

**INVESTOR CALL:**

**IZERVAY™ (AVACINCAPTAD PEGOL INTRAVITREAL SOLUTION)**

**GATHER2 2-YEAR DATA PRESENTED AT AAO 2023**

November 6, 2023 (JST)



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# AAO UPDATE AND GATHER2 SUMMARY AND BACKGROUND

# AAO UPDATE



**Ophthalmology**  
TIMES

**STAT**

**OCULAR SURGERY NEWS**

**HCP Live**

**eyetube**

## SUMMARY OF GATHER2: 2-YEAR DATA

Both monthly (EM) and every other month (EOM) IZERVAY reduced GA growth vs sham

Treatment effect more than doubled over 2 years compared to 1 year for IZERVAY

IZERVAY was well tolerated: over 2 years, there was 1 case of non-serious IOI, 1 case of culture-positive endophthalmitis, and no cases of ION or retinal vasculitis



In year 2, incidence of CNV was similar for sham vs IZERVAY EOM

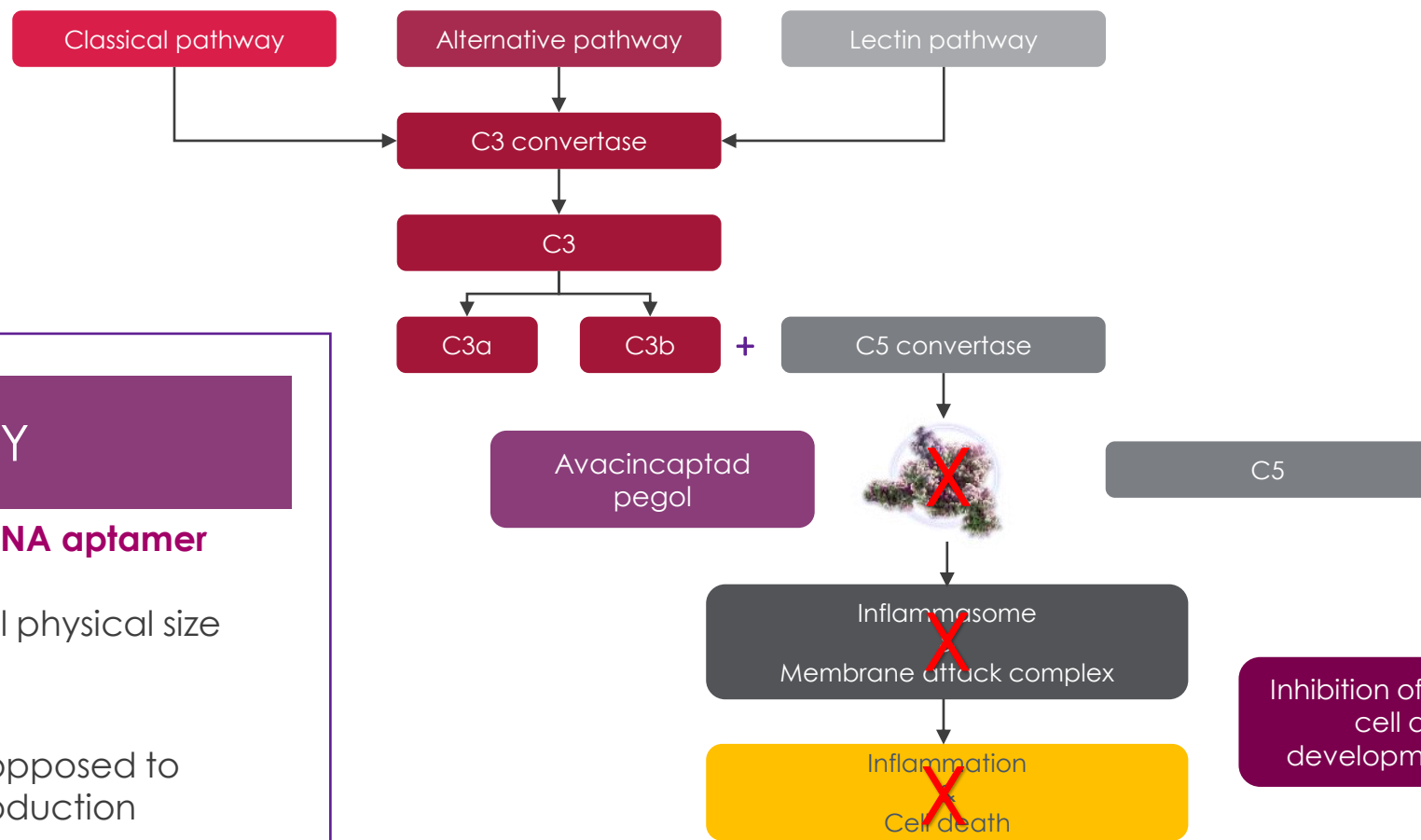
Over 2 years, only a slight increased incidence of CNV was observed for pooled IZERVAY vs sham (11.6% vs 9.0%, respectively)

