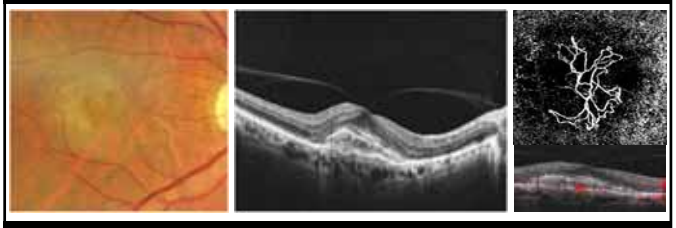
AMD: A Relative Manageable Disease



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DISCLOSURES

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Dr. Majcher Disclosures:
- Paid consultant/speaker for:
  - Carl Zeiss Meditec
  - Iveric Bio (Astellas)
  - Apellis Pharmaceuticals
  - Regeneron Pharmaceuticals
  - Optomed
- Paid advisory board member for LENZ Therapeutics, Notal Vision, Topcon, Tarsus, Genentech

Dr. Haynie Disclosures:
- Paid consultant/advisory board for:
  - Astellas Pharma
  - Apellis Pharmaceuticals
  - Orasis Pharma

All financial relationships have been mitigated

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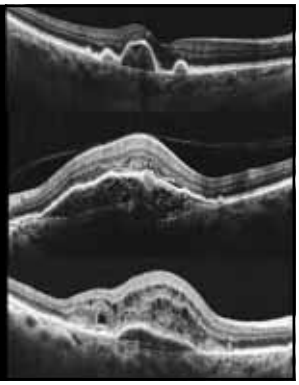
ROAD MAP

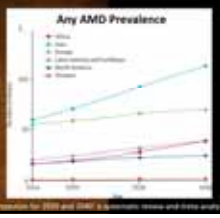
- Intro to AMD
- AMD staging/classification
- Retinal multimodal imaging technologies
- Utility of multimodal imaging in AMD
  - Nonexudative
    - Drusen subtypes
    - GA
    - High risk biomarkers for progression to advanced AMD
  - Neovascular & exudative AMD
- Home monitoring strategies to detect early conversion
- New therapies

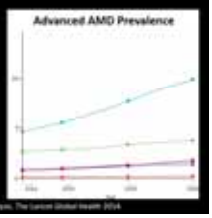


3

AGE RELATED MACULAR DEGENERATION

- Leading cause of blindness in the developed world in persons >50yo
  - Characterized by drusen, RPE abnormalities, geographic atrophy (GA), choroidal neovascularization (CNV)
- Prevalence of AMD is expected to ↑ to 22 million by the year 2050
  - # of cases of advanced AMD is expected to ↑ from 1.7 million in 2010 to 3.8 million in 2050

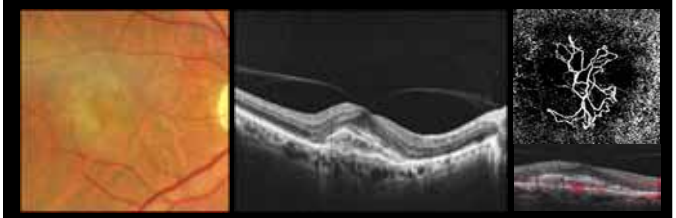




4

AGE-RELATED MACULAR DEGENERATION

- Of all AMD, approx. 80% nonexudative/20% exudative
  - **Neovascular exudative AMD accounts for 90% of severe central VA loss**

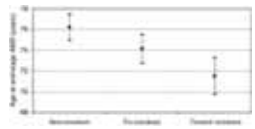


EARLY DETECTION AND PROMPT TREATMENT OF EXUDATIVE AMD IS CRITICAL TO MAXIMIZE VISUAL OUTCOMES!!!

5

RISK FACTORS FOR AMD

Age of end-stage AMD according to smoking status



SMOKERS HAVE EARLIER ONSET END-STAGE AMD

- Older age
- Caucasian
- Genotype/family HX of AMD
  - ARMS2/HTRA1
  - CFH
- **Smoking**
  - Most sig modifiable risk factor for AMD (odds ratios = 2.35-3.12 current vs never)
- HTN &Heart Disease
- High BMI/Obesity - (mild assoc)
- Hypercholesterolemia (high dietary cholesterol intake esp saturated fats and cholesterol
- Diet low in omega 3, vitamins/minerals, carotenoids, antioxidants

American Academy of Ophthalmology PPP Retina/Vitreous Committee. Age-related macular degeneration Preferred Practice Pattern 2019.
Keenan TDL. GA in ARMD: A Tale of Two Stages. Ophthalmol Sci. 2023
Hughes AE, et al. ARMD risk based on CFH, LOC387715/HTRA1, and smoking. PLoS Med. 2007

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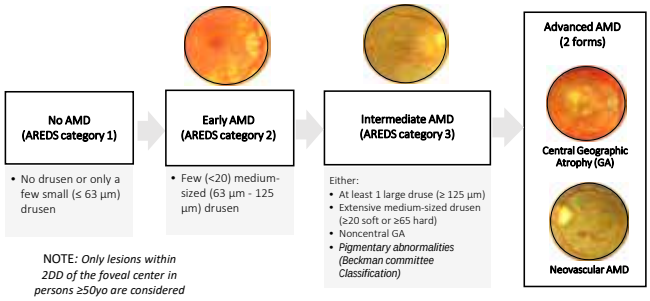
AMD STAGING/CLASSIFICATION



NOTE: *Only lesions within 2DD of the foveal center in persons ≥50yo are considered*

AREDS report no. 8. Arch Ophthalmol. 2001
AMD, age-related macular degeneration. Ferris FL, et al. Ophthalmology. 2013;120(4):844-851.

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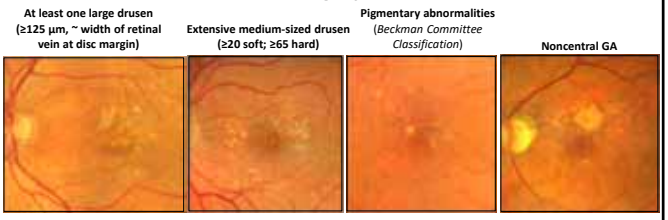
INTERMEDIATE NON-EXUDATIVE AMD

AREDS category 3 Either:



Risk for conversion to advanced AMD is ~ 18% within 5 years

☆ **Image!!! & intentionally look for neo AND GA**

Monitor more frequently (~3 to 6 months), home self-screening (amsler/Foresee home), OTC AREDS 2 supplements, edu on diet & behavior modifications

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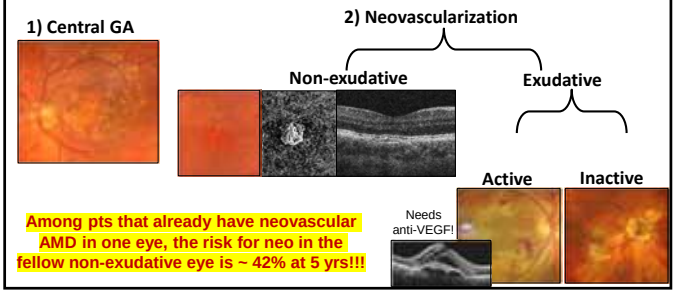
AMD STAGING/CLASSIFICATION

Advanced AMD (AREDS category 4): 2 forms



Among pts that already have neovascular AMD in one eye, the risk for neo in the fellow non-exudative eye is ~ 42% at 5 yrs!!!

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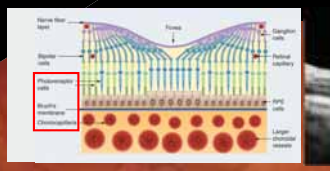
GEOGRAPHIC ATROPHY (GA)



- Advanced/late form of dry AMD
- **Irreversible atrophy of the RPE, photoreceptors & choriocapillaris (in the absence of neovascularization)**
  - Atrophy = tissue loss/attenuation
- Affects > 8 million worldwide (**~20% of ppl with AMD**)
- Accounts for 10-20% of legal blindness from AMD

AREDS Research Group. Change in area of GA in the AREDS: AREDS report number 26. *Arch Ophthalmol* 2009
Keenan TD, et al. AREDS2 Research Group. Progression of GA in ARMD: AREDS2 Report #16. Ophthalmology 2018

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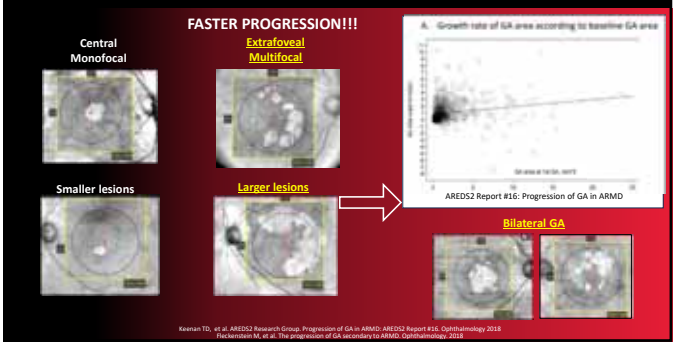
RISK FACTORS FOR GA EXPANSION

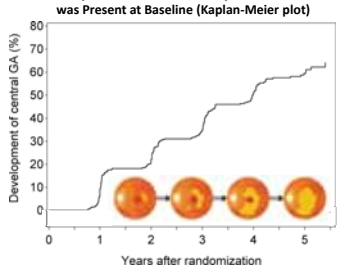
FASTER PROGRESSION!!!



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

11

AREDS 2 Development of Central GA in Eyes Where Non-central GA was Present at Baseline (Kaplan-Meier plot)



GA enlargement is "RELENTLESS and often results in rapid central vision loss!"

In eyes with incident non-central GA, 4-year risk of central involvement was 57%.
In the original AREDs study, the median time from any GA diagnosis to foveal involvement was 2.5 yrs

Keenan TD, et al. AREDS2 Research Group. Progression of GA in ARMD: AREDS2 Report #16. Ophthalmology 2018
Boyer DS, et al. The pathophysiology of GA secondary to ARMD & the complement pathway as a therapeutic target. Retina 2017

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UTILITY OF IMAGING IN AMD

Color Fundus Photography (CFP)/ophthalmoscopy

- DETECTING HEMORRHAGE!

OCT

- Detect new or recurrent neovascular disease activity (esp fluid!)
- Guides anti-VEGF therapy
- Subclassification of CNVM types
- Identify and monitor progression of GA
- Drusen subclassification
- Identify high risk biomarkers for progression to advanced AMD

Near Infrared Reflectance (NIR)

- Detection and monitoring of GA

OCTA

- Detecting and morphologically characterizing CNVMs
- Detecting/monitoring nonexudative CNVMs
- Determining whether PED is vascularized

FAF

- Detection of early GA
- Monitoring GA area
- Predicting GA expansion
- Visualization of reticular pseudodrusen/subretinal drusenoid deposits (SDDs)

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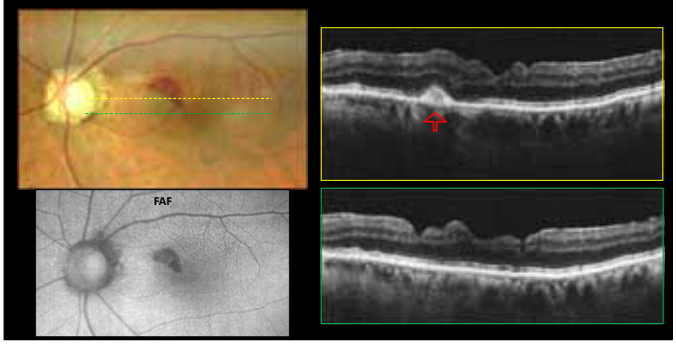
OCT ALONE CANNOT DETECT ALL CONVERTERS!



