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# Pegcetacoplan: Advancing the First Potential Treatment for Geographic Atrophy (GA)

Virtual Investor Event
January 28, 2021

# Forward-looking Statements

Statements in this presentation about future expectations, plans and prospects, as well as any other statements regarding matters that are not historical facts, may constitute “forward-looking statements” within the meaning of The Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements relating to the implications of preliminary clinical data. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: whether the company’s clinical trials will be fully enrolled and completed when anticipated; whether preliminary or interim results from a clinical trial will be predictive of the final results of the trial; whether results obtained in preclinical studies and clinical trials will be indicative of results that will be generated in future clinical trials; whether pegcetacoplan will successfully advance through the clinical trial process on a timely basis, or at all; whether the results of the company’s clinical trials will warrant regulatory submissions and whether pegcetacoplan will receive approval from the FDA or equivalent foreign regulatory agencies for GA, PNH, CAD, HSCT-TMA, C3G, IC-MPGN, ALS or any other indication when expected or at all; whether, if Apellis’ products receive approval, they will be successfully distributed and marketed; and other factors discussed in the “Risk Factors” section of Apellis’ Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 2, 2020 and the risks described in other filings that Apellis may make with the Securities and Exchange Commission. Any forward-looking statements contained in this press release speak only as of the date hereof, and Apellis specifically disclaims any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise.

# Disclosures

| | |
|---|---|
| CAROLINE R. BAUMAL | *Consultant*: Apellis, Genentech, Novartis, Gemini Therapeutics, Zeiss |
| NANCY M. HOLEKAMP | *Consultant:* Allergan, Acucela, Apellis, Bayer, Lineage Cell Therapeutics, Clearside Biosciences, Gemini, Genentech, Gyroscope, Katalyst Surgical, Nacuity, Notal Vision, Novartis, Polyactiva, Regeneron<br>• *Speakers Bureau:* Allergan, Genentech, Novartis, Regeneron, Spark<br>• *Contracted Research*: Genentech, Gemini, Gyroscope, Notal Vision<br>• *Intellectual Property/Patent:* Katalyst Surgical |
| JEFFREY S. HEIER | *Consultant*: 4DMT, Adverum, Aerie, Aerpio, Aldeyra, Allegro, Alzheon, Annexon, Apellis, Aprea, Asclepix, Aviceda, BVT, Dark Horse, DTx, Eloxx, Galimedix, Genentech, Graybug, Gyroscope, Iveric, jCyte, Kanghong, LensGen, NGM, Novartis, Ocular Therapeutix, OcuTerra, Oxurion, Palatin, Regeneron, Regenxbio, Stealth, Thea, Verseon, Vinci, Voyant<br>*Research*: Apellis, Asclepix, Bayer, Genentech, Graybug, Gyroscope, Hemera, Iveric, Kanghong, Kodiak, NGM, Notal Vision, Novartis, Regeneron, Regenxbio, Stealth |
| PEARSE A. KEANE | *Consultant*: DeepMind, Roche, Novartis, and Apellis. Dr. Keane is an equity owner in Big Picture Medical and has received speaker fees from Heidelberg Engineering, Topcon, Allergan, and Bayer. |

# Agenda

| | | |
|---|---|---|
| **Introductions** | FEDERICO GROSSI, M.D., PH.D<br>*Chief Medical Officer*, Apellis | CEDRIC FRANCOIS, M.D., PH.D.<br>*Chief Executive Officer*, Apellis |
| **Overview of Age-related Macular Degeneration (AMD)** | CAROLINE R. BAUMAL, M.D.<br>*Professor of Ophthalmology*<br>Tufts Medical Center, New England Eye Center, Retina Department | |
| **Natural History and Unmet Need in GA** | NANCY M. HOLEKAMP, M.D.<br>*Director, Retina Services*<br>Pepose Vision Institute | |
| **Role of Complement C3 in AMD** | LUKAS SCHEIBLER, PH.D.<br>*Chief Innovation Officer*, Apellis | |
| **Pegcetacoplan: Phase 2 FILLY Results** | JEFFREY S. HEIER, M.D.<br>*Director, Retina Service and Director, Retinal Research*<br>Ophthalmic Consultants of Boston | |
| **Pegcetacoplan: Phase 3 DERBY and OAKS Studies** | JEFFREY EISELE, PH.D.<br>*Local Chronic Program Lead*, Apellis | |
| **Early Detection of Geographic Atrophy with Artificial Intelligence** | PEARSE A. KEANE, M.D.<br>*Consultant Ophthalmologist*, Moorfields Eye Hospital NHS Foundation Trust<br>*Associate Professor*, University College London | |
| **Q&A** | ALL | |

# Apellis: Global Leader in Complement

| OUR STRATEGY | 2021 KEY MILESTONES |
| --- | --- |
| Establish systemic pegcetacoplan as a **disruptive therapy** across rare, complement-driven diseases | **PNH launch in H1 2021** and progress 4 additional registrational programs |
| Be **#1** in the **retina** | **Phase 3 GA results in Q3 2021** a blockbuster opportunity |
| Develop **new technologies** to control complement | **Advance 3 compounds into clinical development** in the next 24 months |

**Focused on compassion and commitment to patients**

# Key Misconceptions We'll Address Today

"Other complement inhibitors have failed. Why should pegcetacoplan work?"

"Pegcetacoplan has no impact on visual acuity. It will take years to notice a difference. Why would people take this drug?"

"How can we trust the FILLY data?"

"The FILLY trial had safety issues. Pegcetacoplan causes 'wet AMD' and had two cases of infectious endophthalmitis."

# Living with Geographic Atrophy

Carolyn’s Story

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# Overview of Age-related Macular Degeneration (AMD)

Caroline R. Baumal, M.D.
*Professor of Ophthalmology,* Tufts Medical Center
New England Eye Center, Retina Department
Boston, MA

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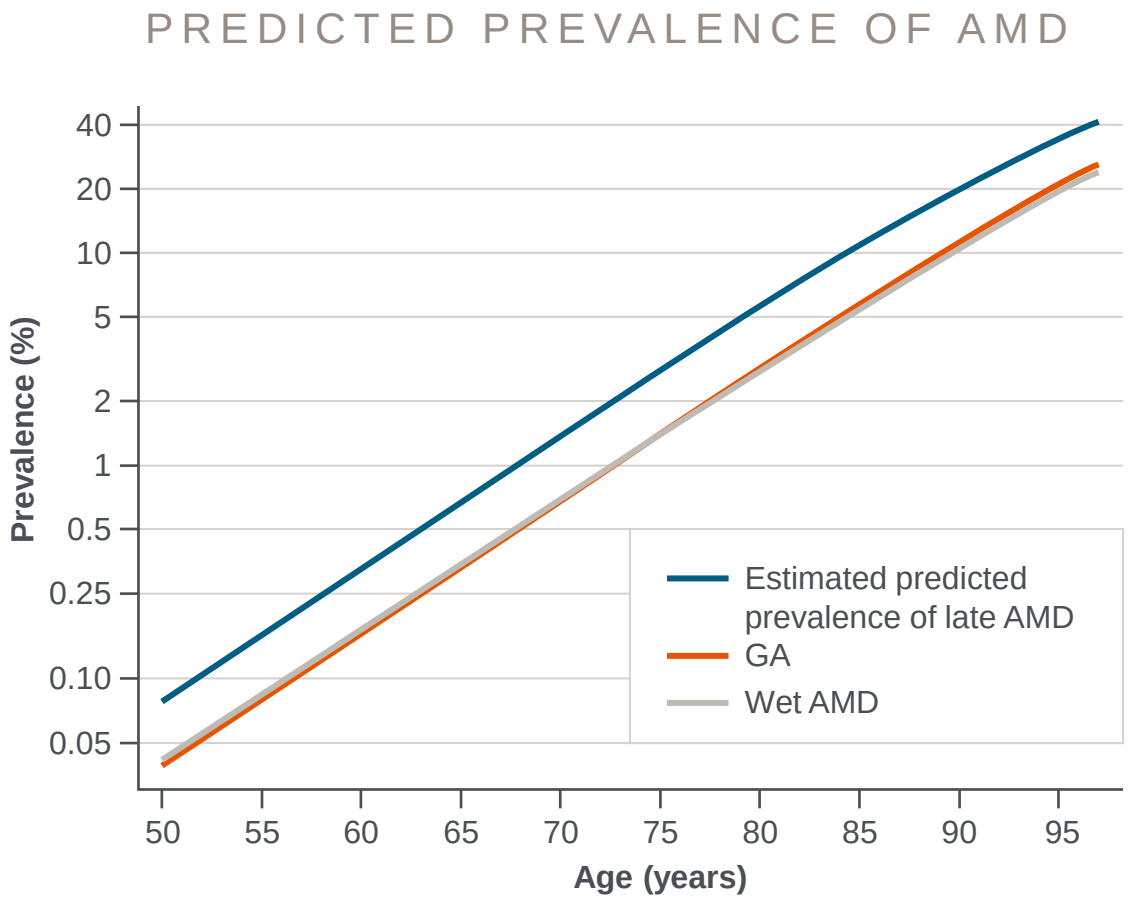
# AMD Causes Progressive Loss of Central Vision

- AMD is a degenerative disease of the macula, part of the retina important for detailed and color vision
- Risk factors include age, genetics, and lifestyle/environmental factors
- Can be classified as dry or wet, as well as by severity
- Global prevalence of AMD:
  - >196 million projected for 2020[1]
  - >288 million projected by 2040[1]
  - From age 50, prevalence approximately quadruples with every 10 years of age[2]




Adapted from Rudnicka AR, et al, 2012.


1. Mitchell P, Liew G, Gopinath B, Wong TY. Age-related macular degeneration. The Lancet. 2018;392(10153):1147-59.
2. Rudnicka AR, et al. *Ophthalmology* 2012; 119:571-80.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# AMD Progresses through Stages




## EARLY AMD

combination of multiple small drusen, few intermediate drusen (63-124 µm), or mild retinal pigment epithelium (RPE) atrophy

## INTERMEDIATE AMD

large drusen (>125 µm), presenting as sharply defined, usually round or oval areas of atrophy in the RPE

## LATE AMD

may present as wet AMD or geographic atrophy (GA). GA is characterized by large, confluent regions of atrophied RPE

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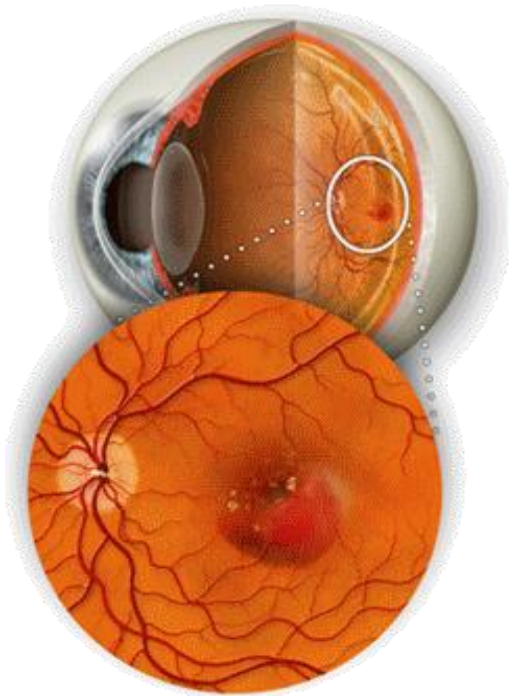
Ambati J, et al. *Nat Rev Immunol*. 2013;13:438-51. Images from: https://webeye.ophth.uiowa.edu/eyeforum/atlas/pages/AMD.htm https://imagebank.asrs.org/file/6296/age-related-macular-degeneration-geographic-atrophy

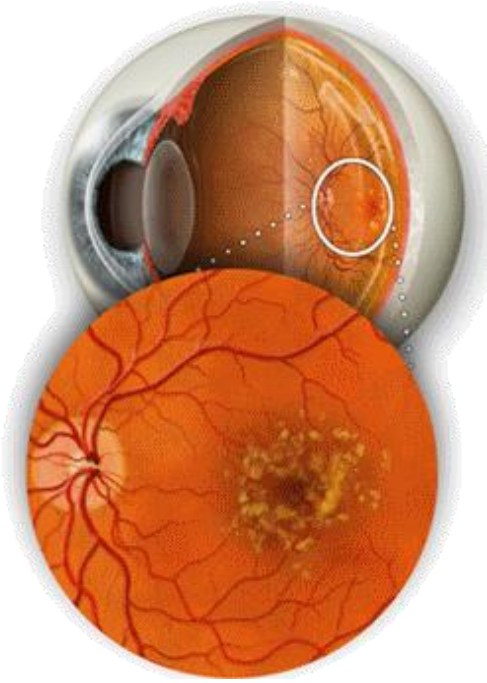
# Late AMD Is either Wet AMD or Geographic Atrophy (GA)

- Early AMD is typically asymptomatic
- Intermediate AMD is associated with some vision loss
- People with late AMD (Wet AMD or GA) experience significant vision loss

WET AMD



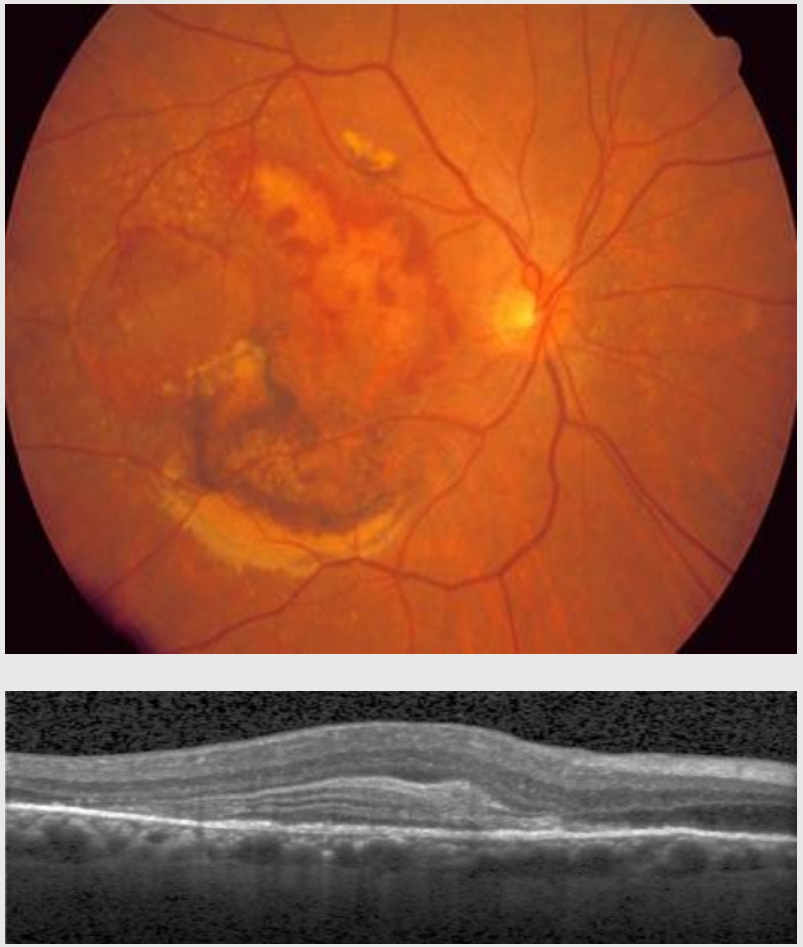
GEOGRAPHIC ATROPHY



Mitchell P, Liew G, Gopinath B, Wong TY. Age-related macular degeneration. The Lancet. 2018;392(10153):1147-59.I
llustration image source: https://amarketresearchgazette.com/age-related-macular-degeneration-market-to-witness-the-highest-growth-globally-in-coming-years/

# Wet AMD Is Treatable

- Approximately 15 million North Americans have AMD
- 10-15% of this population has wet AMD
- Wet AMD can be effectively treated with anti-VEGF therapy



