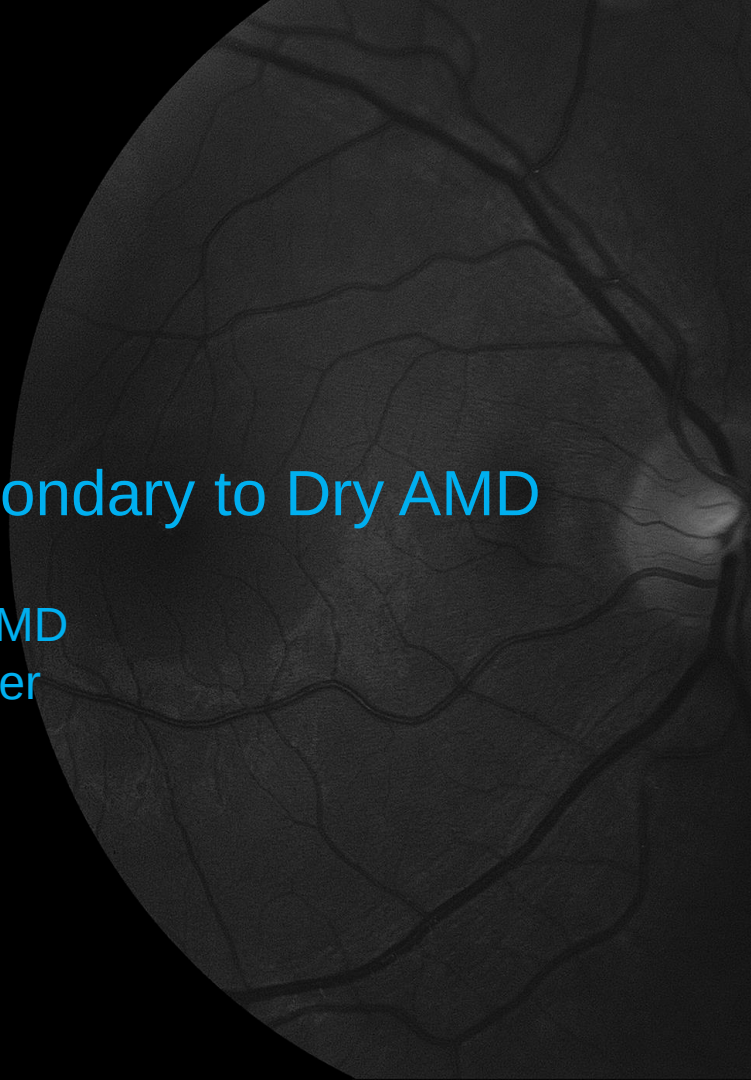
Zimura Pivotal Program in GA Secondary to Dry AMD

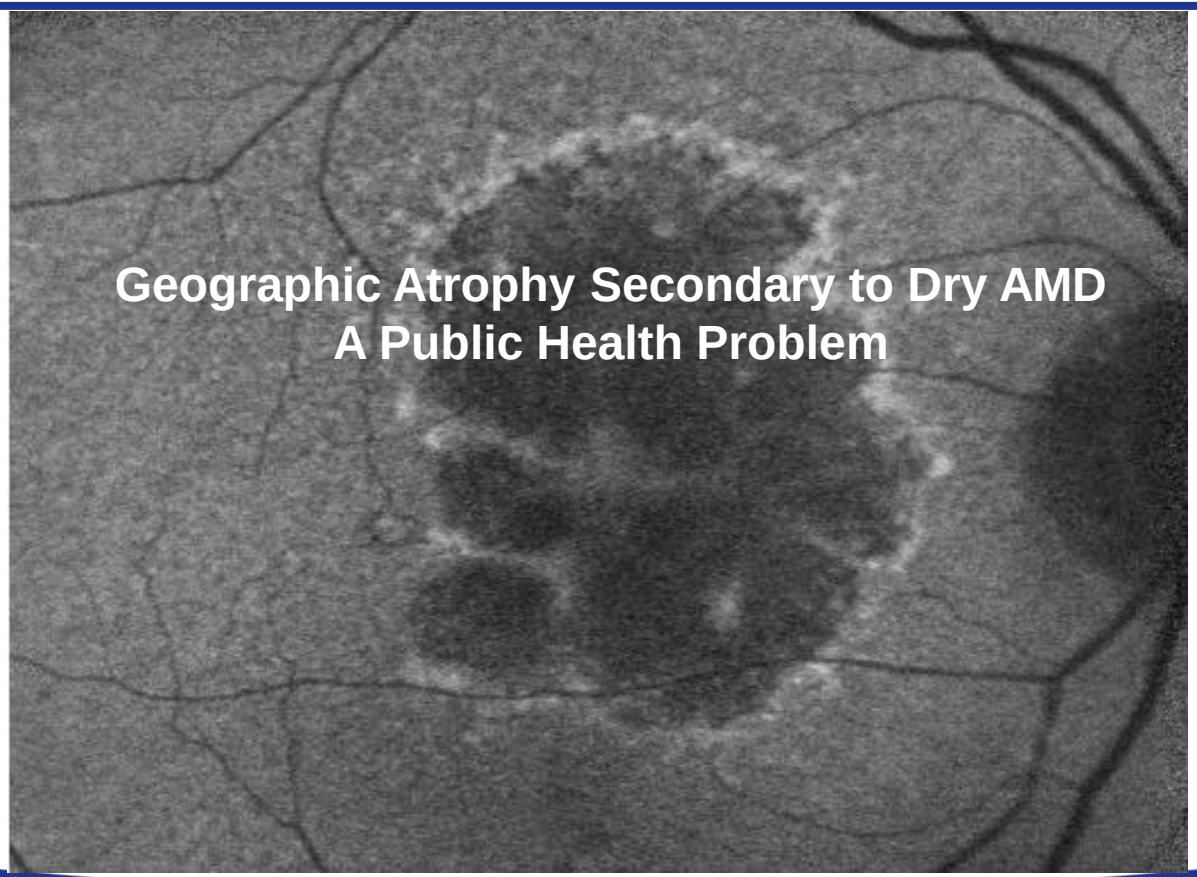
Kourous A. Rezaei, MD
Chief Medical Officer



January 2020
NASDAQ: ISEE

Forward-looking Statements

Any statements in this presentation about the Company's future expectations, plans and prospects constitute forward-looking statements for purposes of the safe harbor provisions under the Private Securities Litigation Reform Act of 1995. Forward-looking statements include any statements about the Company's strategy, future operations and future expectations and plans and prospects for the Company, and any other statements containing the words "anticipate," "believe," "estimate," "expect," "intend", "goal," "may", "might," "plan," "predict," "project," "seek," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions. In this presentation, the Company's forward looking statements include statements about its expectations to use its previously announced clinical trial of Zimura for the treatment of geographic atrophy as a pivotal trial, its development strategy for Zimura, the Company's hypotheses regarding complement inhibition as a mechanism of action for the treatment of geographic atrophy, the projected use of cash and cash balances, the timing, progress and results of clinical trials and other research and development activities, the potential utility of its product candidates, estimates regarding the number of patients affected by the diseases and indications the Company's product candidates are intended to treat, and statements regarding the potential for the Company's business development strategy. Such forward-looking statements involve substantial risks and uncertainties that could cause the Company's development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, those related to the initiation and the progress of research and development programs and clinical trials, availability of data from these programs, reliance on university collaborators and other third parties, establishment of manufacturing capabilities, expectations for regulatory matters, need for additional financing and negotiation and consummation of business development transactions and other factors discussed in the "Risk Factors" section contained in the quarterly and annual reports that the Company files with the Securities and Exchange Commission the ("SEC"). Any forward-looking statements represent the Company's views only as of the date of this presentation. The Company anticipates that subsequent events and developments will cause its views to change. While the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so except as required by law.

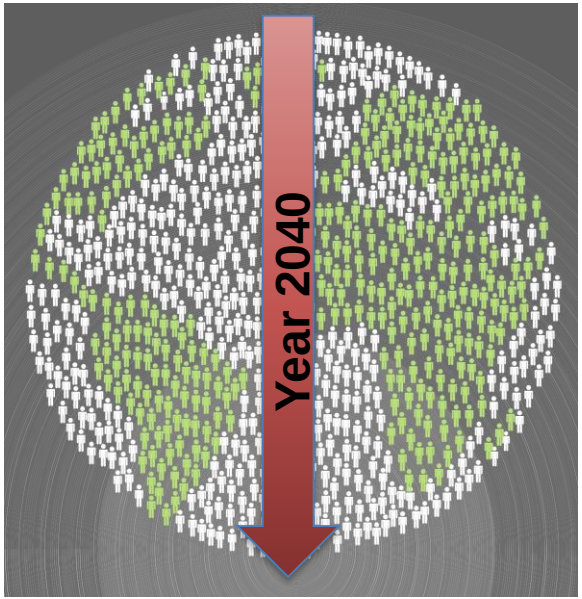


Ophthalmol Ther 2017;6:69-77.

AMD: The Leading Cause of Visual Disability in the Industrialized World

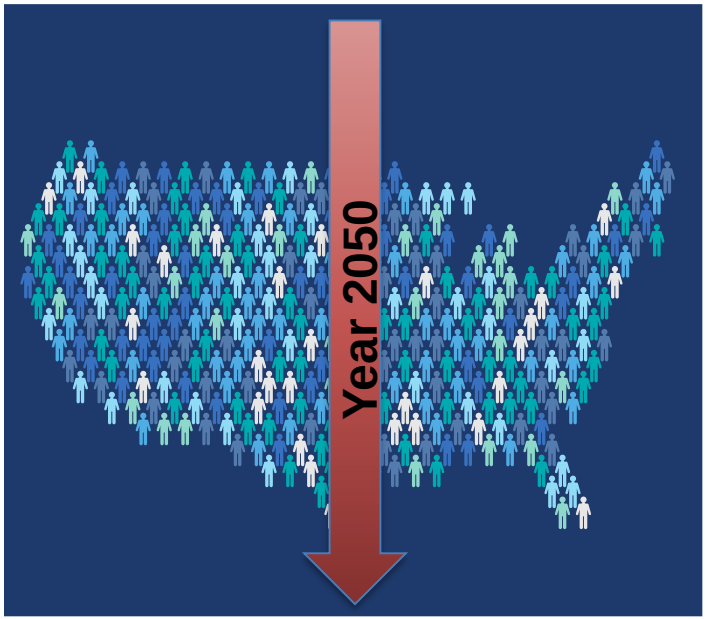
Reported Estimates for AMD Prevalence

~170 Million



~288 Million

~11 Million



~22 Million

Source: Eye Vis (Lond) 2016;22;3:34.