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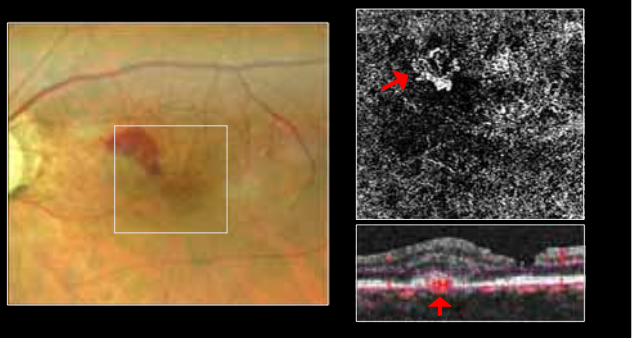
OCT ALONE CANNOT DETECT ALL CONVERTERS!



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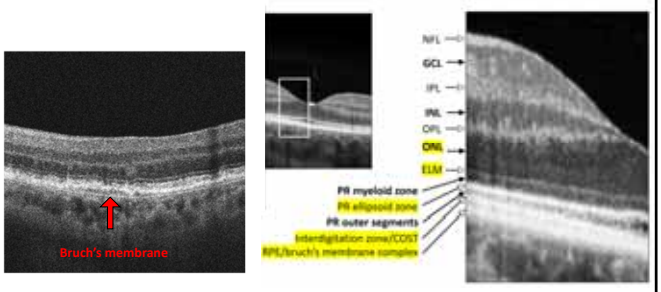
OCT RETINAL ANATOMY



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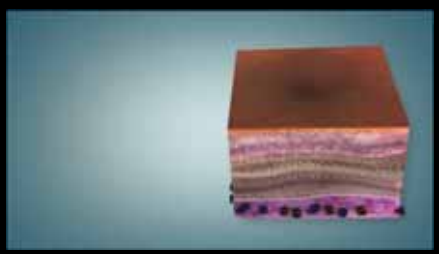
En-Face ANALYSIS



An en face image represents a slab of several retinal layers compressed into a 2D plane

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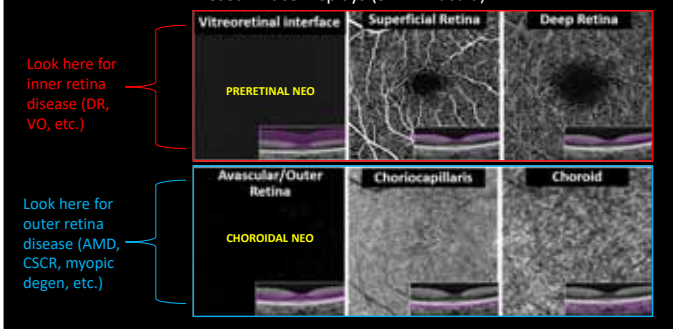
OCTA En Face Display

Preset Enface Displays (3mm macula)



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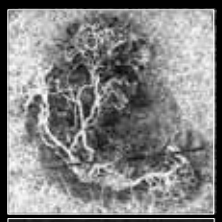
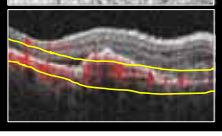
OCTA DISPLAY En Face - Outer Retina Choriocapillaris (ORCC)



- Includes some combination of photoreceptors, RPE, & choriocapillaris
- Designed to detect subretinal & choroidal neo

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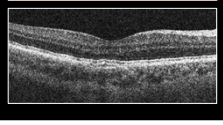
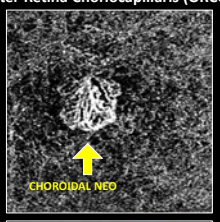
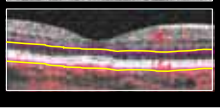
OCTA – only tool able to detect nonexudative CNVM



Outer Retina Choriocapillaris (ORCC)




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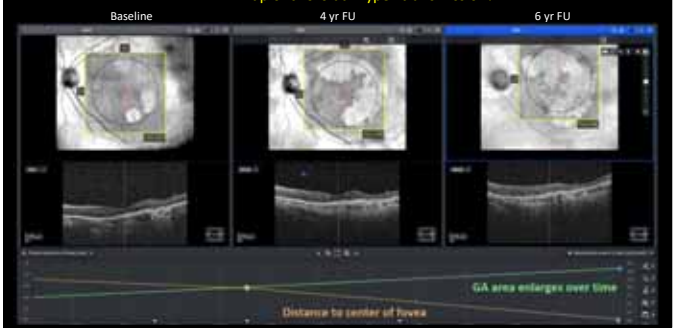
OCT En-Face ANALYSIS (Sub-RPE Slab) - GA

AKA 2D map of choroidal hyper-transmission!



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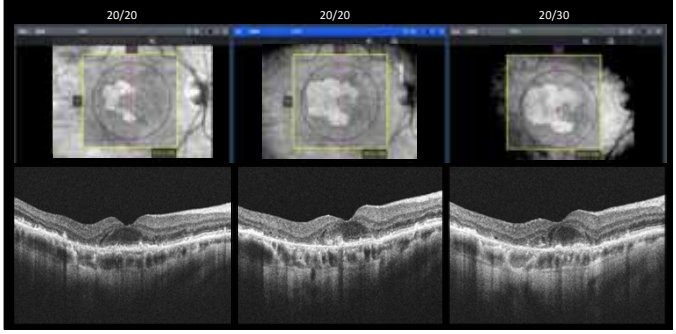
Patterns of Geographic Atrophy Progression (3 years)



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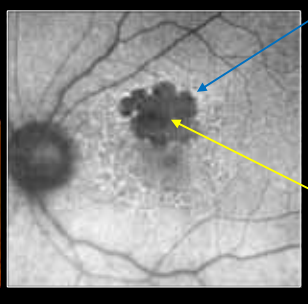
FUNDUS AUTOFLUORESCENCE (FAF)

Hyperfluorescence

- **Impending RPE damage/GA EXPANSION!**
- Advancing zones of degeneration
- Lipofuscin deposition

Hypofluorescence

- **Disruption/loss of the RPE** and/or photoreceptors
- Blockage

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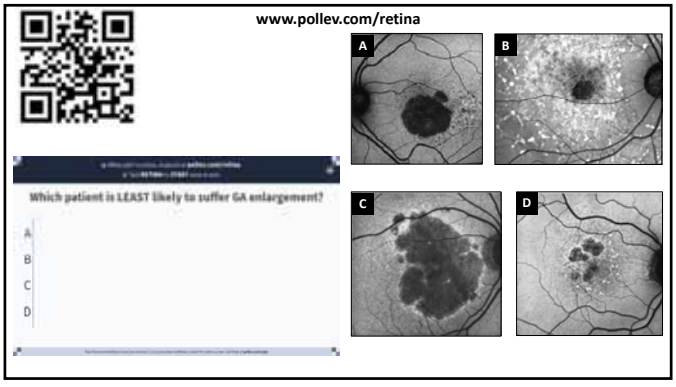
www.pollev.com/retina



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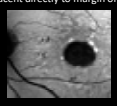
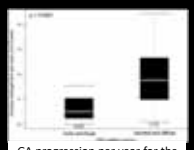
PROGNOSTIC VALUE OF GA PHENOTYPIC FAF PATTERNS

Slow Progression — Rapid Progression

No abnormality (0.38 mm²/yr)

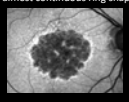
Focal (0.81 mm²/yr)
Single or individual small spots of ↑ FAF adjacent directly to margin of GA





GA progression per year for the pooled data groups

Banded (1.81 mm²/yr)
↑ FAF adjacent directly to margin of GA in an almost continuous ring shape



Diffuse (1.77 mm²/yr)
↑FAF at the margin and elsewhere

The GAIN Study. Am J Ophthalmol. 2015;160: 345–353.e5.
Holz FG, et al (FAM-Study Group). Progression of GA and impact of FAF patterns in ARMD. Am J Ophthalmol. 2007 Mar;143(3):463-72.

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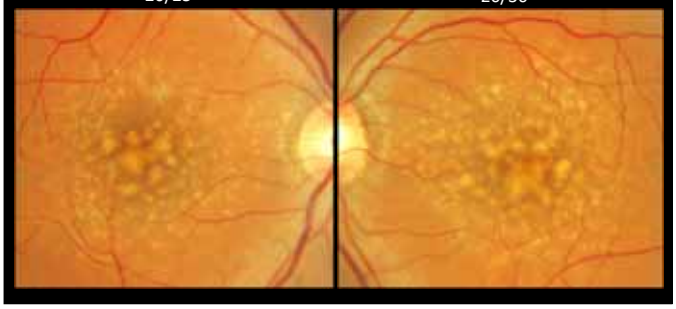
CASE IN POINT

20/25^{-1} — 20/30^{+1}



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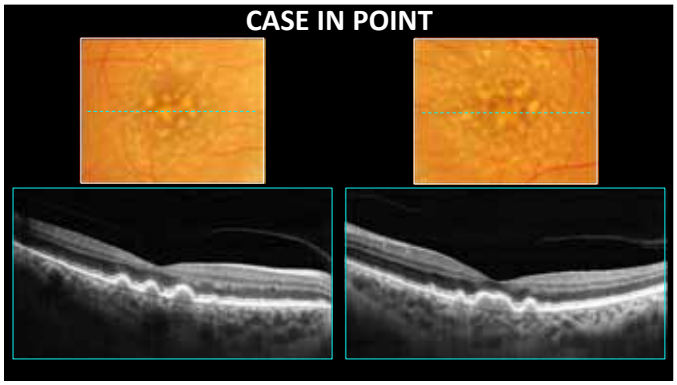
CASE IN POINT



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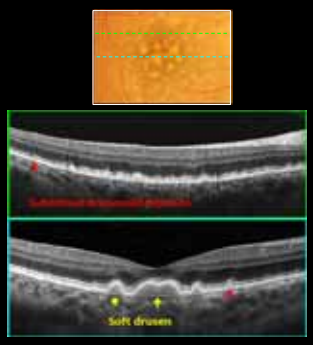
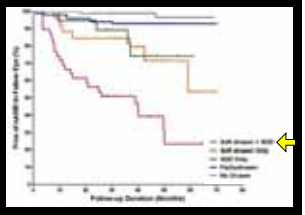
OCT CLASSIFICATION OF DRUSEN – PROGNOSTIC VALUE





THE COMBINATION OF SOFT DRUSEN AND RPD/SDDs POSES THE GREATEST RISK FOR EXUDATIVE CONVERSION!!!