# IZERVAY IS DESIGNED TO BE A SPECIFIC INHIBITOR OF COMPLEMENT C5

IZERVAY

Anti-C5 pegylated RNA aptamer

- 
Relatively small physical size
- 
Synthetic, as opposed to biological, production

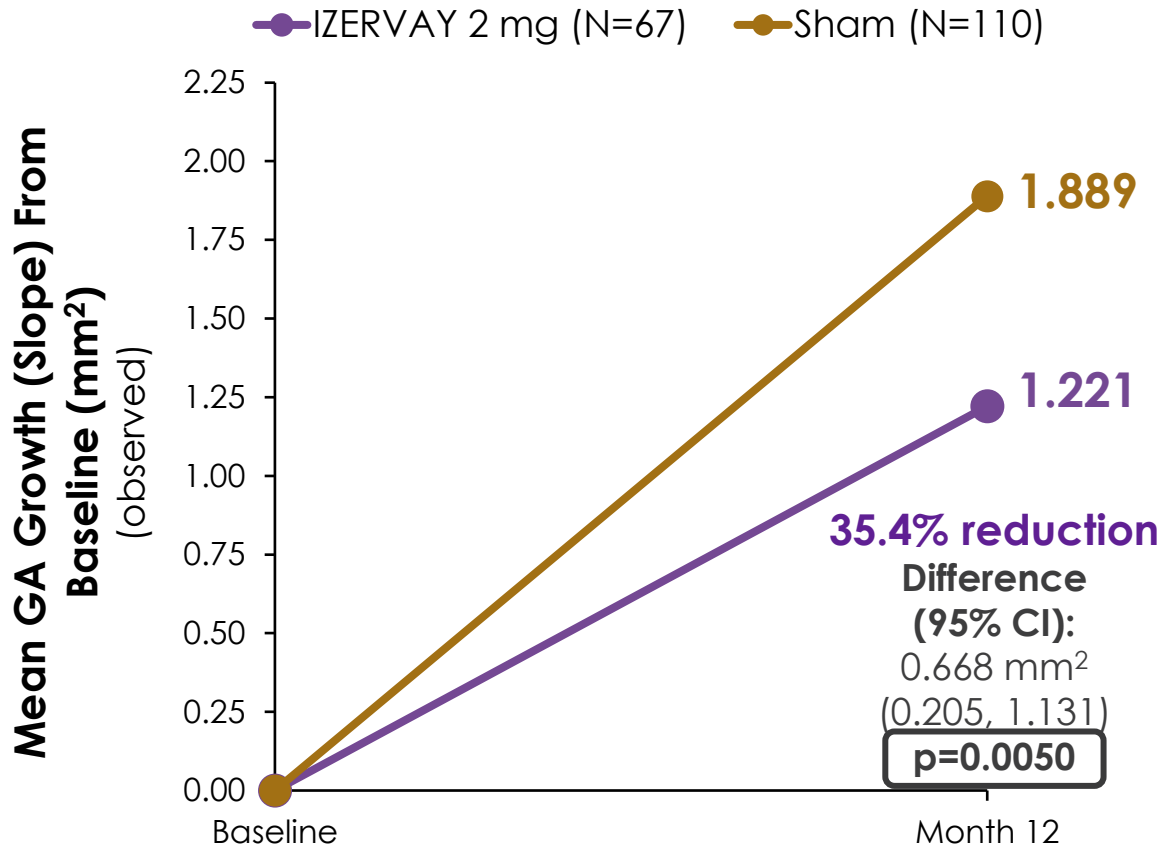


Inhibition of C5 slows inflammation and cell death associated with development and progression of GA

