LONG-TERM DATA

IZERVAY 3.5-year GATHER2 Open-Label Extension (OLE) Trial:

Safety and treatment observations

These OLE analyses help us better understand IZERVAY's role in GA management."

– **Dr. Arshad M. Khanani,** Vitreoretinal Surgeon

INDICATION

IZERVAY® (avacincaptad pegol intravitreal solution) is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD)

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

IZERVAY is contraindicated in patients with ocular or periocular infections and in patients with active intraocular inflammation.

WARNINGS AND PRECAUTIONS

Endophthalmitis and Retinal Detachments

- Intravitreal injections, including those with IZERVAY, may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering IZERVAY in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.

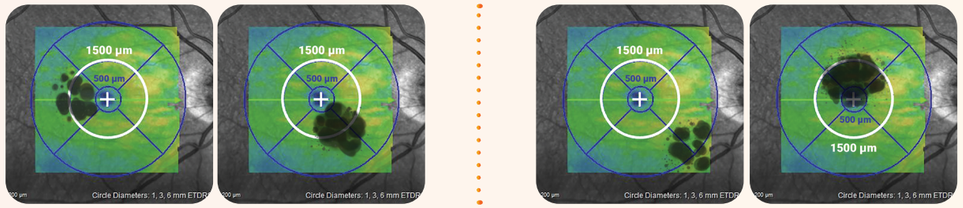
Please see additional Important Safety Information on page 9 and full Prescribing Information for more information.

izervay® (avacincaptad pegol intravitreal solution) 2 mg

IZERVAY was evaluated in patients with GA secondary to AMD[1]

The efficacy and safety of IZERVAY were demonstrated in 2 randomized, multicenter, double-masked, sham-controlled studies in patients with GA due to AMD (GATHER1 and GATHER2).[1]

✓ Included ✓ Included ✗ Not Included ✗ Not Included



Within 1500 µm of, but not involving, the foveal center point[2]

Outside of 1500 µm from the foveal center point[2]

Foveal center point involvement[2]

~84% of patients had disease within 500 µm of the foveal center point[2]

Additional inclusion criteria[3,4]

- ≥50 years
- BCVA between 20/25 and 20/320
- GA lesions:
  - Total area between 2.5 mm^2 and 17.5 mm^2 (1-7 DA, respectively)
  - If multifocal lesions, at least 1 lesion had to be ≥1.25 mm^2 (0.5 DA)

Additional exclusion criteria[3,4]

- Evidence of CNV or any sign of diabetic retinopathy in either eye at baseline
- GA secondary to any condition other than AMD in either eye
- Any prior treatment for AMD or any prior intravitreal treatment for any indication in either eye (except oral vitamin or mineral supplements)
- Any ocular condition in study eye that could progress during the study and potentially affect central vision or otherwise act as a confounding factor

Additionally, a Phase 3, open-label, multicenter, 18-month extension study enrolled 278 participants who completed GATHER2 through the Month 24 visit. Unlike the GATHER1 and GATHER2 inclusion criteria, the OLE study allowed participants with center point–involving GA to enroll in the study (32.7% [91/278]).[2]