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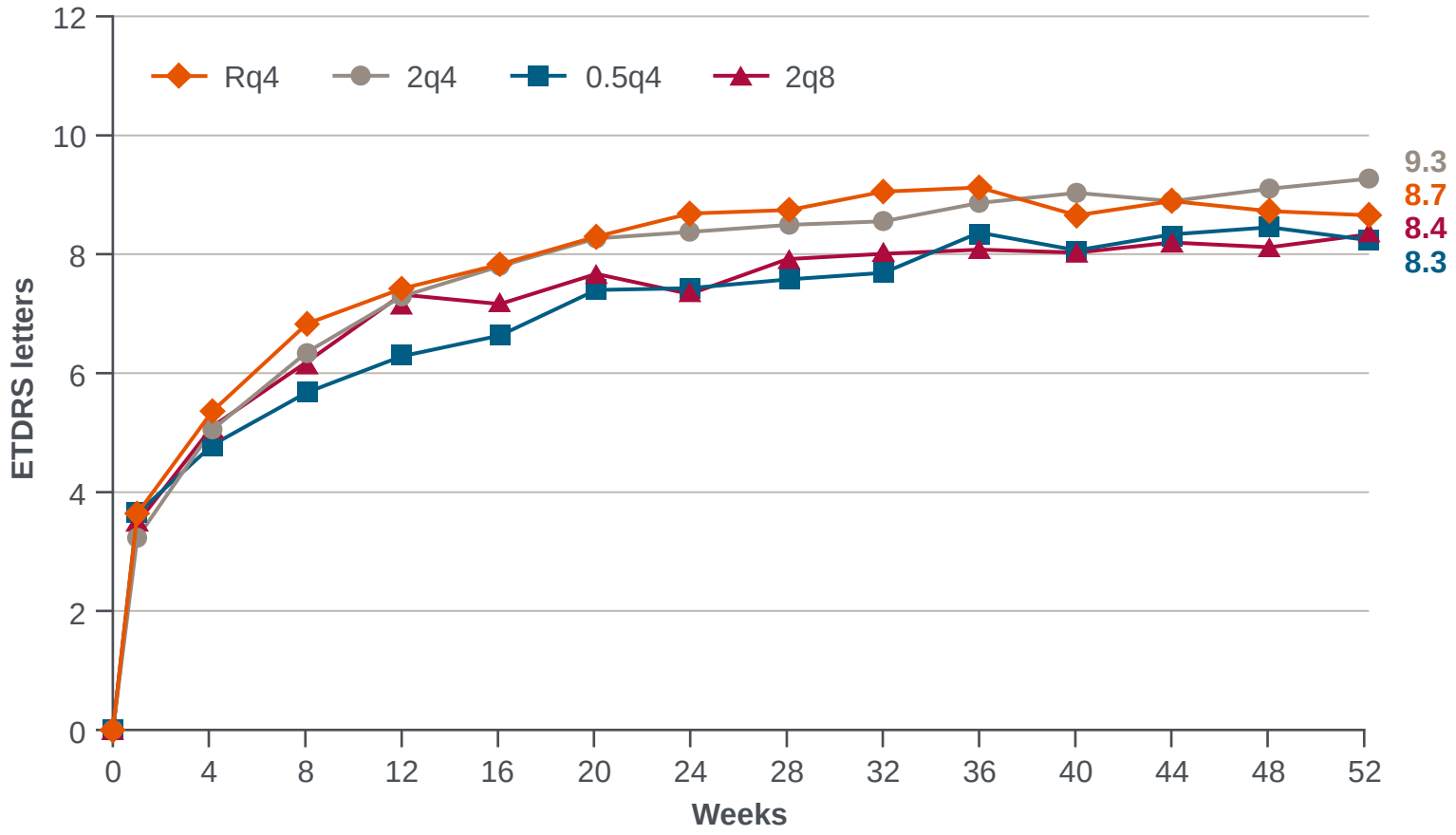
https://www.nei.nih.gov/learn-about-eye-health/resources-for-health-educators/eye-health-data-and-statistics/age-related-macular-degeneration-amd-data-and-statistics
Fundus image from https://www.aao.org/eye-health/diseases/amd-macular-degeneration-pictures-videos
OCT image from Serener, Serte Published 2019, Medicine2019 Scientific Meeting on Electrical-Electronics & Biomedical Engineering and Computer Science (EBBT)

# Anti-VEGF Therapies Have Reduced Global Burden of Wet AMD

- Treatment of wet AMD with anti-VEGF therapy improves visual acuity[1]
- A systematic literature review reported that introduction of anti-VEGF therapies in clinical practice has been associated with a significant reduction in the prevalence of blindness[2]




**Most significant remaining unmet need within AMD is for effective therapies to address geographic atrophy**


1. Heier et al., 2012. *Ophthalomology* 2012.
2. Finger et al., *BMC Ophthalmology* 2020

Figure adapted from Heier et al., 2012.

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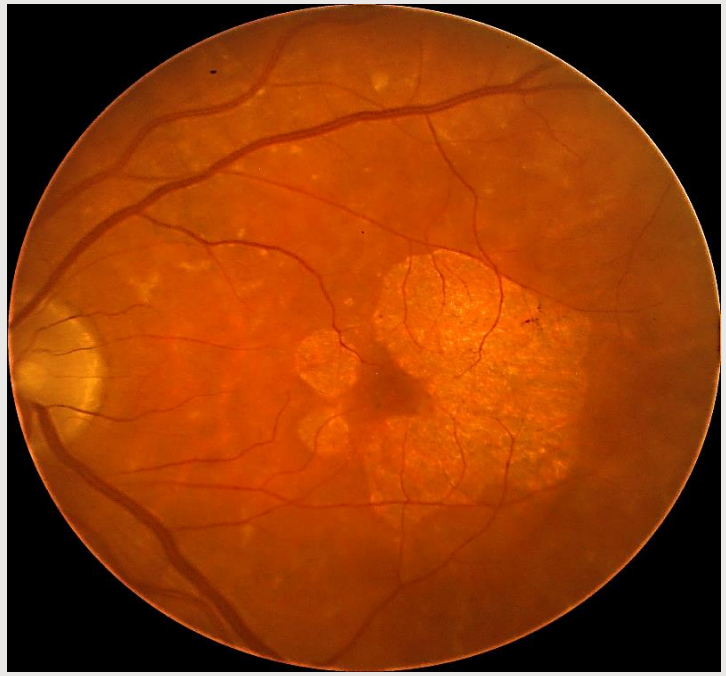
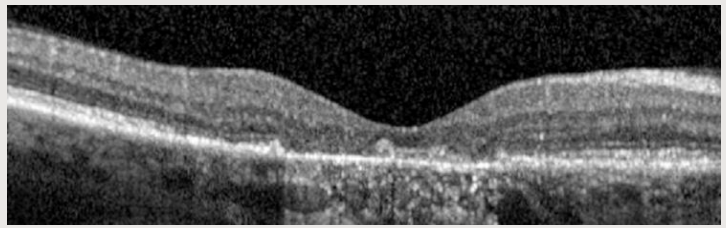
# There Is No Treatment for GA, a Leading Cause of Blindness

- There are **5 million people** living with GA worldwide; 1 million are in the US[1]
- GA accounts for **20% of all legal blindness** attributed to AMD[2, 3]
- There is **no approved treatment** for GA[1]

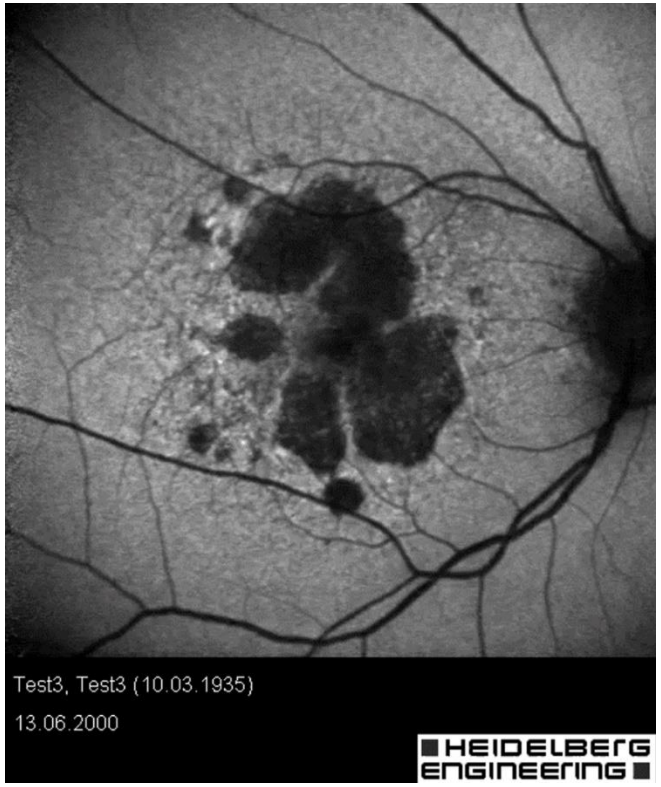





1. Boyer DS et al., *Retina* 2017.
2. Ferris FL 3rd et al., *Arch Ophthalmol.* 1984
3. Klaver CC, et al., *Arch Ophthalmol.* 1998

Image from Holz FG et al., *Ophthalmology* 2014.

# GA Lesion Growth Is Progressive, Constant, and Irreversible



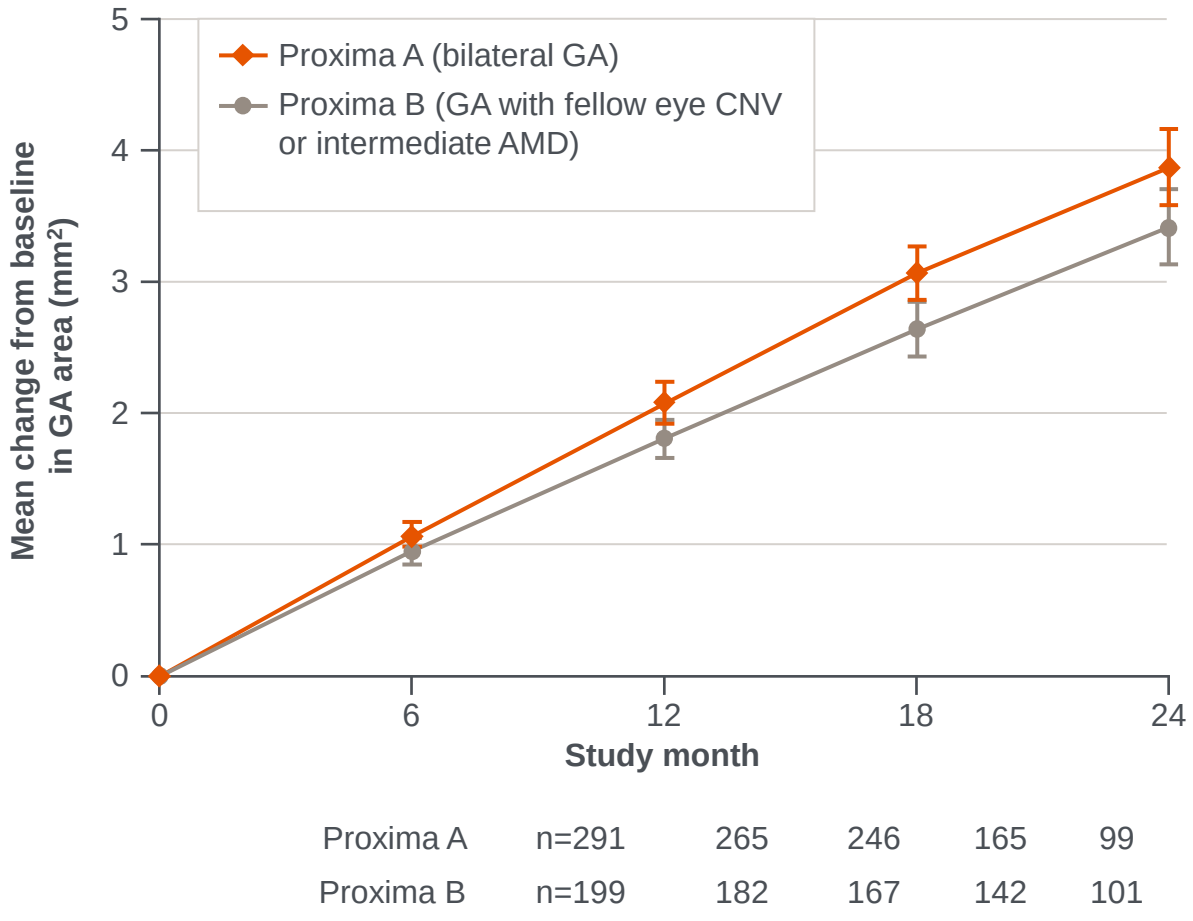




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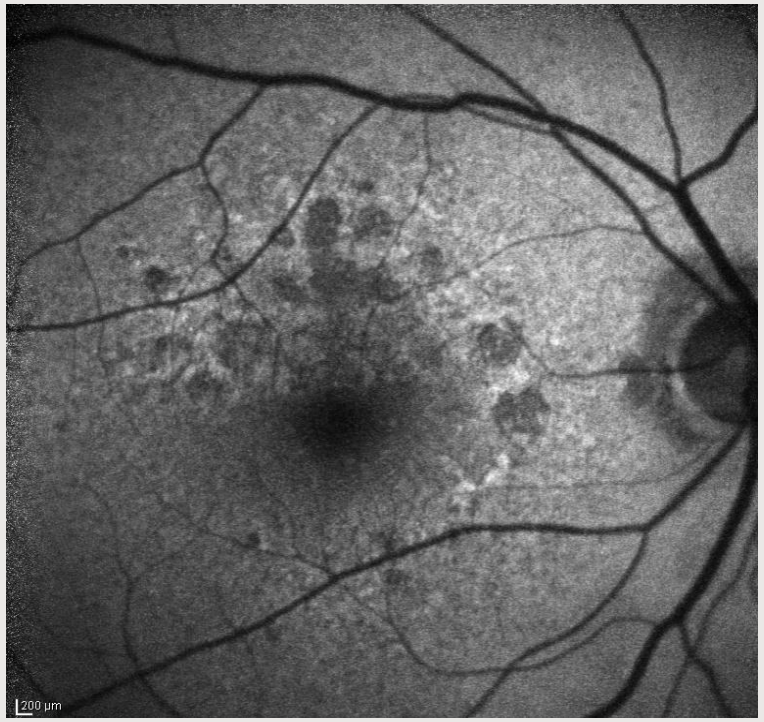
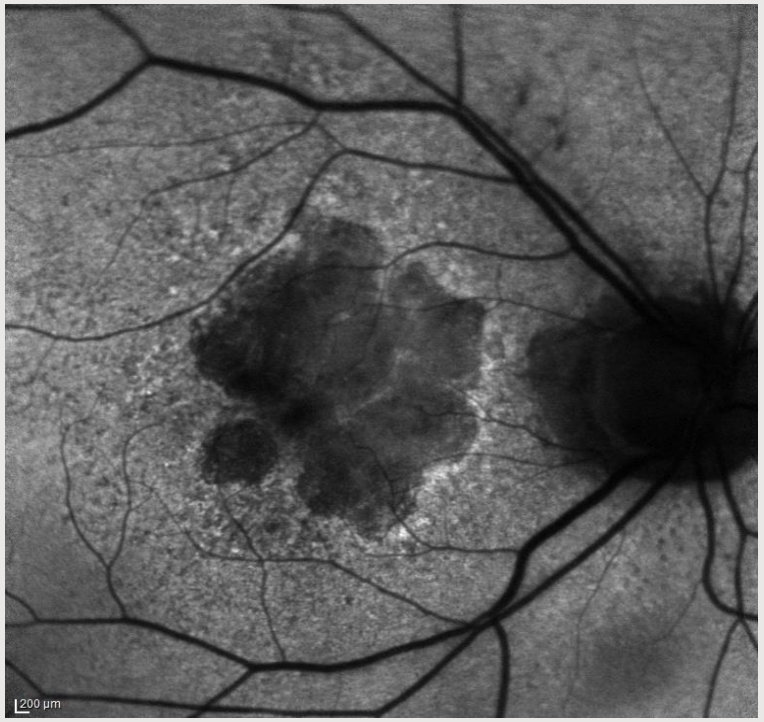
Figure adapted from Holekamp, et al. *Ophthalmology*. 2020; 127(6): 769-783. Image and video courtesy of Dr. Nathan Steinle.

