Astellas Pharma Inc.

IZERVAY Online Meeting

November 6, 2023

Event Summary

[Company Name]	Astellas Pharma Inc.	
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[Event Type]	Special Announcement	
[Event Name]	IZERVAY Online Meeting	
[Date]	November 6, 2023	
[Time]	07:30 – 08:20 (Total: 50 minutes, Presentation: 19 minutes, Q&A: 31 minutes)	
[Venue]	Webcast	
[Number of Speakers]	4	
	Hiromitsu Ikeda	Chief Communications & IR Officer
	Dhaval Desai	Senior Vice President and Chief Development Officer, Iveric Bio, An Astellas Company
	Erin Henry	Vice President, Product Strategy and Innovation, Iveric Bio, An Astellas Company
	Carolyn Sasse	Vice President, Head of Cell & Gene Therapy Development
[Questioner]	Hidemaru Yamaguchi	Citigroup Global Markets
	Shinichiro Muraoka	Morgan Stanley MUFG Securities
	Kazuaki Hashiguchi	Daiwa Securities Group
	Kasumi Haruta	Credit Suisse Securities
	Miki Sogi	Sanford C. Bernstein
	Shinya Tsuzuki	Mizuho Securities

Presentation

Ikeda: Good morning. Thank you very much for joining Astellas Pharma Inc.'s IZERVAY online meeting today, taking time out of your very busy schedules. I'm delighted to serve as the emcee today. I'm Hidemaru Ikeda, Chief Communications & IR Officer. Thank you very much for your time.

Today, GATHER2 study's 24-month data presented at the AAO, the American Academy of Ophthalmology, will be explained by our clinical development persons-in-charge. Today's participants are Iveric Bio's Senior Vice President and Chief Development Officer, Dhaval Desai; Iveric Bio's Vice President, Product Strategy and Innovation, Erin Henry; Vice President, Head of Cell & Gene Therapy Development, Carolyn Sasse.

Today, we will provide simultaneous interpreting between Japanese and English, including Q&A. We cannot guarantee the accuracy of simultaneous translation. On the Zoom menu screen, please select your preferred language. If you select the original option, you can listen to the original sound without going through simultaneous interpretation.

Today, we're going to provide an explanation based on the explanatory meeting materials posted on our website. This material or presentation by representatives for the Company and their answers and statements in the Q&A session include forward-looking statements based on assumptions and beliefs in light of the information currently available to management and are subject to significant risks and uncertainties. Actual results may differ materially depending on a number of factors. They contain information on pharmaceuticals, including compounds under development. This information is not intended to make any representations or advertisements nor provide medical advice of any kind.

We'd now like to go into the presentation. Dhaval, please start your presentation.

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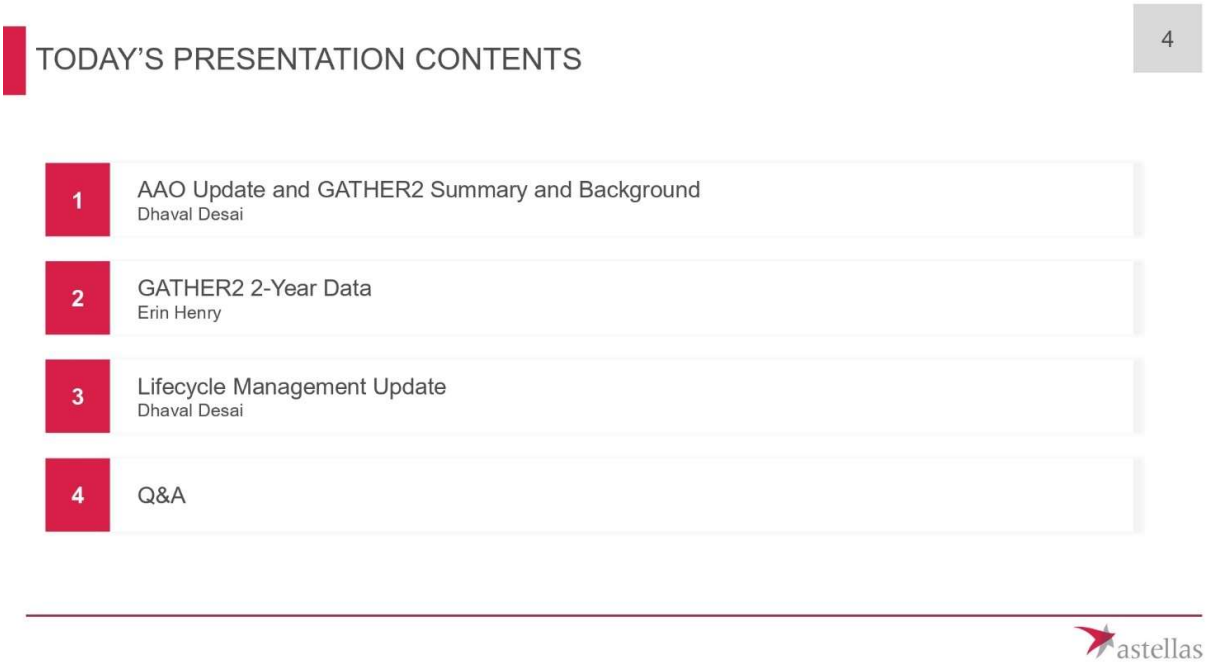
Desai: Hi, everyone. My name is Dhaval Desai, and I'm the Chief Development Officer at Iveric Bio, an Astellas company.



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Today, my colleague Erin Henry and I will be providing updates on IZERVAY and recapping the GATHER2 year two data that was presented yesterday at the American Academy of Ophthalmology.

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I will start with an update on our presentation at AAO and a brief background on the GATHER2 clinical trial.

AAO UPDATE

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We presented the IZERVAY two-year results for the first time yesterday at the AAO Annual Meeting. The reaction among attendees was highly positive, and we have already conducted a number of interviews with key media.

SUMMARY OF GATHER2: 2-YEAR DATA

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- 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)

CNV, choroidal neovascularization; GA, geographic atrophy; IOI, intraocular inflammation; ION, ischemic optic neuropathy.

