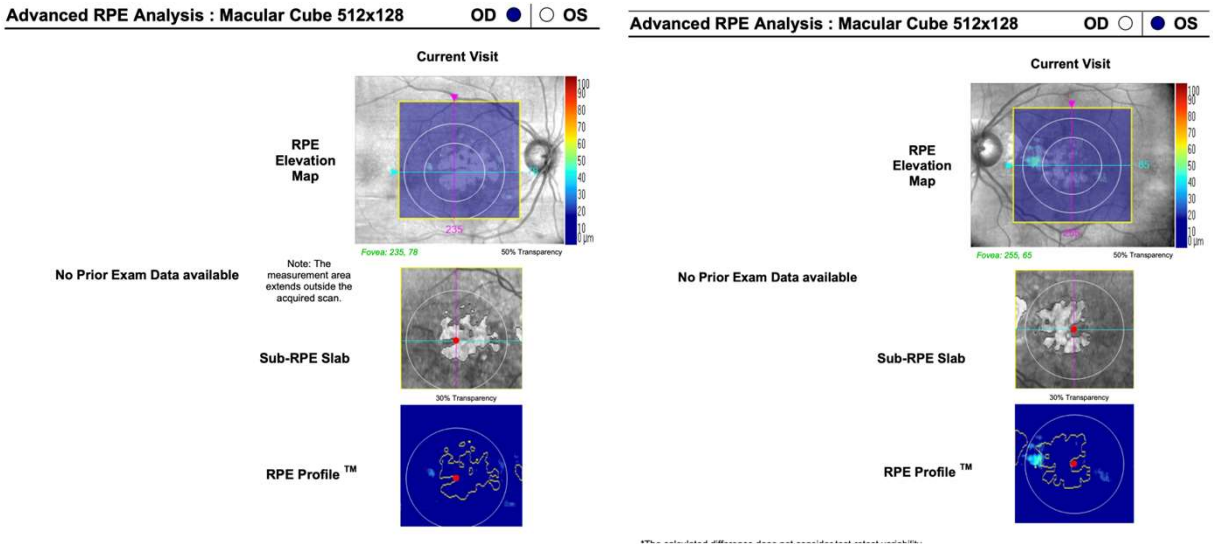


Case 1

- 79 year old caucasian female with history of ARMD
- Distance BCVA OD: 02/200 OS: 20/25
- Ocular SX: cataract extraction OU
- Medications: Aspirin 81 mg







Recommended Izervay OS q 4-6 weeks, AREDS II

Future Therapeutic Options for GA

- Gene therapy-trials currently investigating complement cascade inhibition and enhancing regulatory proteins
  - HMR59/Hemera Biosciences and Janssen Pharmaceuticals- intravitreal injection that augments expression of CD59 that prevents formation of MAC-withdrawn in phase 2
  - GT005/Gyroscope Therapeutics and Novartis-recombinant adenoids-associated viral vector encoding Complement Factor I (CFI) which keeps complement in check. EXPLORE/HORIZON was a subretinal injection-both phase 2 trials terminated in 06/2024. ORACLE phase 2 study estimated completion is 2028

Future GA Treatment

- Stem cell therapy-OpRegen subretinally transplanted RPE cells from human embryonic stem cells (NCT013449993)
- Neuroprotective agents- Brimonidine intravitreal injection or implant (BEACON) Brimonidine stimulates upregulation of ganglion cells and survival cells to release brain-derived neurotrophic factor (BDNF) NCT 00658619-completed with results.

Thank you!