Increase in Age: AMD Progression to Geographic Atrophy

Early AMD

Intermediate AMD

Advanced AMD

Anti-VEGF

Wet AMD

GEOGRAPHIC ATROPHY

Age-related macular degeneration

Paul Mitchell, Gerald Liew, Bamini Gopinath, Tien Y Wong *Lancet* 2018; 392: 1147–59

Incidence and Growth of Geographic Atrophy during 5 Years of Comparison of Age-Related Macular Degeneration Treatments Trials

Juan E. Grunwald, MD,[1] Maxwell Pistilli, MS,[1] Ebenezer Daniel, MBBS, MD,[1] Gui-Shuang Ying, PhD,[1] Wei Pan, MS,[1] Glenn J. Jaffe, MD,[2] Cynthia A. Toth, MD,[3] Stephanie A. Hagstrom, PhD,[3] Maureen G. Maguire, PhD,[1] Daniel F. Martin, MD,[3] for the Comparison of Age-Related Macular Degeneration Treatments Trials Research Group*

PROGRESSION OF MACULAR ATROPHY IN PATIENTS WITH NEOVASCULAR AGE-RELATED MACULAR DEGENERATION UNDERGOING ANTIVASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY

NIZAR SALEH ABDELFATTAH, MD,*† HONGYANG ZHANG, MD,*†‡ DAVID S. BOYER, MD,§ SRINIVAS R. SADDA, MD*†

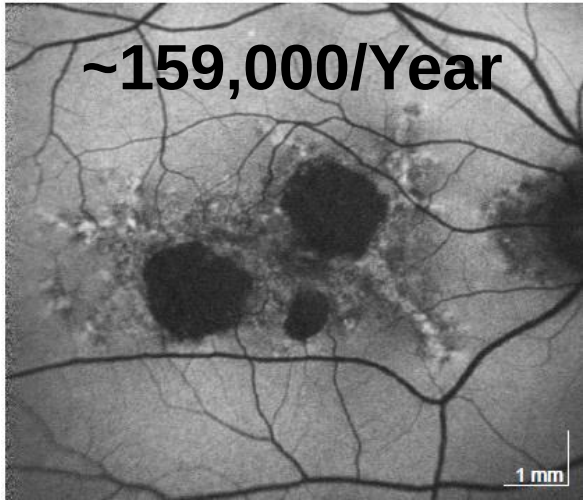
Macular Atrophy Progression and 7-Year Vision Outcomes in Subjects From the ANCHOR, MARINA, and HORIZON Studies: the SEVEN-UP Study*

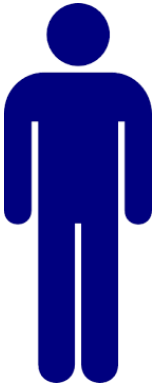
ROBERT B. BHISITKUL, THAIS S. MENDES, SORAYA ROFAGHA, WAYNE ENANORIA, DAVID S. BOYER, SRINIVAS R. SADDA, AND KANG ZHANG

Advanced AMD: Estimated Prevalence & Incidence in the United States

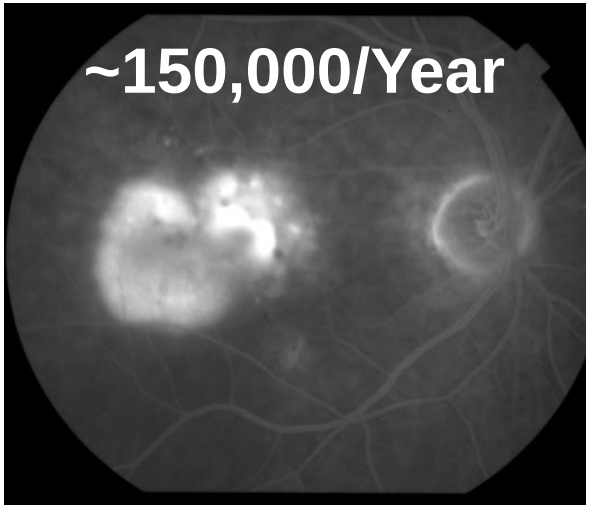
Prevalence of GA in 2020: ~1.5 Million in the US

Incidence of GA





Incidence of Wet AMD



Am J Ophthalmol 2015; 160:85-9. Arch Ophthalmol. 2004;122(4):564-572.3.

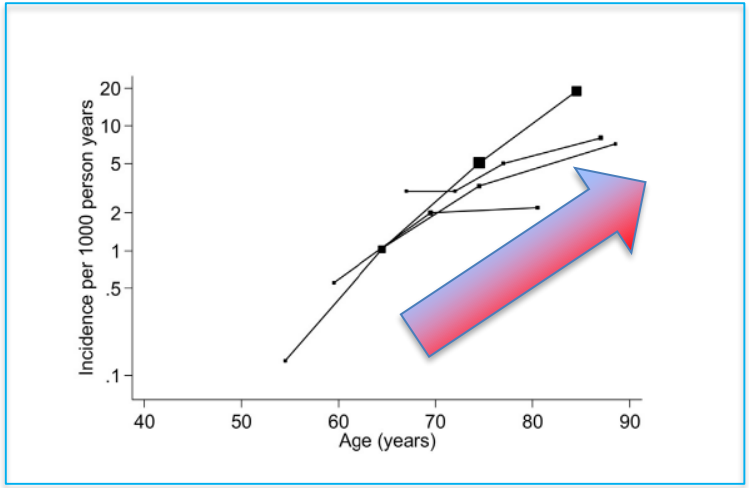
Estimated Prevalence of GA in the United States in 2020: ~1.5 Million

Real World Translation

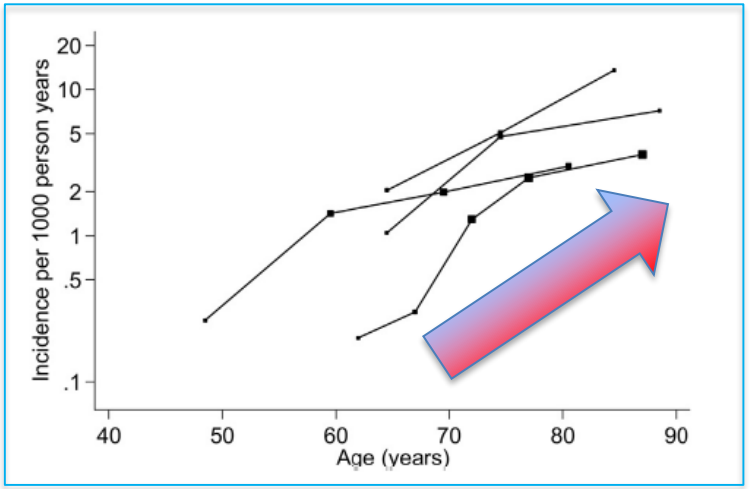
Arch Ophthalmol. 2004;122(4):564-572.3. www.factfinder.census.gov.

Advanced AMD: Incidence Rates Quadruple by Decade of Age

Geographic Atrophy



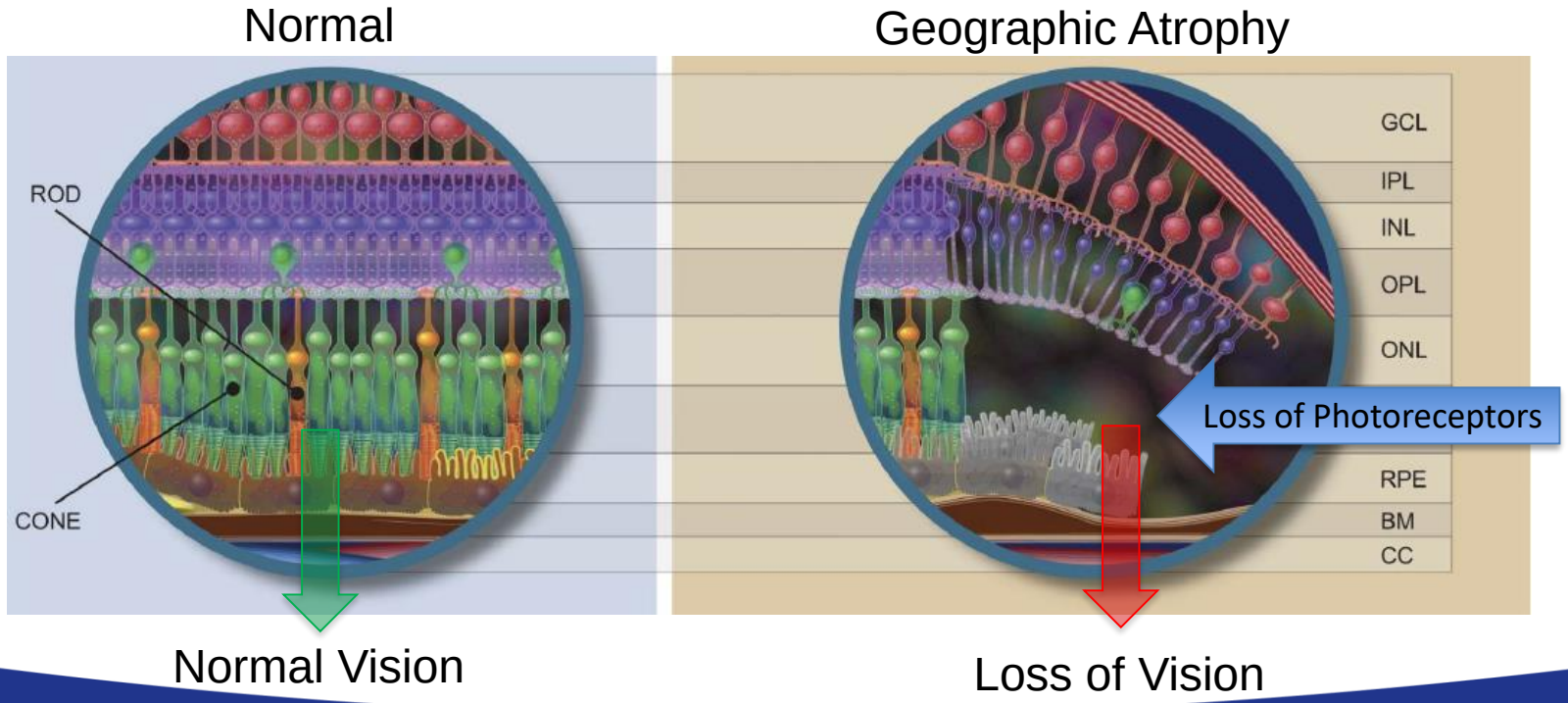
Wet AMD



Am J Ophthalmol 2015; 160:85-93.