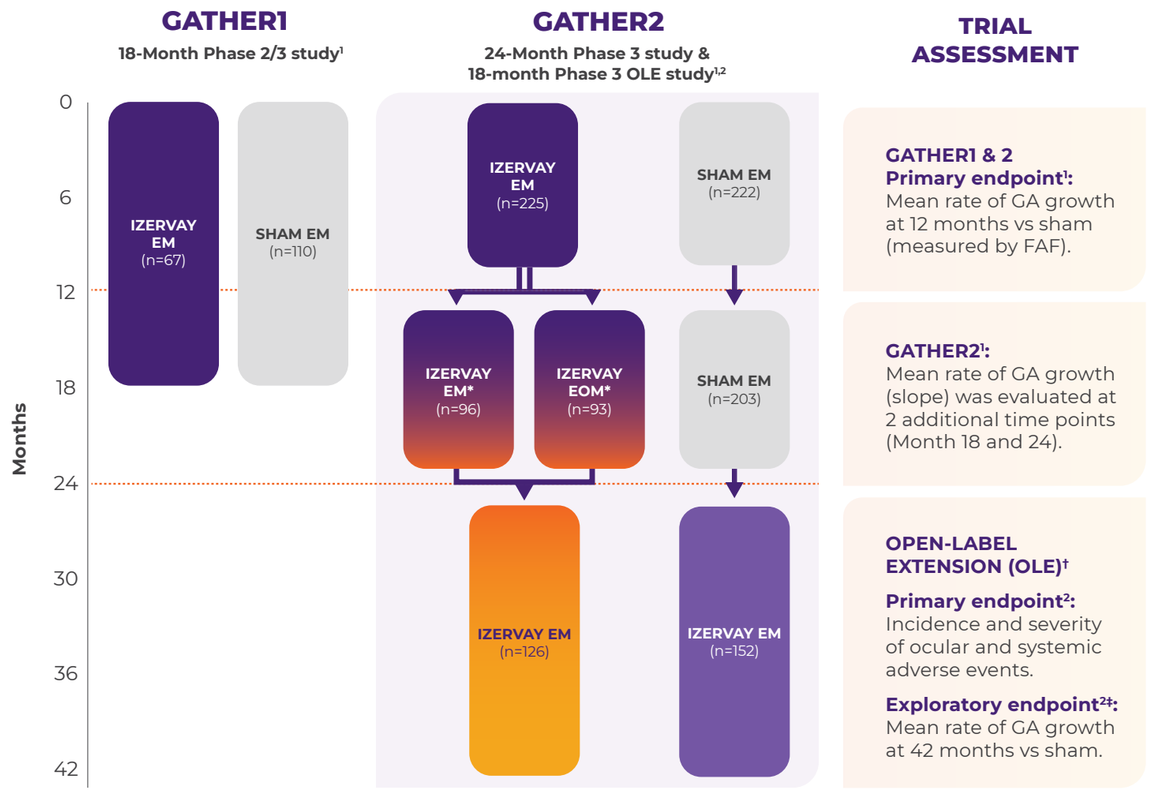
DA=disc area; BCVA=best corrected visual acuity; CNV=choroidal neovascularization.

IMPORTANT SAFETY INFORMATION (CONT'D)
WARNINGS AND PRECAUTIONS (CONT'D)

Neovascular AMD

- In clinical trials, use of IZERVAY was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (7% when administered monthly and 4% in the sham group) by Month 12. Over 24 months, the rate of neovascular (wet) AMD or choroidal neovascularization in the GATHER2 trial was 12% in the IZERVAY group and 9% in the sham group. Patients receiving IZERVAY should be monitored for signs of neovascular AMD.

IZERVAY was assessed in two Phase 3 trials and an open-label extension study through 3.5 years[1,2]



*Patient re-randomization.
†All participants, regardless of prior GATHER2 treatment (IZERVAY or sham), received IZERVAY in the study eye. All participants were to have a final follow-up visit or follow-up procedure at Month 42 if the study was terminated early. The end of the study was defined as the date of the last study assessment for the last participant in the study globally.
‡Exploratory endpoints include the following ophthalmic variables: BCVA, LLVA, LLD, IOP, OE, and GA area.

The recommended dose for IZERVAY is 2 mg once monthly (approximately 28 +/- 7 days)[1]

EM=every month; EOM=every other month; FAF=fundus autofluorescence; IOP=intraocular pressure; LLD=low luminance deficit; LLVA=low luminance visual acuity; OE=ophthalmic examination.

Please see additional Important Safety Information on page 9 and full Prescribing Information for more information.

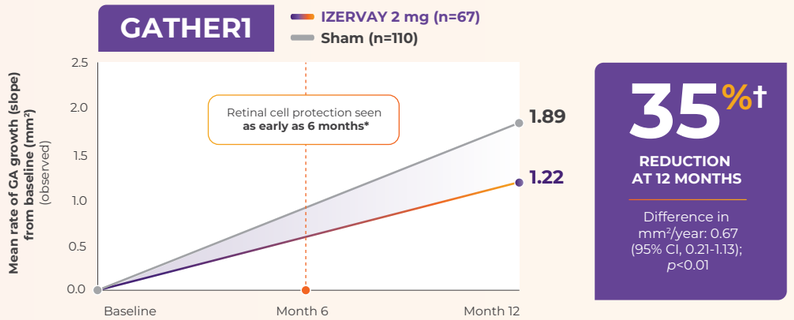
izervay (avacincaptad pegol intravitreal solution) 2 mg

Primary endpoint data

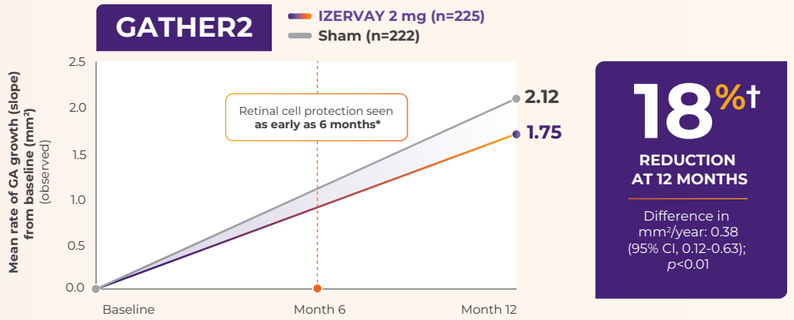
IZERVAY provided significant protection of healthy retinal cells in just one year of treatment[1]