Lee J, et al. Neovascularization in Fellow Eye of Unilateral Neovascular AMD According to Different Drusen Types. Am J Ophthalmol. 2019

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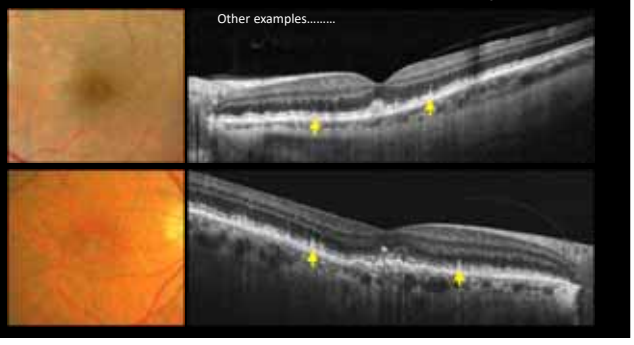
Reticular Pseudodrusen (RPD)/Subretinal Drusenoid Deposits (SDDs)

Other examples……



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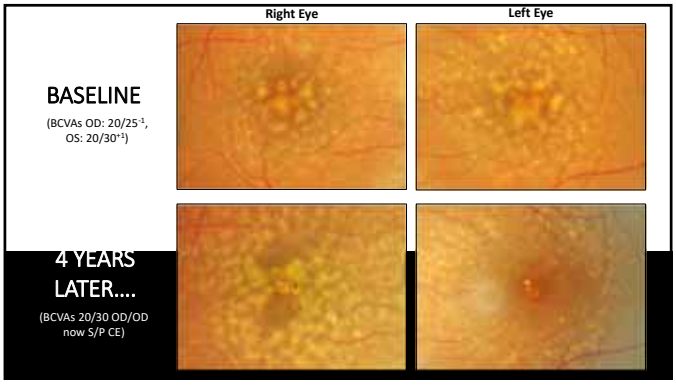

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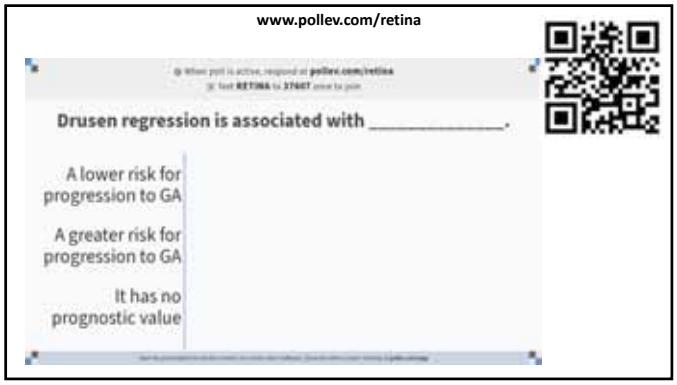

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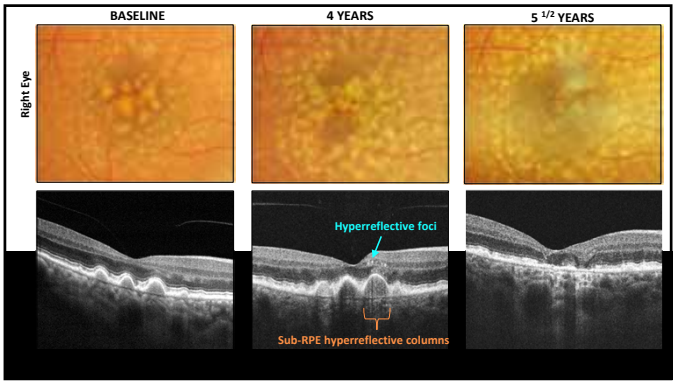

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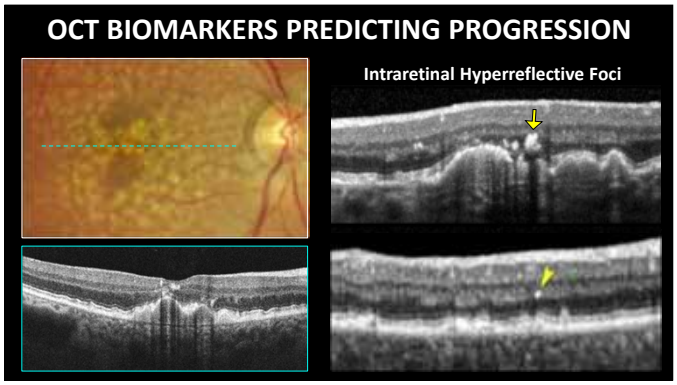

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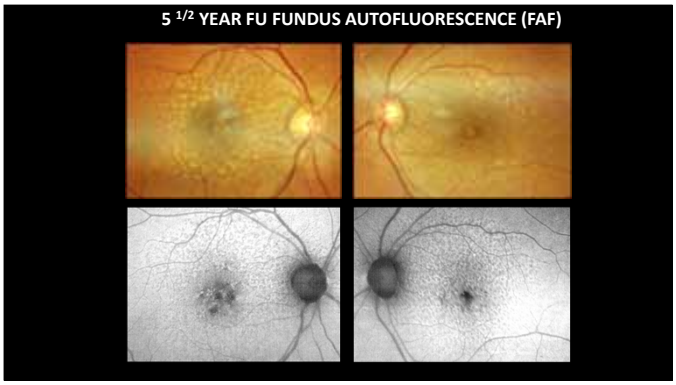
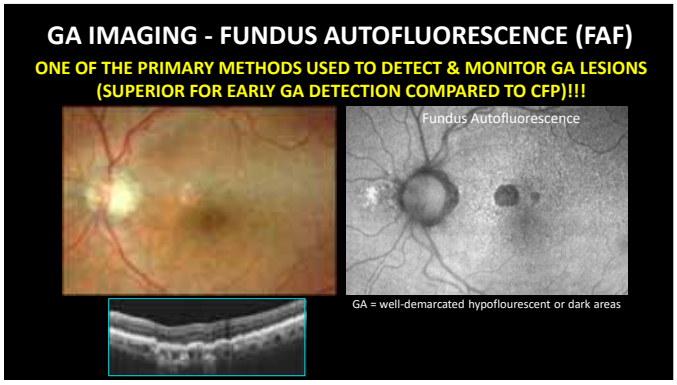


34



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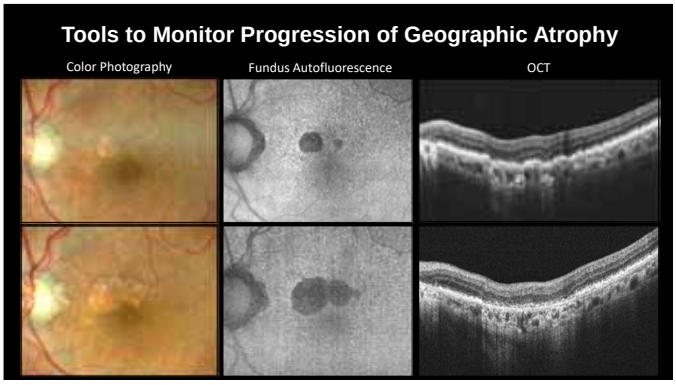

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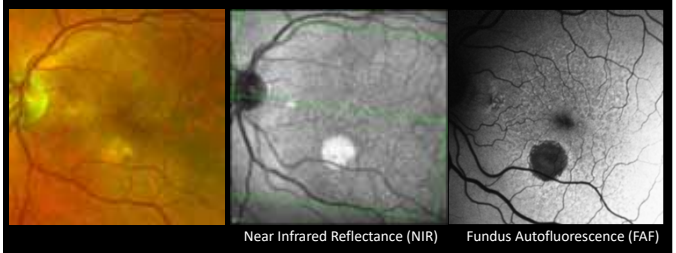
Subretinal Drusenoid Deposits/Reticular Pseudodrusen



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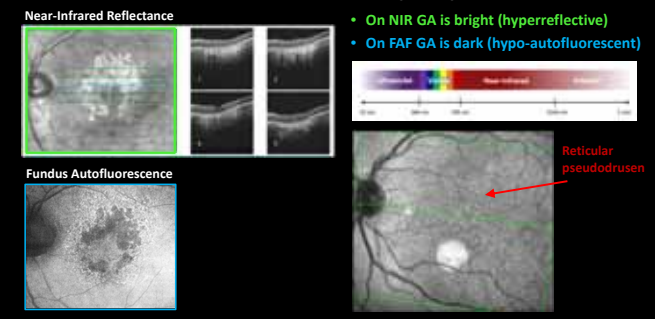
GA IMAGING: NEAR-INFRARED (NIR) REFLECTANCE



M. Pfau et al. Green-Light Autofluorescence Versus Combined Blue-Light Autofluorescence and NIR Imaging in GA Secondary to AMD. IOVS 2017

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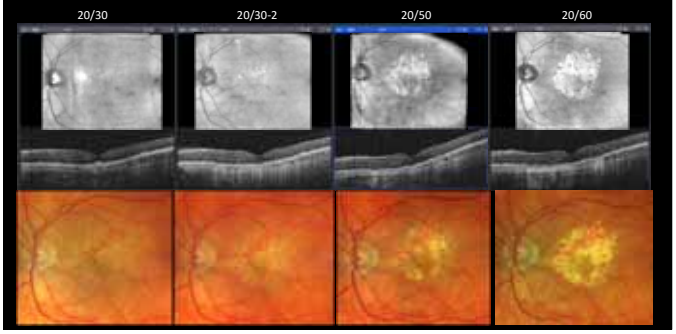
MONITORING GA PROGRESSION WITH NIR (3 YEARS)



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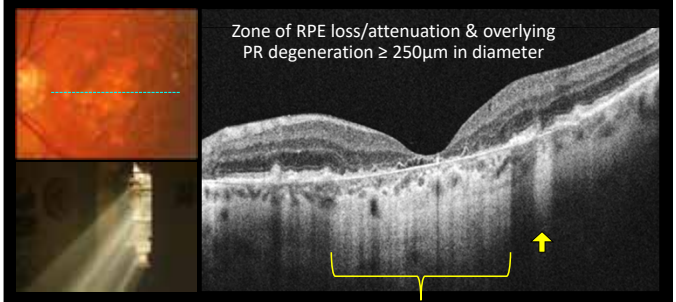
Geographic Atrophy Features on OCT



Homogenous choroidal hyper-transmission

40

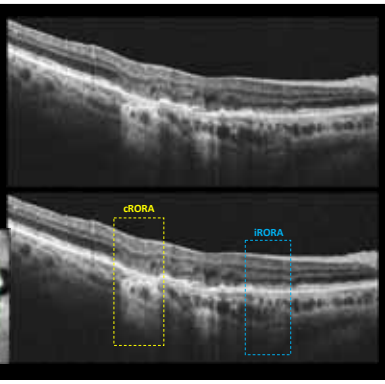
cRORA

Complete RPE & Outer Retinal Atrophy

VS

iRORA

Incomplete RPE & Outer Retinal Atrophy



41

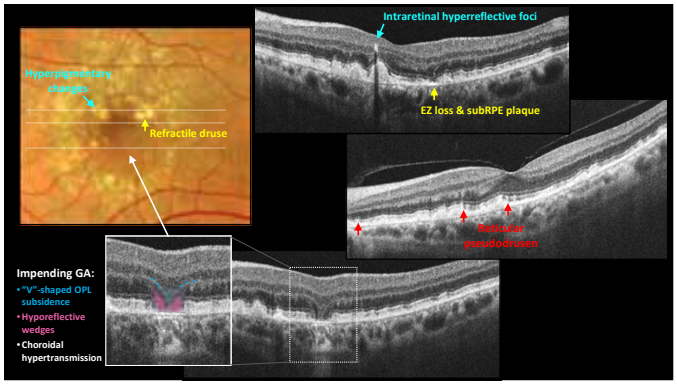
OCT BIOMARKERS PREDICTING GA DEVELOPMENT

- Subsidence of inner nuclear layer (INL) and outer plexiform layer (OPL)
- External limiting membrane (ELM) descent
- ELM and/or photoreceptor ellipsoid zone (EZ) loss
- Hyporeflective wedges
- Intraretinal hyperreflective foci
- Drusen with hyporeflective cores
- Refractile drusen & hyperreflective crystalline deposits
- Drusenoid pigment epithelial detachment (PED) collapse

HIGH RISK OCT FEATURES THAT PREDISPOSE TO FUTURE GA DEVELOPMENT

Jaffe GJ, et al. Imaging Features Associated with Progression to GA in ARMD: Classification of Atrophy Meeting Report 5. Ophthalmol Retina. 2021
Angelica Ly, et al. Developing prognostic biomarkers in intermediate ARMD: their clinical use in predicting progression. Clin Exp Optom 2018

42



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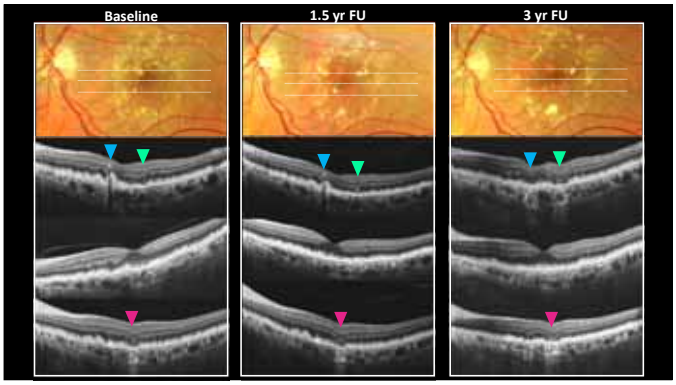