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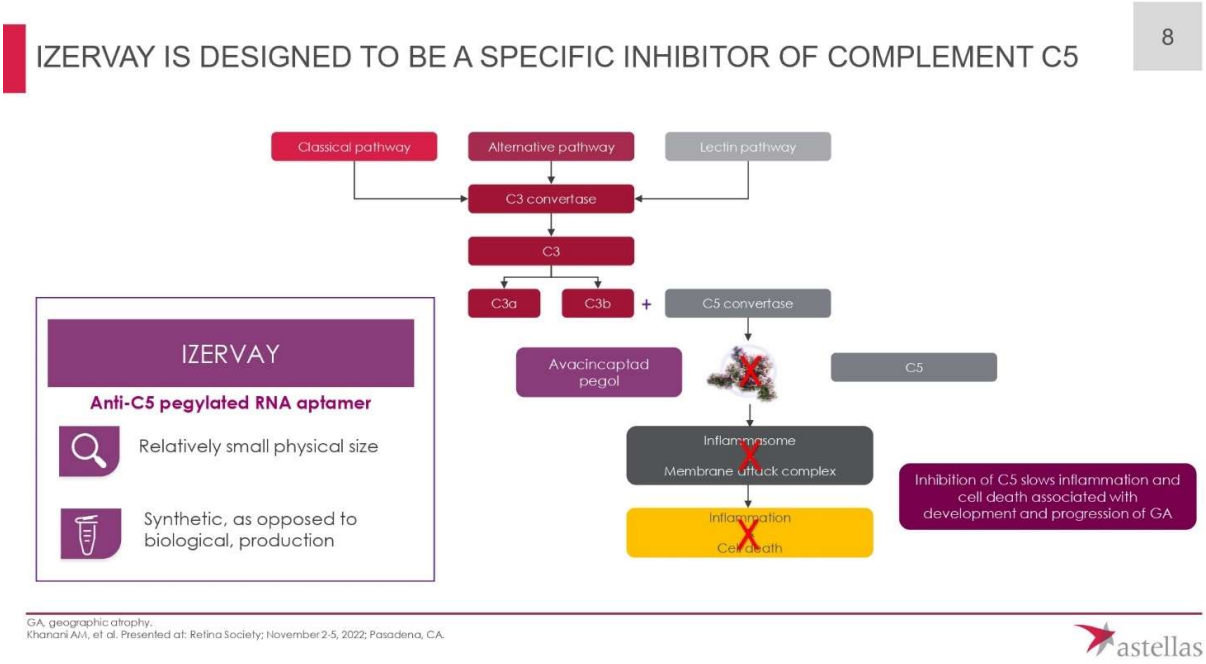
To summarize the major findings: after two years of treatment, IZERVAY dosed monthly and every other month had a similar effect on reducing the growth of geographic atrophy, or GA, versus the sham.

Compared to the first year, the treatment effect more than doubled over two years for IZERVAY treated monthly or every other month compared to the sham.

IZERVAY continued to be well-tolerated. After two years of treatment, there was one case of nonserious intraocular inflammation, one case of culture-positive endophthalmitis, and no cases of ischemic optic neuropathy or retinal vasculitis.

In the second year of treatment, the incidence of choroidal neovascularization or CNV, was similar between the sham group and IZERVAY dosed every other month.

Over the same time period, there was only a slightly increased incidence of CNV between the pooled IZERVAY treatment groups versus sham.



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To give you a quick background, IZERVAY is a pegylated RNA aptamer designed to be a specific inhibitor of complement C5. Inhibition of C5 slows inflammation and cell death associated with the development and progression of GA. By inhibiting this terminal-most effector, IZERVAY may preserve beneficial upstream areas in the complement system, including the anti-inflammatory benefit of C3a.

IZERVAY ACHIEVED THE 12-MONTH PRESPECIFIED PRIMARY OBJECTIVE IN 2 PIVOTAL PHASE 3 STUDIES[1,2]

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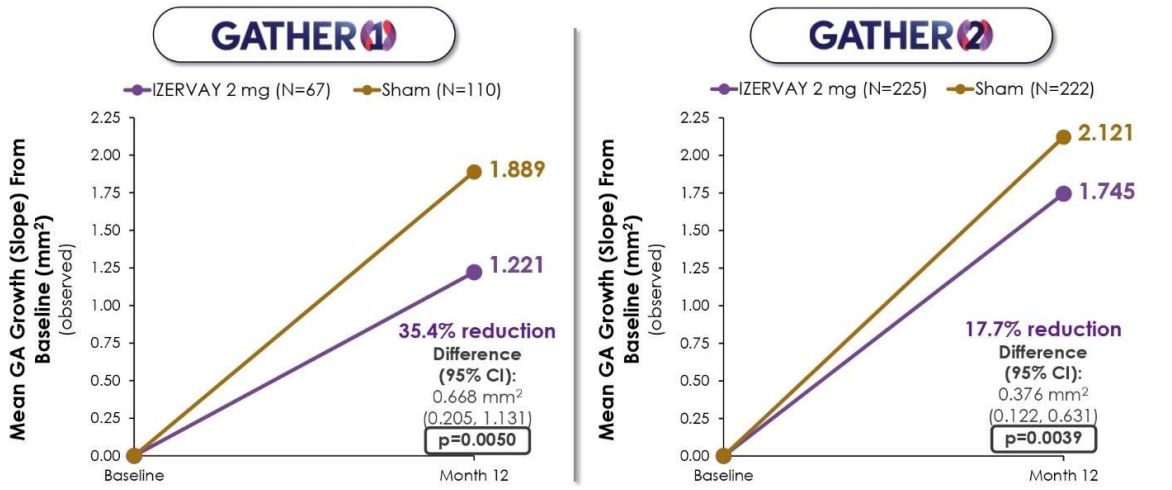

CI, confidence interval; GA, geographic atrophy. 1. Iveric Bio press release; 2. Khanani AM, et al. *Lancet*. 2023;402(10411):1449-1458.

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As a reminder, IZERVAY is the first treatment for GA to achieve a statistically significant reduction in GA lesion versus sham over 12 months across two pivotal Phase III studies. These reductions observed in GA growth are consistent with the broader landscape of complement inhibition for the treatment of GA. Furthermore, these results validate IZERVAY's status as the only breakthrough therapy for GA and the expedited approval IZERVAY received from the FDA.