# GA Lesions Can Impact Extrafoveal and Foveal Regions

- Lesions typically appear first in the perifoveal macula sparing the fovea **(foveal sparing)** before expanding to include the fovea
- Extrafoveal lesions tend to progress more quickly than foveal lesions




EXTRAFOVEAL




FOVEAL

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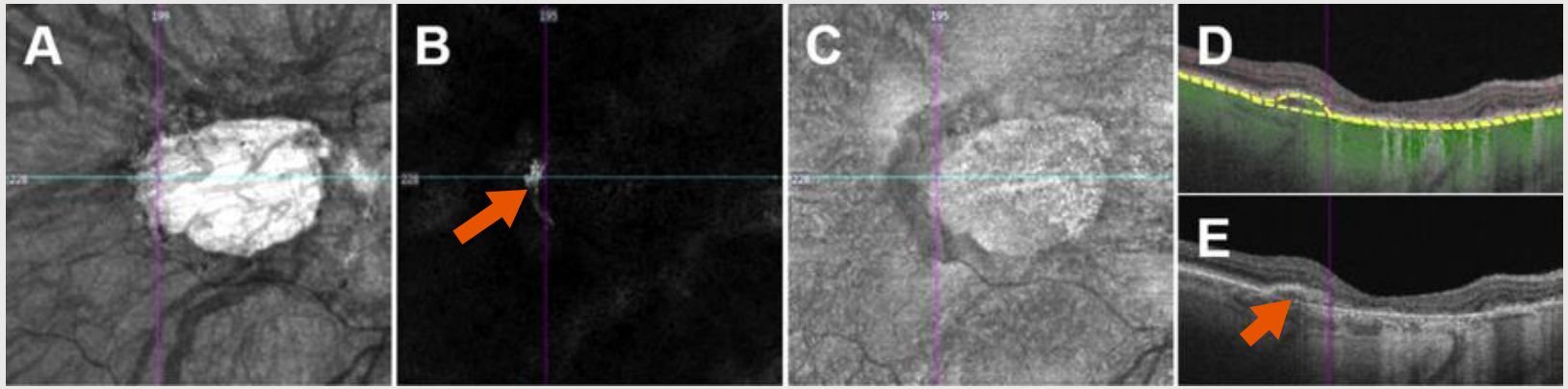
Fleckenstein, et al. *Ophthalmology*. 2018
Images from data on file.

# GA and Wet AMD Can Coexist

- Some GA patients may exhibit **choroidal neovascularization** (CNV) or new blood vessel growth in the choroid
- An **exudation** is defined as leakage from these blood vessels
- **Wet AMD** is characterized by CNV and edema, RPE detachment, and subretinal hemorrhage




**A:** En face structure image under Bruch's membrane (BM)

**B:** En face angiographic image (RPE to BM), showing CNV (arrow)

**C:** En face structure image of B

**D:** OCT B-scan through **type 1 subclinical MNV**

**E:** OCT B-scan showing **double-layer sign adjacent to GA**

OCT=optical coherence tomography;
MNV=macular neovascularization

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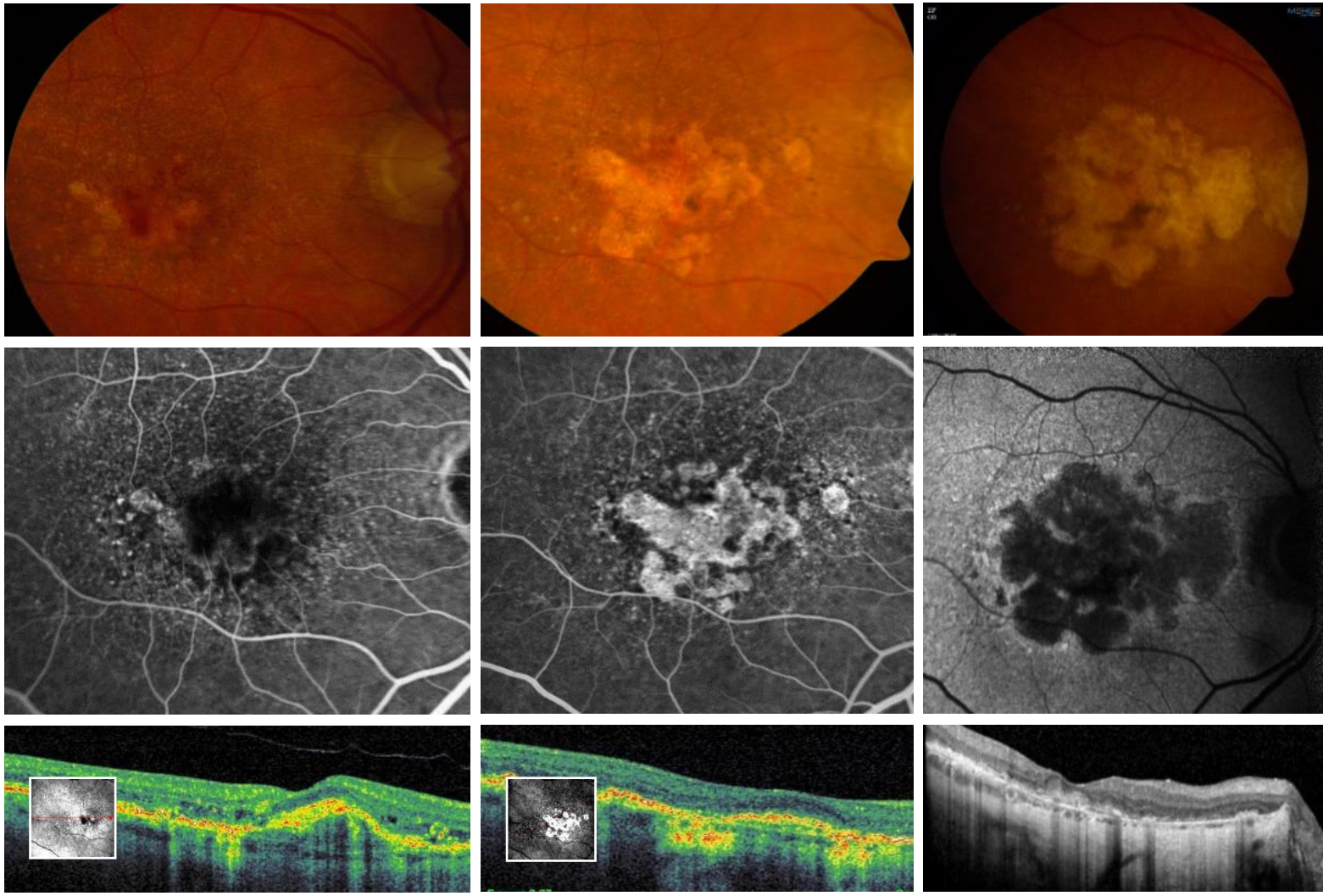
Shi et al., *Ophthalmology Retina* 2019

# GA Is also Responsible for Vision Loss in Patients with Wet AMD Despite Treatment with Anti-VEGF

- In the Seven-UP study, 98% of wet AMD patients on anti-VEGF therapy developed GA over 7 years of follow up (n=58)[1]
- In the CATT study, 38% of wet AMD patients on anti-VEGF therapy developed GA over 5 years of follow up (n=1024)[2]



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1. Rofagha et al., Ophthalmology 2013
2. Grunwald et al., Ophthalmology 2014

# Key Takeaways

- **GA secondary to AMD is a leading cause of blindness**
- **GA and wet AMD can coexist**
- **There is no treatment for the 5 million people worldwide who have GA**

# Natural History and Unmet Need in GA

Nancy M. Holekamp, M.D.
*Director, Retina Services*
Pepose Vision Institute
St. Louis, MO

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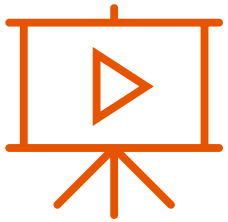

# Video from NIH National Eye Institute

Demonstrates vision with advanced GA

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# GA Causes Loss of Retinal Tissue and Progressive Vision Loss

## VISUAL SYMPTOMS

- Loss of ability to see objects clearly (especially in dim light conditions)
- Straight lines appear to be wavy or distorted
- Loss of color vision
- Dark areas of gray and white spots may appear in the center of vision

NORMAL VISION

VISION WITH ADVANCED GA

Boyer DS, et al. *Retina*. 2017;37(5):819-35.
Holz FG, et al. *Ophthalmology*. 2014;121:1079-91
Images: NIH National Eye Institute video on AMD

# GA Interferes with Essential and Enjoyable Activities

"I can't see cars coming from a distance. I can see when they're near, but that's too late then if you've crossed over"


"Like when I'm getting tablets out, I can look and think, I've only got one and then I'll look again and I've got two … It's difficult to differentiate things"

"I just miss being able to read my books … I mean going into the library and just selecting a book … I've read all my life you know, and I just miss it so much"

"Same when I'm fishing I get so mad with myself at times I should be able to do that and this and I should be able to see that and I can't"



Carlton, J, et al. 2019. *British and Irish Orthoptic Journal*. 2019;1:133-141.

# Apellis and Verana Health Collaboration: IRIS® Registry Natural History Study of ~69,000 GA patients

- **Objective:** To evaluate clinical characteristics and disease progression in patients diagnosed with GA secondary to AMD in real-world clinical practice using the American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight) database

- The IRIS Registry is the world's largest specialty clinical data registry, with >59.99 million unique patients and includes 18,209 clinicians in ophthalmology practice, as of September 1, 2020

| **Cohort 1 – GA:GA** (n=44,120) | | **Cohort 2 – GA:wet AMD** (n=25,321) | |
|---|---|---|---|
| **Study Eye: GA Lesion Location** | | | |
| **1A** | **1B** | **2A** | **2B** |
| Extrafoveal GA **(n=22,791)** | Foveal GA **(n=21,329)** | Extrafoveal GA **(n=12,309)** | Foveal GA **(n=13,012)** |

GA and wet AMD based on report of treating physician per ICD10 codes

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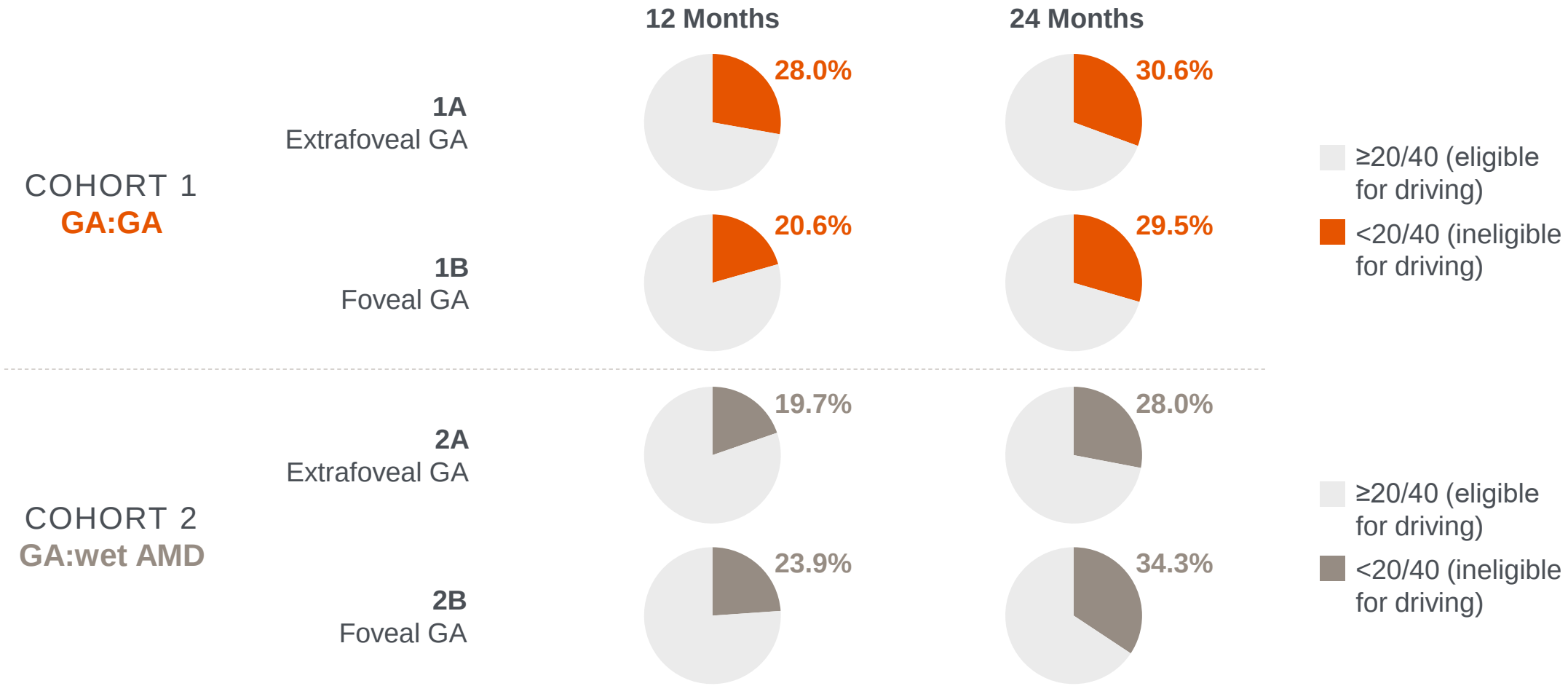
Rahimy E et al. Late-breaking presentation at AAO 2020.

# Up to 1/3 of Study Eyes Progress to Loss of Driving Eligibility in 24 Months

PERCENTAGE WITH STUDY EYE NO LONGER ELIGIBLE FOR DRIVING

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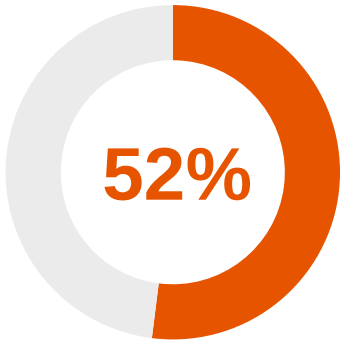
Rahimy E et al. Late-breaking presentation at AAO 2020.