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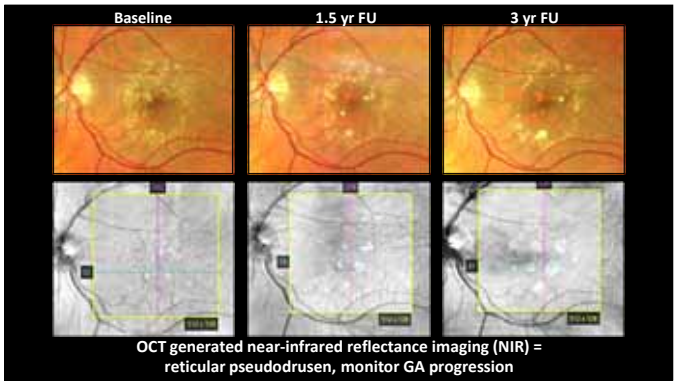

45

Valeda Light Delivery System (photobiomodulation PBM)

- First FDA approved therapy for Dry AMD using Photobiomodulation
  - Nov 4th 2024
- LIGHTSITE III 24-month study
- ~200 patients across multiple completed and enrolled trials
- 9 sessions over 3-5 weeks, repeated every 4 months for a total of 2 years

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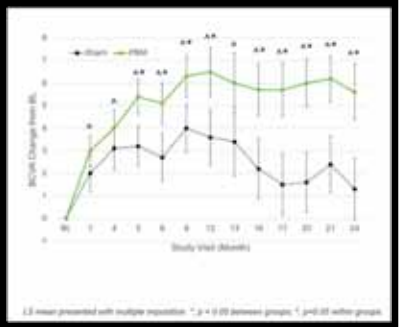
Valeda Light Delivery System (photobiomodulation PBM)

LIGHTSITE III 24-month study

- Met the predetermined primary efficacy BCVA endpoint at Month 21 (mean letter difference of 3.8 letters, p = 0.0036) with a statistically significant difference between the PBM group versus Sham
- A mean letter difference of 4.3 letters (p = 0.0024) was maintained at Month 24.
- Within group analysis showed improved BCVA with a mean > 5 letter gain in PBM eyes from:
  - Month 13 (LS mean 6.0 letters) (p = < 0.0001)
  - Month 21 (LS mean 6.2 letters) (p < 0.0001)
  - Month 24 (LS mean 5.6 letters) (p < 0.0001)



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Valeda Light Delivery System (photobiomodulation PBM)

Post Hoc Analysis on Treatment Benefit on Incident GA (LIGHTSITE III 24-month study)

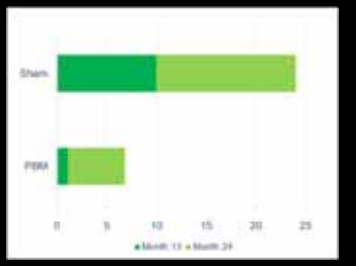
Incidence of New GA:

Month 13 (M13), p = 0.024
- Sham group: 5/50 (10.0%)
- PBM group: 1/87 (1.1%)

Month 24 (M24), p = 0.007
- Sham group: 12/50 **(24.0%)**
- PBM group: 6/87 **(6.8 %)**

Incident GA Significantly Higher in the Sham Group at Month 24

Incident GA was evaluated as a safety endpoint for disease progression and not a prespecified endpoint



48

Oral Antioxidant and Lutein/Zeaxanthin Supplements Slow Geographic Atrophy Progression to the Fovea in Age-Related Macular Degeneration

- Post hoc analysis of AREDS and AREDS 2 to determine the effects of supplementation on slowing GA progression
- Looked at change in proximity to central macula and change in GA area over time
- AREDS: In eyes with **non-central GA** antioxidants slowed GA progression towards the center of the fovea
- AREDS 2: In eyes with **non-central GA** lutein/zeaxanthin slowed GA progression towards the center of the fovea
- Supplementation did not significantly affect area-based progression

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Newly Approved Complement Inhibition Therapy for GA

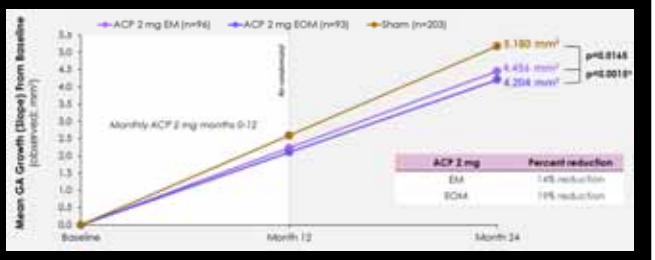
	Avacincaptad Pegol (C5)		Pegcetacoplan (C3)
	Approved Aug 2023	FDA Approval	Approved Feb 2023
	GA secondary to AMD/2mg intravitreal injection monthly for up to 12 months	FDA Indication/ Dosing	GA secondary to AMD/15mg intravitreal injection every 25-60 days (monthly or EOM)
	C5	MOA/Target	C3
	Gather 1 & Gather 2	Clinical Trials	OAKS & DERBY
	Only non-center point involving GA in part within 1500 µm from the foveal center included	Key differences in study design	GA lesions with (~65%) and without subfoveal involvement included
	Pts with CNV in fellow eye excluded		CNV in the fellow eye was not exclusionary

Inclusion criteria in all trials: - BCVA 20/320 or better, **no neo or exudation in study eye**
- Total GA area between 2.5 - 17.5 mm² (**1 - 7 disc areas**) via FAF

Primary endpoint: **Change in total GA lesion area on FAF**

50

Avacincaptad Pegol: GATHER 2: Mean Rate of GA Growth From Baseline at 24 Months



APPROX 20% REDUCTION IN GA GROWTH OVER 24 MONTHS COMPARED TO SHAM WITH EVERY OTHER MONTH DOSING DURING THE 2ND YEAR

Khanani AM, et al. Presented at: AAO 2023; Nov 3-6, 2023. San Francisco, CA.

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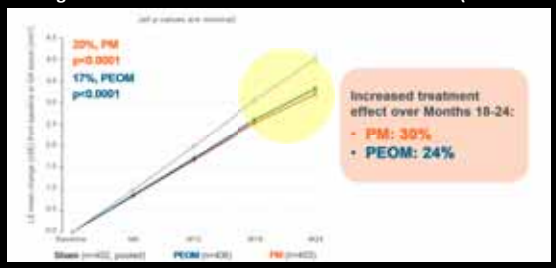
Pegcetacoplan: Mean Change From Baseline in GA Lesion Area at 24 Months (OAKS & DERBY)

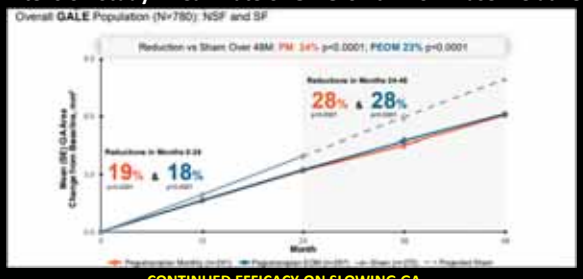


20% REDUCTION IN GA GROWTH OVER 24 MONTHS COMPARED TO SHAM WITH MONTHLY DOSING: TREATMENT EFFECT ↑ OVER TIME

Chiang A, et al. Assessment of GA Lesion Progression in the Phase 3 OAKS and DERBY Trials. IOVS. 2023;64:986., https://sylvreecp.com/oaks-and-derby-efficacy/

52

Pegcetacoplan: Gale Extension Study: Mean Rate of GA Growth From Baseline at 48M



CONTINUED EFFICACY ON SLOWING GA

Khanani AM, et al. Presented at: AAO 2023; Nov 3-6, 2023. San Francisco, CA.

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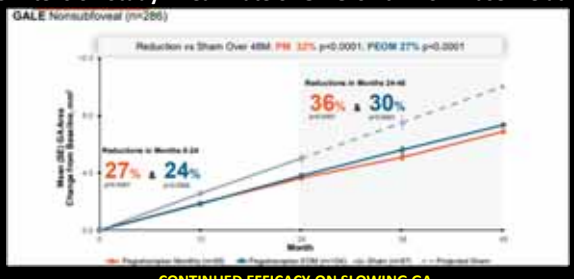
Pegcetacoplan: Gale Extension Study: Mean Rate of GA Growth From Baseline at 48M



CONTINUED EFFICACY ON SLOWING GA

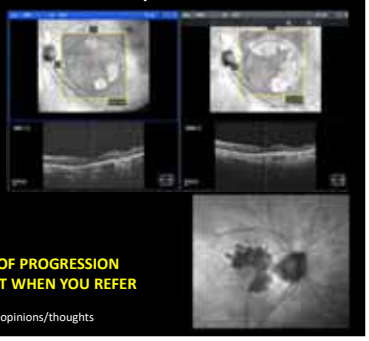
Khanani AM, et al. Presented at: AAO 2023; Nov 3-6, 2023. San Francisco, CA.

54

Which patients with GA should you refer?

Those most **likely** to benefit:

- Extrafoveal GA esp those demonstrating progression over time (or with surrounding FAF hyperautoFL) or those with central involving GA in the fellow eye
- Pts motivated to undergo intravitreal injection at least every other month
- Pts that have enough life left to live to experience a benefit from treatment



IF YOU HAVE DOCUMENTATION OF PROGRESSION
SEND IT TO THE RETINAL SPECIALIST WHEN YOU REFER

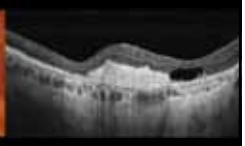
Disclaimer* These are my own personal opinions/thoughts

55

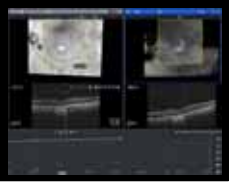
Which patients with GA should you **NOT** refer?

Those **unlikely** to benefit:

- Neovascular/exudative AMD or hx of anti-VEGF treatment in the affected eye? (fellow eye OK)
- Disciform macular scars
- Extensive central-involving GA with poor acuity
- Stable GA lesions (no surrounding FAF hyperautoFL)
- RPE atrophy from other cause (POHS, AOFVD, IRD, etc.)
- Presence of other confounding disease limiting BCVA (end stage glaucoma, etc.)