Geographic Atrophy: Loss of Retinal Cells

Retinal Cell Layers: Cone Photoreceptors Responsible for Sharp Vision

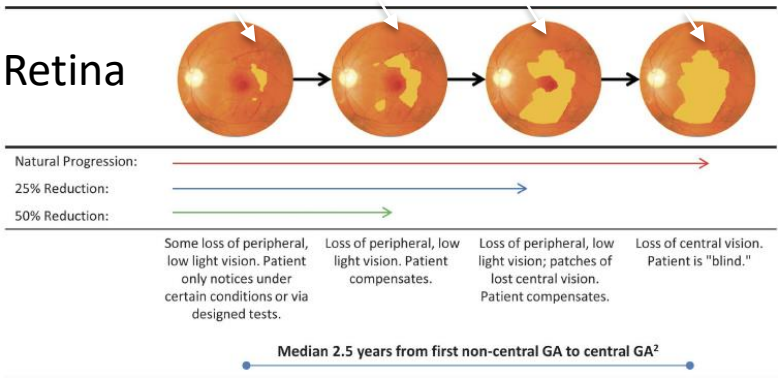


Source: Retina 2017;37:819-835.

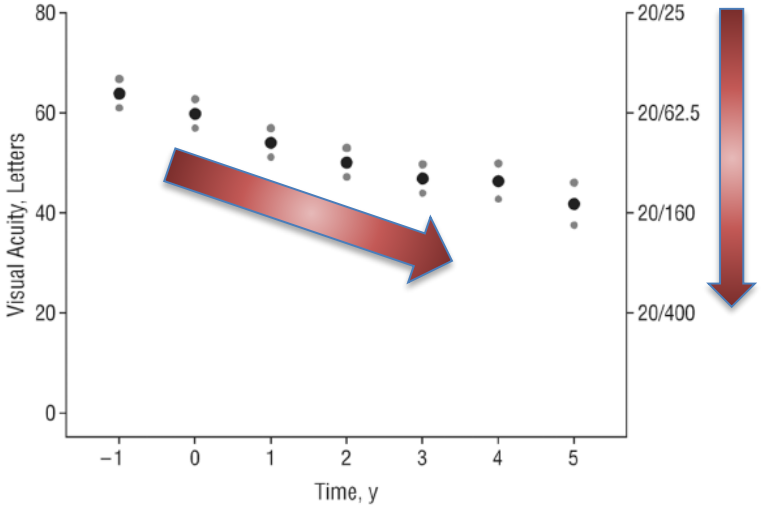
Geographic Atrophy Secondary to Dry AMD

Geographic Atrophy: Loss of Photoreceptors (Cells that Perceive Light) Over Time

Increase in Area of Degeneration Over Time

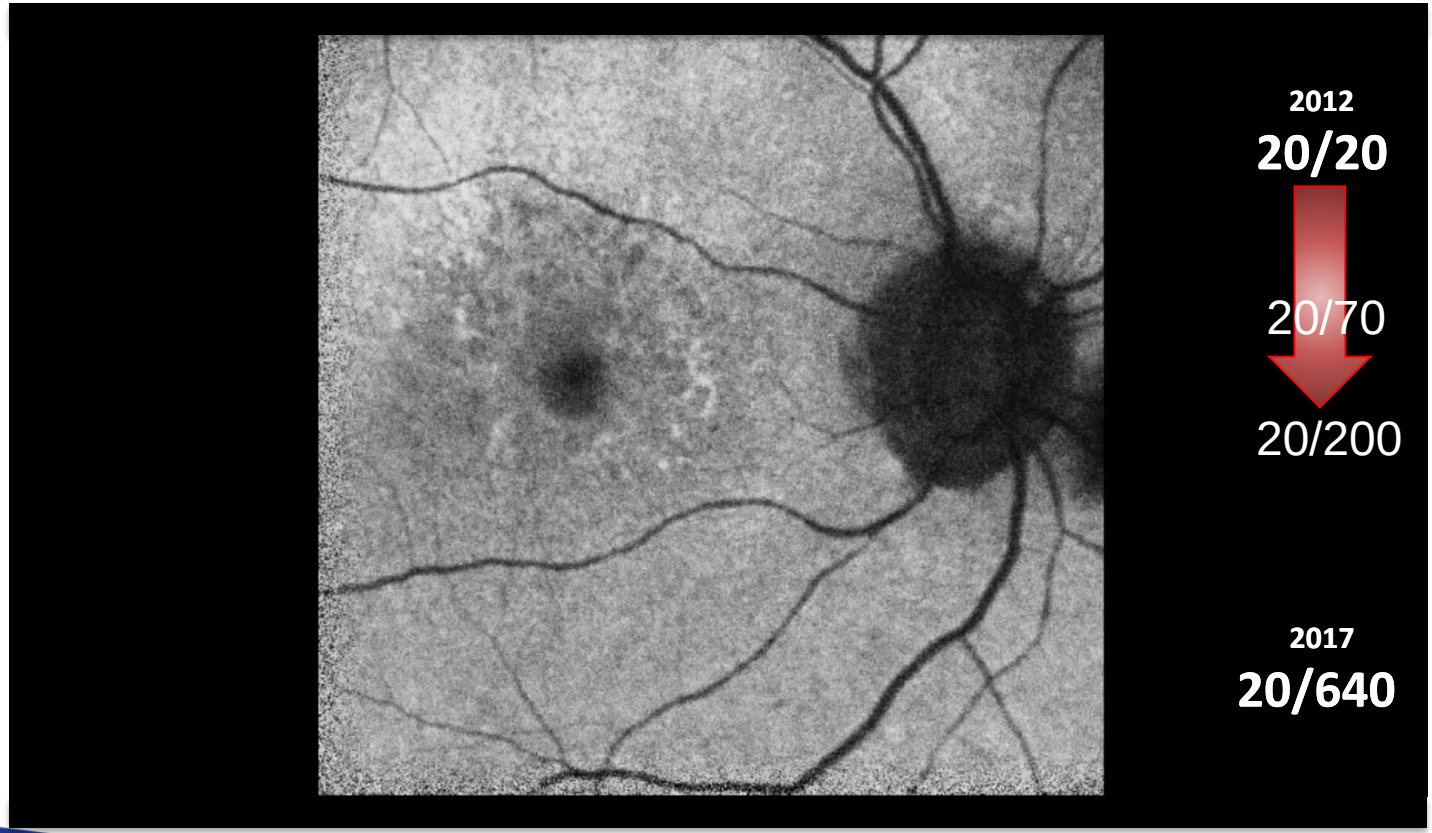


Loss of Vision Over Time



Source: Ophthalmology 2014;121:1079-1091. Retina 2017;27:819-835. Arch Ophthalmol 2009;127:1168-1174.

Geographic Atrophy: Growth Over Time



Lower limit for driving in many US states

Legal Blindness

Courtesy: Jordi Mones, MD

Number of Subjects Reporting Significant Negative Impact From GA

Living with Geographic Atrophy: An Ethnographic Study

Sobha Sivaprasad · Elizabeth A. Tschosik · Robyn H. Guymer · Audrey Kapre · Ivan J. Suñer · Antonia M. Joussen · Paolo Lanzetta · Daniela Ferrara

- Reading: 100%
- Driving: 75%
- Watching TV: 69%
- Recognizing Faces: 63%
- Household Activities: 63%
- Fear of Worsening: 44%

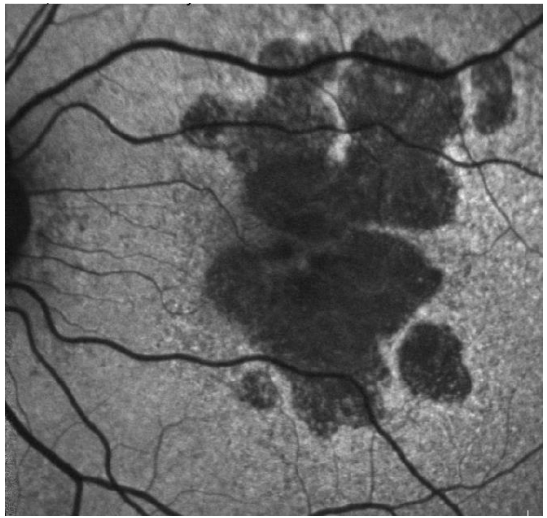
"Can't read a menu if it's too small and it's too dark"

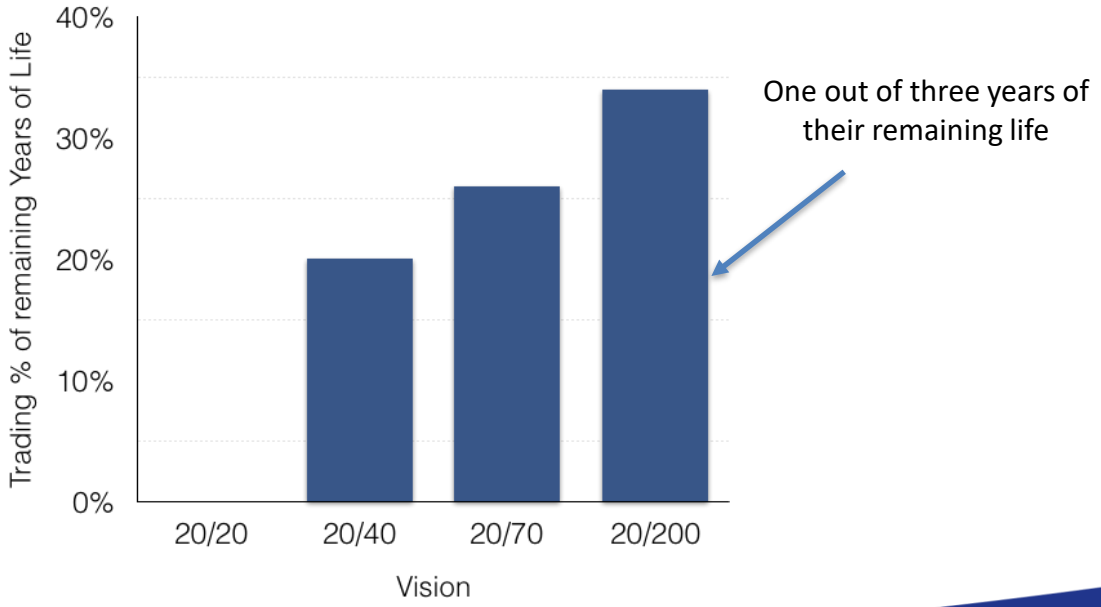
"Well, horrible, that you can't see, you can't drive… You have to depend on other people for taking care of you. You lose your independence"

"Because there's a fear creeps into all this…Will I go blind eventually?"