The primary endpoint in GATHER1 and 2 evaluated the mean rate of GA growth (slope) from baseline to Month 12, measured by FAF at 3 time points (baseline, Month 6, and Month 12). In GATHER2, the mean rate of GA growth (slope) measured by FAF was evaluated at 2 additional time points (Month 18 and Month 24).[1]

Reductions in mean rate of growth (MMRM analysis) at 12 months vs sham[1]



35%†
REDUCTION AT 12 MONTHS
Difference in mm²/year: 0.67 (95% CI, 0.21-1.13); *p*<0.01



18%†
REDUCTION AT 12 MONTHS
Difference in mm²/year: 0.38 (95% CI, 0.12-0.63); *p*<0.01

IZERVAY is the only GA treatment to demonstrate statistically significant efficacy at one year in two Phase 3 trials[1,5]

CI=confidence interval; MMRM=mixed models for repeated measures.
*6-month time point was not part of the primary analysis, is observational in nature and should be interpreted with caution, and cannot be considered conclusive.
†Percent difference is calculated by 100×(difference)/(least squares mean from sham).

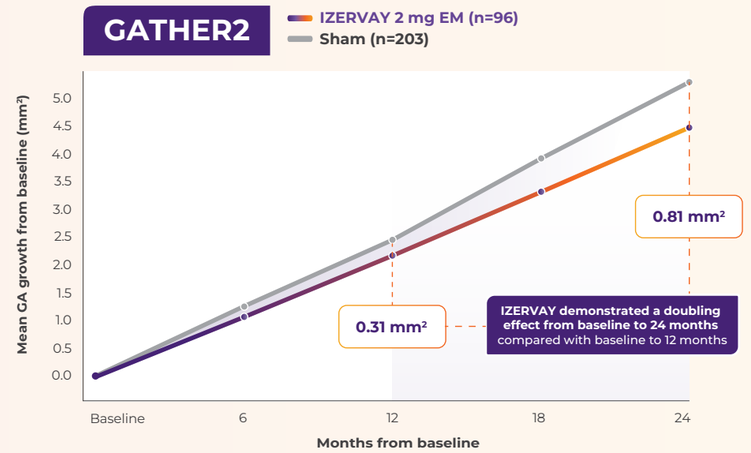
IMPORTANT SAFETY INFORMATION (CONT'D)
WARNINGS AND PRECAUTIONS (CONT'D)
Increase in Intraocular Pressure

- Transient increases in intraocular pressure (IOP) may occur after any intravitreal injection, including with IZERVAY. Perfusion of the optic nerve head should be monitored following the injection and managed appropriately.

24-Month data

IZERVAY demonstrated an increasing treatment effect over 2 years[1,6]

Analysis of mean growth in GA area (mm²) at Month 24 vs sham[2,6‡]



Piecewise spline multivariate slope.

The annualized rate of GA growth (MMRM analysis)[§] at 24 months in GATHER2[1]

IZERVAY 2 mg EM

- **2.23 mm²/year**
- 14% reduction at 24 months; difference vs sham (95% CI) mm²/year=0.36 (0.07-0.66); *p*=0.0165[‖]

IZERVAY 2 mg EM to EOM

- **2.10 mm²/year**
- Due to the hierarchical testing procedure, no statistical test was performed for the EOM treatment group

The recommended dose for IZERVAY is 2 mg once monthly (approximately 28 +/- 7 days)[1]

‡Analysis is based on MMRM assuming a piecewise linear trend at Month 6, 12, 18, including effects for treatment, time, and time by treatment interaction.
§Non-transformed GA growth slope analysis.
‖Percent difference is calculated by 100×(difference)/(least squares mean from sham).