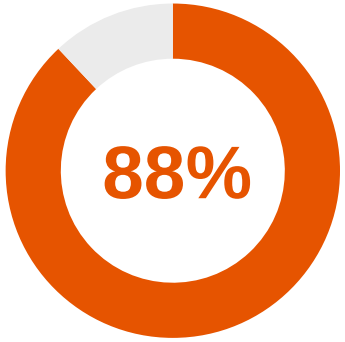
# Patients with GA Reported Problems with Transportation in a Retrospective Burden of Illness Study (n=137)

**Among patients with GA who had a driver's license (n = 76),**

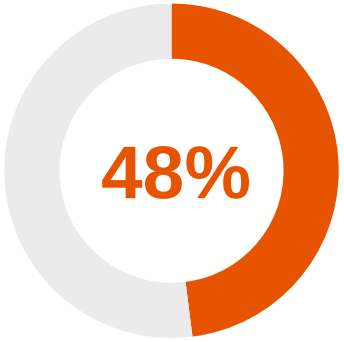



said they did not feel confident driving during the day

AND



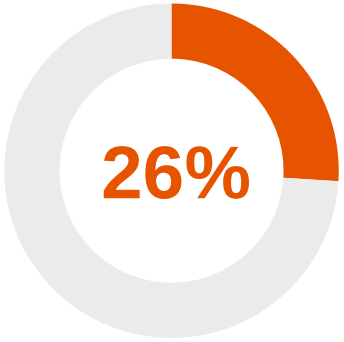

said they did not feel confident driving at night




reported using public transport

AND

**Although 55% had a driver's license, only**




said they drive their own vehicle

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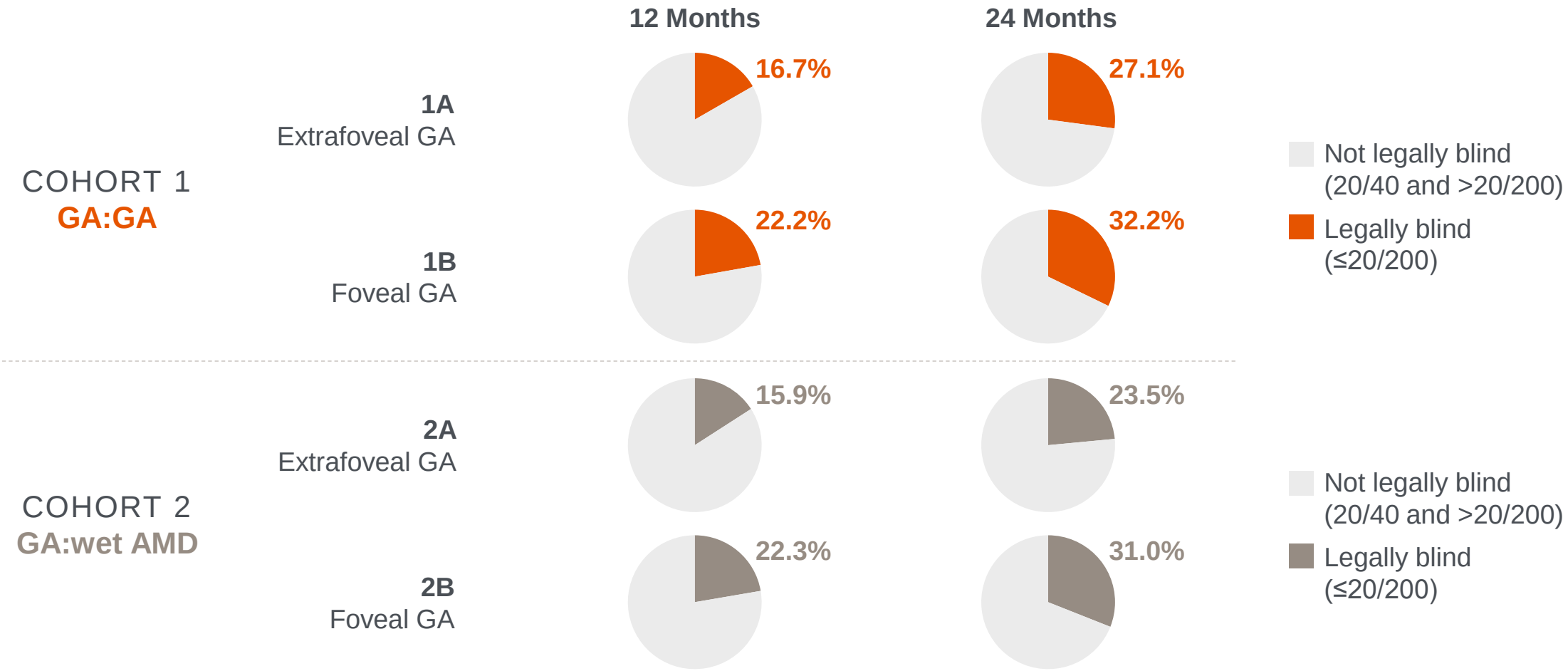
Patel PJ, et al. *Clin Ophthalmol*. 2020;14:15.

# Up to 1/3 of Study Eyes Progress to Legal Blindness in 24 Months

PERCENTAGE WITH STUDY EYE PROGRESSING TO LEGAL BLINDNESS

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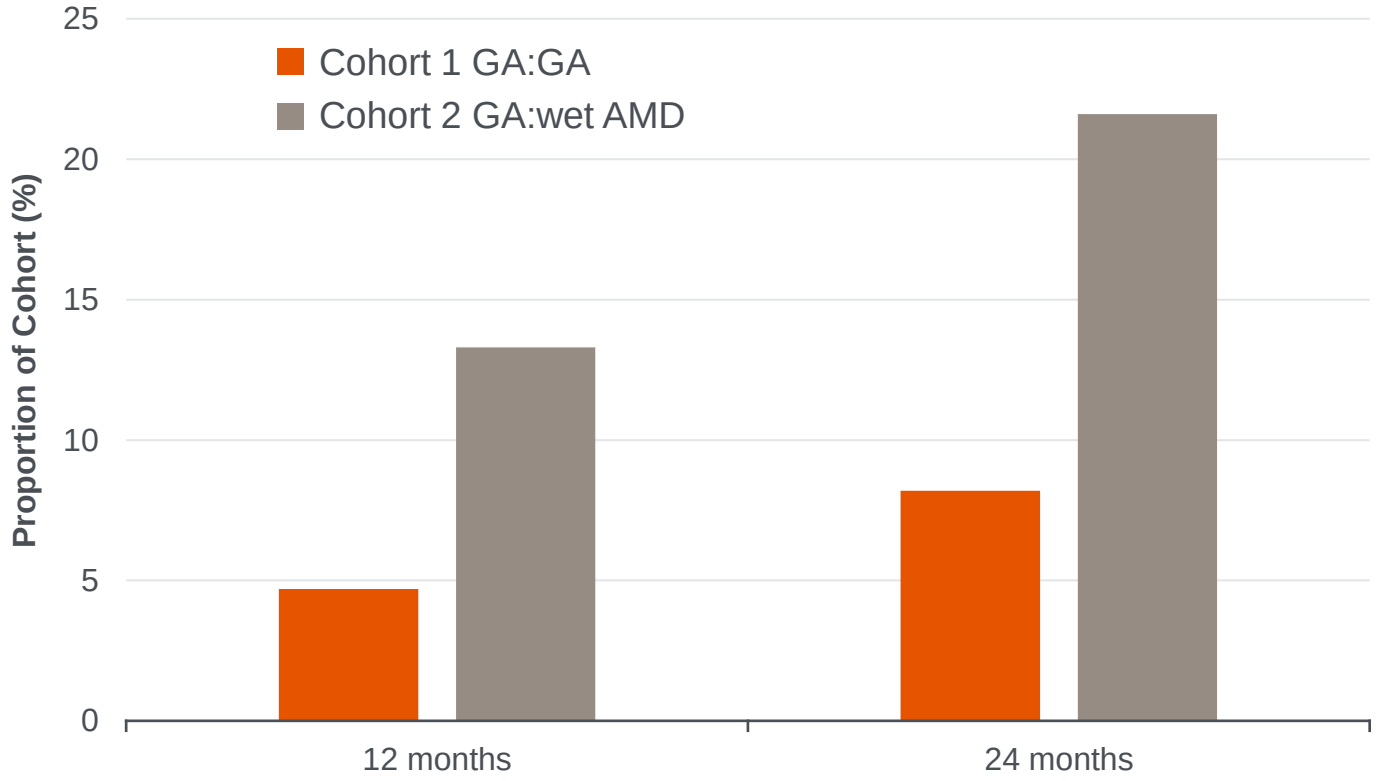
Rahimy E et al. Late-breaking presentation at AAO 2020.

# Wet AMD Is Not a Rare Occurrence in Patients with GA

- Progression from GA to new onset wet AMD was observed in 4.7% of patients with bilateral GA (GA in both eyes) and 13.3% of patients with wet AMD in the contralateral eye during the first 12 months
- The rate at 24 months was 8.2% and 21.6% in bilateral GA and wet AMD in the contralateral eye, respectively




**Patients were nearly three times more likely to develop new-onset wet AMD in an eye with GA when wet AMD had already been detected in the contralateral eye**

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Rahimy E et al. Late-breaking presentation at AAO 2020.
https://investors.apellis.com/news-releases/news-release-details/apellis-announces-late-breaking-presentation-largest

# Key Takeaways

- **GA lesion growth is progressive and irreversible**
- **Wet AMD can occur in GA patients and its occurrence is considerably higher if wet AMD is present in the fellow eye**
- **Many patients lose the ability to drive within two years, and vision-related quality of life is significantly impacted**

**There is significant unmet medical need in patients with GA**

# Role of Complement C3 in AMD

Lukas Scheibler, Ph.D.
*Chief Innovation Officer*
Apellis Pharmaceuticals

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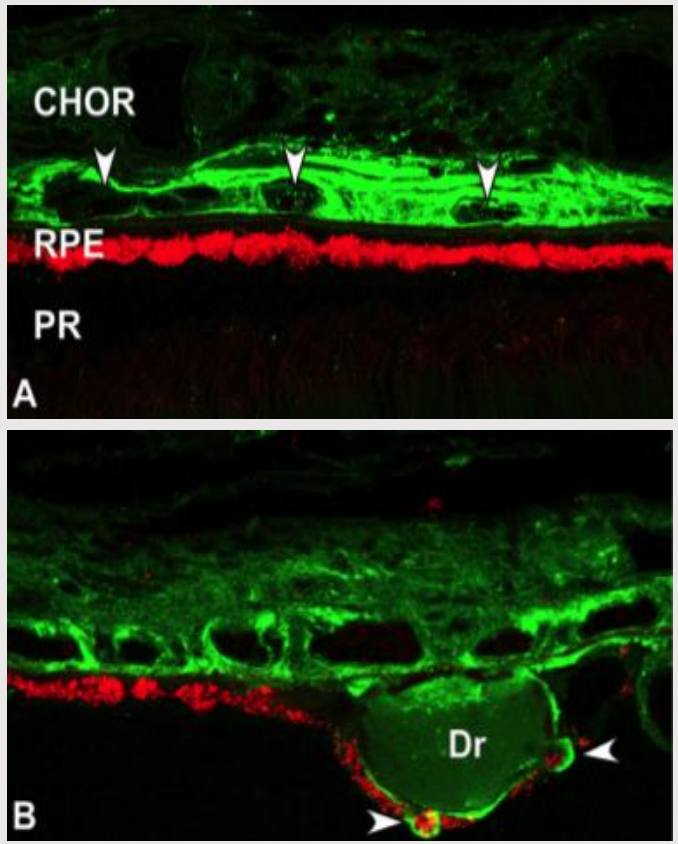
# Excessive Complement Activation and Geographic Atrophy: Key Lines of Evidence

**HISTOLOGICAL:**
Complement proteins in drusen, choroid, and sub-RPE space[1]

**PHYSIOLOGICAL:**
Elevated levels of complement activation products can be observed in the plasma and ocular tissues of patients with AMD[2]

**GENETIC:**
Variants in complement system genes have been implicated in AMD pathogenesis[3,4]




Source: Anderson DH, et al. *Prog Retin Eye Res*. 2010;29(2):95-112.


1. Anderson, DH et al. *Am J Ophthalmol*. 2002;134(3):411-31.
2. Boyer DS, et al. *Retina*. 2017;37(5):819-35.
3. Handa JT, et al. *Nat Commun*. 2019;26;10(1):3347.
4. Fritsche LG, et al. *Nat Genet*. 2016;48(2):134-43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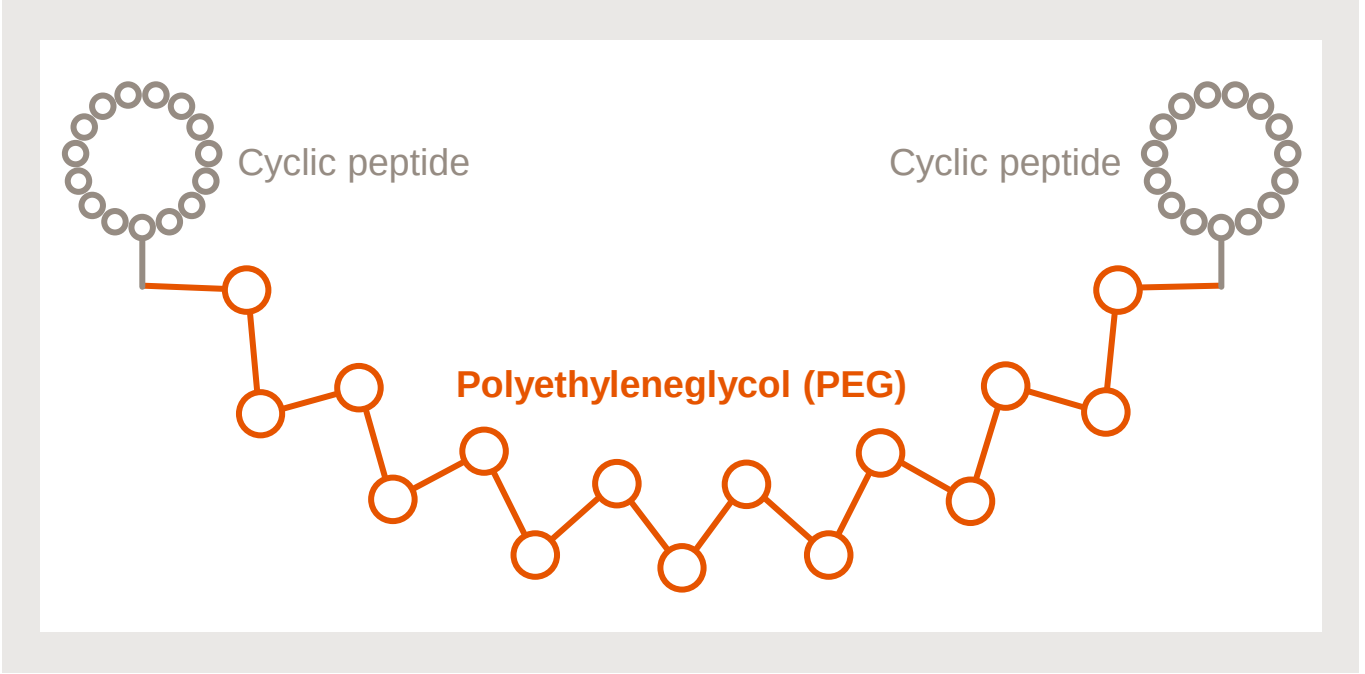
# Pegcetacoplan: Targeted C3 Therapy

Pegcetacoplan is an investigational, targeted C3 therapy designed to regulate the overactivation of complement and improve the standard of care for patients with complement-mediated conditions, including GA[1]

Pegcetacoplan is composed of two 15-amino acid fragment cyclic peptides linked by a PEG molecule[2]

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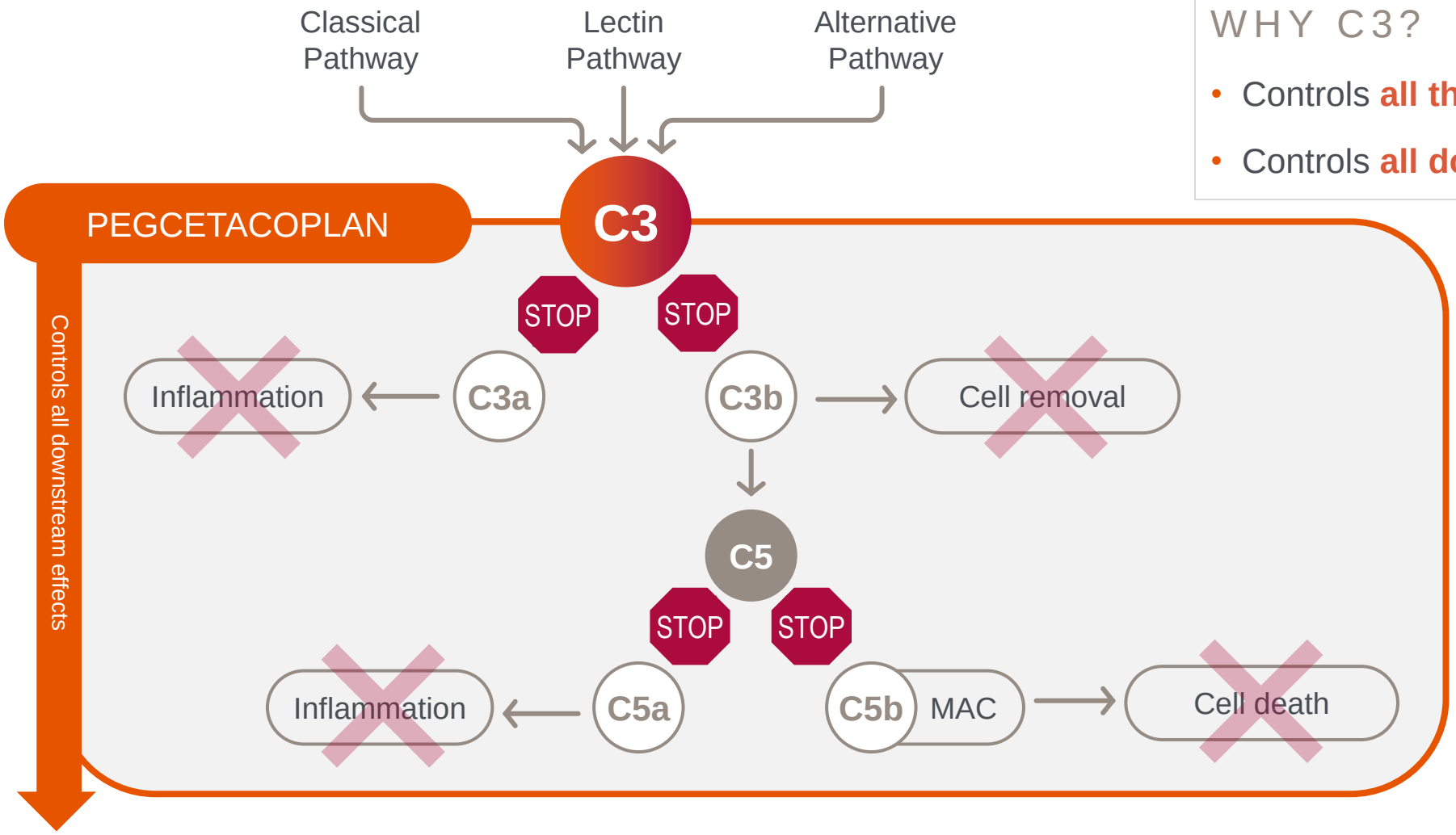
1. Data on file, Apellis Pharmaceuticals. 2. Apellis Pharmaceuticals. Recruiting patients for geography atrophy secondary to AMD. 2019. https://gastudy.com/

# Targeting C3 for Comprehensive Control of Complement




WHY C3?