Patients with Poor Vision: Number of Years Willing to Trade off for Better Vision

Major Impact on Patient's Quality of Life

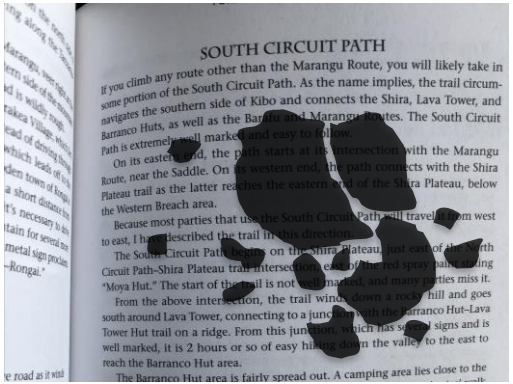




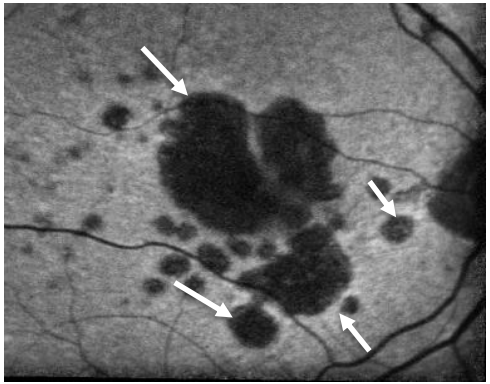
Surv Ophthalmol 48: 204–223, 2003.

Geographic Atrophy: Impact on Functional Vision in Daily Life

Treatment Goal: Slow Down the Growth of Geographic Atrophy



Areas of missing vision (scotoma)



Areas of geographic atrophy
(Dead retinal cells)

Areas of missing vision (scotoma)

AMD Progression to Geographic Atrophy: Potential for Complement Inhibition

Complement Inhibition

Early AMD

Intermediate AMD

Advanced AMD

Anti-VEGF

Wet AMD

GEOGRAPHIC ATROPHY

Age-related macular degeneration

Paul Mitchell, Gerald Liew, Bamini Gopinath, Tien Y Wong *Lancet* 2018; 392: 1147–59

Incidence and Growth of Geographic Atrophy during 5 Years of Comparison of Age-Related Macular Degeneration Treatments Trials

Juan E. Grunwald, MD,[1] Maxwell Pistilli, MS,[1] Ebenezer Daniel, MBBS, MD,[1] Gui-Shuang Ying, PhD,[1] Wei Pan, MS,[1] Glenn J. Jaffe, MD,[2] Cynthia A. Toth, MD,[2] Stephanie A. Hagstrom, PhD,[3] Maureen G. Maguire, PhD,[3] Daniel F. Martin, MD,[3] for the Comparison of Age-Related Macular Degeneration Treatments Trials Research Group*

PROGRESSION OF MACULAR ATROPHY IN PATIENTS WITH NEOVASCULAR AGE-RELATED MACULAR DEGENERATION UNDERGOING ANTIVASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY

NIZAR SALEH ABDELFATTAH, MD,*† HONGYANG ZHANG, MD,*†‡ DAVID S. BOYER, MD,§ SRINIVAS R. SADDA, MD*†

Macular Atrophy Pro and 7-Year Vision Outcomes in Subje the ANCHOR, MARINA, and H N Studies: the SEVEN dy*

ROBERT B. BHISITKUL, THAIS S. MENDES, SO , WAYNE ENANORIA, DAVID S. BOYER, SRINIVAS R. SA G ZHANG

Zimura®

Pivotal Clinical Trial in Geographic Atrophy Secondary to Dry AMD
12-Month Topline Results

Pivotal Trial Highlights

Zimura Pivotal Trial in geographic Atrophy Secondary to AMD

- Both Zimura 2mg and 4mg were well tolerated over 12 months
- Primary efficacy endpoint was achieved for both Zimura 2mg and Zimura 4mg dose, leading to a ~27% reduction in GA growth over 12 months
- The overall data suggested a dose response relationship
- Initiating the second pivotal clinical trial with the goal of enrolling the first patient in the first quarter of 2020

Zimura Pivotal Clinical Trial for GA Secondary to Dry AMD

A Randomized, Double-Masked, Sham Controlled Trial to Assess the Safety and Efficacy of Intravitreous Administration of Zimura (Complement C5 Inhibitor) in Subjects with Geographic Atrophy Secondary to Dry Age-Related Macular Degeneration (AMD)

Screening Clinical Trial Design

- If the estimated effect size indicates low levels of benefit: would not move forward with a subsequent trial
- If the estimated effect size is moderate, but clinically relevant: move forward with subsequent Phase 3 clinical trials
- If the estimated effect size is more efficacious than the sham control with the strength of evidence meeting the level of statistical significance, as was the case in the Zimura trial for both the 2 mg and 4 mg dose groups, then the trial could potentially serve as a registration trial and only one more pivotal trial would be required for regulatory approval

Source: Fleming & Richrdson, J Infections Diseases. 2004;190:666-74.

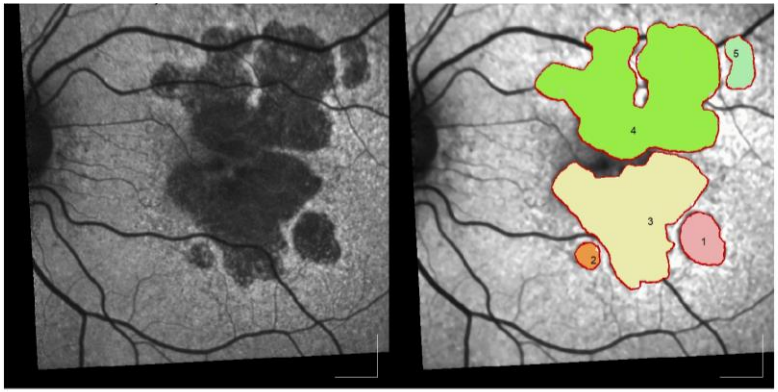
Zimura in GA Secondary to Dry AMD Pivotal Clinical Trial

- Randomized, double masked, sham controlled clinical trial
- Cohorts included in the pre-specified statistical analysis of the primary endpoint at Month 12*:
  - Zimura 4 mg dose
  - Zimura 2 mg dose
  - Sham
- 286 subjects were enrolled for monthly treatment with Zimura or Sham for 18 months
  - ~75% of the patients were enrolled in the US

*Descriptive analysis was performed for the Zimura 1mg cohort

Primary Efficacy Endpoint

Mean rate of change in GA over 12 months measured by fundus autofluorescence (FAF) at three time points: Baseline, Month 6, and Month 12 (square root transformation of GA lesion)



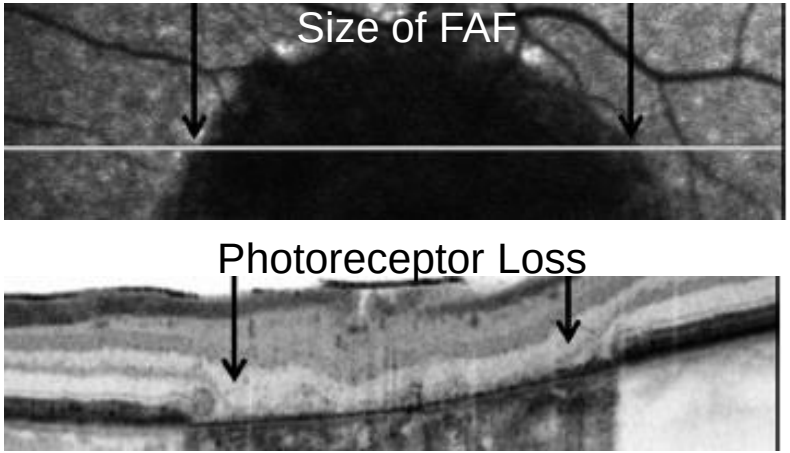
“Preventing Photoreceptor Loss”: “Clinically Meaningful End-point”

“Preventing photoreceptor loss, for example, would be considered a clinically meaningful end- point, given the established link between photoreceptor loss and visual function. The threshold of such a therapeutic effect remains to be established, but if photoreceptor loss can be prevented at least to the extent of the fuzzy border, as seen on OCT, around the GA lesion, that might be considered a potential trial endpoint.”

Research Opportunities

Report From the NEI/FDA Endpoints Workshop on Age-Related Macular Degeneration and Inherited Retinal Diseases

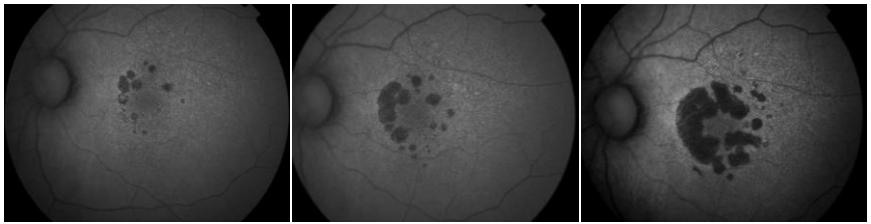
Karl Csaky,[1] Frederick Ferris III,[2] Emily Y. Chew,[2] Prashant Nair,[3] Janet K. Cheetham,[4] and Jacque L. Duncan[5]

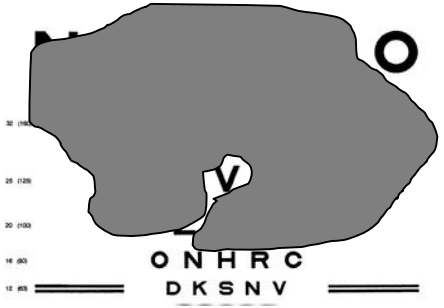


Source: Investigative Ophthalmology & Visual Science January 2011, Vol.52, 1-6. Investigative Ophthalmology & Visual Science 2017 Jul 1;58(9):3456-3463.