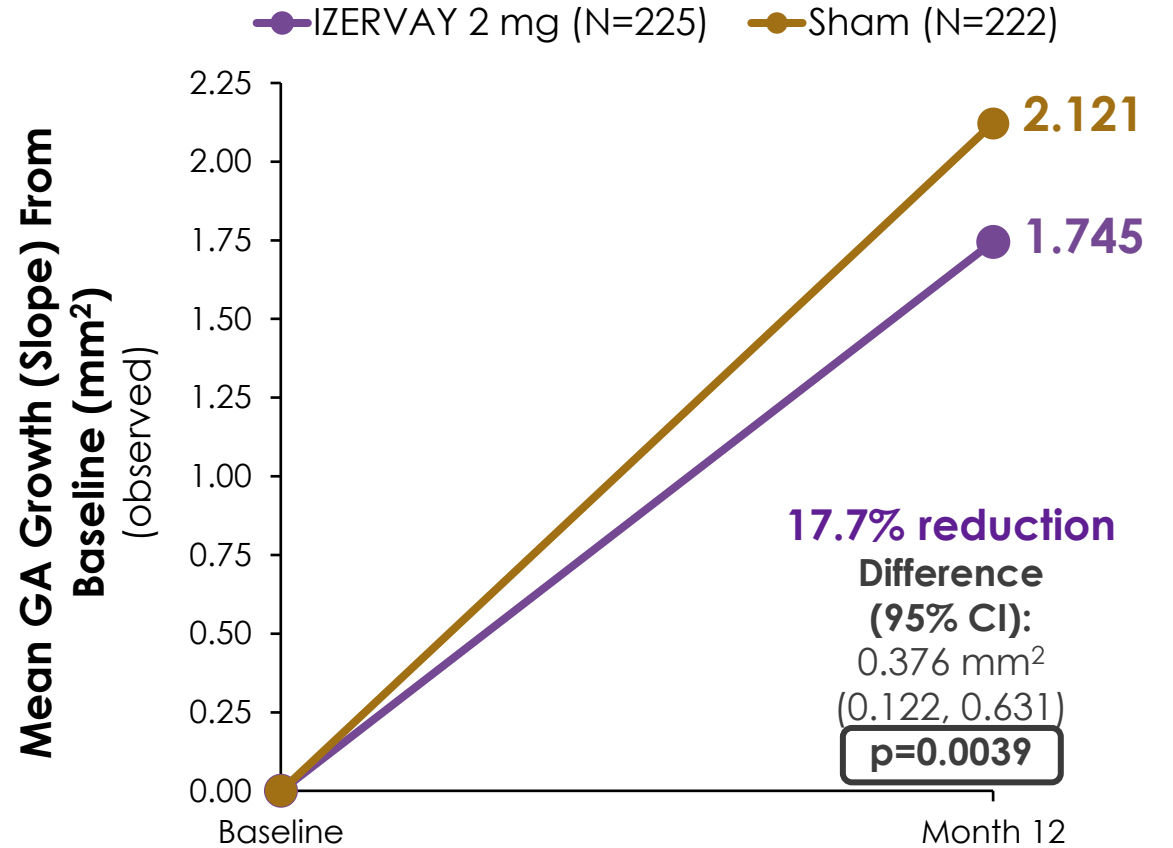


# IZERVAY ACHIEVED THE 12-MONTH PRESPECIFIED PRIMARY OBJECTIVE IN 2 PIVOTAL PHASE 3 STUDIES<sup>1,2</sup>

## GATHER 1

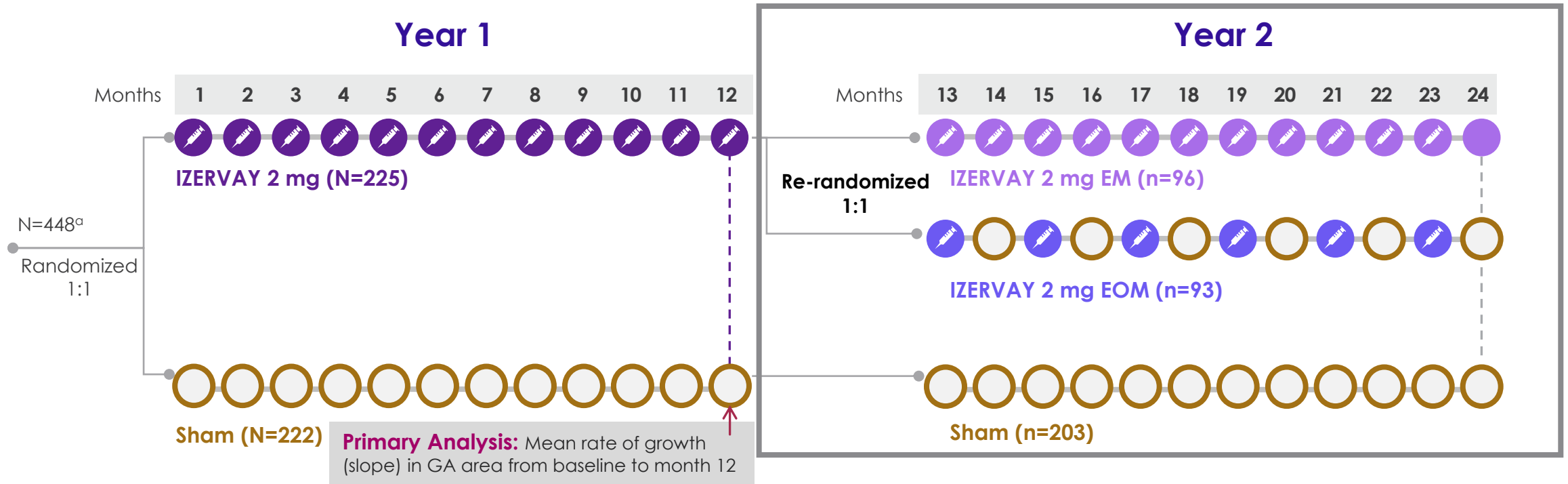


## GATHER 2



CI, confidence interval; GA, geographic atrophy. 1. Iveric Bio press release; 2. Khanani AM, et al. *Lancet*. 2023;402(10411):1449-1458.

# GATHER2 IS A 2-YEAR, PHASE 3, INTERNATIONAL, MULTICENTER, PROSPECTIVE, RANDOMIZED, DOUBLE-MASKED, SHAM-CONTROLLED STUDY (NCT04435366)



**Year 2 Objectives:**  
Evaluate efficacy and safety of re-randomized population of IZERVAY monthly (EM) and every other month (EOM) through year 2

**Statistical Methodology:**  
To control for multiplicity, year 2 statistical significance was conducted sequentially on prespecified outcomes:

1. Reduction in GA growth for IZERVAY EM vs sham
2. Reduction in rate of persistent vision loss for IZERVAY pooled vs sham
3. Reduction in GA growth for IZERVAY EOM vs sham

GA, geographic atrophy.  
Khanani AM, et al. *Lancet*. 2023;402(10411):1449-1458.  
Note: The 24-month objective used observed data. <sup>a</sup> 448 randomized, with 447 treated (1 patient in sham did not receive treatment after randomization).