- Controls **all three** pathways
- Controls **all downstream effects**

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Merle NS, et al. Cell Research. 2010; 20:34-50.

# Pegcetacoplan: Phase 2 FILLY Results

Jeffrey S. Heier, M.D.
*Director, Retina Service and Director, Retinal Research*
Ophthalmic Consultants of Boston

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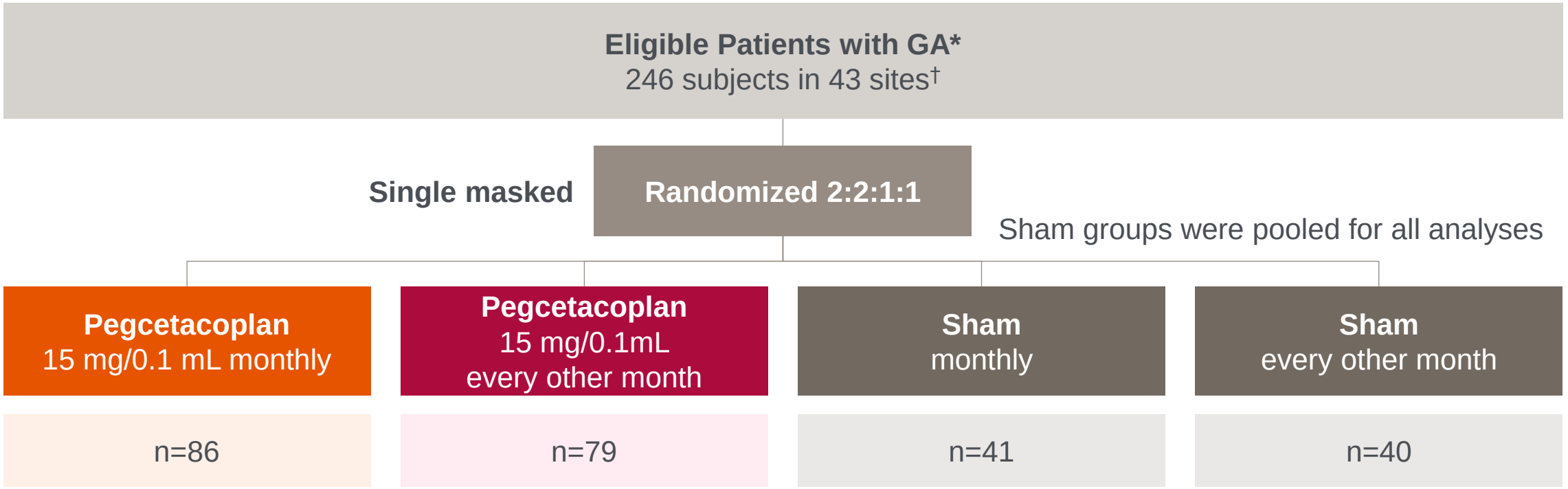
# Phase 2 FILLY Study: Design




**Population:** patients with geographic atrophy* secondary to AMD

**Design:** single masked, randomized 2:1:2:1

**Duration:** 18 months

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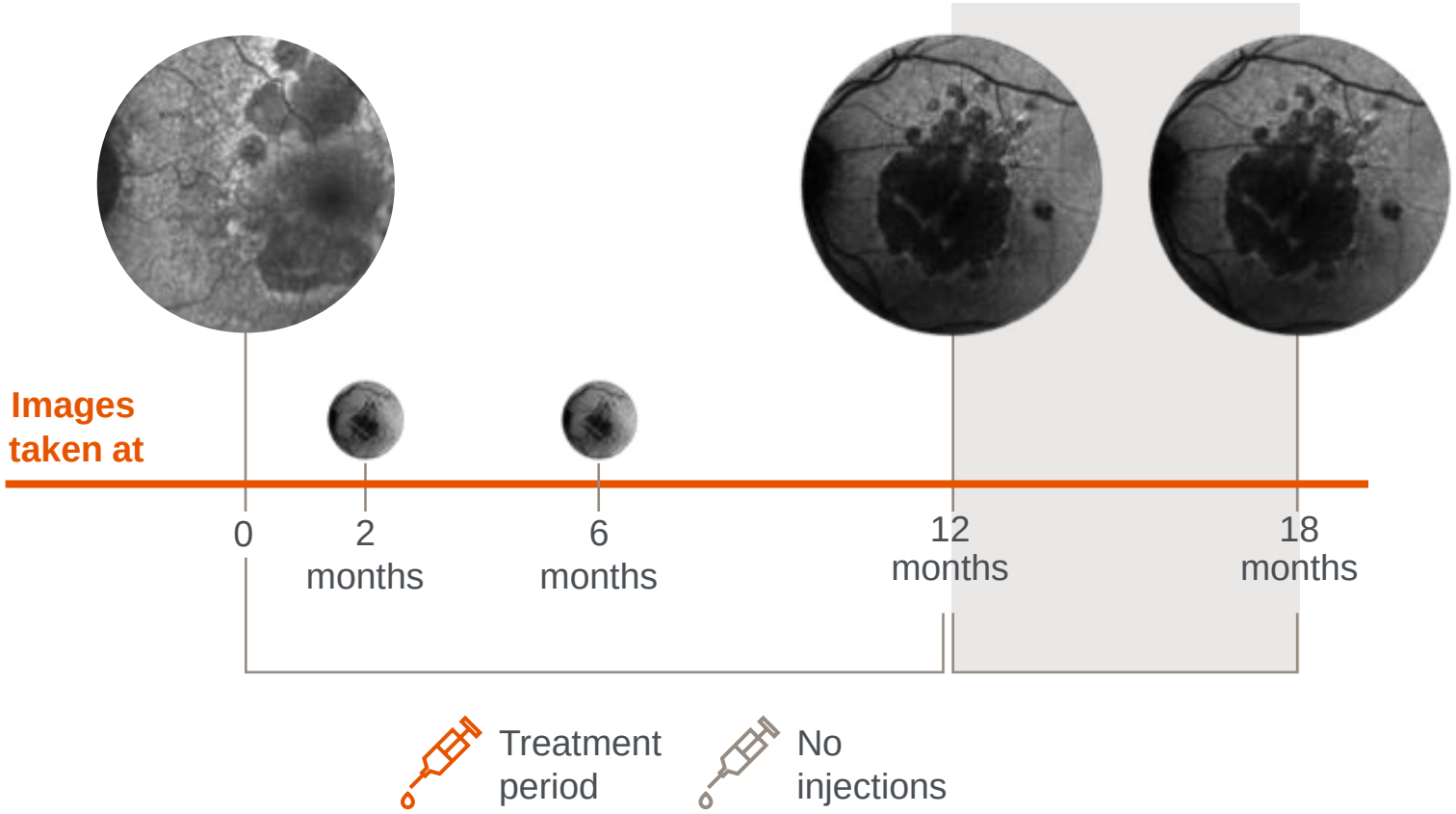
Liao DS, et al. *Ophthalmology*. 2020;127

*Confirmed by the central reading center using fundus autofluorescence images.
†Not counting the 3 satellite sites

# Phase 2 FILLY Study: Timeline and Endpoints




**Primary efficacy endpoint**

Change in geographic atrophy (GA) lesion size from baseline at month 12

**Primary safety endpoint**

Number and severity of local and systemic treatment emergent adverse events (TEAEs)

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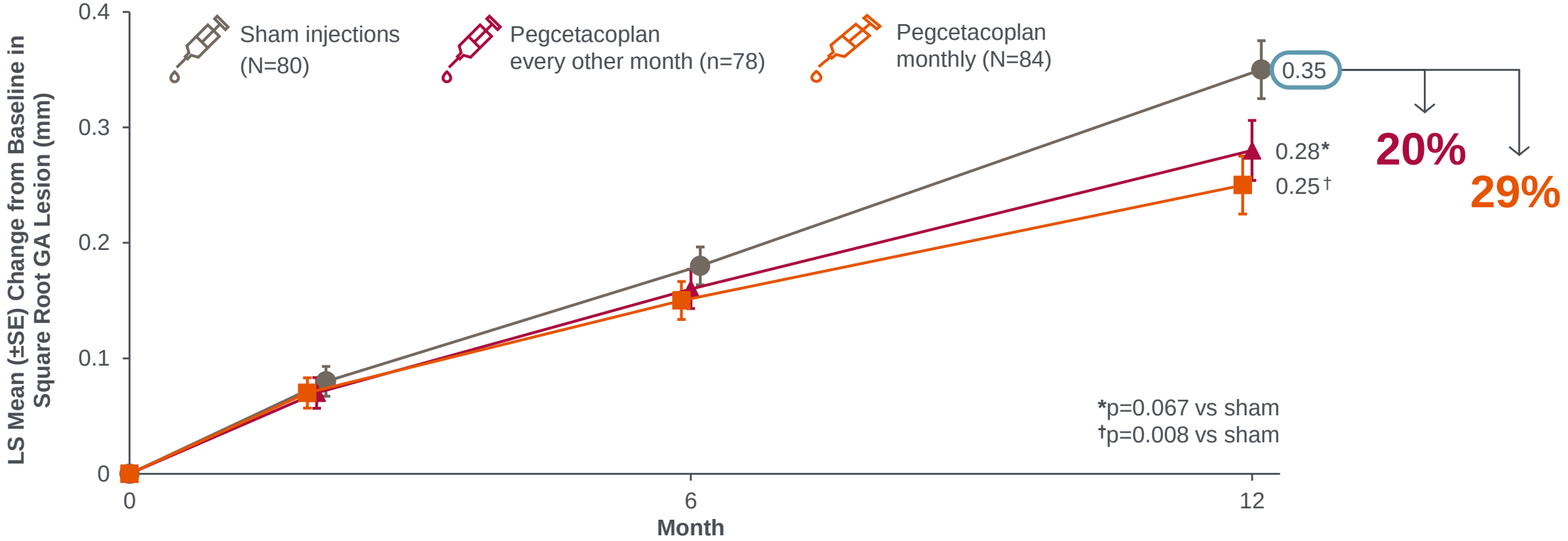
Liao DS, et al. *Ophthalmology*. 2020;127

# Phase 2 FILLY Study: Pegcetacoplan Met Primary Endpoint, Reducing GA Lesion Growth

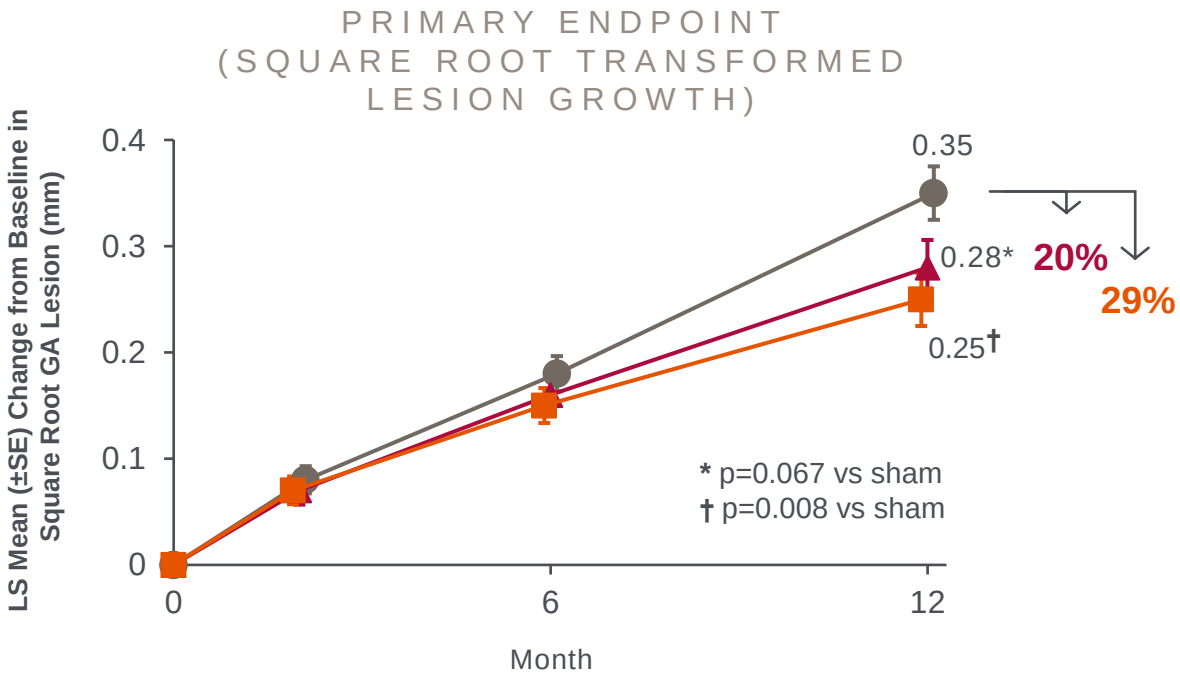


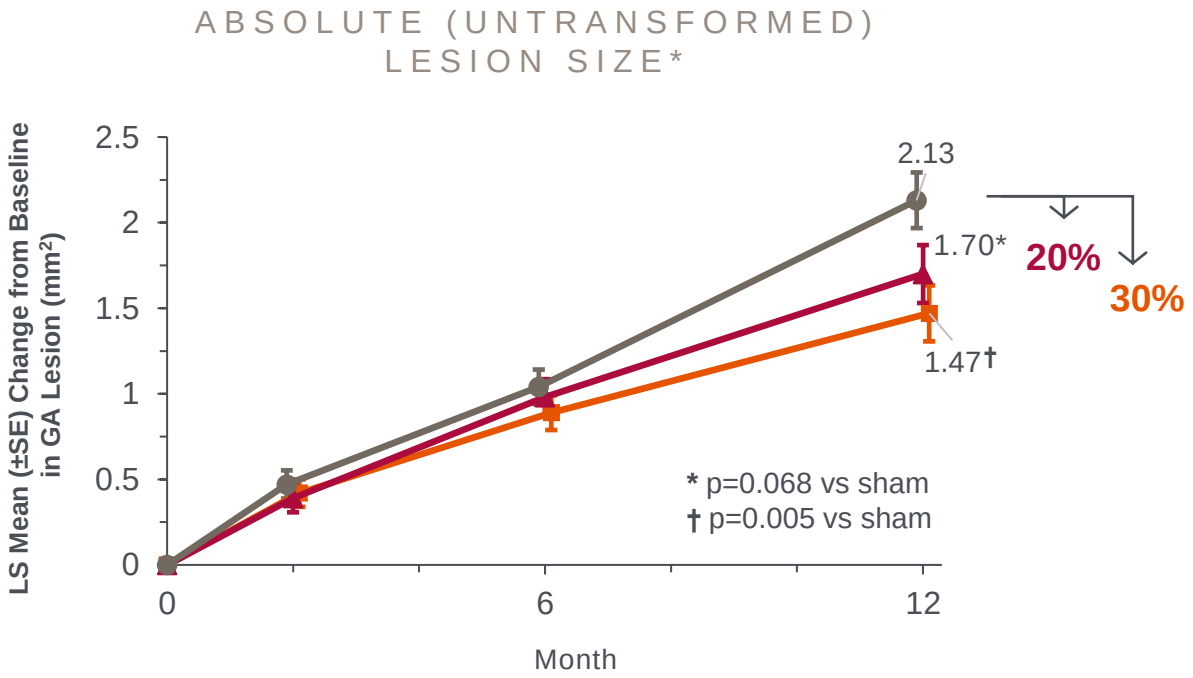

| Chroma and Spectri Phase 3 Trials | |
|---|---|
| Change from baseline in square root of GA area at 48 wk, mm | **Sham Pooled (n=598)** |
| Adjusted mean (SE) | 0.342 (0.007) |

*,†Square root. Modified intention-to-treat (mITT) population was used for the efficacy analysis; defined as all patients who received at least 1 injection and underwent at least 1 follow-up examination at month 2 or later at which primary efficacy data were collected. 2-sided t tests at the alpha = 0.1 level

Liao DS, et al. Ophthalmology. 2020;127:186-95. Holz et al. JAMA Ophthalmol. 2018

# Phase 2 FILLY: Impact of Pegcetacoplan on Absolute GA Lesion Growth Is Consistent with the Primary Endpoint




Sham injections (N=80)

Pegcetacoplan every other month (n=78)

Pegcetacoplan monthly (N=84)

*Post hoc analysis

**mITT, Observed, Mixed-Effect Model**

A mixed effect model with main effects of treatment, visit and GA lesion at baseline, and interactions of treatment × visit, visit × baseline.