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

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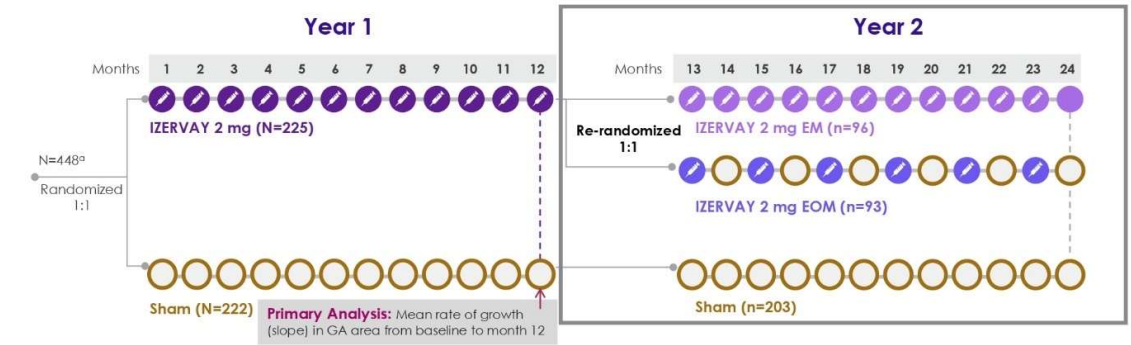

Year 2 Objectives:
Evaluate efficacy and safety of re-randomized population of IZERVAY monthly (EM) and every other month (EOM) through year 2

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. [a]448 randomized, with 447 treated (1 patient in sham did not receive treatment after randomization).

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Now I'd like to take a moment to talk about the design of GATHER2, which is an international, randomized, sham-controlled study.

As shown on the prior slide, in year one, the study met the primary endpoint of a statistically significant reduction in the mean rate of geographic atrophy growth from baseline to month 12 compared to the sham.

After the first year of treatment, patients treated with IZERVAY were rerandomized to continue with monthly treatment or receive every other month until month 24. Sham patients continued to receive monthly sham treatment up to month 24.

In year two, we were excited to explore whether reducing the dose intensity to every other month resulted in a meaningful treatment effect as well as to better understand the long-term safety profile at this dosing regimen compared to the sham. As we've already stated in the summary, we're pleased that the findings support both effectiveness and a well-tolerated safety profile with IZERVAY dosed every other month in year two.

As a background for the statistical design for GATHER2 in year two, to control for multiplicity, testing for statistical significance was conducted sequentially on the study's prespecified outcomes.

The first test was reduction on GA growth for IZERVAY monthly versus the sham. The second test was reduction in the rate of persistent vision loss for the pooled IZERVAY groups versus the sham. The third test was a reduction in GA for every-other-month IZERVAY versus the sham.

If a result was not statistically significant, we stopped formal testing. P-values were still calculated but would be considered nominal.

With that, I'm going to turn the presentation over to my colleague Erin Henry.

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GATHER2 2-YEAR DATA

ERIN HENRY

VICE PRESIDENT, PRODUCT STRATEGY AND INNOVATION,
IVERIC BIO, AN ASTELLAS COMPANY

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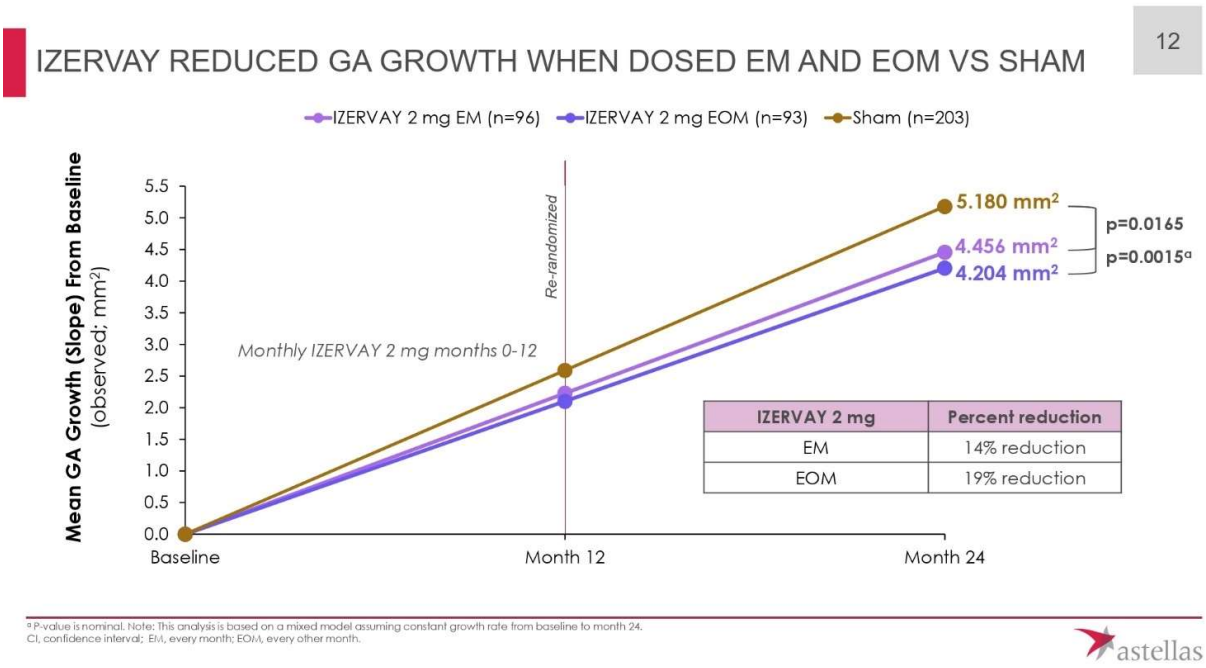
Henry*: Thank you, Dhaval. Hello, everyone. My name is Erin Henry, Vice President of Product Strategy and Innovation at Iveric Bio, an Astellas company.



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Pictured here are the results for the primary efficacy outcome in year two, reduction in GA growth for monthly and every other month by IZERVAY versus the sham.

As Dhaval just mentioned, the monthly treatment arm achieved statistical significance, and the every-other-month treatment arm had a nominal p-value of 0.0015. We believe both IZERVAY dosing arms represent robust reductions in GA growth versus the sham, irrespective of the sequential statistical testing. As we've seen, nominal p-values are common in this therapeutic space and are considered meaningful to physicians.

As I will discuss on the next slide, when we examine the difference in millimeter squared reduction after two years of treatment, we are seeing a trend of YoY improvement in efficacy and impact on GA regions compared to year one.