Primary Efficacy Endpoint

- GA: Visual function can be a poor indicator of functional vision
- Patients' visual disabilities are usually underestimated





Courtesy: Jordi Mones, MD

Duke Reading Center

- Established in 2001
- Experienced physicians, imaging and functional testing experts
- Extensive experience with AMD:
  - 35 treatment trials
  - 10 treatment trials for GA
- Largest AMD trials to date (CATT, VIEW1, HAWK, etc…)
- ~17,000 OCT technicians and photographers certified

Source: Duke Reading Center

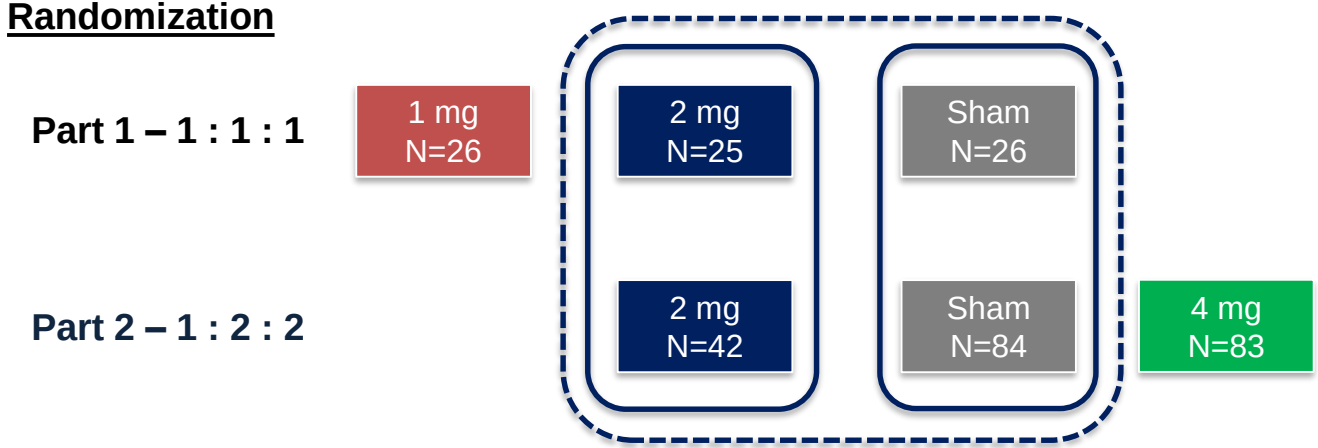
Duke Reading Center

- Completely masked assessment
- Each visit evaluated independently
- Two experienced primary readers analyze the GA lesion size on FAF with RegionFinder
- > 10% discrepancy arbitrated by Reading Center Director: Glenn Jaffe, MD
- Supportive modalities: OCT and NIR imaging

Source: Duke Reading Center

Zimura in GA Secondary to Dry AMD Clinical Trial

Randomization

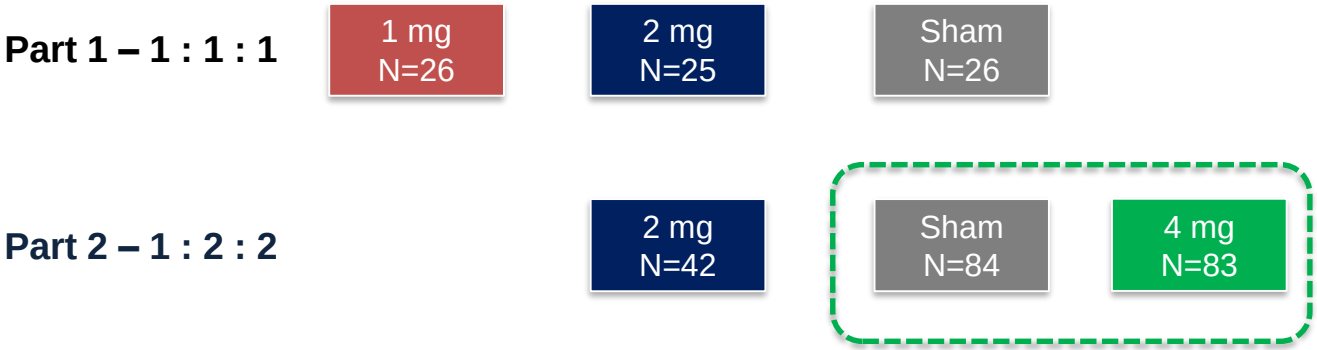


Efficacy Evaluation

- Zimura 2 mg vs. Sham: subjects randomized from Part 1 were combined with the subjects randomized from Part 2, where the analysis included a regression factor by part.

Zimura in GA Secondary to Dry AMD Clinical Trial

Randomization

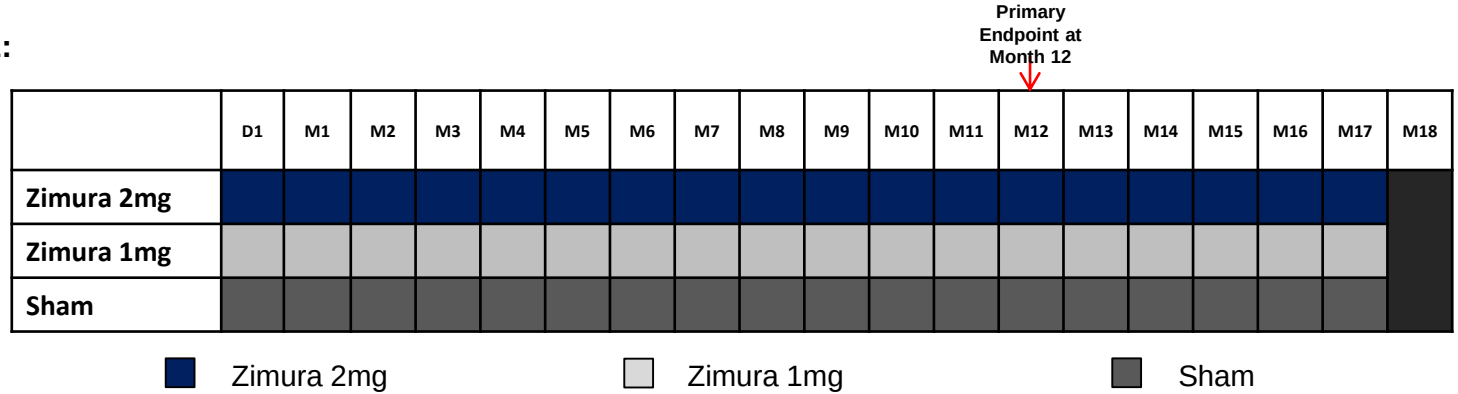


Efficacy Evaluation

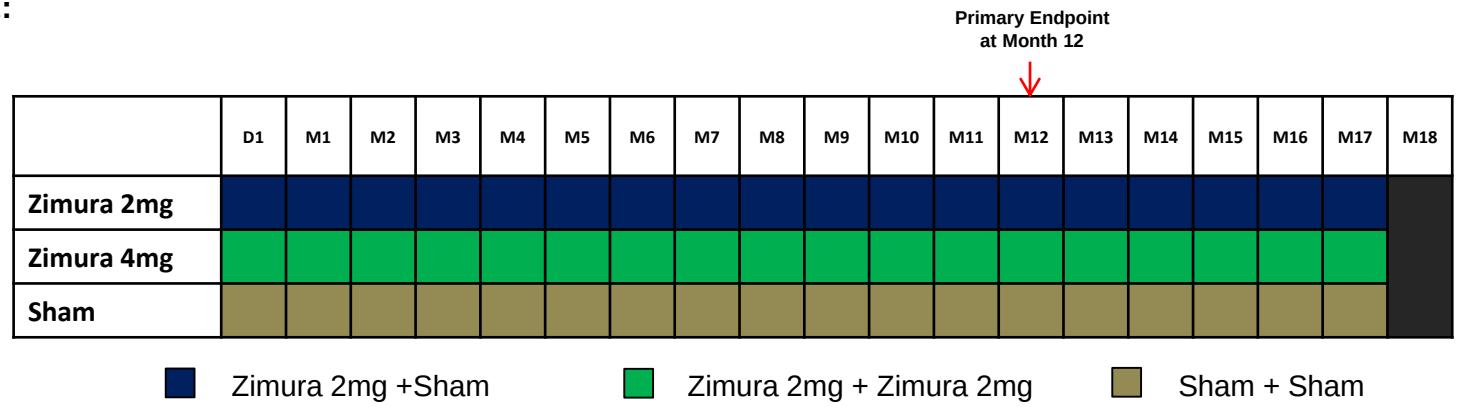
- Zimura 4 mg vs. Sham: based only on subjects randomized in Part 2

Zimura in GA Secondary to Dry AMD Clinical Trial

Part 1:



Part 2:



Key Ophthalmic Inclusion Criteria (Study Eye)

- Non-foveal GA secondary to dry AMD
- Total GA area ≥ 2.5 and ≤ 17.5 mm^2 (1 and 7 disk areas [DA] respectively), determined by screening images of FAF
- If GA is multifocal, at least one focal lesion should measure ≥ 1.25 mm^2 (0.5 DA)
- GA in part within 1500 microns from the foveal center
- The atrophic lesion must be able to be photographed in its entirety
- Best corrected visual acuity in the SE between 20/25 – 20/320, inclusive

Key Ophthalmic Exclusion Criteria

- GA secondary to any condition other than AMD in either eye (e.g., drug-induced)
- Any prior treatment for AMD or any prior intravitreal treatment for any indication in either eye, except oral supplements of vitamins and minerals
- Evidence of CNV in either eye. If CNV develops in the SE during the course of the study, the subject will be withdrawn from the study
- Any ocular condition in the SE that would progress during the course of the study that could affect central vision or otherwise be a confounding factor

Statistical Analysis

- A Mixed-Effects Repeated Measures (MRM) model was used to assess the differences between Zimura 2mg or 4mg dose and their corresponding sham in rate of change of GA area (square root transformation) over 12 months

- The model included the following fixed and *random effects*:
  - Treatment: Sham *vs* dose
  - Study part (1 *vs* 2): only for 2 mg
  - Baseline VA: < 50 letters *vs* ≥ 50 letters
  - Size of baseline GA: < 4 disc area *vs* ≥ 4 disc area
  - Pattern of FAF at the junctional zone of GA: none/focal *vs* banded/diffuse
  - *Visit (0, 6 mos or 12 mos) with unstructured correlation*
  - *Interaction terms between visit and all other factors*