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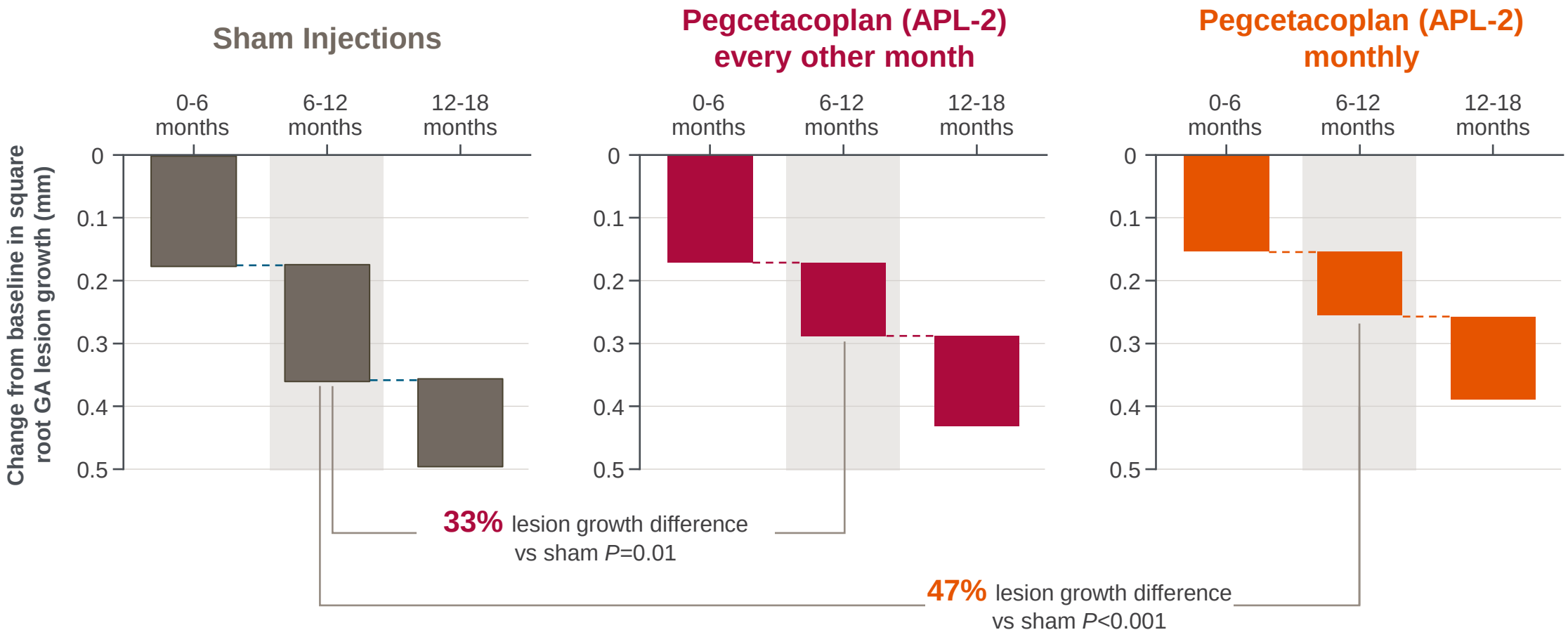
M12DBL Data

# FILLY Post Hoc Analysis of Lesion Growth by 6-Month Periods – Increasing Effect Size with Longer Duration of Treatment




Data from subjects with a measurable GA lesion size at Months 6, 12, and 18.

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Liao DS, et al. Ophthalmology. 2020;127:186-95
Data on file

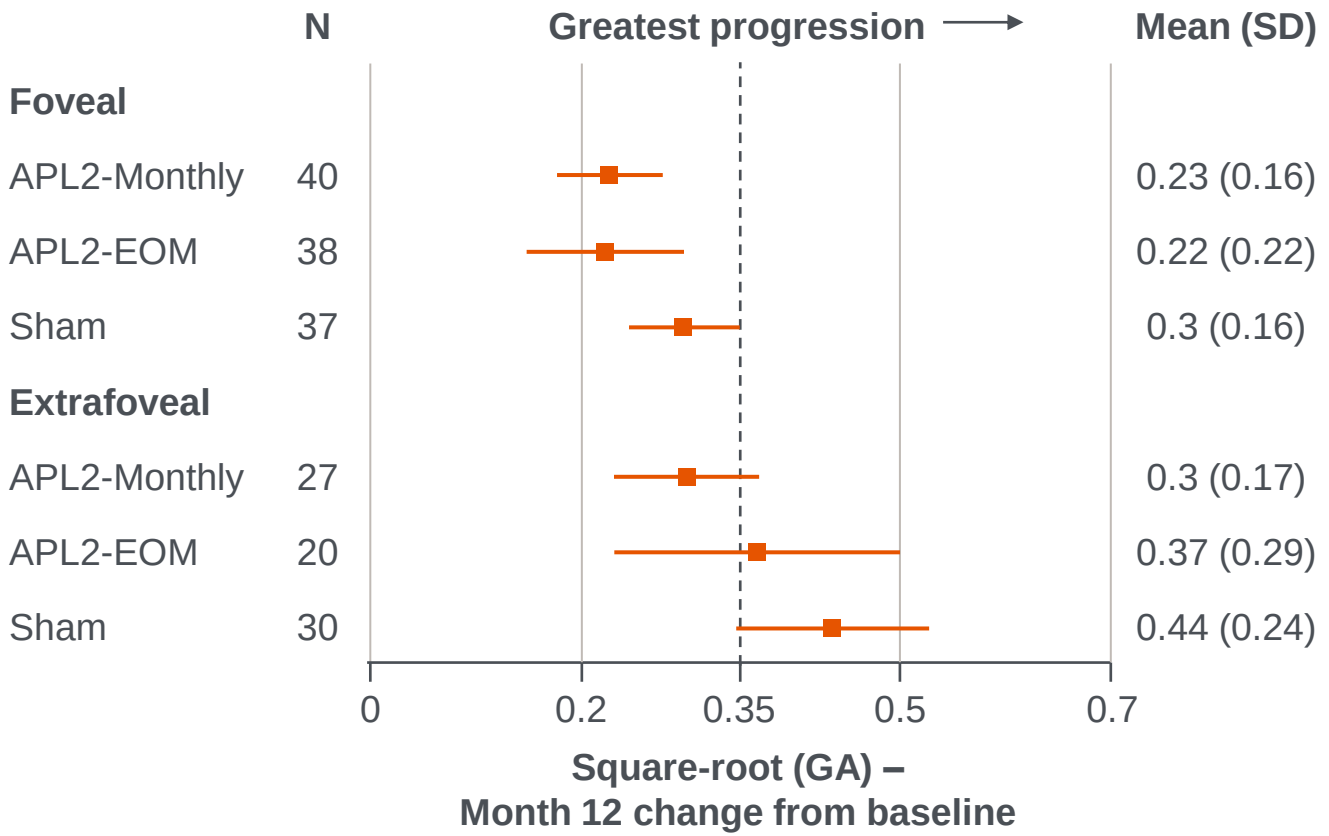
# FILLY Post Hoc Multivariate Analysis

## OBJECTIVE

- Post hoc analysis of FILLY to examine efficacy of pegcetacoplan across subgroups; to determine risk factors that predicted GA progression, and whether the efficacy of pegcetacoplan remained significant after adjusting for these risk factors

## RESULTS

- Efficacy of pegcetacoplan was consistent across subgroups
- Risk factors identified as predictors of GA progression in the FILLY study were in line with those described in the literature
- **Treatment effect of pegcetacoplan remained significant when population was controlled for these key risk factors**

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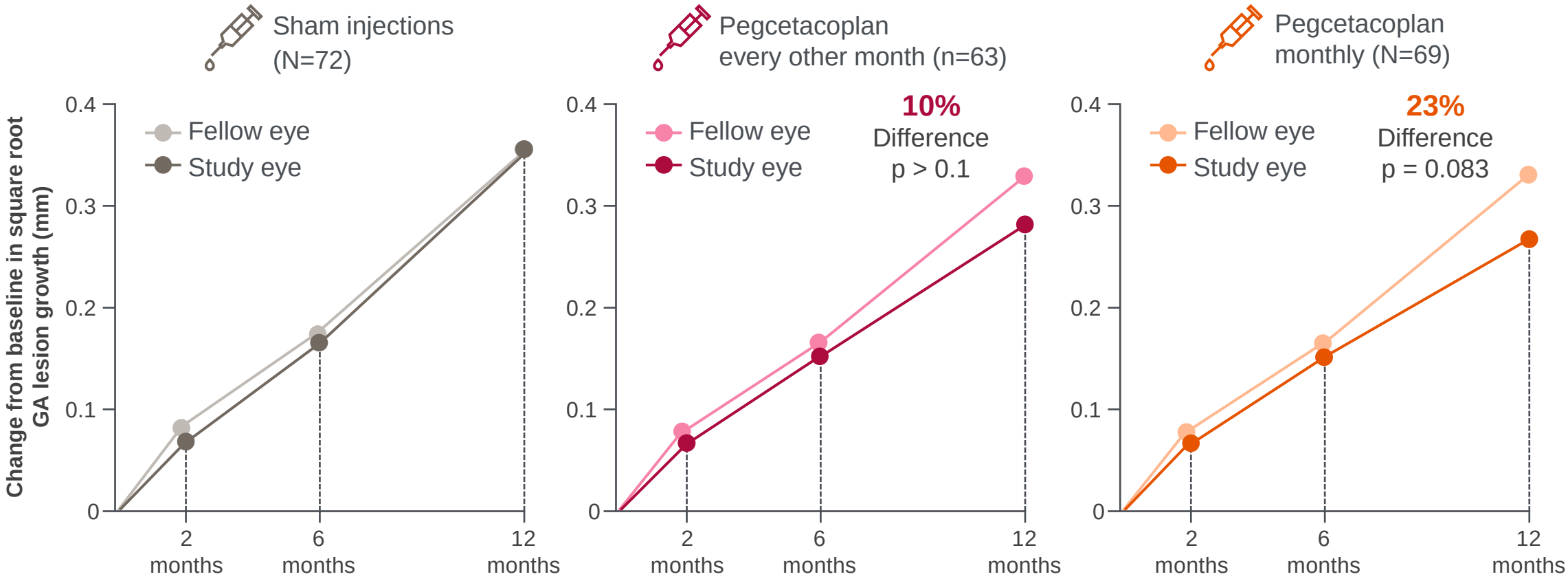
Steinle et al., ARVO 2019. Submitted for publication.

# Phase 2 FILLY Post Hoc Analysis: Decreased Lesion Growth in Treated Eye vs. Untreated Fellow Eye




Liao DS, et al. Ophthalmology. 2020;127:186-95.
Data on file.

# Phase 2 FILLY Study: Safety

- Exudations at 12 Months (treatment period):
  - 16% monthly, 6% every-other-month, 1% sham*
  - 0 cases of classical CNV
  - No clinically significant impact on vision
  - Most treated with anti-VEGF therapy
- Safety in line with other studies of intravitreally administered agents
- Serious adverse events in the study eye were reported in 4 of 86 (4.7%), 2 of 79 (2.5%), and 1 of 81 (1.2%) of patients in the pegcetacoplan monthly, pegcetacoplan every-other-month, and sham groups, respectively.

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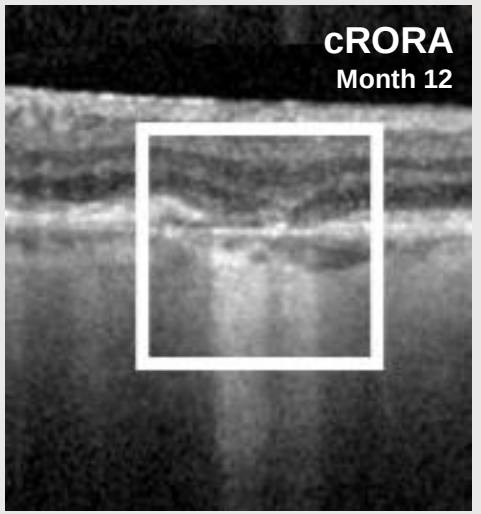
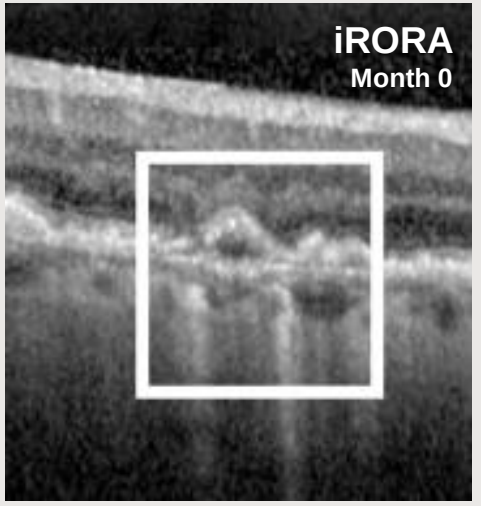
Liao DS, et al. Ophthalmology. 2020;127:186-95.
* Data on file

# Earlier Endpoints for Retinal Atrophy

- Therapeutic trials for geographic atrophy are focused on the end-stage (**complete** RPE and outer retinal atrophy or **cRORA**); e.g., GA lesions

- Earlier endpoints in the atrophy pathway have been defined: incomplete RPE and outer retinal atrophy (**iRORA**); e.g., consistent with intermediate AMD




iRORA: incomplete RPE and outer retinal atrophy; cRORA: complete RPE and outer retinal atrophy; RPE: retinal pigment epithelium
Sadda et al., EURETINA 2020 late-breaking presentation.