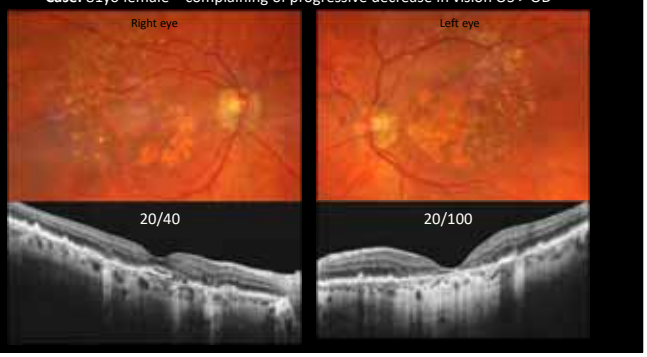
BCVA CFs



Disclaimer* These are my own personal opinions/thoughts

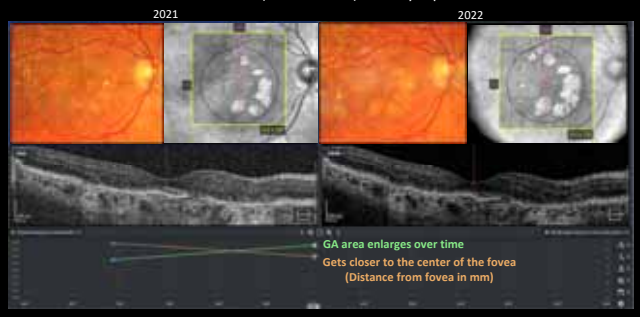
56

Case: 81yo female – complaining of progressive decrease in vision OS > OD



57

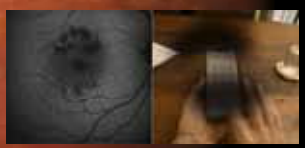
Enface OCT (sub-RPE Slab) OD: 1 yr apart



58

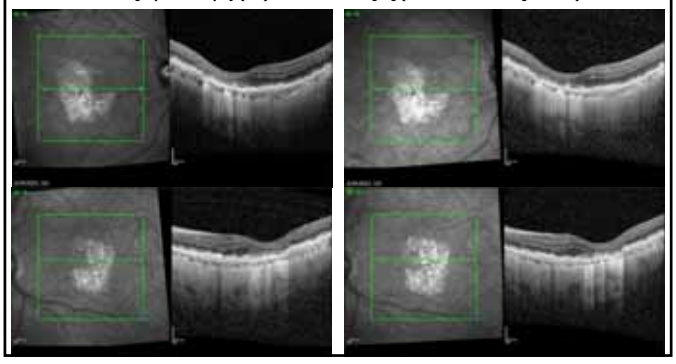
PATIENT EDUCATION

- GA is progressive and irreversible
- Set realistic expectations: Treatment **slows progression**, does not halt GA enlargement
  - Vision will continue to get worse even with tx
- Administered via **INTRAVITREAL INJECTION** monthly or every other month
- **Chronic therapy**
- Importance of home self-screening for exudative conversion



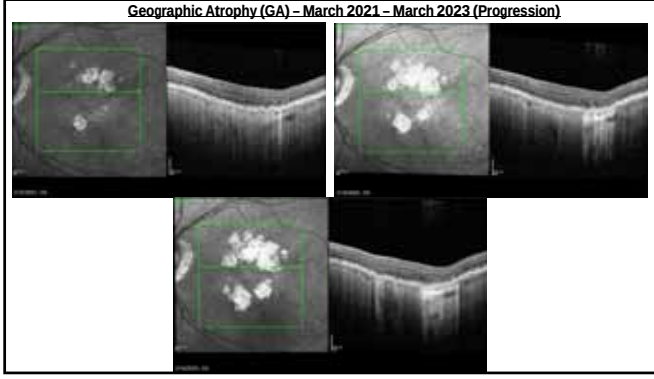
59

Geographic Atrophy (GA) – 14 Month imaging (Minimal to No Progression)



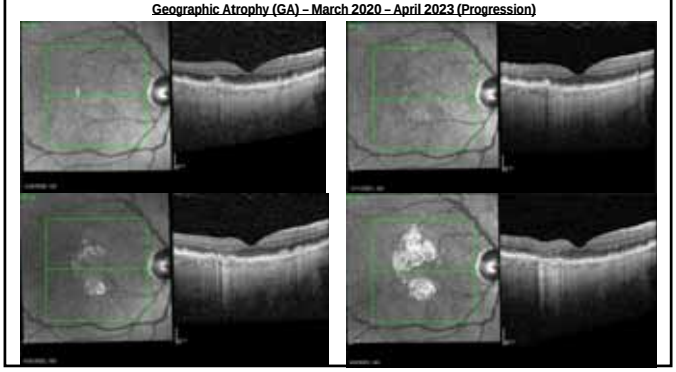
60

Geographic Atrophy (GA) – March 2021 – March 2023 (Progression)



61

Geographic Atrophy (GA) – March 2020 – April 2023 (Progression)

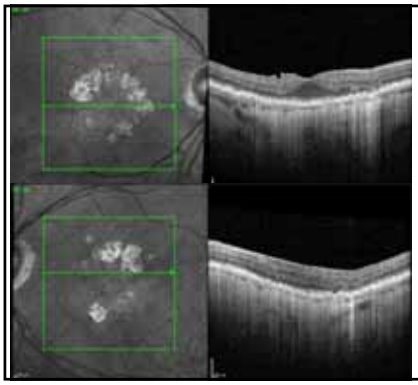


62

76 YO WF with a history of AMD

PMHx: HTN, Hyperlipidemia

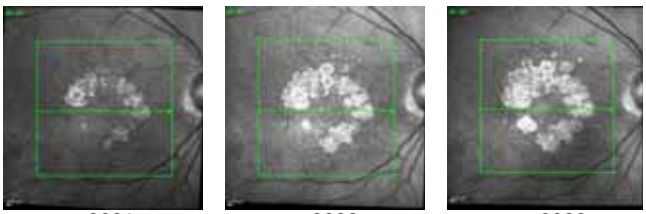
63



- 76 YO WF with a history of AMD
- PMHx: HTN, Hyperlipidemia
- Initial Examination 2021
- VA 20/25 OD
- VA 20/25 OS

64

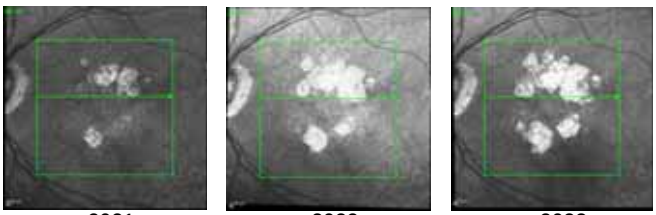
- 76 YO WF with a history of AMD: Initial Examination 2021
- Progressive GA noted OD



2021 2022 2023

65

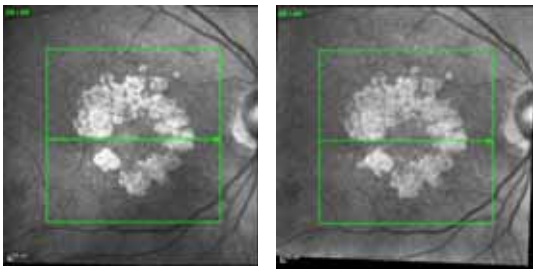
- 76 YO WF with a history of AMD: Initial Examination 2021
- Progressive GA noted OS



2021 2022 2023

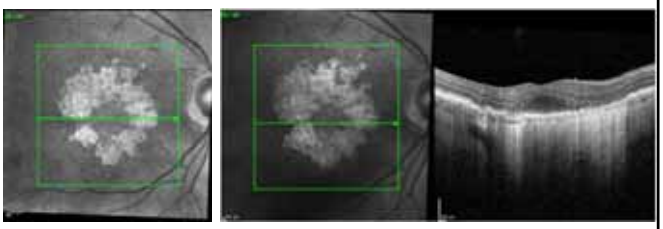
66

- 76 YO WF with a history of AMD: Initial Examination 2021
- Treated OD with Syfovre (3 doses to date)



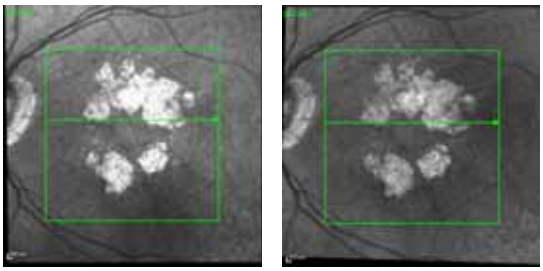
67

- 76 YO WF with a history of AMD: Initial Examination 2021
- Treated OD with Syfovre (3-15 doses to date – 20/40)



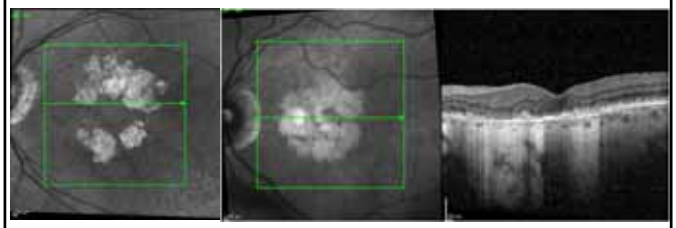
68

- 76 YO WF with a history of AMD: Initial Examination 2021
- Treated OS with Syfovre (3 doses to date)



69

- 76 YO WF with a history of AMD: Initial Examination 2021
- Treated OS with Syfovre (3-15 doses to date – vision 20/50)



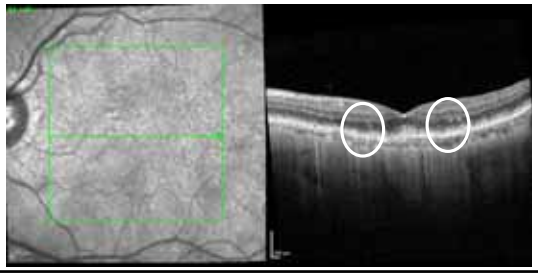
70

79 YO WF with a history of AMD

PMHx: HTN, Hyperlipidemia, Breast Cancer

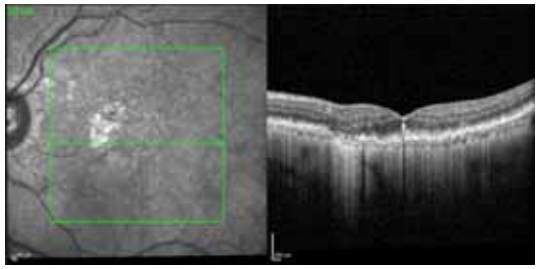
71

- 79 YO WF with a history of AMD
- PMHx: HTN, Hyperlipidemia, Breast Cancer
- VA 20/30 OS - OCT reveals biomarkers for GA - 2020



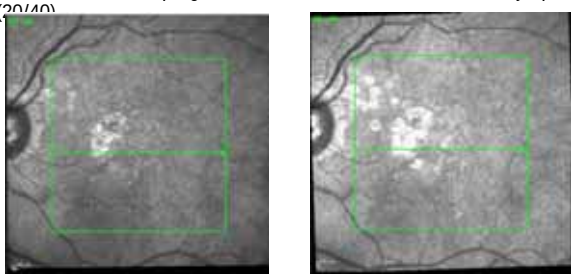
72

- 79 YO WF with a history of AMD
- OCT in 2022 reveals parafoveal GA lesion with associated symptoms in dark illumination and missing letters with reading



73

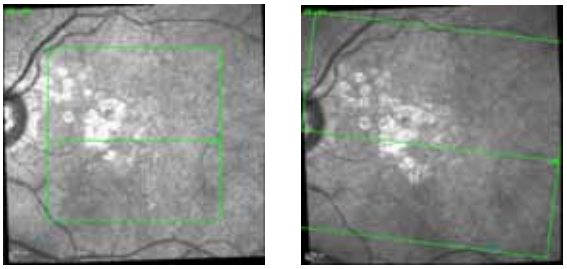
- 79 YO WF with a history of AMD
- OCT 2023 confirms progression of GA lesion with associated symptoms (20/40)



2022 2023

74

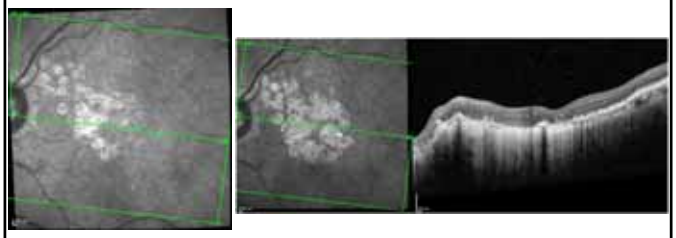
- 79 YO WF with a history of AMD
- Treated with Syfovre (4) – Vision 2040



2023 Syfovre (4)

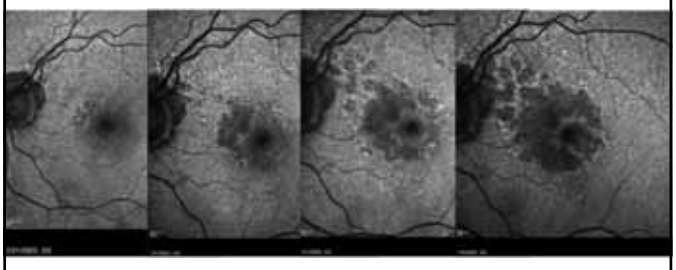
75

- 79 YO WF with a history of AMD
- Treated with Syfovre (13) Vision 20/80



76

- 79 YO WF with a history of AMD
- Progression of GA noted on FAF 2022, 2023 (IVS), 2024 (7), 2025 (Total - 13)
- Vision 20/40 – 20/80