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

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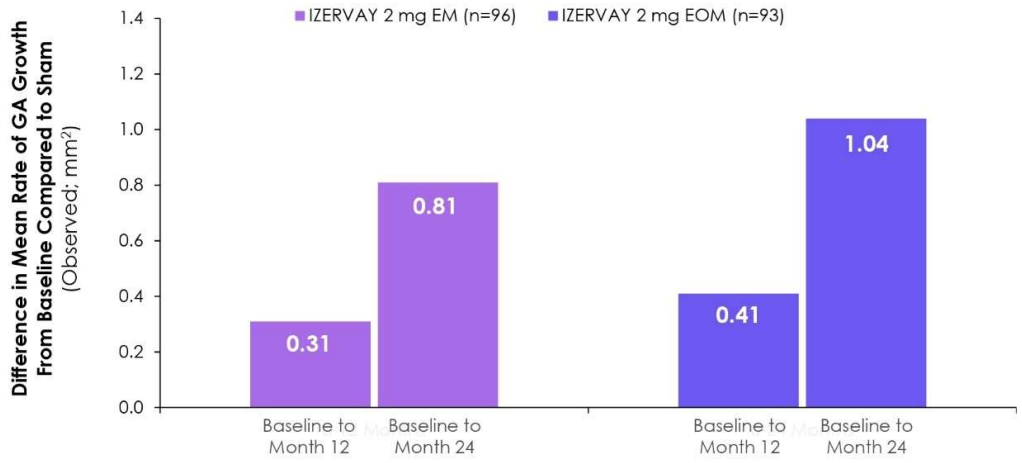

Note: This is a simplified piecewise slope spline Mixed model with Repeated Measures analysis. The analysis is based on a mixed effects model for repeated measures assuming a piecewise linear growth slope every 6 months. The EOM group received monthly IZERVAY in the first year.
EM, every month; EOM,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

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Here is another way to look at the increased treatment effect over time for both IZERVAY monthly and every other month versus the sham. This graph clearly illustrates how for both IZERVAY and every-other-month groups, the treatment effects more than doubled over two years compared to one year.

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

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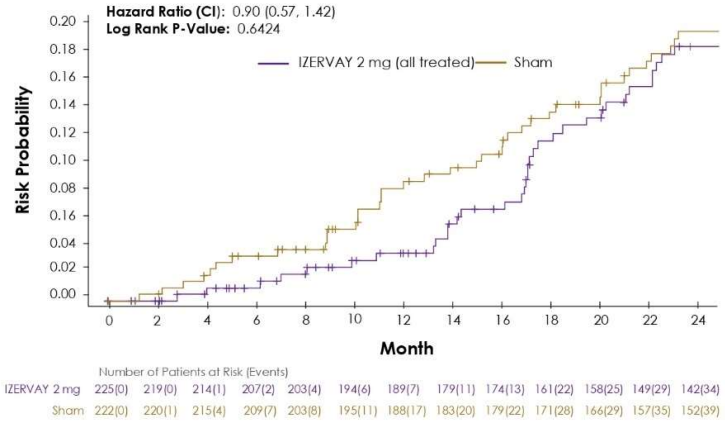
~ Mean change in BCVA and LL-BCVA from baseline between IZERVAY and sham was similar at two-years



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.

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The prespecified objective demonstrating that IZERVAY reduced the rate of greater than or equal to 15-letter persistent vision loss compared to the sham over two years was not statistically significant.

The mean change in best-corrected visual acuity and low luminance best-corrected visual acuity from baseline between IZERVAY and the sham was similar at two years.

We will continue to explore persistent vision loss across several sensitivity analyses and look forward to presenting more data in the future.

TREATMENT EMERGENT ADVERSE EVENTS (TEAES) OVER 2 YEARS WERE SIMILAR AND CONSISTENT WITH YEAR 1[1]

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

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In terms of top line safety, the overall treatment-emergent adverse events, or TEAES, were similar and consistent with year one.

For ocular treatment-emergent adverse events, there was an incident of 64% versus 48.2% in IZERVAY versus sham study eyes, respectively.

Serious ocular treatment-emergent adverse events in the study eye were the same between groups, less than 2%.

Treatment-emergent adverse events leading to study drug discontinuation were less than 2% and 0% in the IZERVAY and sham groups, respectively.

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SERIOUS OCULAR TEAEs – NO NEW SAFETY SIGNALS IN YEAR 2

	Year 1[1]		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)
Serious ocular TEAEs in study eye, n (%)	**2 (0.9)**	**2 (0.9)**	**2 (2.1)**	**0 (0.0)**	**0 (0.0)**	**4 (1.8)**	**2 (0.9)**
Choroidal neovascularization	2 (0.9)	1 (0.5)	0	0	0	2 (0.9)	1 (0.5)
Visual acuity reduced	0	1 (0.5)[a]	0	0	0	0	1 (0.5)[a]
Visual acuity reduced transiently	0	1 (0.5)[a]	0	0	0	0	1 (0.5)[a]
Endophthalmitis	0	0	1 (1.0)[b]	0	0	1 (0.4)[b]	0
Subluxated intraocular lens	0	0	1 (1.0)	0	0	1 (0.4)	0

[a] Occurred in the same patient; [b] 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.

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Serious ocular adverse events in the study eye were less than 2% over two years.

Focusing on the year two results, you can see that there were two serious ocular adverse events reported in the pooled IZERVAY groups, including one case of culture-positive endophthalmitis and one case of subluxated intraocular lens in the IZERVAY monthly group.

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CHOROIDAL NEOVASCULARIZATION (CNV)

	Year 1[1]		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)
CNV in study eye, n (%)	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.
1. Khanani AM, et al. *Lancet*. 2023;402(10411):1449-1458.