# GATHER2 2-YEAR DATA

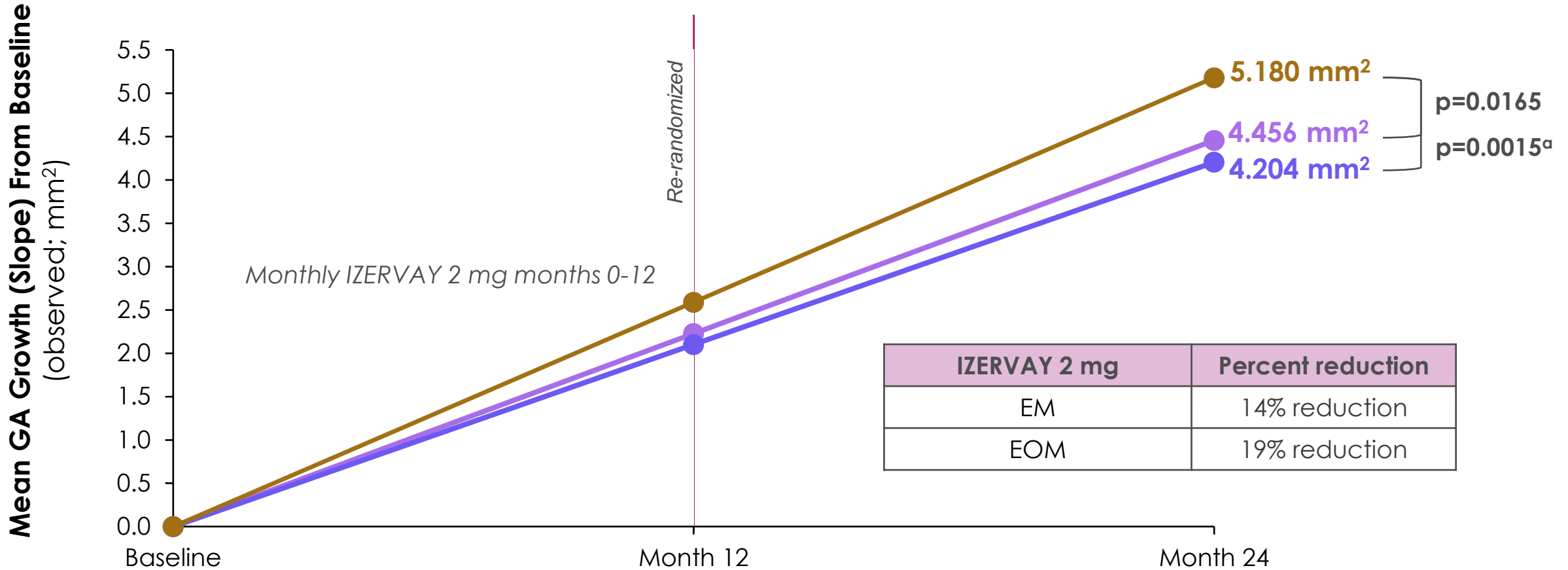


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