77

Potential Complications of Syfovre

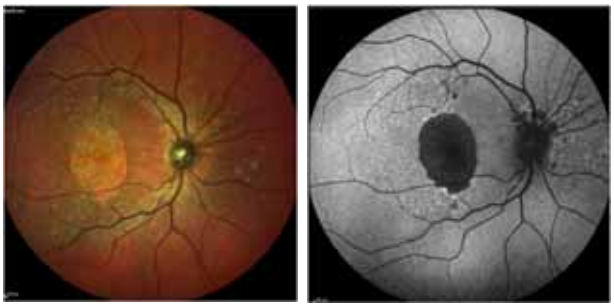
Conversion to Neovascular AMD
Secondary Intraocular Inflammation (IOI)

78

- 65 YO WF with a history of AMD presents for second opinion on AMD
- Vision loss OD for 3 years and gradual decline OS over 12M with increased trouble in lower light settings
- PMHx: Hyperlipidemia, OSA (non compliant with CPAP therapy)
- Vision 20/150 OD – drusen with central GA
- Vision 20/30- OS with intermediate drusen
- Diagnosis:
  - Advanced AMD OD with subfoveal involvement
  - Intermediate Dry AMD OS

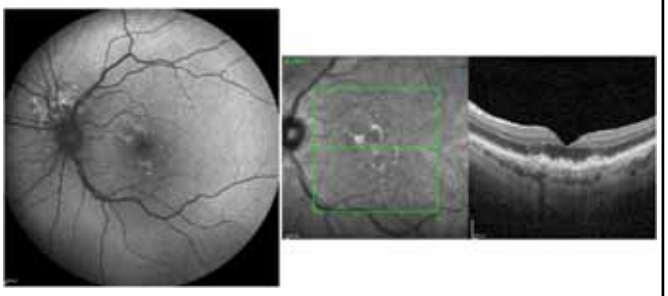
79

- 65 YO WF with a history of AMD – Initial Imaging in 2019 OD



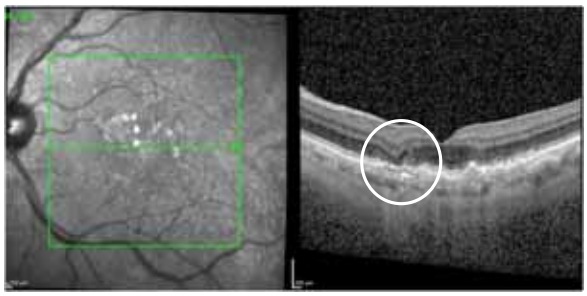
80

- 65 YO WF with a history of AMD – Initial Imaging in 2019 OS



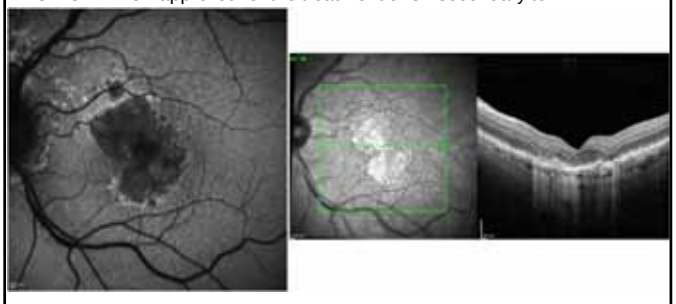
81

- 67 YO WF with AMD –Imaging in 2021 OS BIOMARKERS for GA



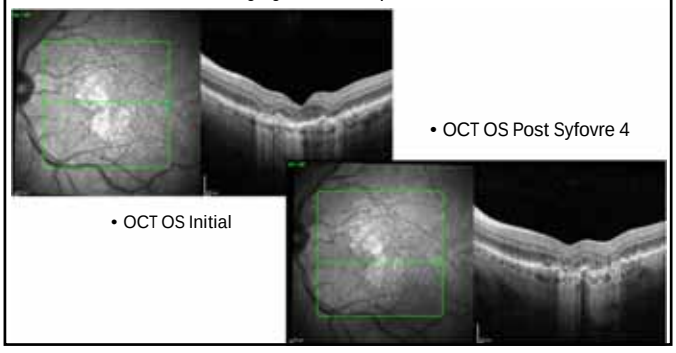
82

- 69 YO WF with AMD –Imaging in 2023 OS GA present
- SYFOVRE now approved for the treatment of GA secondary to AMD



83

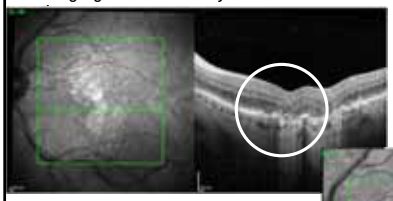
- 70 YO WF with AMD –Imaging in 2024 OS post IVS 4



- OCT OS Post Syfovre 4
- OCT OS Initial

84

- 70 YO WF with AMD - She returns for Syfovre 5
- Imaging confirms early conversion to neovascular AMD OS – Vabysmo

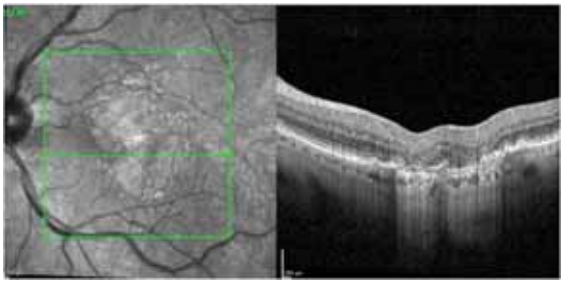


- OCT OS Early CNV

- OCT OS Post Syfovre 4

85

- 70 YO WF with AMD – Imaging 2024 post Syfovre / Vabysmo
- History of Syfovre 7 and Vabysmo 2 to date – Treated with both compounds

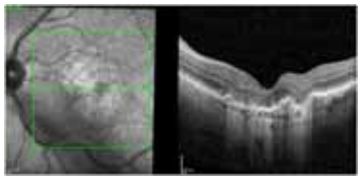


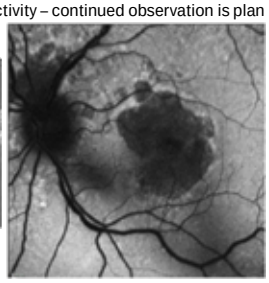
86

- 70 YO WF with AMD – Imaging 2024 post Syfovre / Vabysmo
- Patient returns with significant increased floaters with blurred vision 20/100

87

- 71 WF with AMD – Developed Intermediate Uveitis post combined Syfovre/Vabysmo
- Despite aggressive topical Durezol the vitreous haze remained and she ultimately required Vitrectomy surgery (this was her better eye)
- 1 year post Vitrectomy and observation her vision remains stable at 20/30-2
- FAF confirms GA lesion borders show minimal activity – continued observation is plan for now





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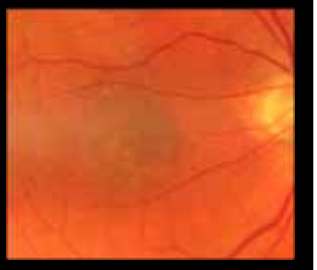
CASE

- **69yo male**
- CC: No visual complaints (DM exam)
- Oc Hx:
  - Cataracts OU
- Med Hx:
  - HTN, Type 2 DM, chol
- Vision: BCVAs @dist
  - **OD 20/40 PHNI (was 20/25 last year)**
  - OS 20/20



89

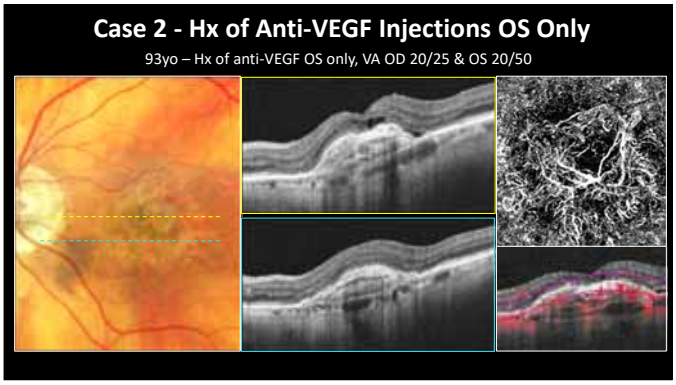
Images from 1 yr ago….

20/25

20/20

90

91



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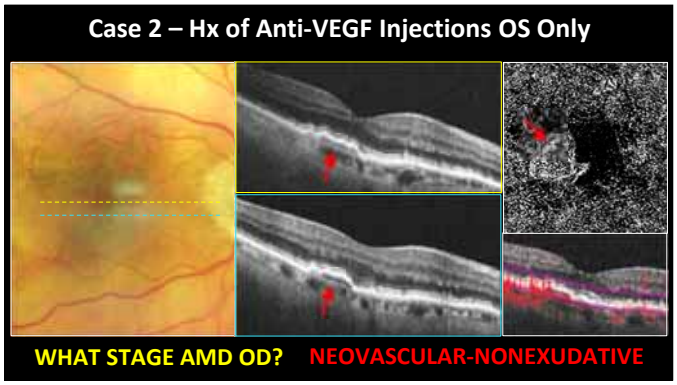

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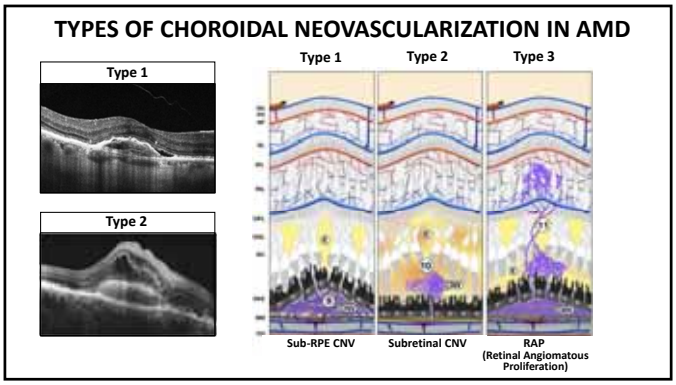

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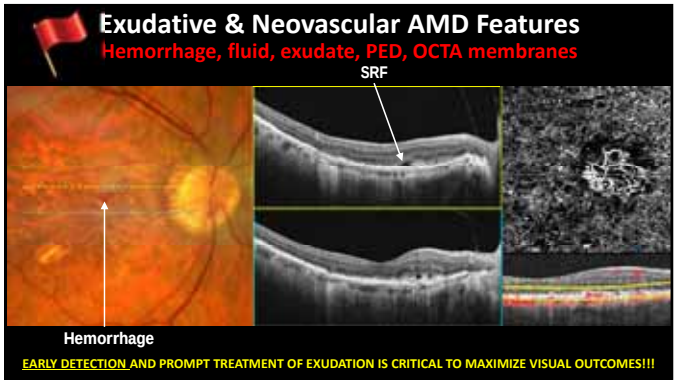

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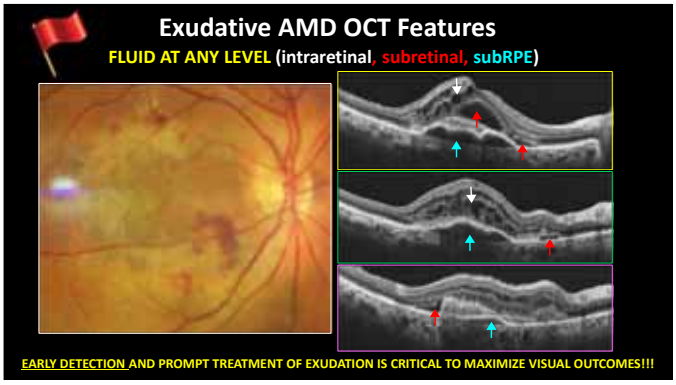