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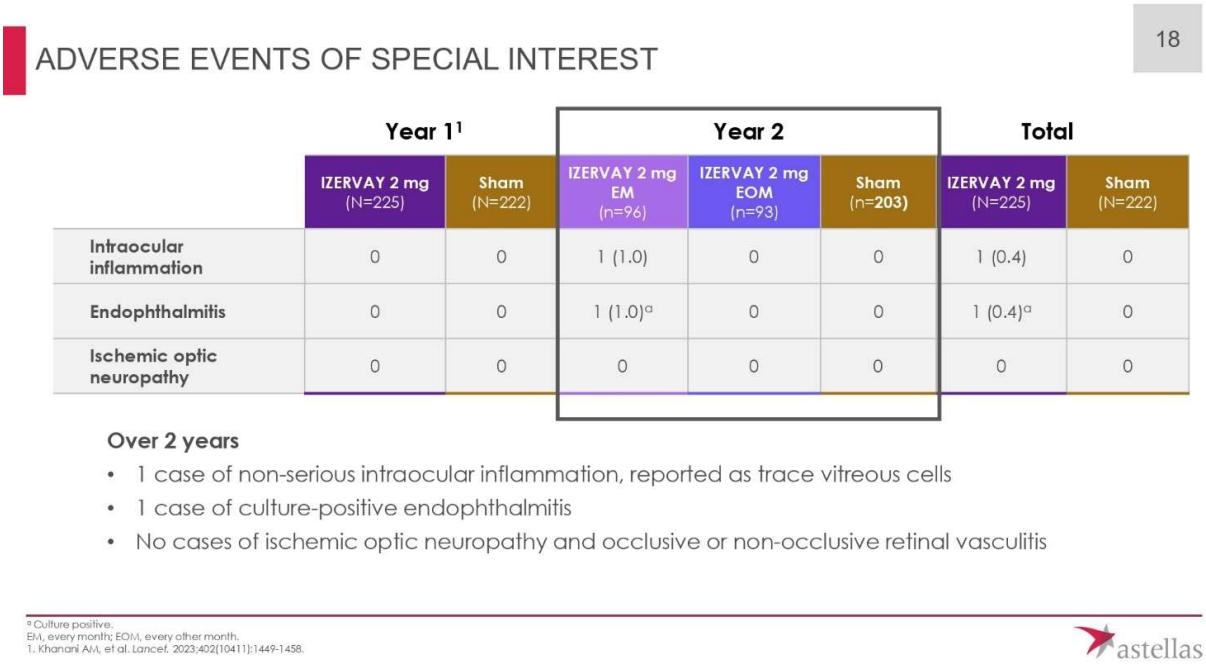
In GATHER2, if a diagnosis of choroidal neovascularization was confirmed, the patient was provided with study-supplied aflibercept or ranibizumab and remained in the study.

Of the 26 total choroidal neovascularization cases over two years in the pooled IZERVAY dosing groups, two were considered serious. Of the 20 total choroidal neovascularization cases in the sham arm over two years, one was considered serious.

In year two, as highlighted in the center box, the incidence of choroidal neovascularization was similar for the sham and the IZERVAY every-other-month groups. Over two years, we've only seen a slight increase in the incidence of choroidal neovascularization in the pooled IZERVAY dosing groups versus the sham group.



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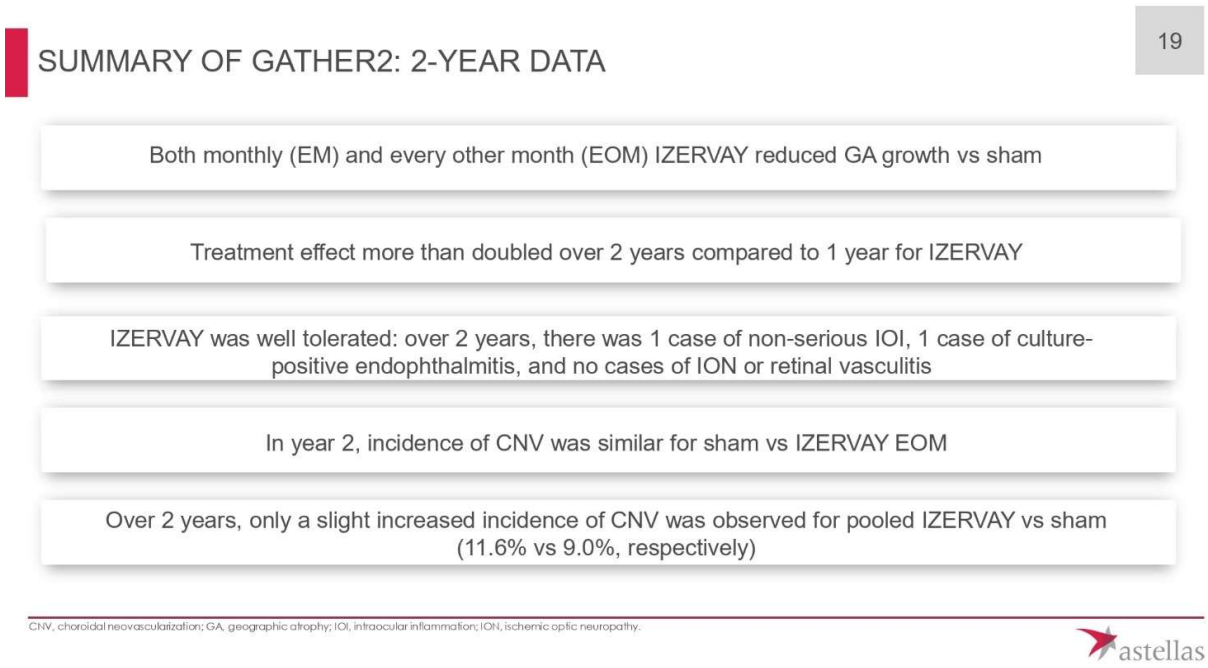
More importantly, there were no cases of ischemic optic neuropathy or retinal vasculitis over two years. In year two, there was one case of nonserious intraocular inflammation reported as trace vitreous cells and one case of culture-positive endophthalmitis. Overall, these two-year safety data are critical because they provide evidence that IZERVAY is not associated with inflammatory side effects.

Ocular inflammation has been a concern with complement inhibitors in geographic atrophy, but after two years of treatment, we're seeing no evidence to support a concern with IZERVAY.



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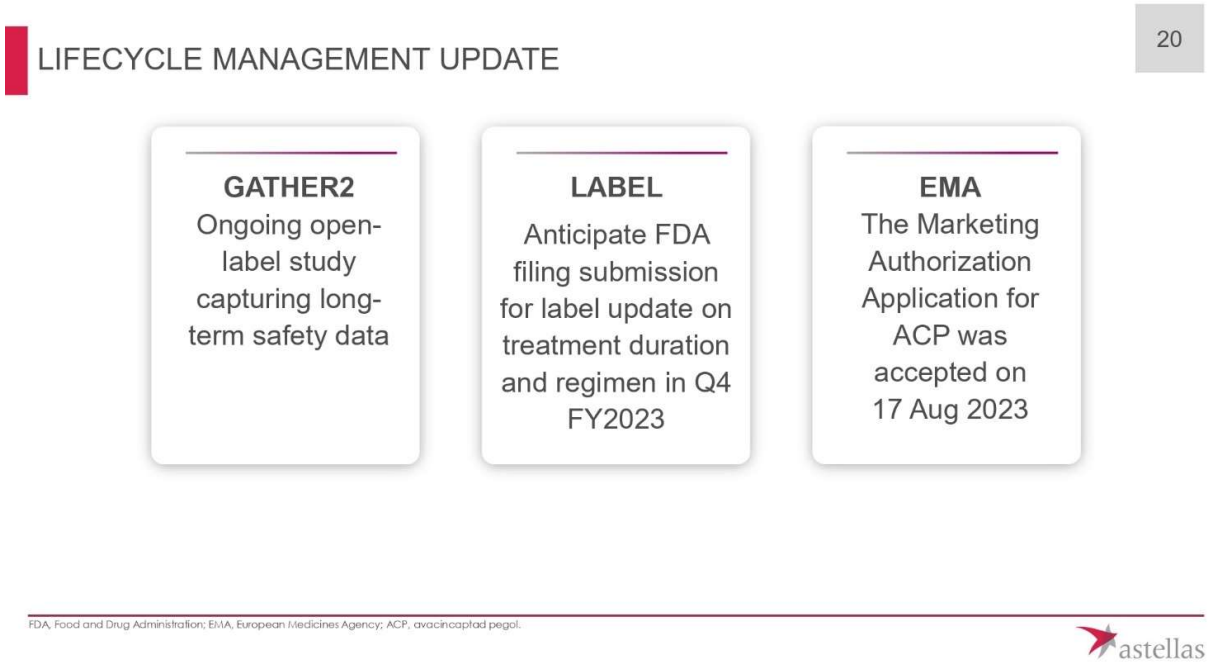
To summarize, we're excited that in the second year of GATHER2, IZERVAY showed a consistent impact on reducing GA growth in both the monthly and every-other-month dosing arms compared to the sham arm.