Please see additional Important Safety Information on page 9 and full Prescribing Information for more information.

izervay (avacincaptad pegol intravitreal solution) 2 mg

Safety

Proven safety through 2 years in the GATHER trials[1]

IZERVAY is the only FDA-approved GA treatment with no warning and precaution for intraocular inflammation or retinal vasculitis[1,5]

Common ocular adverse reactions (≥2%) and greater than sham in study eye through 12 months[1]	GATHER1 and GATHER2 IZERVAY (n=292)	GATHER1 and GATHER2 Sham (n=332)
Conjunctival hemorrhage	13%	9%
Increased intraocular pressure (IOP)	9%	1%
Blurred vision*	8%	5%
Choroidal neovascularization (CNV)	7%	4%
Eye pain	4%	3%
Vitreous floaters	2%	<1%
Blepharitis	2%	<1%

Adverse events of special interest[2-4]	GATHER1 (0-12 months) IZERVAY (n=67)	GATHER1 (0-12 months) Sham (n=110)	GATHER2 (0-24 months) IZERVAY (n=225)	GATHER2 (0-24 months) Sham (n=222)
Intraocular inflammation (IOI), n†	1	0	1	0
Endophthalmitis, n	0	0	1‡	0
Ischemic optic neuropathy, n	0	0	0	0
Retinal vasculitis, n	0	0	0	0

- Safety data observed in patients with GA secondary to AMD up to 24 months were consistent with those seen at 12 months[1,4]
- Over 24 months, the rate of neovascular (wet) AMD or choroidal neovascularization in the GATHER2 trial was 12% in the IZERVAY group and 9% in the sham group[1]

The real-world safety profile across more than 500k vials of IZERVAY remains consistent with findings from the GATHER trials[1,2§]

*Blurred vision includes visual impairment, vision blurred, visual acuity reduced, visual acuity reduced transiently.
†In GATHER1, one case of IOI was reported at Month 7 without any antechamber inflammation. This event was mild with no effect on visual acuity. Per the investigator, the event was not drug- or injection procedure-related. In GATHER2, one case of nonserious IOI occurred during Year 2 of treatment. This event was reported as trace vitreous cells and was not related to the study drug or injection procedure.
‡Culture positive.
§As of 12/25. Based on samples and commercially distributed vials.

OLE data

No cases of retinal or occlusive vasculitis were reported through 3.5 years[2]

Ocular TEAEs ≥2% during open-label extension	IZERVAY to IZERVAY EM (n=125)	Sham to IZERVAY EM (n=151)
Ocular TEAEs in the study eye, % (n)	59.2% (74)	58.3% (88)
Increased intraocular pressure (IOP)	15.2% (19)	13.2% (20)
Cataract	12.8% (16)	7.3% (11)
Conjunctival hemorrhage	10.4% (13)	9.9% (15)
Vitreous detachment	5.6% (7)	0.7% (1)
Visual acuity reduced	5.6% (7)	13.2% (20)
New-onset CNV‖	5.6% (7)	9.3% (14)
Punctate keratitis	3.2% (4)	6.0% (9)
Transient visual loss	3.2% (4)	2.0% (3)
Posterior capsule opacification	2.4% (3)	4.6% (7)

IZERVAY treatment duration[2]:

- IZERVAY to IZERVAY: 42 months
- Sham to IZERVAY: 18 months

TEAE=treatment emergent adverse event.
‖New-onset CNV includes patients with CNV incidence during open-label extension portion but not CNV that occurred during the GATHER2 trial.

IMPORTANT SAFETY INFORMATION (CONT'D)

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥5%) reported in patients receiving IZERVAY were conjunctival hemorrhage, increased IOP, blurred vision, and neovascular age-related macular degeneration.

Please see additional Important Safety Information on page 9 and full Prescribing Information for more information.

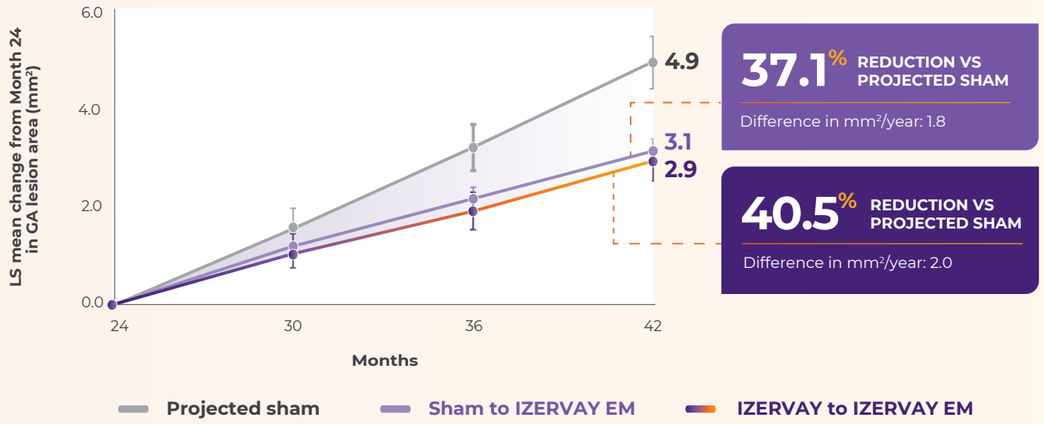
izervay (avacincaptad pegol intravitreal solution) 2 mg

OLE exploratory endpoint

Observed reduction in rate of GA lesion growth vs projected sham by 37.1% and 40.5% from Months 24-42[2]

Given the exploratory nature of the data, these results should be interpreted with caution and cannot be considered conclusive. The OLE analysis used a projected sham and may not reflect rate of change for all GA patients. Although prespecified, there was no statistical testing hierarchy. Open-label studies can allow for selection bias; clinical significance is not established.