Baseline Characteristics: Generally Balanced Across Cohorts*

	Zimura 2mg N = 67	Sham for 2mg arm N = 110	Zimura 4mg N = 83	Sham for 4mg arm N = 84
Mean Age, Years	78.8	78.2	79.2	78.2
Female Gender, Number (%)	45 (67.2%)	79 (71.8%)	58 (69.9%)	61 (72.6%)
Active smoker, Number (%)	25 (37.3%)	36 (32.7%)	26 (31.3%)	29 (34.5%)
Non-Subfoveal GA, Number (%)	62 (92.5%)	104 (94.5%)	81 (97.6%)	82 (97.6%)
Mean GA Area, mm^2	7.33	7.42	7.90	7.45
Mean SQ Root GA Area, mm	2.62	2.63	2.72	2.64
Bilateral GA, Number (%)	67 (100%)	108 (98.2%)	83 (100%)	83 (98.8%)
Hyper Autofluorescence (%)	66 (98.5%)	109 (99.1%)	82 (98.8%)	83 (98.8%)
Mean BCVA (ETDRS Letters)	70.2	69.0	69.5	68.3
Mean LL BCVA (ETDRS Letters)	36.7	34.5	36.8	33.9
Low Luminance Deficit (BCVA-LL BCVA)	33.5	34.5	32.7	34.4

*Detailed baseline characteristics based on part 1 and part 2 are available online

Preliminary Safety Analysis Through Month 12

- Zimura was generally well tolerated after 12 months of administration
- No Zimura related adverse events
- No Zimura related inflammation
- No drug related discontinuations from the trial attributed to Zimura
- No serious ocular adverse events in the study eye
- No cases of endophthalmitis reported in the clinical trial
- The most frequently reported ocular adverse events were related to the injection procedure
- Incidence of CNV in the untreated fellow eyes was 10 patients (3.5%) and in the study eyes was 3 patients (2.7%) in the sham group, 1 patient (4.0%) in the Zimura 1mg group, 6 patients (9.0%) in the Zimura 2mg group, and 8 patients (9.6%) in the Zimura 4mg group

Superior Safety Profile To Date

C5 Inhibition: Potential Safety Advantages

- Complement C3a receptors play roles in endotoxemia, ischemia-reperfusion, neurotrauma, and ALS models

- ***C3aR is protective*** in these models (knockout worsens disease)

- ***C3-CR3 is also protective*** in a retinal degeneration model

- Global blockade of C3 (as opposed to C5) may prevent the beneficial activities of C3a, whilst also increasing infection risk

Source: J. Exp. Med. 2019 Vol. 216 No. 8 1925–1943. J Immunol 2006; 176:4315-4322. J Immunol 2015;194: 3542–3548. Wu et al., 2013, PNAS; Brennan et al., 2019, JCI Insight, Woodruff unpublished data.

C5 Inhibition: Potential Safety Advantages

C3 or CR3 Deficiency: Potential for Increased Microglial Neurotoxicity

C3- and CR3-dependent microglial clearance protects photoreceptors in retinitis pigmentosa

JEM Journal of Experimental Medicine

Sean M. Silverman, Wenxin Ma, Xu Wang, Lian Zhao, and Wai T. Wong

Complement activation has been implicated as contributing to neurodegeneration in retinal and brain pathologies, but its role in retinitis pigmentosa (RP), an inherited and largely incurable photoreceptor degenerative disease, is unclear. We found that multiple complement components were markedly up-regulated in retinas with human RP and the rd10 mouse model, coinciding spatiotemporally with photoreceptor degeneration, with increased C3 expression and activation localizing to activated retinal microglia. Genetic ablation of C3 accelerated structural and functional photoreceptor degeneration and altered retinal inflammatory gene expression. These phenotypes were recapitulated by genetic deletion of CR3, a microglia-expressed receptor for the C3 activation product iC3b, implicating C3-CR3 signaling as a regulator of microglia–photoreceptor interactions. Deficiency of C3 or CR3 decreased microglial phagocytosis of apoptotic photoreceptors and increased microglial neurotoxicity to photoreceptors, demonstrating a novel adaptive role for complement-mediated microglial clearance of apoptotic photoreceptors in RP. These homeostatic neuroinflammatory mechanisms are relevant to the design and interpretation of immunomodulatory therapeutic approaches to retinal degenerative disease.

Source: J. Exp. Med. 2019 Vol. 216 No. 8 1925–1943.

Primary Efficacy Endpoint Achieved for Both Zimura 2mg and 4mg

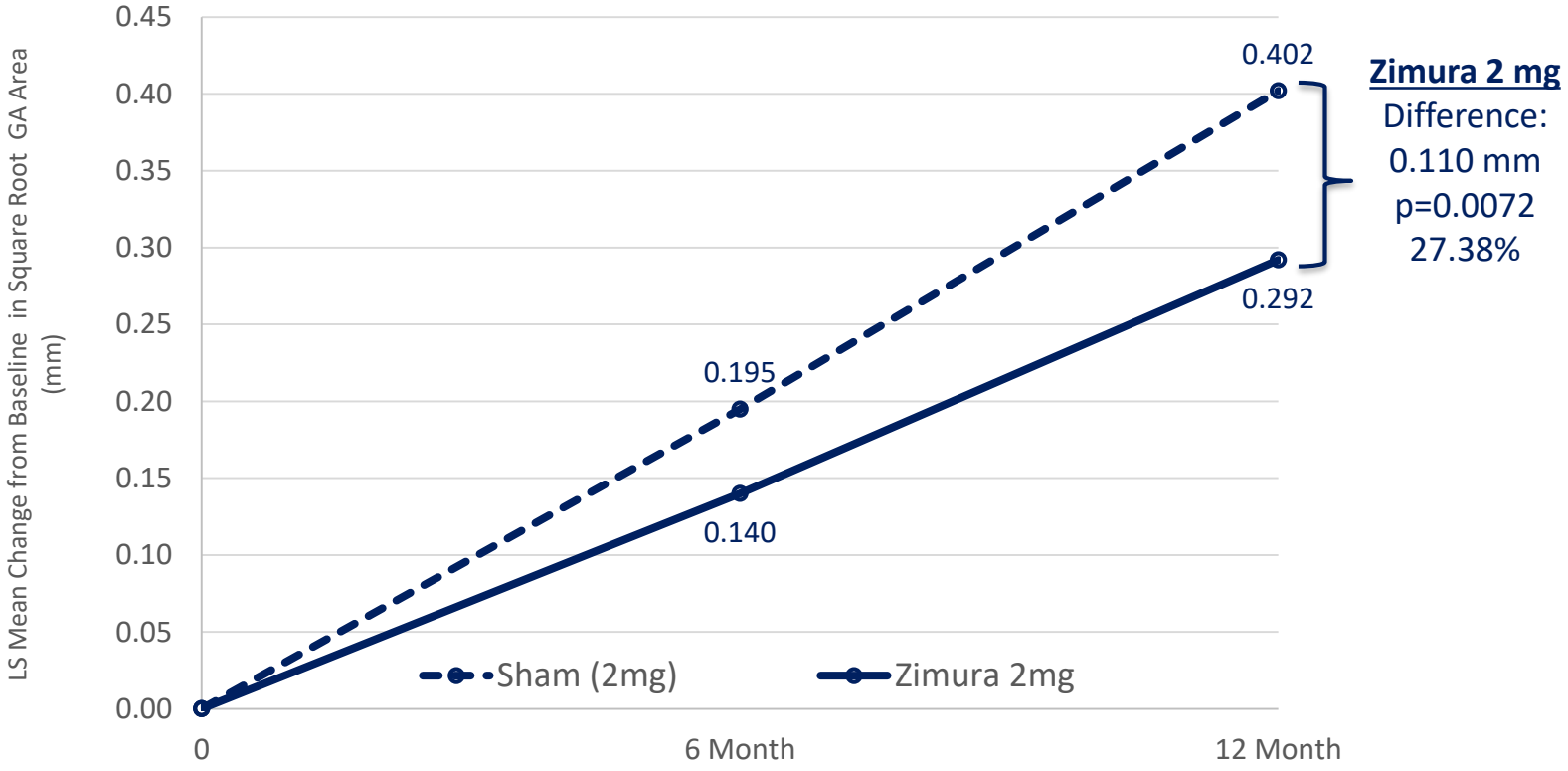
Mean Rate of Change in Geographic Atrophy Area from Baseline to Month 12 (MRM Analysis)
(Square Root Transformation, ITT Population)

Cohort	Zimura 2 mg (N = 67)	Sham 2 mg (N = 110)	Difference	P-value	% Difference
Mean Change in GA[a] (mm)	0.292[c]	0.402[c]	0.110	0.0072[b]	27.38%

Cohort	Zimura 4 mg (N = 83)	Sham 4 mg (N = 84)	Difference	P-value	% Difference
Mean Change in GA[a] (mm)	0.321	0.444	0.124	0.0051[b]	27.81%

(a) = based on the least squared means from the MRM model
(b) = reflects statistically significant p-value; Hochberg procedure was used for significance testing
(c) = these least square means are estimates of the MRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data

Primary Efficacy Endpoint Achieved: Zimura 2 mg vs. Sham



Based on LSMEANS from MRM Model; ITT Population Hochberg procedure used for significance testing. These least square means are estimates of the MRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data.

Mean Rate of Change in GA for Zimura 2 mg by Part

Mean Rate of Change in Geographic Atrophy (GA) Area from Baseline to Month 12
(MRM Analysis) (Square Root Transformation)