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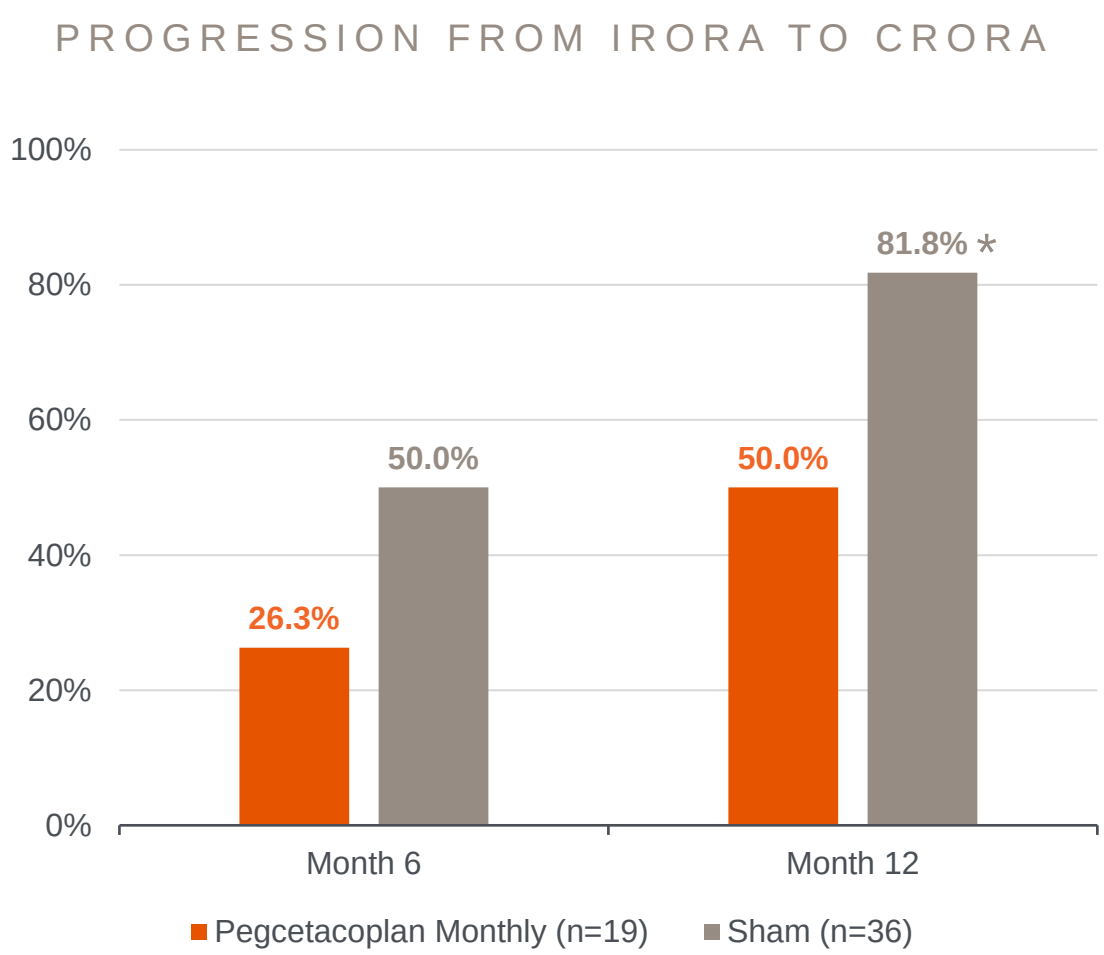
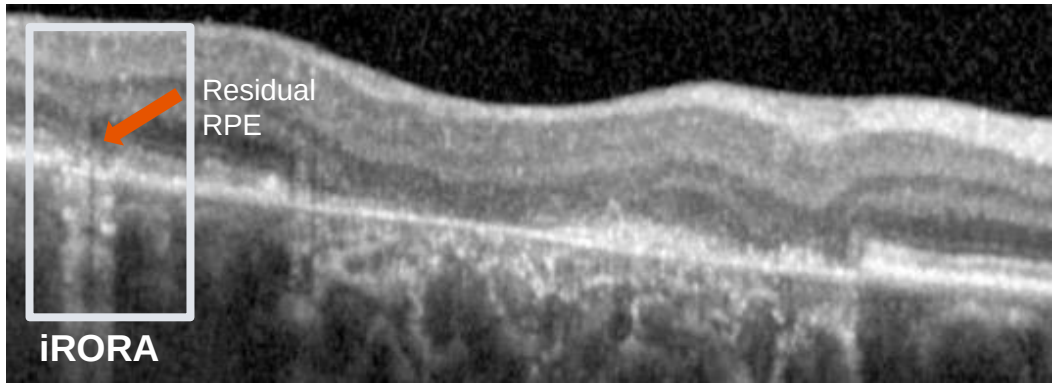
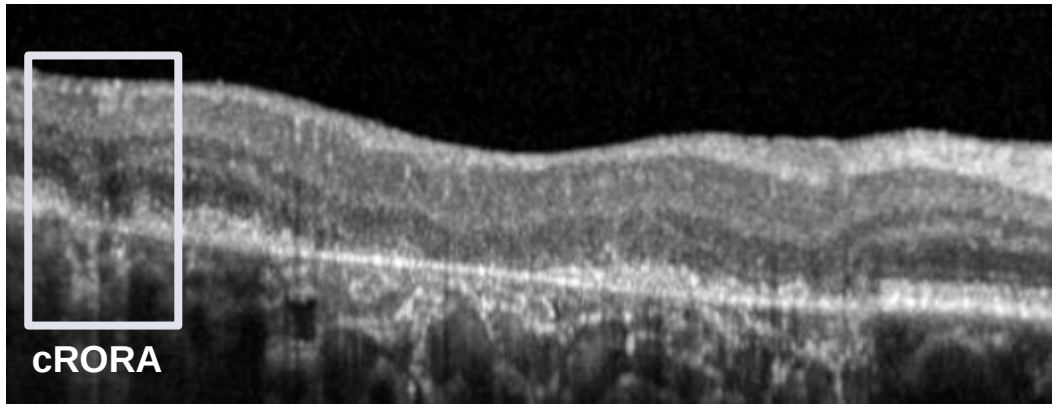
# Phase 2 FILLY Post Hoc Analysis: Pegcetacoplan Slowed Progression from Intermediate AMD to GA




**Pearson Chi-Square:**
Month 6 - P=0.08; *Month 12 - P=0.02
**Relative risk:**
Month 12 - 0.61 (0.37- 1.00)

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Sadda et al., EURETINA 2020 late-breaking presentation.

# Key Takeaways: Pegcetacoplan in GA

- **Phase 2 FILLY study met primary endpoint, reducing GA lesion growth, with benefit across GA phenotypes**
- **Demonstrated a dose response with sham group progressing at expected rate**
- **Effect in treated eye vs. contralateral eye**
- **Slowed progression from intermediate AMD to GA; potential for earlier intervention in course of GA**
- **Safety in line with other studies of intravitreally administered agents**

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# Pegcetacoplan: Phase 3 DERBY and OAKS Studies

Jeffrey Eisele, Ph.D.
*Local Chronic Program Lead*
Apellis Pharmaceuticals

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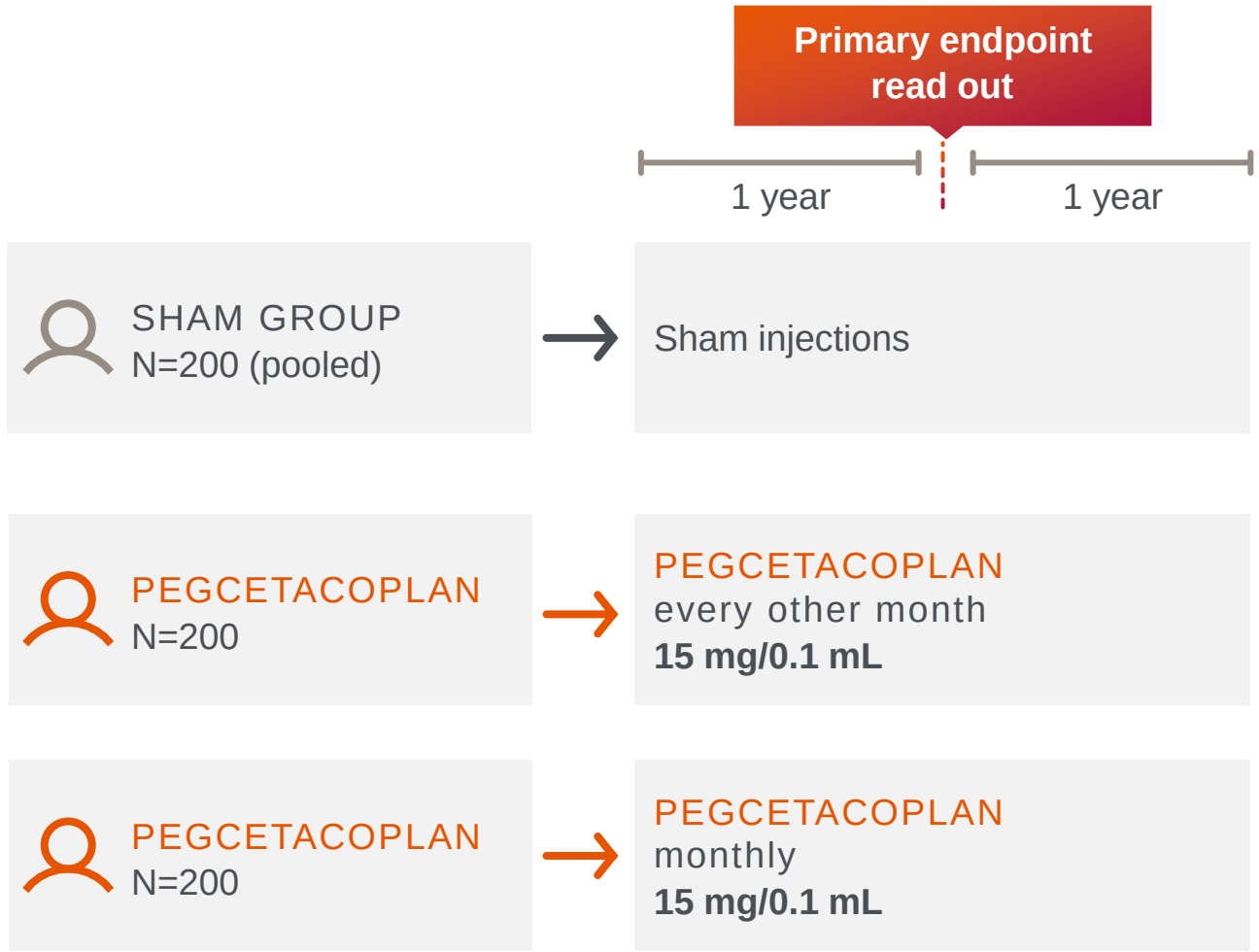
# DERBY and OAKS: Two Phase 3 Studies Enrolled (n=1,256) with Top-line Results Expected in Q3 2021




*Same study population and trial design as FILLY*

**Population:** patients with geographic atrophy secondary to AMD

**Primary endpoint:** change in total area of GA lesion(s) based on Fundus Autofluorescence (FAF) at month 12

**Design:** double masked, randomized 2:1:2:1

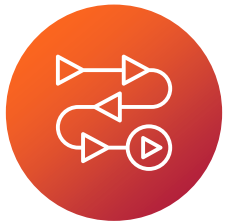
**Treatment:** 15 mg/0.1 mL intravitreal injection vs. sham injection

**Sample size:** >600 subjects from approx. 100 multinational sites per study

**Duration:** 2 years

Apellis NCT03525600, NCT03525613

# DERBY and OAKS: Key Efficacy Endpoints



## PRIMARY

- Change from baseline to Month 12 in total area of GA lesion(s) in the study eye (in $mm^2$) based on FAF

## SECONDARY

- BCVA, LL-BCVA, low-luminance deficit
- Reading speed
- Microperimetry (OAKS study only*) — Macular Integrity Assessment (MAIA) device
- National Eye Institute Visual Functioning Questionnaire 25-Item Version (NEI VFQ-25)
- Functional Reading Independence Index (FRI) composite score

*Subjects must meet following criteria: (a) able to detect fixation target, (b) total elapsed time to complete 68-point exam <30 min, (c) reliability test ratio <20%, (d) willing and able to undertake microperimetry in investigator's opinion.
BCVA=best-corrected visual acuity; FAF=fundus autofluorescence; LL-BCVA=low-luminance BCVA.
NCT03525600, NCT03525613

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# Key Changes from FILLY to DERBY and OAKS

| PARAMETER | FILLY | DERBY AND OAKS | RATIONALE/IMPACT |
|---|---|---|---|
| **Primary endpoint** | Change in lesion size (square root transformed) | Absolute change in lesion size | Followed recommendation from FDA. FILLY absolute change was consistent with square root |
| **Study masking** | Single masked | Double masked | Further minimize potential for bias |
| **Assessment** | Months 0, 2, 6, 12 | Months 0, 2, 4, 6, 8, 10, 12 | Additional data points to better evaluate primary endpoint |
| **Handling of exudations** | Anti-VEGF initiated; pegcetacoplan discontinued | Anti-VEGF initiated; pegcetacoplan treatment continues | Decrease the amount of study treatment discontinuation |

# Why Do We Believe DERBY and OAKS Will Be Successful?

**FILLY results are robust: Same study population and core design as the FILLY trial**

- All sensitivity analyses in FILLY confirmed the efficacy profile
- Conservative approaches to managing missing data maintained treatment effect

**Implemented learnings from FILLY to improve DERBY and OAKS study designs**

- Patients who develop exudative AMD will stay in the study receiving pegcetacoplan and anti-VEGF

**Study masking and confirmation of exudation by reading center may reduce potential for bias in diagnosis of exudation**

**Strategy to mitigate impact of missed injections due to COVID-19; studies still well powered for primary endpoint**

# DERBY and OAKS: Key Takeaways

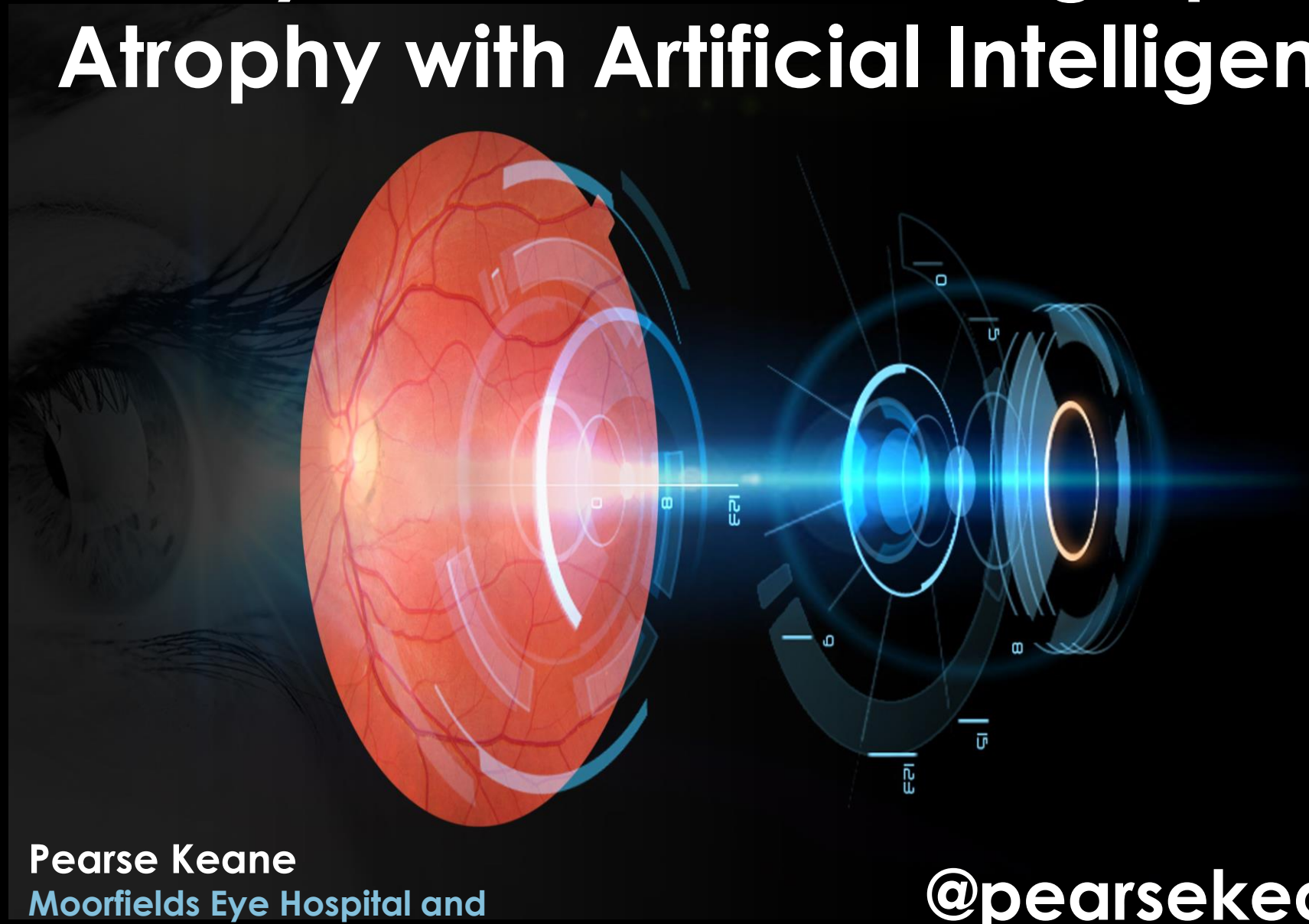
**Broad GA patient population reflective of real-world GA patients**