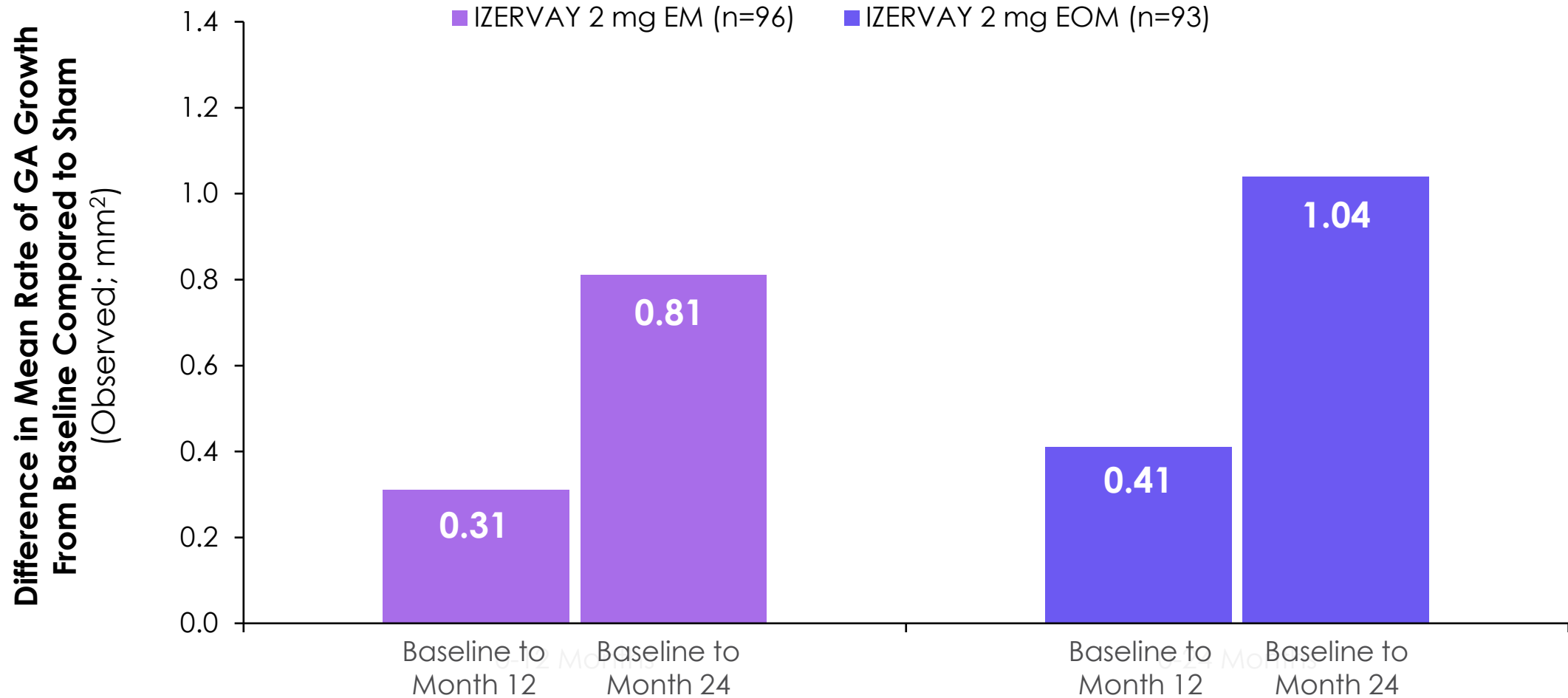
# IZERVAY REDUCED GA GROWTH WHEN DOSED EM AND EOM VS SHAM