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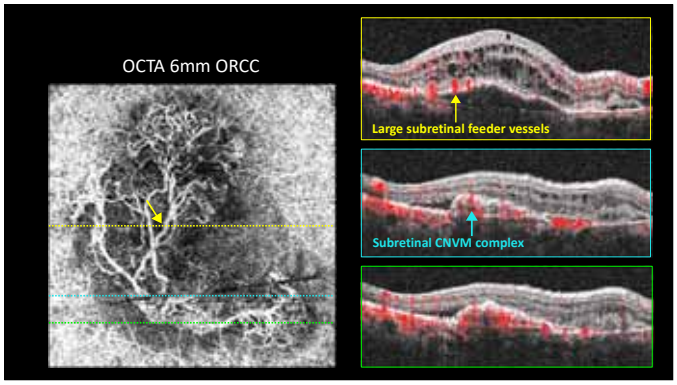

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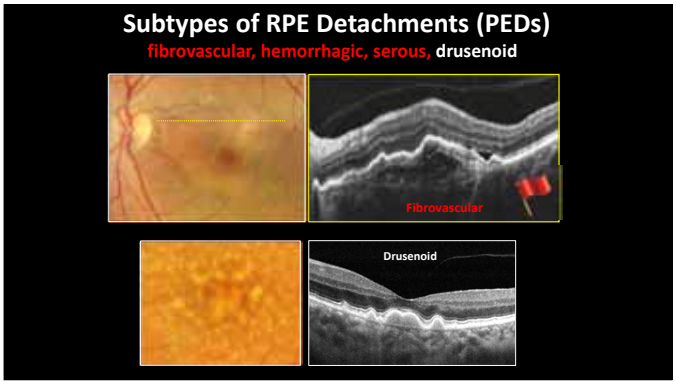

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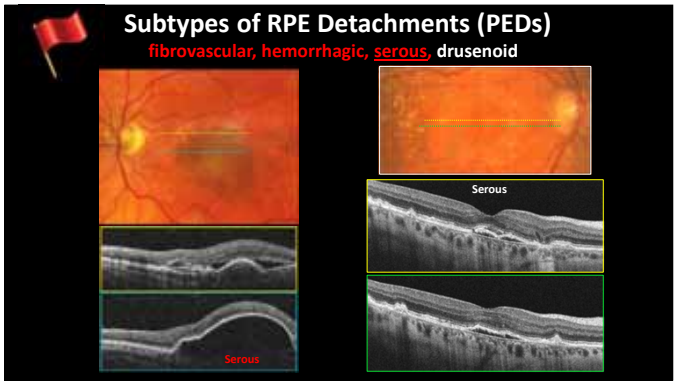

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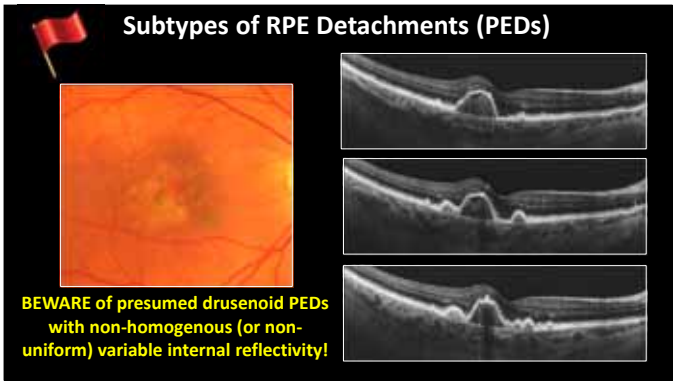

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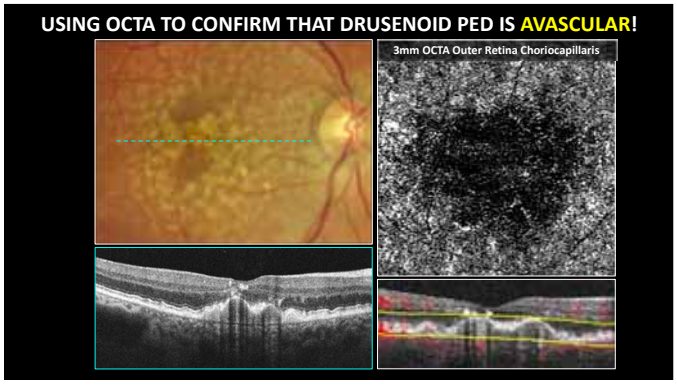

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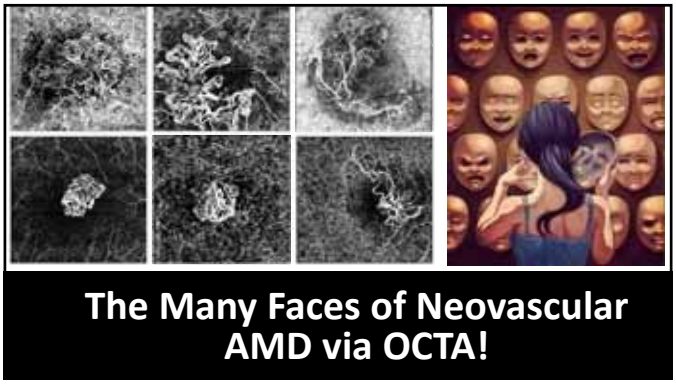

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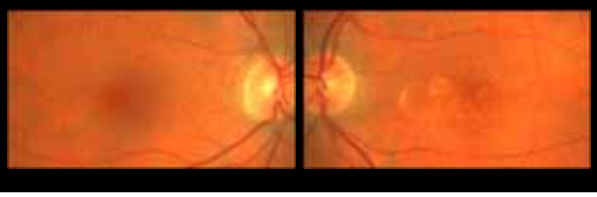
DON'T WAKE THE SLEEPING DRAGON

- CC: **Routine exam**, no visual complaints
- Oc Hx:
  - **Dry AMD x 5 years OU**, taking AREDS 2
  - Cataract NS 1+ OU
- Med Hx:
  - HTN, Type 2 DM
  - Never smoker
- Vision: BCVAs @dist
  - OD 20/20
  - **OS 20/40+1**



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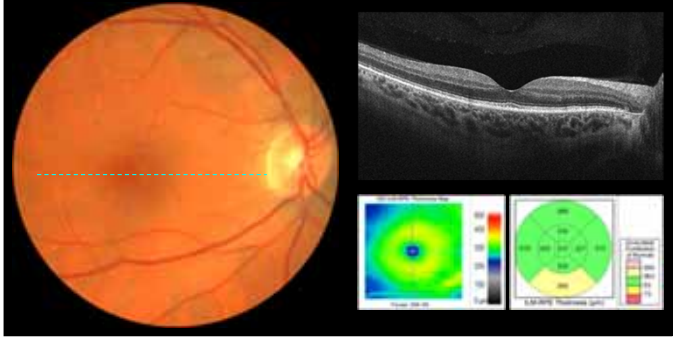
DON'T WAKE THE SLEEPING DRAGON



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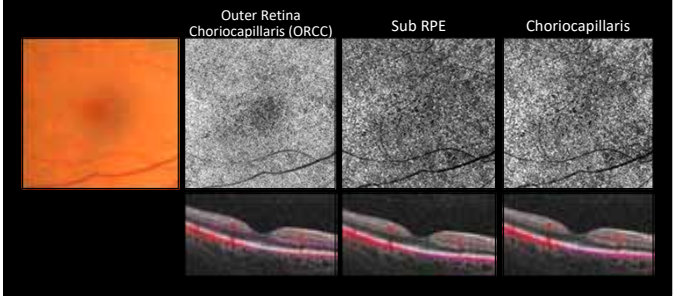
DON'T WAKE THE SLEEPING DRAGON

OCT Angiography 6mm Macula OD



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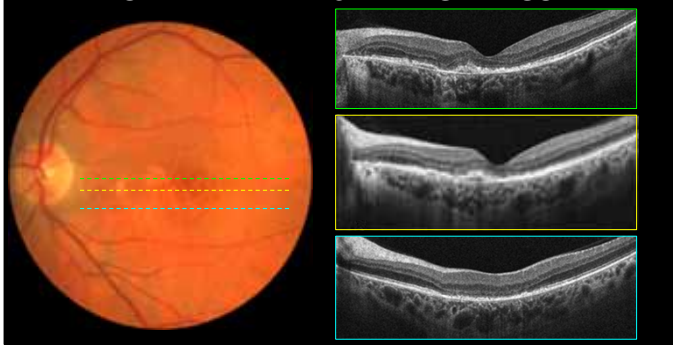
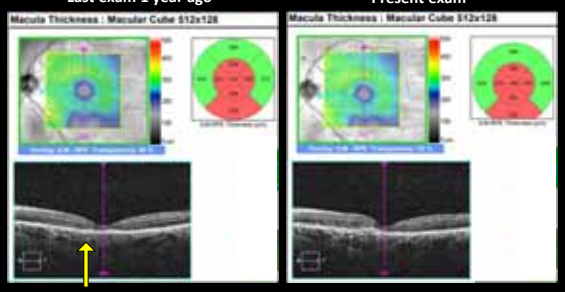
DON'T WAKE THE SLEEPING DRAGON



106

DON'T WAKE THE SLEEPING DRAGON

Last exam 1 year ago **Present exam**



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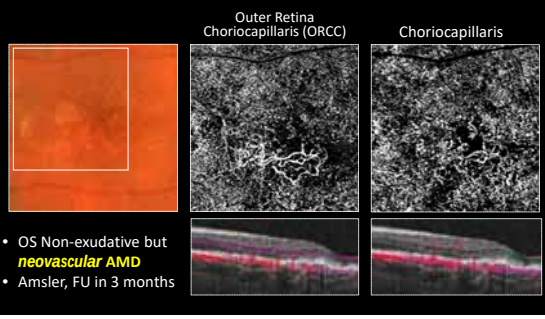
DON'T WAKE THE SLEEPING DRAGON

OCT Angiography 3mm Macula OS



- OS Non-exudative but ***neovascular*** **AMD**
- Amsler, FU in 3 months

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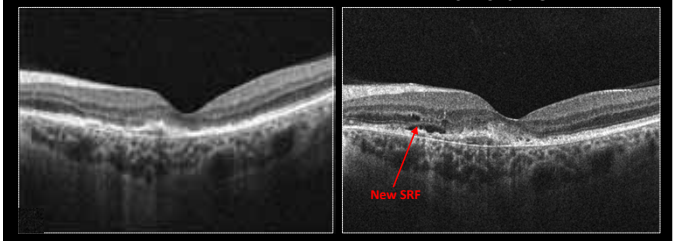
DON'T WAKE THE SLEEPING DRAGON

No shows 3 month FU appt, returns 6 months later (no complaints and stable VA)

Baseline | 6 Month FU



OS EXUDATIVE AMD!!!! Refer to retina for anti-VEGF

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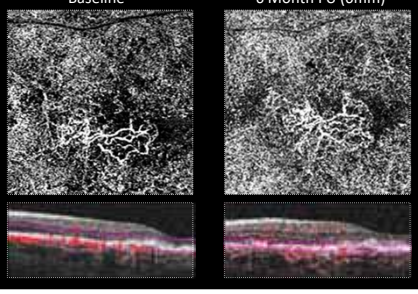
DON'T WAKE THE SLEEPING DRAGON

OCT Angiography 3mm Outer Retina Choriocapillaris OS

Baseline | 6 Month FU (6mm)



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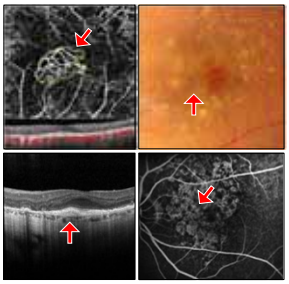
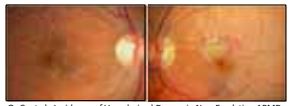
NONEXUDATIVE CNV



1. Well-defined neovascular complex via OCTA
2. No signs of exudation via ophthalmoscopy such as exudate or blood
3. No fluid via structural OCT
4. No leakage with IVFA

Present in approx. 10% of high risk AMD eyes (intermediate AMD, exudative fellow eye)



Carnevali A, et al. OCTA: A Useful Tool for Diagnosis of Treatment-Naïve Quiescent CNV. Am J Ophth. 2016.