- Fellow eye neovascular AMD allowed
- Extrafoveal and foveal GA lesions allowed

**Same study population and design as the FILLY trial**

**Top-line results expected Q3 2021**

# Early Detection of Geographic Atrophy with Artificial Intelligence



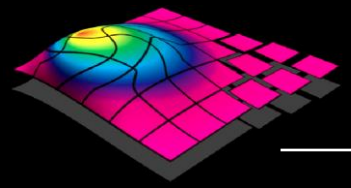
**Pearse Keane**
Moorfields Eye Hospital and
UCL Institute of Ophthalmology

@pearsekeane

# My Background

*Consultant Ophthalmologist*

*Associate Professor*



# “Deep Learning”

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THE SCIENCES

## World Changing Ideas 2015

10 big advances that will improve life, transform computing and maybe even save the planet

By THE EDITORS on December 1, 2015

***https://www.scientificamerican.com/report/world-changing-ideas-20151/***

# July 2016

Moorfields Eye Hospital NHS
NHS Foundation Trust

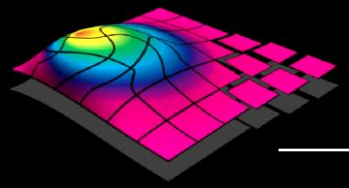
DeepMind

# August 2018



*Fauw, J. D. et al. Clinically applicable deep learning for diagnosis and referral in retinal disease. Nat Med 24, 1342–1350 (2018).*

# Why I'm passionate about helping to cure AMD



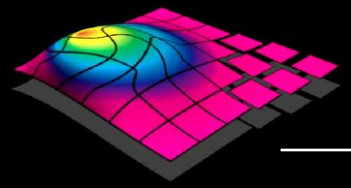
Clinical science

## Prevalence and incidence of age-related macular degeneration in Europe: a systematic review and meta-analysis

Jeany Q Li ,[1] Thomas Welchowski,[2] Matthias Schmid,[2] Matthias Marten Mauschitz,[1] Frank G Holz,[1] Robert P Finger[1]

**~25% of people aged >60 years estimated to have early or intermediate AMD!!!**

*Li, J. Q. et al. Prevalence and incidence of age-related macular degeneration in Europe: a systematic review and meta-analysis. Brit J Ophthalmol (2020)*



# The One Fact?

***"There is no treatment for "dry" AMD"***

# An Opportunity?


MyAOP log in Subscribe | AOP website

al support

ECSA

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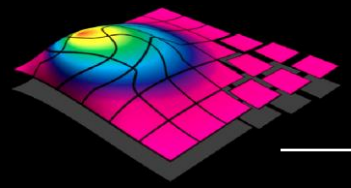
ve

the machine in store.


May 2017



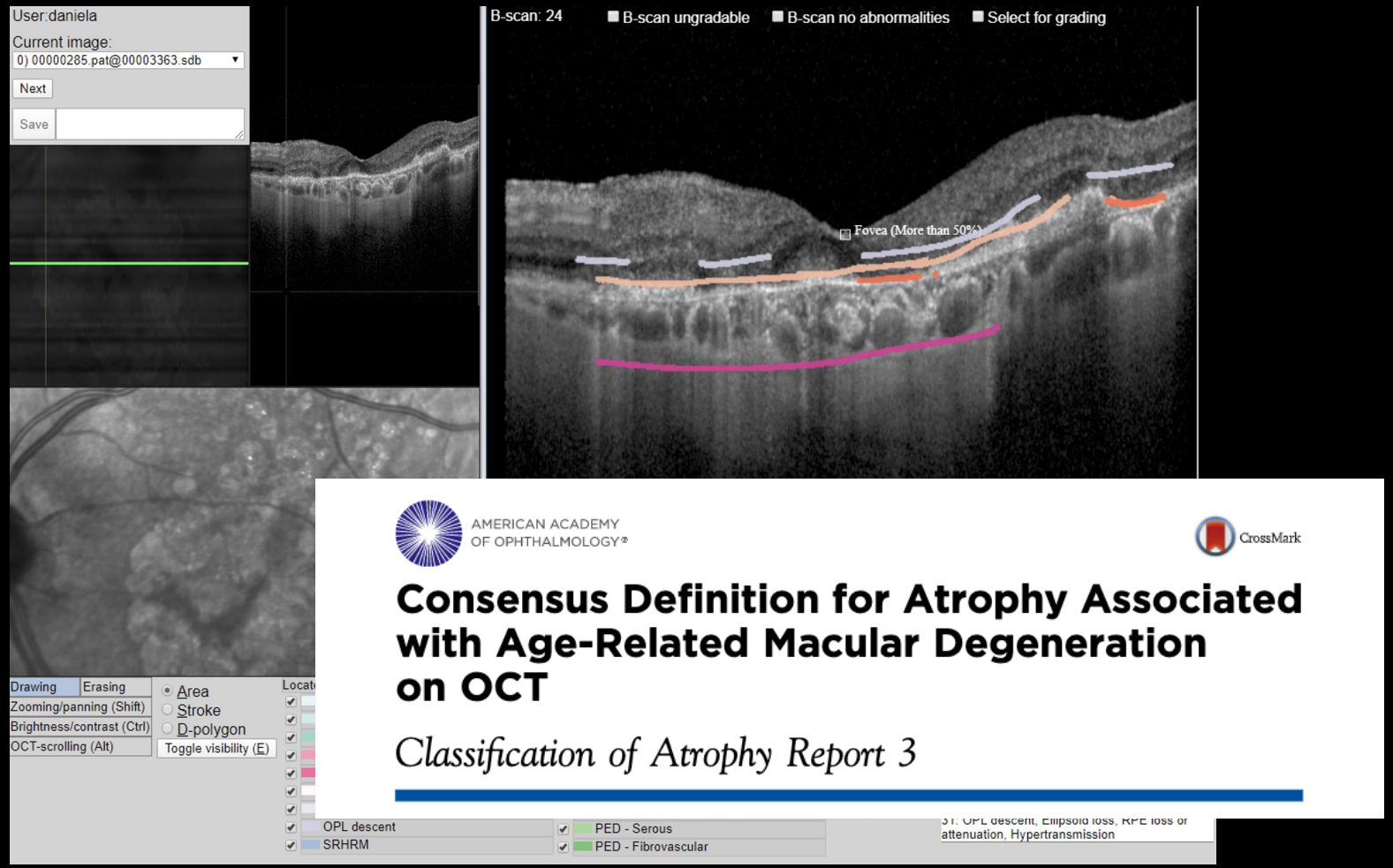
# Aim

# Dataset - Development


**984 OCT volumes - 399 eyes - 200 patients**

*Jaffe, G. J. et al. C5 Inhibitor Avacincaptad Pegol for Geographic Atrophy Due to Age-Related Macular Degeneration: A Randomized Pivotal Phase 2/3 Trial. Ophthalmology (2020) doi:10.1016/j.ophtha.2020.08.027.*

# Labelling Strategy




AMERICAN ACADEMY OF OPHTHALMOLOGY®

CrossMark

**Consensus Definition for Atrophy Associated with Age-Related Macular Degeneration on OCT**

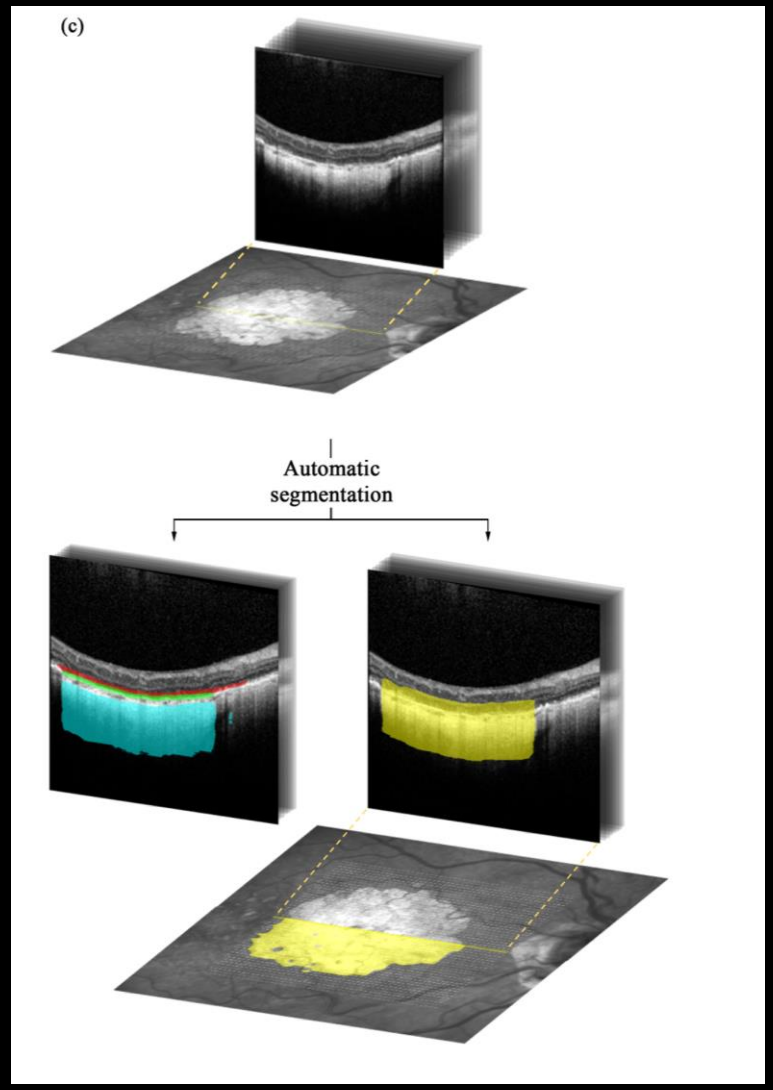
*Classification of Atrophy Report 3*

*Sadda, S. R. et al. Consensus Definition for Atrophy Associated with Age-Related Macular Degeneration on OCT: Classification of Atrophy Report 3. Ophthalmology, (2017).*

# Dataset - external validation


**192 OCT volumes - 192 eyes - 110 patients**

# Image Reconstruction




***Area (mm2)***

# Key Results

| | Internal validation dataset | | | | | External validation dataset All | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Model vs. Consensus grading | | | | | Model vs. Consensus grading | | | | | Human grader 1 vs. Human grader 2 | | | |
| | n | DSC Median | DSC Mean | DSC SD | ICC | n | DSC Median | DSC Mean | DSC SD | ICC | n | DSC Median | DSC Mean | DSC SD | ICC |
| **Geographic atrophy** | | | | | | | | | | | | | | | |
| Approach 1 | 988 | 0.84 | 0.75 | 0.24 | 0.62 | 713 | 0.96 | 0.91 | 0.15 | 0.93 | 806 | 0.80 | 0.69 | 0.30 | 0.79 |
| Approach 2 | 988 | 0.83 | 0.75 | 0.25 | 0.66 | 713 | 0.95 | 0.87 | 0.20 | 0.89 | - | - | - | - | - |
| **GA only** | | | | | | | | | | | | | | | |
| Approach 1 | | | | | | 600 | 0.96 | 0.92 | 0.14 | 0.94 | 657 | 0.75 | 0.59 | 0.38 | 0.78 |
| Approach 2 | | | | | | 600 | 0.96 | 0.89 | 0.18 | 0.91 | - | - | - | - | - |
| **Other retinal pathologies** | | | | | | | | | | | | | | | |
| Approach 1 | | | | | | 113 | 0.93 | 0.86 | 0.17 | 0.89 | 149 | 0.80 | 0.69 | 0.30 | 0.72 |
| Approach 2 | | | | | | 113 | 0.85 | 0.77 | 0.25 | 0.83 | - | - | - | - | - |

# First Manuscript

## TITLE PAGE

**Title** Development and validation of a clinically applicable deep-learning model for detection and quantification of Geographic Atrophy from three-dimensional Optical Coherence Tomography scans


**Author listing**

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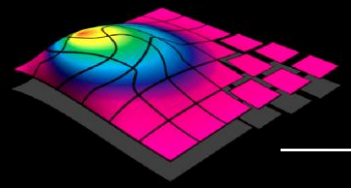
***Under Review**



# Next Steps?

***Structure-Function***

***Fast Progressors?!***

# From Code to Clinic?



p.keane@ucl.ac.uk

**THANK YOU**

*to our presenters!*

Apellis

# Key Misconceptions We Addressed Today

**“Other complement inhibitors have failed. Why should pegcetacoplan work?”**

We believe that GA is the consequence of a failure to clean up C3 deposition in the retina.

↓

Single pathway inhibitors are insufficient to correct this failure.

↓

Pegcetacoplan, a targeted C3 therapy, has the potential to accomplish this with its broad, multi-point control of complement across all three pathways.

**“Pegcetacoplan has no impact on visual acuity. It will take years to notice a difference. Why would people take this drug?”**

- Visual acuity charts don't reflect the real impact of GA in vision due to foveal sparing.
- GA is a relentless, progressive disease that severely impairs patients’ visual function and quality of life.
- A leading cause of blindness, GA has no approved treatments and remains the most significant unmet need in the retina.
- The need and desire for treatment was reflected in the speed of enrollment in DERBY and OAKS.

# Key Misconceptions We Addressed Today

**“How can we trust the FILLY data?”**

- The FILLY study met its primary endpoint, demonstrated a dose response, and the sham group progressed at the expected rate.
- Dropouts were in line with other GA trials. 242 out of 246 patients (modified intent-to-treat: mITT) were included in the primary analysis population, which accounted for missing data with the well-established mixed-effect model for repeated measures (MMRM).
- All sensitivity analyses confirmed the efficacy profile.
- Post hoc analyses also showed that lesion growth slowed in treated eyes vs. contralateral eyes in patients with bilateral GA and that pegcetacoplan slowed progression from intermediate AMD to GA.

**“FILLY had safety issues. Pegcetacoplan causes ‘wet AMD' and had two cases of infectious endophthalmitis.”**

- The FILLY trial had no safety findings that limited DERBY and OAKS, which studies the same broad patient population.
- Exudations are an expected occurrence in GA. No classical CNV was detected and there was no clinically significant impact on vision.
- FILLY was single-masked, which may have led to greater reporting of exudations in subjects randomized to pegcetacoplan than in subjects randomized to sham. DERBY and OAKS are double masked to further minimize potential bias.
- Two cases of infectious endophthalmitis out of ~1,500 intravitreal injections are consistent with reported incidence rates in published studies involving intravitreal injection.

# Q&A

Apellis

# Apellis: Global Leader in Complement

| OUR STRATEGY | 2021 KEY MILESTONES |
| --- | --- |
| Establish systemic pegcetacoplan as a **disruptive therapy** across rare, complement-driven diseases | **PNH launch in H1 2021** and progress 4 additional registrational programs |
| Be **#1** in the **retina** | **Phase 3 GA results in Q3 2021** a blockbuster opportunity |
| Develop **new technologies** to control complement | **Advance 3 compounds into clinical development** in the next 24 months |

**Focused on compassion and commitment to patients**

Apellis

# Pegcetacoplan: Advancing the First Potential Treatment for Geographic Atrophy (GA)

Virtual Investor Event

January 28, 2021