Importantly, we saw a treatment effect that more than doubled over two years compared to one year.

IZERVAY continued to be well-tolerated with no new safety signals and similar rates of choroidal neovascularization in every-other-month IZERVAY versus the sham group in year two.

In totality, we believe this is great news for patients and retina specialists and will build confidence in the use of IZERVAY for geographic atrophy.

I will now turn the presentation back to Dhaval.



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Desai*: Thank you, Erin.

After completing two years of the GATHER2 study, patients had an option to enroll in an open-label extension, which will enable us to capture long-term safety data.

In terms of our US regulatory progress, we anticipate completing our filing with the FDA in early 2024, which is Q4 FY2023 for Astellas. We will be pursuing label changes to remove the restriction on treatment duration and provide an option for every-other-month dose.

The marketing authorization application for IZERVAY was accepted by the European Medicines Agency on August 17, 2023.

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And with that, I will begin the question-and-answer portion of today's call.

Ikeda [M]: Thank you very much. This is all from us.

Now, we would like to entertain your questions. If you have any questions, please use the Raise Hand button. You can find it at the bottom of your Zoom screen. If you're attending from your smartphone, please tap the Details button, then you can find the Raise Hand icon. Please tap that.

I'm going to invite those who ask questions. So if your name is called upon, please unmute yourself and mention your name and affiliate to start your question. Now, please go ahead.

Thank you. The first question, Citigroup Securities, Yamaguchi-san, please.

Yamaguchi [Q]: Good morning, this is Hidemaru Yamaguchi. Can you hear me?

Ikeda [A]: Yes, we can hear you.

Yamaguchi [Q]: Thank you very much. The first question is that every other month, the reduction is down by 19%. Every month, it's down by 14%, which is great data. But every other month's reduction is higher than that of every month, and I'm not quite sure I understand the mechanism of these situations. Can you tell me why the reduction of every other month is more efficacious than every month? Thank you. That's the first question.

Desai [M]: Thank you for your question. I'll ask Erin to take that question.

Henry [A]: Thank you. So what we're seeing over the two years is the rerandomized population of patients, and we believe that both monthly and every-other-month dosing showed a meaningful reduction in GA growth relative to sham growth. The differences between these two arms, we believe, are most likely due to disease heterogeneity and not due to meaningful differences between monthly dosing and every-other-month dosing.

Yamaguchi [Q]: Okay. Thank you. The second question is that you showed us the 15-letter clinical evidence on page 14. It looks pretty good up until 12 months, 14 months, but it's getting closer to the difference between IZERVAY and the sham treatment. The hazard ratio is 90% at the moment, and there is no significant difference. For clinical purposes, is it better to have a clinical difference, even though it's not really the target to have this statistical significance in the future? Or not really? If you show the difference and numerical difference, would it be good enough? What do you think about this clinical evidence? Thank you.

Desai [A]: Yes. So based on the results of year one, we had actually looked to see whether or not we would get a statistically significant finding of this from year two, as was mentioned in the statistical design. We are doing more work on this data set and reviewing each patient individually to further understand what happened over the course of the two-year period, and we're committed to presenting that data once we've completed our review.

Yamaguchi [Q]: Have you already announced the 12-month data or not? Thank you.

Desai [A]: Yes, the 12-month data was presented at a number of meetings, most recently at the ARVO meeting.

Yamaguchi [M]: Okay. Thank you.

Ikeda [M]: Thank you very much. Next, Morgan Stanley MUFG Securities, Mr. Muraoka, please.

Muraoka [M]: Hello, this is Muraoka from Morgan Stanley. Can you hear me?

Ikeda [M]: Yes, we can hear you.

Muraoka [Q]: Thank you very much. I also have a question which is similar to the previous one. First of all, congratulations on the wonderful data.

Regarding the vision loss data, there was no significant difference for 24 months. For your future marketing penetration competition, have you thought about the possibility of a negative impact, including in your discussions with the FDA? I hope you can respond to my question.

Desai [A]: Thank you for the question. As I mentioned previously, we will continue to evaluate this data to understand what happened over the period of two years. Certainly, at 12 months, the data makes it look like the curves are separating. If you look at the sensitivity analyses that were presented at the AAO meeting, the curves for 10, 20, 25 letters do look to have some separation as well.

We'll conduct further analysis on this data. Certainly, it will be submitted to the FDA and EMA, and we'll see what the discussions turn into. But we will continue to work on this data, and we will continue to present it as we learn more.

Muraoka [Q]: Regarding the penetration, what's the current impact on the penetration of the product in the market?

Desai [A]: I don't think we can make a comment on what the penetration of the vision data is. To this date, we have not had vision data for any complement inhibitor in geographic atrophy. What we do believe is that over time, these will separate as patients lose valuable real state in terms of visual acuity.

It's impossible to say what the impact of this data will be. We will continue to commit ourselves to understanding what this data is and share it with the clinical community as soon as we understand it better.

Muraoka [Q]: Thank you very much. I have another question, which is not about the presentation today.

At the AAO, there was a physician survey for complement therapy or complement inhibitors. The slide was reported in the media. Pros and cons were 17% and 83% respectively, according to the information I received. I think it's an extreme response, and it may not be reliable, in my view. But regarding this physician survey, how do you perceive it? How this will affect the future penetration of IZERVAY, in your opinion? I'd like to hear your views.