Or C, et al. Incidence of Vascularized Drusen in Non-Exudative ARMD using SD-OCTA. ARVO 2018.

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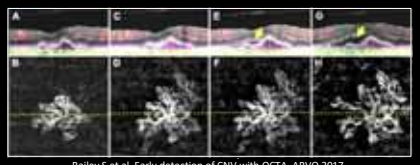
NONEXUDATIVE CNV

Prognosis

- Rate of future exudation, eyes with nonexudative CNV vs eyes without nonexudative CNV
  - **Bailey S ARVO 2017.** 60% vs 4% (5 months)
  - **De Oliveira Dias J Ophthal 2018.** 21% vs 4% (12 months)
    - 15x greater risk of exudation after detection of nonexudative CNV



EYES WITH NONEXUDATIVE CNV ARE AT HIGH RISK FOR EXUDATIVE CONVERSION!

Bailey S et al. Early detection of CNV with OCTA. ARVO 2017.
De Oliveira Dias JR, et al. Natural History of Subclinical Neovascularization in Nonexudative ARMD Using SS-OCTA. Ophthalmol 2018.

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AMD HOME MONITORING SYSTEMS

ForeseeHOME
AMD Monitoring System

Why was it developed?

- AMD is the leading cause of blindness in the developed world in persons >50yo
- Neo accounts for 90% of severe central VA loss from AMD
- Early detection and prompt treatment of neo improves the visual outcomes
- **Need for home monitoring between routine office visits to detect early conversion** from intermediate nonexudative to neovascular AMD

What is it?

- **FDA approved home preferential hyperacuity perimeter (PHP)** that *augments* in-office exams
  - Detects and characterizes central and paracentral metamorphopsia
  - Only available by physician order
  - The Notal Vision Monitoring Center- provides pt training, compliance reminders, & communicates with prescribing eyecare provider

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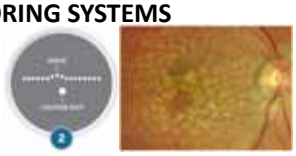
AMD HOME MONITORING SYSTEMS

ForeseeHOME
AMD Monitoring System



Who should use it?

- Patients with **intermediate nonexudative AMD in at least one eye**
  - **BCVA 20/60 or better** (stable vision and fixation)
- Covered by Medicare and some private insurances

What is the test like?

- Pt clicks where a wave or bump appears in a dotted line
  - Takes ~ 3 min per eye
  - Daily testing recommended

How is early conversion detected?

- Each test result is compared to a normative database and the pt's personal baseline
- Clinician is alerted if sig change

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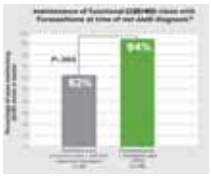
AMD HOME MONITORING SYSTEMS

ForeseeHOME

AMD Monitoring System



DOES RESEARCH SUPPORT ITS USE?

AREDS 2 HOME Study

- Foresee Home identified 64% of converters
  - **Functional vision (≥20/40) at conversion was maintained in 94% of patients using Foresee Home** vs 62% without

ALOFT Study (Analysis of the Long-term visual Outcomes of ForeseeHome Remote Telemonitoring)

- Large retrospective review of clinical data from 2010 to 2020 (3,334 eyes)
- 52% of conversions detected by system alert
- Median acuity measures of converters at:
  - Baseline 20/30
  - Initial conversion 20/39
  - **Final follow-up 20/32**
- 82% of eyes that converted had functional vision (≥20/40) at final follow up

Chew EY, et al. Randomized Trial of the Foreseehome Device for Early Detection of nARMD. Home Study Report Number 1. Contemp Clin Trials 2014.
Ho AC, et al. Real-World Performance of a Self-Operated Home Monitoring System for Early Detection of nARMD. *J Clin Med* 2021.
Mathai M, et al. Analysis of the Long-term visual Outcomes of ForeseeHome Remote Telemonitoring - The ALOFT study. *Ophthalmology Retina* 2022.

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AMD MOBILE MONITORING SYSTEMS

myVisionTrack (mVT®) app

- Smartphone and tablet-based app
- Based on shape discrimination hyperacuity testing
- Monitors progression of DME and AMD
- Prescription required
- Clinician is alerted if significant change in test results

MaculaTester app

- Electronic version of the Amsler grid
- Record areas of distortion by touching screen
- Does NOT automatically detect progression or communicate with doctor
- Can set up reminder notifications

Alleye app

- 2 different app versions:
  1. AlleyeOne: for those at increased risk of retinal disease
  2. Alleye: for those with existing retinal disease (AMD & DME)
- Assesses vernier acuity using an alignment task
- In studies, 52-66% of the pts who came to the clinic bc of a + test result received an intravitreal injection
- Register as a provider online (https://alleye.io/provider)

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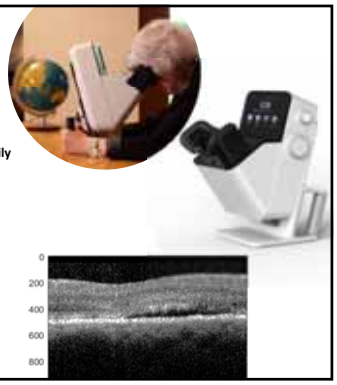
AMD HOME MONITORING SYSTEMS

Home OCT



- **Monitoring of intra- and subretinal fluid based on daily patient self-imaging**
  - **Easy-to-use, patient-operated device**
  - **AI algorithm analyzes images on cloud**
  - **Remote diagnostic clinic, provider of monitoring program, reports changes meeting physician-selected fluid volume thresholds to referring physician**
  - **24/7 physician access to all data**
- **Personalize Injection schedule**

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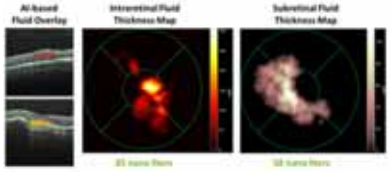
Home OCT for monitoring chronic therapy of neovascular AMD between office visits

- **3mm x 3mm (10 x 10 degree) field of view**
- **88 B-scans with 34 um spacing**
- **Scanning takes < 1 min per eye**



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Anti-VEGF

Medications

- 1st generation
  - Bevacizumab (off label)
  - Lucentis® (ranibizumab) 0.5 or 0.3mg (0.05 mL): nAMD, mCNV, RVO, DR, DME
  - Eylea® (aflibercept) 2 mg (0.05 mL) : nAMD, RVO, DME, DR
- 2nd generation (extended duration)
  - **Vabysmo® (faricimab-svoa) 6 mg (0.05 mL of 120 mg/mL solution): nAMD, DME, RVO**
  - **Eylea HD ® (aflibercept) 8mg (0.07mL) : nAMD, DME, DR**
  - Beovu® (brolucizumab) 6 mg (0.05 mL of 120 mg/mL solution): nAMD, DME
- **Biosimilars**
  - Byooviz® (ranibizumab-nuna) 0.5 mg (0.05 mL): nAMD, RVO, mCNV
  - Cimerli ® (ranibizumab- -eqrn) 0.5 mg(0.05 mL) for nAMD, RVO, mCNV) or 0.3 mg(0.05 mL) (biosimilar for DR/DME)

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Anti-VEGF Biosimilars

Per the FDA:

- "A biosimilar is a biological product that is approved based on data showing that it is highly similar to a biological product already approved by the FDA (reference product) and has no clinically meaningful differences in terms of safety, purity and potency (i.e., safety and effectiveness) from the reference product, in addition to meeting other criteria specified by law."

Currently, 2 FDA approved Ranibizumab Biosimilars

- Byooviz (Samsung) approved Sept 2021
- Cimerli (Coherus) approved Oct 2022

www.reviewofophthalmology.com/article/an-update-on-the-antivegf-biosimilar-pipeline

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Extended Duration Anti-VEGF Therapies

High Dose Aflibercept (8mg Eylea)

- FDA approved in Aug 2023 for nAMD, DME, & DR
- 8mg high dose vs 2mg standard dose
- **Phase III PULSAR (nAMD)** & PHOTON (DME) clinical trials
  - Demonstrated non-inferior and clinically equivalent vision gains at 48 wks with 8 mg at 12 and 16 week dosing after 3 initial doses compared to 2mg Eylea every 8 weeks after initial dosing
  - Recommended dose 1 injection every 4 weeks for first 3 mos for all indications, then every 8-16 weeks (2-4 mos) for AMD and DME and every 8-12 weeks (2-3 mos) for DR
  - No new safety signals

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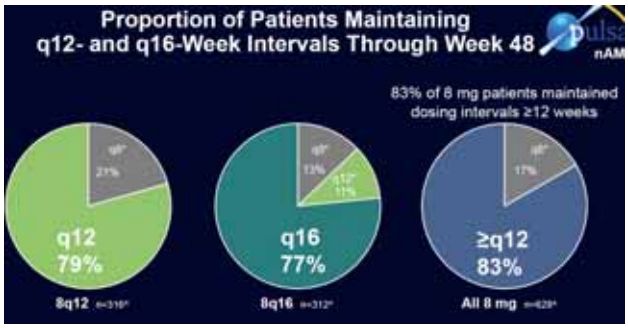

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Extended Duration Anti-VEGF Therapies

Faricimab (Vabysmo)

- FDA approved in Jan 2022 for nAMD & DME, Oct 2023 for RVO
- Dual MOA (bi-phasic antibody) inhibits VEGF-A **& Angiopoietin-2 (Ang-2)**

- Phase III DME clinical trials **TENAYA & LUCERNE**
  - Dosing monthly x4 months than flexible dosing based on pt need
  - **At week 48, ~80% of the patients in the faricimab arm had achieved a 12- or 16-week treatment interval and 45% achieved a 16-week interval**

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Port Delivery System (Susvimo)

- Port delivery system of ranibizumab
- FDA approved 10/2021 for treatment of neovascular AMD
- Permanent refillable reservoir that passively diffuses ranibizumab into vitreous cavity

Holekamp, Nancy M., et al. "Archway Randomized Phase 3 Trial of the Port Delivery System With Ranibizumab for Neovascular Age-Related Macular Degeneration." Ophthalmology (2021).

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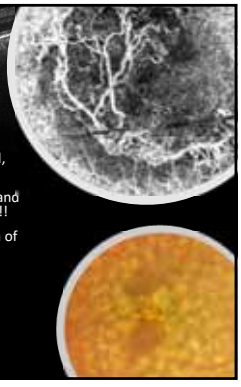
Take Home Message

- Be familiar with features suggestive of exudative AMD (blood, fluid, PED, etc)
- OCT/OCTA allows for earlier detection of neovascularization and exudation in AMD = Earlier treatment = Vision preservation!!!
- OCTA is the only method of detecting and monitoring growth of non-exudative CNV membranes
- Look (with FAF & OCT) and refer patients with GA that may benefit from newly approved therapies
- Recognize OCT biomarkers for conversion from intermediate nonexudative AMD to advanced AMD



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Thank You!

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DrJay@soundretina.com

NSU OCO

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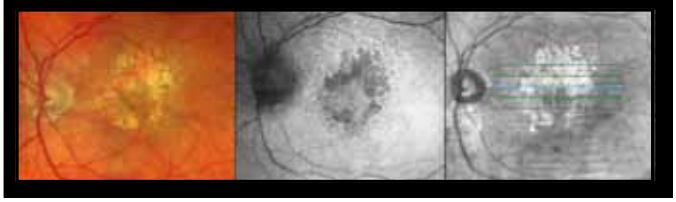

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On behalf of Vision Expo, we sincerely thank you for being with us this year.

Reminder to Complete Your Session Evaluations!

Please be sure to complete your digital session evaluations for each course you attended! Your feedback is important to us as our Education Planning Committee considers content and speakers for future meetings to provide you with the best education possible.

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