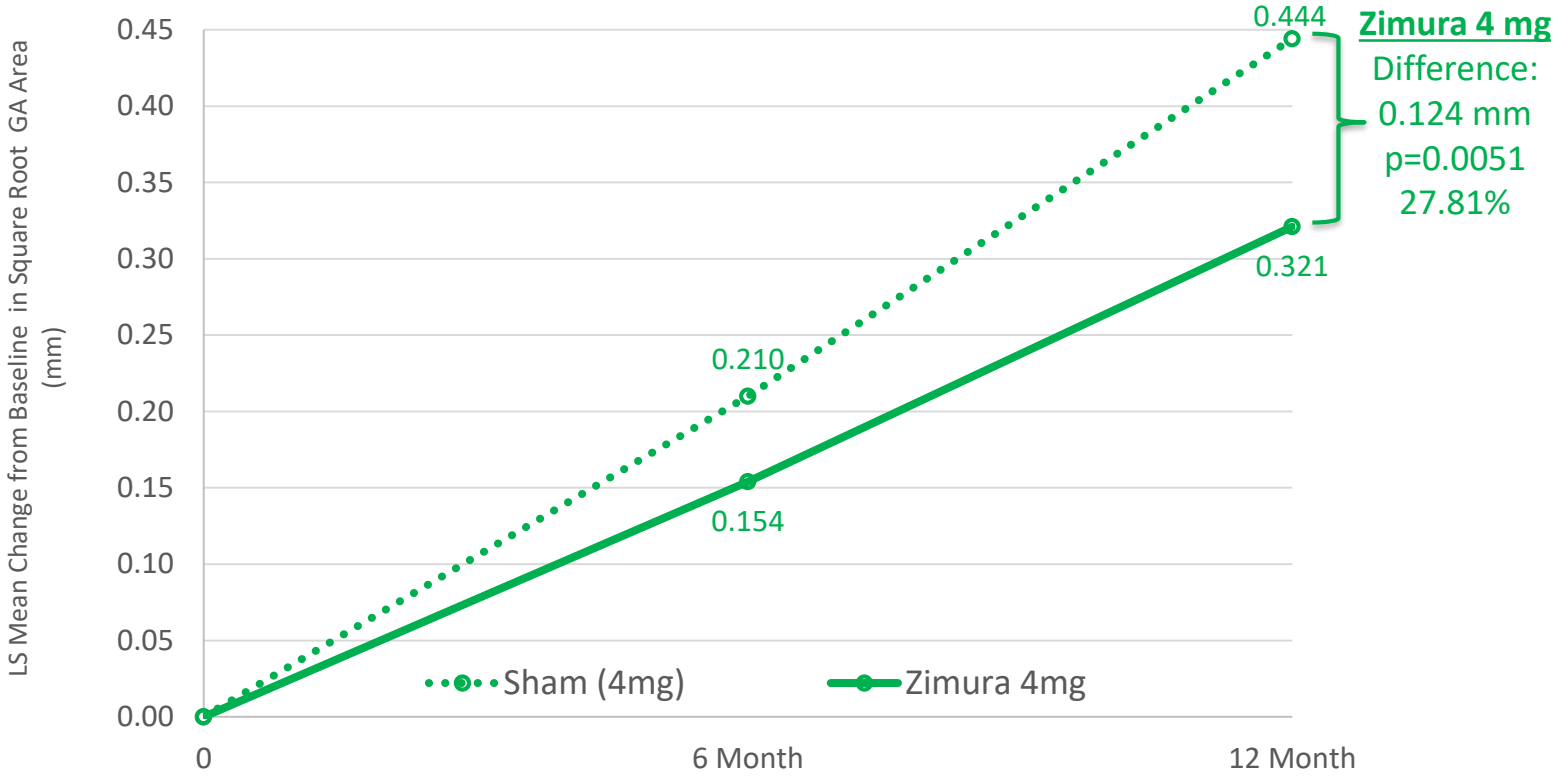
Cohort		Zimura 2mg (N = 25)	Sham 2mg (N = 26)	Difference
Part 1	Mean Change in GA[(a)] (mm)	0.329	0.422	0.093

(a) = based on the least squared means from the MRM model

Cohort		Zimura 2mg (N = 42)	Sham 2mg (N = 84)	Difference
Part 2	Mean Change in GA[(a)] (mm)	0.308	0.422	0.114

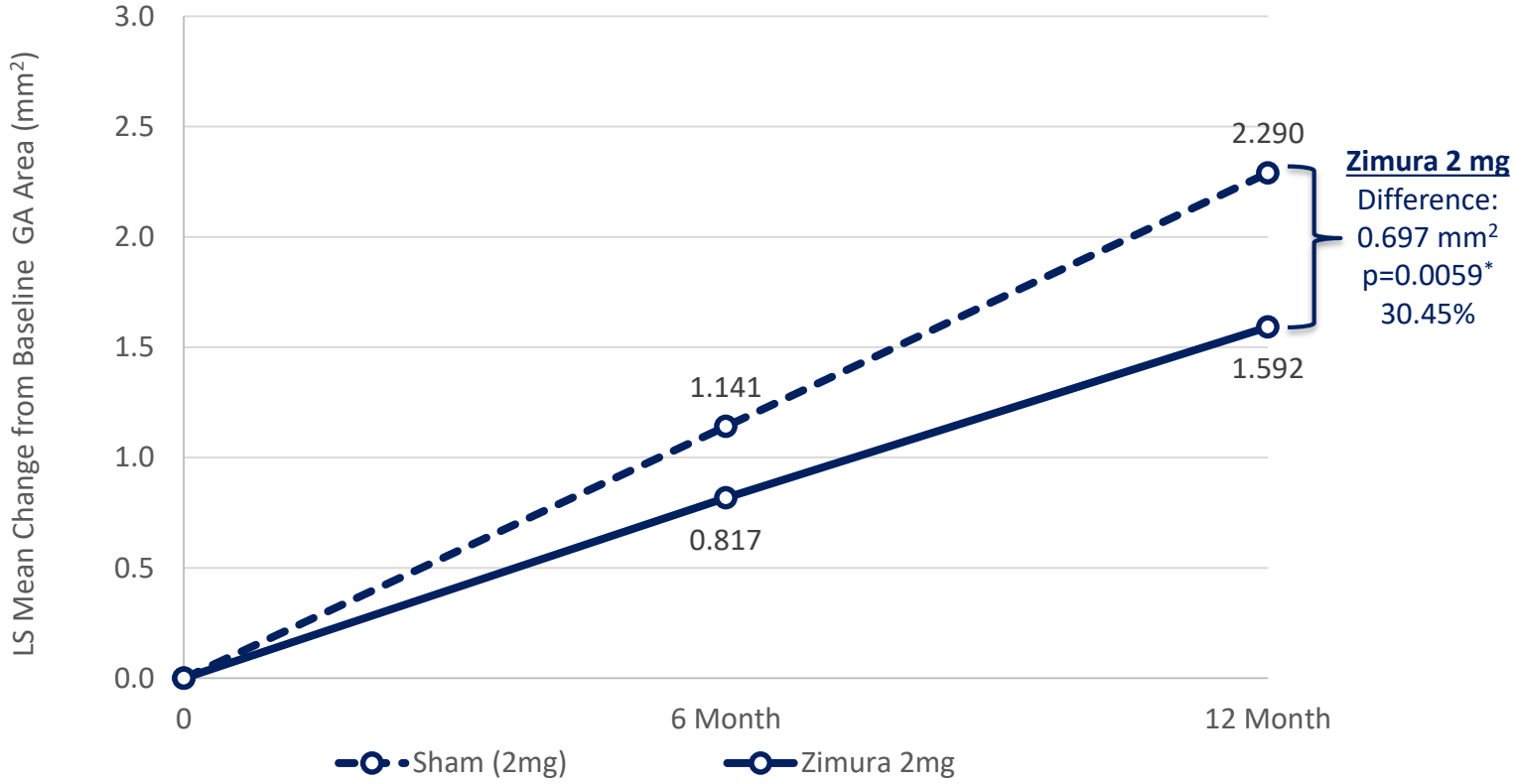
(a) = based on the least squared means from the MRM model

Primary Efficacy Endpoint Achieved: Zimura 4 mg vs. Sham



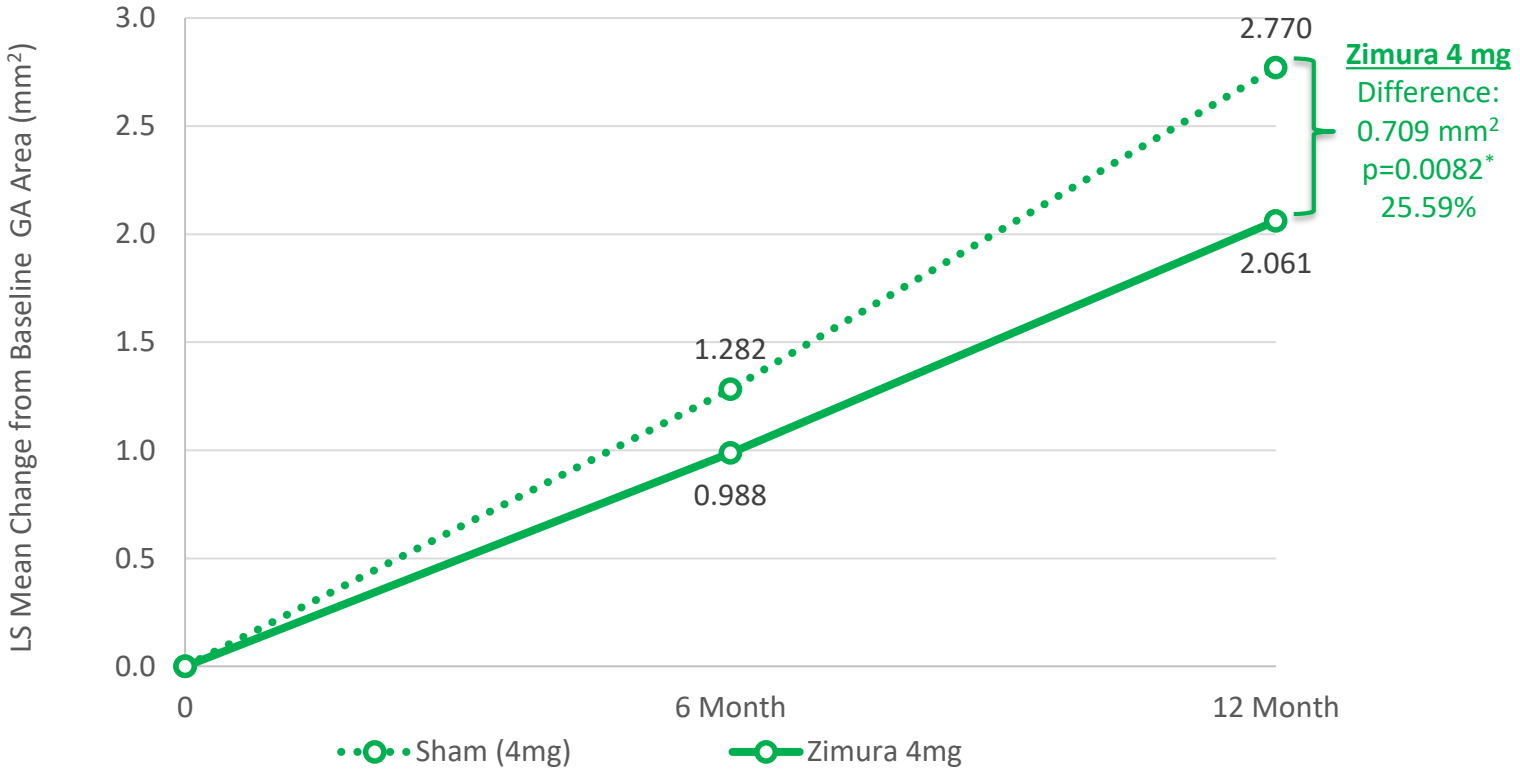
Based on LSMEANS from MRM Model; ITT Population Hochberg procedure used for significance testing

Supportive Efficacy Endpoint: Zimura 2 mg vs. Sham (Non-Square Root)



Based on LSMEANS from MRM Model; ITT Population Hochberg procedure used for significance testing. These least square means are estimates of the MRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2 and should not be interpreted as directly observed data. *Prespecified and descriptive analysis.