Desai [A]: Yes. Thank you for the question. I think a couple of things that you have to understand about any of these surveys is that they were probably done a handful of months ago. If you would remember, a handful of months ago, we were right in the middle of unveiling of a lot of safety findings from another compound in this class, and so that certainly potentially has the ability to color the opinions of physicians.

What I will tell you is that we believe that the consistent safety profile that we saw in year two, combined with the efficacy seen with monthly and every-other-month dosing, is really going to provide both the clinical community and their patients something to think about. I think we have to take those results with a little bit of a grain of salt, understanding that they were probably done during a highly sensitive time in the retina community.

Now, we have two-year results from the GATHER2 study, which really hold up an efficacy profile that is similar for every other month and monthly, and a safety profile that is really well tolerated with no cases of ischemic optic neuropathy, no cases of vasculitis, and a low case of intraocular inflammation.

Henry [A]: Dhaval, if I may add one additional comment. The percentages that were reported were in the retina subspecialty day debate session. That happened a day before we had an opportunity to present the GATHER2 two-year results.

I'd say this is a new field, and people are still very much trying to understand the data. But I think being able to provide our results, I'd be curious how that may have changed people's perspective. Of course, there isn't another opportunity for that survey, at least not in this meeting.

Muraoka [M]: Thank you very much. That's all from me.

Ikeda [M]: Thank you for the question. Next, Daiwa Securities, Hashiguchi-san, please?

Hashiguchi [Q]: This is Hashiguchi from Daiwa Securities. Thank you very much for giving me this opportunity. In AAO, another complement inhibitor with 36 months data was also presented. Based upon such a presentation, what kind of comments do specialists have about the selection of treatment options? It's been shown a while after the presentation of other products and your product clinical trial data. What kind of view do the specialists have for the differentiation of usage of the drug? For this kind of patient, this drug will be used. For that kind of patient, another drug will be used. What do they think? If you know any information about that, we would be very happy to hear an actual voice from the field.

Desai [M]: Erin, can I ask you to take that one, please?

Henry [A]: Absolutely. Our results were just presented yesterday morning. We've heard generally positive results. People were very interested to see the details of the results, to begin to digest the results.

We heard a lot of positive responses on the outcomes of the IZERVAY every-other-month dosing group compared to the sham group. I think there had been some questions about what that would look like.

I've also heard a lot of positive comments on the safety results over two years. The exceptionally low number of adverse events is of special interest. The intraocular inflammation rate, the lack of ischemic optic neuropathy, the single case of endophthalmitis are all things that I think practitioners are feeling better about seeing that additional follow-up.

It's still early days, and I would say that we look forward to continuing to get more insights from doctors in the community. That's the preliminary feedback that I can share here.

Hashiguchi [M]: Thank you very much, [inaudible]. Thank you very much.

Ikeda [M]: Thank you very much. Next, UBS Securities, Ms. Haruta, please.

Haruta [Q]: I'm Haruta from UBS Securities. Thank you very much for this opportunity. Statistical testing in the study was done sequentially. This was done at the timing of after 12 months. When it comes to every-other-month dosing, there's a mention of a nominal p-value. Because of the nature of the testing, you explained you stopped when there was no statistical significance. So until what timing this nominal p-value? Could you elaborate on that, please?

Desai [M]: Yes. I think the question is asking if you could please confirm when did we stop, at what time point did we stop the testing for the every-other-month. Is that correct?

Haruta [Q]: Yes. For every other month, yes, I'd like to ask you about the timing. Regarding the 24-month data, is it 24 months or after 12 months? I'd like to confirm.

Desai [A]: Yes. Thank you. So the statistical testing that was done for year two was done at the end of year two. So all patients that were in that 24-month cohort, when the patient's last visit happened at month 24, that is when the analysis was done for every other month in terms of the efficacy and the nominal p-value.

Haruta [Q]: Understood. So that is a p-value as of month 24.

Desai [A]: That is as of month 24, correct.

Haruta [Q]: Understood. My second question is regarding the CNV rate. That is not really high in the study. Looking at the real world, I think dry AMD, VEGF IVT, and GA, and dry AMD IVT are utilized more. With this in mind, how do you view the situation?

Desai [M]: I think the question is regarding looking at the difference between the CNV rates of IZERVAY and the sham, that is, how are we looking at the difference between the two? Could you please confirm the question?

Haruta [Q]: Apologies, the way I asked my question was a bit complicated. I'm so sorry.

CNV rate was not really high in this study. But in the real world, for wet AMD treatment that is ongoing and I think for GA as well, this treatment will be used. If both drugs are used, what would be the points needed to be concerned about?

Desai [M]: Erin, can I pass that one to you?

Henry [A]: Yes, absolutely.

In this population, if patients were to develop choroidal neovascularization during the course of the GATHER2 study, they were able to receive anti-VEGF, either aflibercept or ranibizumab, and remain on their study dose.

While we don't have many patients in total that received both IZERVAY and anti-VEGF, and you can see here we only had 26, they did have the opportunity to receive both the study drug and the anti-VEGF. In this small population, we did not find that to be a problem or an issue. There were no concerns based on what we've seen in the small number of patients.

When you think about real world, we know that there are many patients with neovascular AMD that are treated regularly with anti-VEGF. Geographic atrophy is the other advanced form of age-related macular degeneration. Up until now, we haven't had treatment options. So we imagine that clinicians will use this data to figure out the right patients to treat with IZERVAY, and they will manage them accordingly if they were to have this small but real risk of conversion to choroidal neovascularization with an anti-VGEF agent that they think is most appropriate.

Haruta [M]: Understood. Thank you very much.

Ikeda [M]: Next, Sanford C. Bernstein, Ms. Sogi, please.

Sogi [Q]: Thank you very much for taking my questions. I have a few questions about the data first. On page 12, I've been always wondering why you've only shown us the 12-month and 24-month data while Apellis Pharmaceuticals' SYFOVRE had a more actually granular data. That's my first question.

Desai [M]: So can you help us understand what you're referring to in terms of granular data?

Sogi [Q]: I'm sorry, more data points. That's what I meant.

Desai [A]: Right. A couple of things as it relates to showing the 12- and 24-month data:

The first thing that you need to understand about geographic atrophy is that it is a chronic disease, and that once a patient starts a treatment, they are on it essentially for the rest of their lives. And so there's not a decision point where at six months or at 18 months that we're going to say, look, we're going to stop treating you.