Reductions in mean rate of growth (MMRM analysis) from Months 24 to 42 vs projected sham[2]



37.1% REDUCTION VS PROJECTED SHAM

Difference in mm²/year: 1.8

40.5% REDUCTION VS PROJECTED SHAM

Difference in mm²/year: 2.0

Methodology: For projected sham, GA growth rate from Month 24 to Month 42 was first calculated as the average transformed growth rates across four 6-month intervals (baseline through Month 24) in the GATHER2 sham group and subsequently converted to the untransformed scale.[2]

For the IZERVAY groups, a separate piecewise MMRM was applied using square root transformed GA area data. The least squares mean of the square root transformed GA area was calculated and converted to the untransformed scale.[2]

LS=least squares.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

IZERVAY is contraindicated in patients with ocular or periocular infections and in patients with active intraocular inflammation.

Please see additional Important Safety Information on page 9 and full Prescribing Information for more information.

INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION

IZERVAY® (avacincaptad pegol intravitreal solution) is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD)

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

IZERVAY is contraindicated in patients with ocular or periocular infections and in patients with active intraocular inflammation.

WARNINGS AND PRECAUTIONS

Endophthalmitis and Retinal Detachments

- Intravitreal injections, including those with IZERVAY, may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering IZERVAY in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.

Neovascular AMD

- In clinical trials, use of IZERVAY was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (7% when administered monthly and 4% in the sham group) by Month 12. Over 24 months, the rate of neovascular (wet) AMD or choroidal neovascularization in the GATHER2 trial was 12% in the IZERVAY group and 9% in the sham group. Patients receiving IZERVAY should be monitored for signs of neovascular AMD.

Increase in Intraocular Pressure

- Transient increases in intraocular pressure (IOP) may occur after any intravitreal injection, including with IZERVAY. Perfusion of the optic nerve head should be monitored following the injection and managed appropriately.

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥5%) reported in patients receiving IZERVAY were conjunctival hemorrhage, increased IOP, blurred vision, and neovascular age-related macular degeneration.

Please see full Prescribing Information for more information.

Physician featured has been compensated.

izervay (avacincaptad pegol intravitreal solution) 2 mg

izervay (avacincaptad pegol intravitreal solution) 2 mg

Treat to protect with IZERVAY[1]

The #1 prescribed FDA-approved treatment for new GA patients[2]*

Visit IZERVAYecp.com to learn more

*Based on Symphony data from 3/24-10/25. May not represent entire patient population.

References: 1. Izervay. Package insert. Northbrook, IL: Astellas Pharma US, Inc.; 2025. **2.** Astellas Pharma US, Inc. Izervay. Data on File. **3.** Patel SS, Lally DR, Hsu J, et al. Avacincaptad pegol for geographic atrophy secondary to age-related macular degeneration: 18-month findings from the GATHER1 trial. *Eye*. 2023;37(17):3551-3557. Erratum in: *Eye*. 2023;37(17):3705. **4.** Khanani AM, Patel SS, Staurenghi G, et al. Efficacy and safety of avacincaptad pegol in patients with geographic atrophy (GATHER2): 12-month results from a randomised, double-masked, phase 3 trial. *Lancet*. 2023;402(10411):1449-1458. **5.** Syfovre. Package insert. Waltham, MA: Apellis Pharmaceuticals, Inc.; 2025. **6.** Khanani AM, Danzig CJ, Heier JS, et al. Avacincaptad pegol for geographic atrophy secondary to age-related macular degeneration: 2-year efficacy and safety results from the GATHER2 phase 3 trial [published online ahead of print December 15, 2025]. *Ophthalmology*. 2025. https://www.aaojournal.org/action/showPdf?pii=S0161-6420(25)00790-0.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS

Endophthalmitis and Retinal Detachments

- Intravitreal injections, including those with IZERVAY, may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering IZERVAY in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.

Please see additional Important Safety Information on page 9 and full Prescribing Information for more information.

astellas