Supportive Efficacy Endpoint: Zimura 4 mg vs. Sham (Non-Square Root)



Based on LSMEANS from MRM Model; ITT Population Hochberg procedure used for significance testing. *Prespecified and descriptive analysis.

Secondary Endpoints

- Mean change in best corrected visual acuity (ETDRS letters) from Baseline to Month 12

Cohort	Zimura 2mg (N = 67)	Sham 2mg (N = 110)	Difference
Mean Change in BCVA[a]	-7.90[b]	-9.29[b]	1.39

Cohort	Zimura 4mg (N = 83)	Sham 4mg (N = 84)	Difference
Mean Change in BCVA[a]	-3.79	-3.51	-0.28

- Mean change in low luminance best corrected visual acuity (ETDRS letters) from Baseline to Month 12

Cohort	Zimura 2mg (N = 67)	Sham 2mg (N = 110)	Difference
Mean Change in LL BCVA[a]	-1.03[b]	-1.41[b]	0.38

Cohort	Zimura 4mg (N = 83)	Sham 4mg (N = 84)	Difference
Mean Change in LL BCVA[a]	1.53	2.97	-1.44

(a) = based on the least squared means from the MRM model; ITT population

(b) = these least square means are estimates of the MRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data

Trial not designed to demonstrate differences in mean changes in BCVA or LL BCVA with statistical significance

Analyzed Geographic Atrophy Data

	N (%) [1]
Missing at baseline[2]	1 (<1%)
Missing at 6 months and at 12 months[2]	36 (14%)
Missing at 6 months only	11 (4%)
Missing at 12 months only	30 (12%)
No missing	182 (70%)
	260 (100%)

[1]Sham, 2mg and 4mg groups
[2]*Excluded from model for 2mg and 4mg*

Sensitivity Analysis

Several pre-specified sensitivity analyses conducted for primary endpoint:

- Replaced missing data using multiple imputations, with an added “shift” increased until significance is lost
- Replaced missing data by
  - mean value of same treatment arm
  - mean value of opposite treatment arm
  - mean value of both treatment arms
  - mean value of sham arm
- Replaced missing data using “pattern mixture model”
  (useful to investigate “missing not at random” assumptions)

Sensitivity Analyses

Replace missing data using multiple imputations, with an added “shift” increase until significance is lost

Data Imputation Method	Zimura 2mg vs. Sham		Zimura 4mg vs. Sham	
	Difference**	*P*	Difference**	*P*
No imputation (primary analysis)	0.110	0.0072*	0.124	0.0051*
Impute mean value of same arm	0.119	0.0005*	0.152	<0.0001*
Impute mean value of opposite arm	0.075	0.031*	0.107	0.0033*
Impute mean value of both arms	0.097	0.0047*	0.129	0.0003*
Impute mean value of sham arm	**0.093**	**0.0056***	**0.120**	**0.0008***

** Statistically significant (without adjustment for multiplicity)*
*** Difference in means of GA area (square root transformation)*

Sensitivity Analysis

Statistical interpretation:

- All analyses indicated a small impact of missing data on our overall conclusion on the primary endpoint
- The shift imputation analyses showed that statistical significance would only be lost for large shifts (~40% of observed treatment effect)
- Analysis results were robust to missing data

Conclusions

Zimura Pivotal Trial in geographic Atrophy Secondary to AMD

- Both Zimura 2mg and 4mg were well tolerated over 12 months
- Primary efficacy endpoint was achieved for both Zimura 2mg and Zimura 4mg dose, leading to a ~27% reduction in GA growth over 12 months
- The overall data suggested a dose response relationship
- Initiating the second pivotal clinical trial with the goal of enrolling the first patient in the first quarter of 2020

Initiating Second Pivotal Trial: Plan to Begin Enrolling 1Q 2020

- Our understanding of the regulatory requirements for registration*:
  - **Safety**
    - Rule of 3: To identify adverse events occurring at a rate of 1% or greater:
      - 300 patients exposed to the dose seeking approval (or a higher dose) for a duration of at least 1 year
      - These patients do not need to be only treated for the indication seeking approval
      - A portion of these patients need to be followed for 2 years
  - **Efficacy:** Adequate and well controlled trials
    - Clear statement of the objectives: Slowing down the progression of GA growth
    - Valid Comparison and minimize bias:
      - Two independent randomized, double masked, sham controlled clinical trials
    - Well defined and reliable method of assessment for primary endpoint:
      - Objective endpoint
      - Progression of geographic atrophy over 12 months, measured at 3 timepoints
      - Assessed by an independent and masked reading center
    - Robust statistical analysis to show effect (statistical significance)

*Formal and informal correspondence with regulatory agency
ASRS 2018 Annual Meeting, Vancouver, BC, Presentation by Wiley Chambers, MD

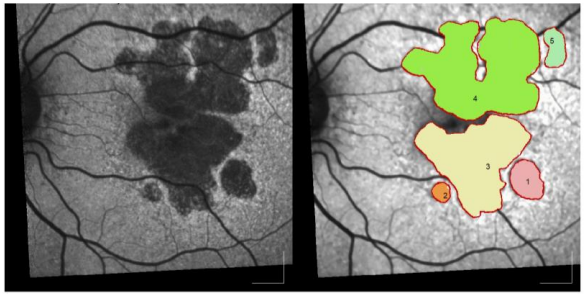
A PHASE 3 MULTICENTER, RANDOMIZED, DOUBLE-MASKED, SHAM CONTROLLED CLINICAL TRIAL TO ASSESS THE SAFETY AND EFFICACY OF INTRAVITREAL ADMINISTRATION OF ZIMURA™ (COMPLEMENT C5 INHIBITOR) IN SUBJECTS WITH GEOGRAPHIC ATROPHY SECONDARY TO DRY AGE-RELATED MACULAR DEGENERATION

Zimura in GA Secondary to Dry AMD Pivotal Clinical Trial

- ~400 subjects will be enrolled for treatment with Zimura or Sham for 24 months
- Randomization: 1:1

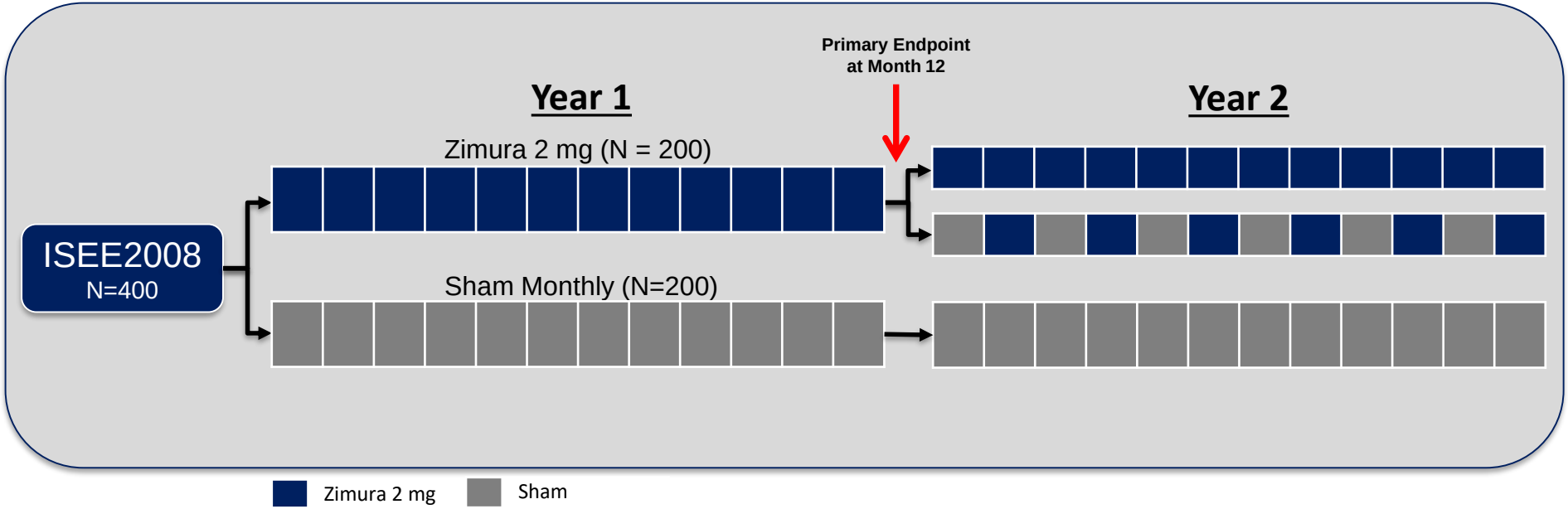
Zimura 2 mg N=200	Sham N=200

- **Primary Efficacy Endpoint:**
  - Mean rate of change in GA over 12 months measured by fundus autofluorescence (FAF) at three time points: Baseline, Month 6, and Month 12 (square root transformation of GA lesion)



Zimura in GA Secondary to Dry AMD Pivotal Clinical Trial

Primary Efficacy Endpoint: Mean rate of change in GA over 12 months measured by fundus autofluorescence (FAF) at three time points: Baseline, Month 6, and Month 12 (square root transformation)



Key Ophthalmic Inclusion Criteria (Study Eye)

- Non-foveal GA secondary to dry AMD
- Total GA area ≥ 2.5 and ≤ 17.5 mm^2 (1 and 7 disk areas [DA] respectively), determined by screening images of FAF
- If GA is multifocal, at least one focal lesion should measure ≥ 1.25 mm^2 (0.5 DA)
- GA in part within 1500 microns from the foveal center
- The atrophic lesion must be able to be photographed in its entirety
- Best corrected visual acuity in the SE between 20/25 – 20/320, inclusive

Key Ophthalmic Exclusion Criteria

- GA secondary to any condition other than AMD in either eye (e.g., drug-induced)
- Any prior treatment for AMD or any prior intravitreal treatment for any indication in either eye, except oral supplements of vitamins and minerals
- Evidence of CNV in either eye
- If subject develops CNV in the SE during the course of the trial, the subject remains in the study and continues to receive Zimura/Sham treatment (in addition to the standard of care anti-VEGF)
- Any ocular condition in the SE that would progress during the course of the study that could affect central vision or otherwise be a confounding factor

Thank You