● IZERVAY 2 mg EM (n=96) ● IZERVAY 2 mg EOM (n=93) ● Sham (n=203)



<sup>a</sup> P-value is nominal. Note: This analysis is based on a mixed model assuming constant growth rate from baseline to month 24. CI, confidence interval; EM, every month; EOM, every other month.

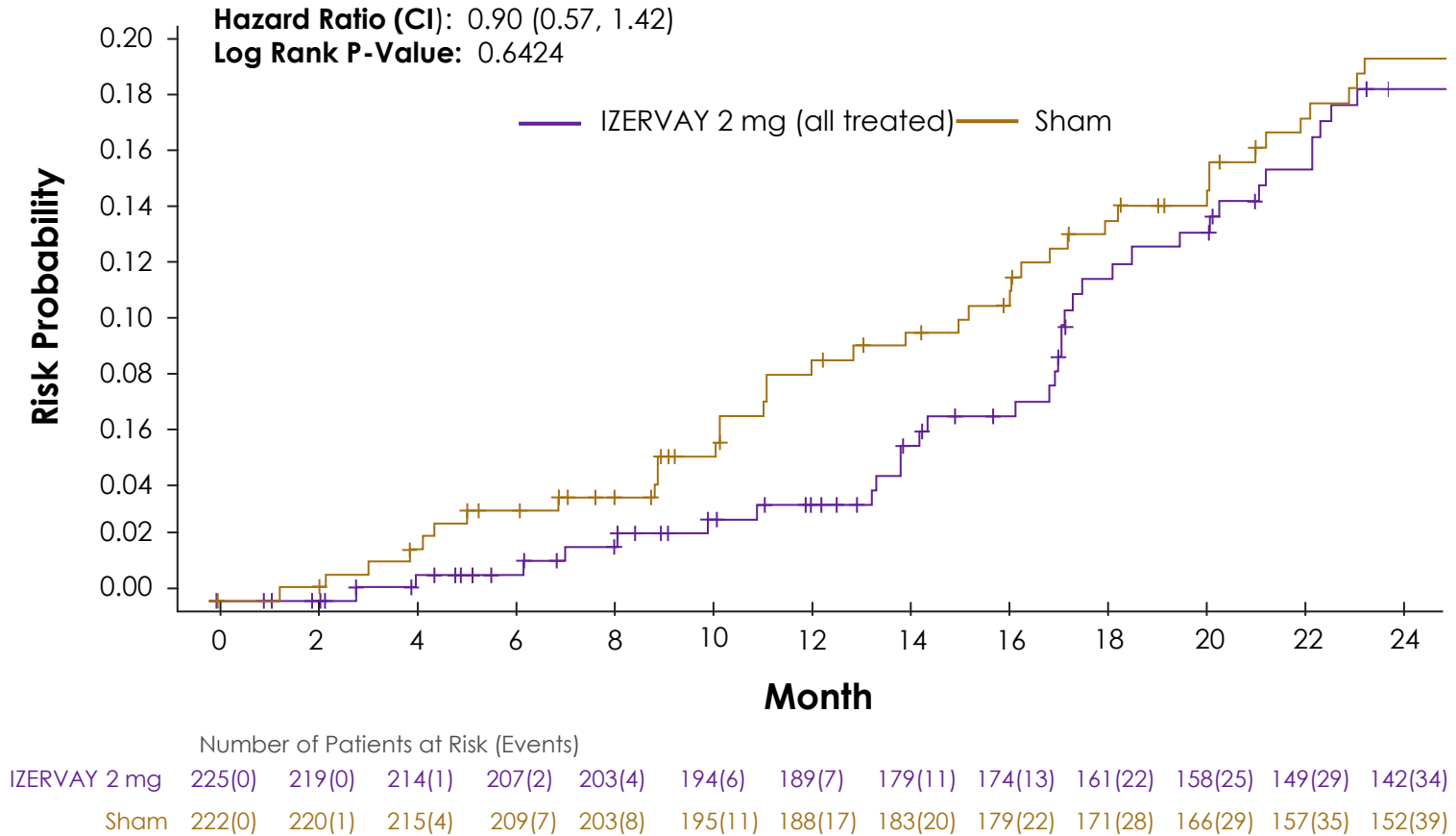
## TREATMENT EFFECT MORE THAN DOUBLED WITH IZERVAY OVER 2 YEARS COMPARED TO 1 YEAR



Note: This is a simplified piecewise slope spline Mixed model with Repeated Measures analysis. The analysis is based on a mixed effects model for repeated measures assuming a piecewise linear growth slope every 6 months. The EOM group received monthly IZERVAY in the first year. EM, every month; EOM, every other month

# NO STATISTICALLY SIGNIFICANT DIFFERENCE IN ≥15-LETTER PERSISTENT VISION LOSS BETWEEN IZERVAY AND SHAM

~ Mean change in BCVA and LL-BCVA from baseline between IZERVAY and sham was similar at two-years



Note: Persistent vision loss was defined as loss ≥15 letters in BCVA at 2 consecutive visits. Mean BCVA change from baseline at month 24 was -7.309 for ACP 2 mg (N=225) and -6.475 for sham (N=222). Mean LL-BCVA change from baseline at month 24 was -10.583 for ACP 2 mg (N=225) and -9.096 for sham (N=222). BCVA, best-corrected visual acuity; CI, confidence interval; LL-BCVA, low-luminance BCVA.

# TREATMENT EMERGENT ADVERSE EVENTS (TEAES) OVER 2 YEARS WERE SIMILAR AND CONSISTENT WITH YEAR 1<sup>1</sup>

	<b>IZERVAY (N=225)</b>	<b>Sham (N=222)</b>
<b>TEAEs, n (%)</b>	<b>208 (92.4)</b>	<b>184 (82.9)</b>
Ocular in study eye	144 (64.0)	107 (48.2)
Non-ocular	172 (76.4)	160 (72.1)
<b>Serious TEAEs, n (%)</b>	<b>60 (26.7)</b>	<b>51 (23.0)</b>
Ocular in study eye	4 (1.8)	2 (0.9)
Non-ocular	55 (24.4)	49 (22.1)
<b>TEAEs leading to study drug discontinuation, n (%)</b>	<b>11 (4.9)</b>	<b>9 (4.1)</b>
Ocular in study eye	4 (1.8)	0
Non-ocular	7 (3.1)	9 (4.1)

Note: n = study eyes with events.