The data that we're showing you at 24 months basically shows you that with IZERVAY, what you see, and you can see clearly from the lines, is that there's an early separation of those curves that starts at six months, continues through 12, and is expanding through 18 and 24. That is what we believe that clinicians and their patients will ultimately find the most useful in terms of making treatment decisions for treating geographic atrophy.

Sogi [Q]: Right. Thank you very much.

The next question is how to look at the data on page 13. First of all, when you look at both the data from every month and every other month, the baseline to month 12, I assume that these are coming from the same one single arm. I'm having a little bit hard time understanding why the number is different, 0.31 versus 0.41.

The next one is the difference in mean rate for baseline to 24 months in the data for every other month. Does it mean that the growth rate is almost the same as the sham?

Desai [M]: Yes. Erin, you answered this one previously, so maybe I'll just kick it back to you to answer this one as well.

Henry [A]: Absolutely. What this bar graph is demonstrating is that in the first year for both what we're calling the monthly arm here and the arm for every other month arm, you can see the difference between the sham arm with respect to differences between monthly and sham arms, then the arms for every other month and the sham, which in the first year has everyone receiving monthly dosing. While we saw that in these rerandomized populations that baseline characteristics remained relatively balanced, there are slight differences in year one when everyone is dosed monthly. We believe this is most likely due to heterogeneity of the disease.

I think what's the important point is regardless of that one-year difference, when you look from the baseline to two years, that's the difference in the monthly arm that continues on monthly through the second year, and the treatment effect over that two years is 0.81. That's an absolute difference between the sham arm and the monthly arm. That's more than a doubling from one year to two years. The difference from 12 to 24 is the difference between this baseline to 12 and baseline to 24, so 0.5 millimeter squared.

And then, when we look at the every-other-month arm, again, similarly, when we look from baseline to 12, it's 0.41 millimeter squared. That's the difference between the every-other-month arm and sham. And then, when we look baseline to 24 months, it's 1.04 millimeter squared. So again, more than a doubling. If you look at the difference, that's about 0.6 millimeters squared.

So regardless of whether or not they stayed on monthly dosing or they moved to every-other-month dosing in the second year, we see a similar increased treatment effects in that second year, and so that over 2 years, you're seeing this absolute difference of 0.81 millimeter squared for the monthly arm and 1.04 millimeter squared for the every-other-month arm. We think these are both meaningful reductions in GA growth relative to the sham arm.

Sogi [Q]: Thank you very much for the clarification. It's very clear.

It looks like, interestingly, every-other-month over 24 months, of course, over the first 12 months patients were receiving the every-month treatment, but every-other-month seems to be slightly better. So I'd like to see if there's any hypothesis why every-other-month seems to be even slightly better than every month.

Also, I assume that based on how this trial has been designed the actual label will be that the patients can receive every-other-month treatment after the completion of 12-month treatment. Is that correct?

Desai [M]: Erin, can I ask you to take that one as well?

Henry [A]: Sure. So you're correct in that we see a slightly bigger delta in the every-other-month arm relative to the sham over two years. Again, there's nothing that we have seen in terms of the baseline characteristics of the rerandomized population that gives us a reason why this arm would perform a little bit better. We think that geographic atrophy is a heterogeneous disease, and so I think both of these demonstrate meaningful reductions relative to the sham arms. I think it adds to our knowledge that moving from monthly dosing in the first year to every-other-month dosing in the second year still provided this meaningful treatment reduction with p-values that was 0.0015.

In terms of submission to the FDA and other health authorities, we will submit the totality of these two-year results, and we will have that conversation with the health authorities about what they believe is appropriate in terms of potential updates to the label.

Sogi [Q]: Thank you very much. One final question. We understand that from the clinical trial you show really robust safety data. But at the same time, I think the issue emerging is the concern around adverse events, about those very rare adverse events that won't be able to be probably detected in the clinical trial with a limited population. What is your plan moving forward to ease this type of adverse event?

Desai [A]: Thanks for the question. Just to clarify, to date, there's only been one case of retinal vasculitis that has been reported in a patient that does not have GA but has Stargardt disease.

In terms of our plan, Astellas is committed to transparently reporting safety data, and what we find in both our clinical trials as well as in our post-marketing setting will be transparently communicated to the retina community over the course of the coming years.

Sogi [M]: Thank you very much.

Ikeda [M]: Thank you very much. Next, Mizuho Securities, Mr. Tsuzuki, please.

Tsuzuki [M]: This is Tsuzuki from Mizuho Securities. Can you hear me?

Ikeda [M]: Yes, we can hear you.

Tsuzuki [Q]: Thank you very much. I have one question regarding GATHER2; I'm looking at page nine.

Regarding the GATHER2 data, if I look at it at 12 months, there is a 17.7% reduction for GA growth. Regarding this data, if you look at page 12, at 24 months, monthly dosing, there is a 14% reduction. For you, considering the results at 24 months, and having an original reduction of 17.7% at 12 months, you could have been expecting a higher value, a higher reduction. Or is this what you expected? Do you think you could have expected a higher reduction here? Any comment on your side?

Desai [A]: Yes. Thank you for the question.

A couple of points as it relates to the statistical analysis and the year one results versus the year one results: remember that in year one of GATHER2, all patients, all 225 patients, were on monthly dosing and treated as one singular group. If you go to the year two results for GATHER2, the difference is that the single group of 225 patients has now been split into two separate groups, and the analysis goes all the way back to baseline. The numbers that you saw in year one cannot be used to put the year two numbers in reference because the entire analysis has changed.

What is more relevant is to look at the difference in absolute lesion size. And what you see with the absolute lesion size is that the number that you see at year one and the reduction with monthly dosing more than doubles whether you use monthly or every-other-month dosing out to month 24. That is the data that treating clinicians will see when they are treating patients in their office, when they're looking at their fundus autofluorescence images. That's what we believe is the most appropriate and relevant number, not necessarily percentage reduction that has been changed due to a statistical analysis and how you treat the data.

Tsuzuki [M]: Very clear. Thank you very much for your response.

Ikeda [M]: Thank you very much. There are some others who are raising their hand but we are running over, so we'd like to close this meeting here.

Regarding other questions we could not handle, the IR team will be happy to receive them. If you have any questions, please contact us.

Thank you very much for joining us so early in the morning. Thank you very much. We'd like to close this meeting here. Thank you very much.

[END]

Document Notes

1. *Speaker speech is classified based on whether it [Q] asks a question to the Company, [A] provides an answer from the Company, or [M] neither asks nor answers a question.*

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