1. Khanani AM, et al. *Lancet*. 2023;402(10411):1449-1458.

# SERIOUS OCULAR TEAEs – NO NEW SAFETY SIGNALS IN YEAR 2

	Year 1 <sup>1</sup>		Year 2			Total	
	IZERVAY 2 mg (N=225)	Sham (N=222)	IZERVAY 2 mg EM (n=96)	IZERVAY 2 mg EOM (n=93)	Sham (n=203)	IZERVAY 2 mg (N=225)	Sham (N=222)
<b>Serious ocular TEAEs in study eye, n (%)</b>	<b>2 (0.9)</b>	<b>2 (0.9)</b>	<b>2 (2.1)</b>	<b>0 (0.0)</b>	<b>0 (0.0)</b>	<b>4 (1.8)</b>	<b>2 (0.9)</b>
Choroidal neovascularization	2 (0.9)	1 (0.5)	0	0	0	2 (0.9)	1 (0.5)
Visual acuity reduced	0	1 (0.5) <sup>a</sup>	0	0	0	0	1 (0.5) <sup>a</sup>
Visual acuity reduced transiently	0	1 (0.5) <sup>a</sup>	0	0	0	0	1 (0.5) <sup>a</sup>
Endophthalmitis	0	0	1 (1.0) <sup>b</sup>	0	0	1 (0.4) <sup>b</sup>	0
Subluxated intraocular lens	0	0	1 (1.0)	0	0	1 (0.4)	0

<sup>a</sup> Occurred in the same patient; <sup>b</sup> Culture positive.

Note: Choroidal neovascularization = eMNV, neMNV, peripapillary NV.

EM, every month; eMNV, exudative macular neovascularization; MNV, macular neovascularization; EOM, every other month; neMNV, nonexudative MNV; NV, neovascularization; TEAE, treatment emergent adverse event.

1. Khanani AM, et al. *Lancet*. 2023;402(10411):1449-1458.



# CHOROIDAL NEOVASCULARIZATION (CNV)

	Year 1 <sup>1</sup>		Year 2			Total	
	IZERVAY 2 mg (N=225)	Sham (N=222)	IZERVAY 2 mg EM (n=96)	IZERVAY 2 mg EOM (n=93)	Sham (n=203)	IZERVAY 2 mg (N=225)	Sham (N=222)
<b>CNV in study eye, n (%)</b>	15 (6.7)	9 (4.1)	7 (7.3)	4 (4.3)	11 (5.4)	26 (11.6)	20 (9.0)

**Incidence of CNV in year 2 was similar for sham and the IZERVAY groups**

Note: Choroidal neovascularization = eMNV, neMNV, peripapillary NV.

EM, every month; eMNV, exudative macular neovascularization; MNV, macular neovascularization; EOM, every other month; neMNV, nonexudative MNV; NV, neovascularization.

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# ADVERSE EVENTS OF SPECIAL INTEREST

	Year 1 <sup>1</sup>		Year 2			Total	
	IZERVAY 2 mg (N=225)	Sham (N=222)	IZERVAY 2 mg EM (n=96)	IZERVAY 2 mg EOM (n=93)	Sham (n=203)	IZERVAY 2 mg (N=225)	Sham (N=222)
Intraocular inflammation	0	0	1 (1.0)	0	0	1 (0.4)	0
Endophthalmitis	0	0	1 (1.0) <sup>a</sup>	0	0	1 (0.4) <sup>a</sup>	0
Ischemic optic neuropathy	0	0	0	0	0	0	0

## Over 2 years

- 1 case of non-serious intraocular inflammation, reported as trace vitreous cells
- 1 case of culture-positive endophthalmitis
- No cases of ischemic optic neuropathy and occlusive or non-occlusive retinal vasculitis

<sup>a</sup> Culture positive.  
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# LIFECYCLE MANAGEMENT UPDATE

## **GATHER2**

Ongoing open-label study capturing long-term safety data

## **LABEL**

Anticipate FDA filing submission for label update on treatment duration and regimen in Q4 FY2023

## **EMA**

The Marketing Authorization Application for ACP was accepted on 17 Aug 2023



# Q&A

