Transcript Details
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Persistent Fluid in Wet Age-related Macular Degeneration: Understanding Treatment Implications

DR. BIRNHOLZ:
This is ReachMD. I'm Dr. Matt Birnholz and joining me to explore key data on the impacts of EYLEA on persistent fluid in patients with wet age-related macular degeneration, or Wet AMD for short, is Dr. John Kitchens. Dr. Kitchens, welcome to you.

DR. KITCHENS:
Matt, thanks for having me.

DR. BIRNHOLZ:
Excellent. Wonderful to have you.

Before we begin, let's take a moment to review some important safety information for EYLEA.

ANNOUNCER:
IMPORTANT SAFETY INFORMATION AND INDICATIONS

CONTRAINDICATIONS
EYLEA is contraindicated in patients with ocular or periocular infections, active intraocular inflammation, or known hypersensitivity to aflibercept or to any of the excipients in EYLEA.

WARNINGS AND PRECAUTIONS
Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately. Intraocular inflammation has been reported with the use of EYLEA.
Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA. Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with VEGF inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately.

There is a potential risk of arterial thromboembolic events (ATEs) following intravitreal use of VEGF inhibitors, including EYLEA. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of reported thromboembolic events in Wet AMD studies during the first year was 1.8% (32 out of 1824) in the combined group of patients treated with EYLEA compared with 1.5% (9 out of 595) in patients treated with ranibizumab; through 96 weeks, the incidence was 3.3% (60 out of 1824) in the EYLEA group compared with 3.2% (19 out of 595) in the ranibizumab group. The incidence in the DME studies from baseline to week 52 was 3.3% (19 out of 578) in the combined group of patients treated with EYLEA compared with 2.8% (8 out of 287) in the control group; from baseline to week 100, the incidence was 6.4% (37 out of 578) in the combined group of patients treated with EYLEA compared with 4.2% (12 out of 287) in the control group. There were no reported thromboembolic events in the patients treated with EYLEA in the first six months of the RVO studies.

DR. BIRNHOLZ:
Now, with that important safety information in mind, let's touch on VIEW 1 and VIEW 2. And Dr. Kitchens, can you just talk about these two clinical trials and give us an overview?

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DR. KITCHENS:
Sure Matt. So, VIEW 1 and VIEW 2 are really the largest phase 3 anti-VEGF trials completed to date looking at patients with wet age-related macular degeneration. They're multi-centered, double masked, clinical studies involving more than 2,400 patients with Wet AMD treatment-naïve patients, by the way. Mean age 76 years old for these patients and they were randomized to really four groups; they were randomized to receive either EYLEA 2 mg every other month following three initial monthly doses, EYLEA 2 mg every month throughout the first year, EYLEA half a mg every month, which is not an approved dose, um, and ranibizumab 0.5 mg every month. In both studies, the primary efficacy endpoint was the proportion of patients with Wet AMD who maintained vision, which really is losing less than 15 ETDRS, or early treatment diabetic retinopathy study letters of best corrected visual acuity at year one compared to their baseline.

DR. BIRNHOLZ:
That's a great background for us, Dr. Kitchens. Thanks so much. But what were some of the key findings from the VIEW 1 and VIEW 2 trials?

DR. KITCHENS:
If we really look at the primary endpoint at Year 1, uh, that's at maintenance of vision, losing less than three lines of ETDRS visual acuity it was maintained in 95% of patients in the monthly group, 94% in the every other month group, once again followed by the three initial monthly doses, and 94% of the patients treated with monthly ranibizumab. That's VIEW 1. And VIEW 2, 95% of patients in each treatment group maintained their vision. When we look at the integrated VIEW 1 and VIEW 2 secondary efficacy endpoints, the mean change in best corrected visual acuity from baseline to Year 1 was around 8.4 to 9.3 letters across the three treatment groups. In years one through two, the mean change from baseline when they presented was 7.6 to 7.9 letters across all the treatment groups.

DR. BIRNHOLZ:
And Dr. Kitchens, can you walk us through the visual outcomes of the patients with persistent fluid as evaluated in post-hoc subgroup analyses?

DR. KITCHENS:
As you mentioned, Matt, these, these persistent fluid patients, the patients that have fluid at baseline, this could be intraretinal, subretinal, month 1, month 2, and month 3 while receiving those first dose injections, 11.7 letters. Whereas the patients that were then with persistent fluid extended out to every other month dosing, they gained about a line and a half of visual acuity. And so I think we have an opportunity here for these patients that require more frequent treatment to A, spell that out ahead of time so we can say, look, you are somebody that's probably going to require more treatments here in the first year.

DR. BIRNHOLZ:
And let's dig into this a little bit deeper, Dr. Kitchens and focus on what dosing is supported by EYLEA clinical trials and the product label. Now, which patients do you think would need every month treatment for longer timeframes?

DR. KITCHENS:
When we look at the FDA approval what's really nice is, is that we have the opportunity to utilize EYLEA every month for the first three months and then every other month or we can use it every month through the first year and beyond if we need to.

DR. BIRNHOLZ:
And on that note then, what about the importance of dosing flexibility, especially in more difficult-to-treat patient populations. What can you tell us?

DR. KITCHENS:
You know, it's really important, uh, when we look we wanna be able to treat our patients in an individualized and custom fashion. Wet AMD is not just a cookie cutter disease, this is something that you're gonna have patients that respond really well early on and you can extend those patients out and treat 'em less often throughout that first year. But you're also conversely gonna have those patients, particularly this 20% with this persistent fluid that is a great biomarker for our patients going forward. So, everybody's an individual with this disease and we wanna treat them as such.

DR. BIRNHOLZ:
Specifically, from your vantage point, would you leave patients with early persistent fluid on a monthly long-term or treat with a longer dosing interval in Year 2?

DR. KITCHENS:
I certainly think the majority of these patients when we've treated them really aggressively in this first year, we're able to actually get those patients out beyond just monthly injections in Year 2. You can start to do like we do, treat-and-extend where we'll treat the patient, bring 'em back maybe a week or two later than they were coming back for their intervals and see 'em.

DR. BIRNHOLZ:
And how 'bout a patient who presents with fluid recurrence but stable vision? I'm interested in whether you would treat a patient like that with more frequency or not?

DR. KITCHENS:
I really think it depends on the type of recurrence, uh, the volatility if you will of the recurrence. So, if you have dry retina and then suddenly you have a 150 microns of fluid that just comes back in a week, the patient is subjectively or objectively has a decline in their vision I think I would treat those patients more aggressively. If someone comes back with just a l- early bit of subretinal fluid with, with stable vision and no subjective vision loss, I think we can maintain and extended duration in between those injections. And in some instances actually even be able to extend the patient out very, very carefully. Once again, I don't have much tolerance for intraretinal fluid. We're really talking only about subretinal fluid, here.

DR. BIRNHOLZ:
I see. Yeah, of course. And I'm also interested in whether there's a threshold that you use for the amount of fluid or amount of change in vision which you'll chose to either accept or treat more frequently?

DR. KITCHENS:
Yeah, Matt, I certainly don't wanna see any patients who have subjective vision loss. So, a patient feels like they're getting worse, I have very little tolerance for that. That being said, there's numerous studies that actually show that even up to 100 microns of subretinal fluid can be well-tolerated and have no deleterious effect on the vision. So, I will, in some instances tolerate subretinal fluid. I, I'm finding that I have to increase my tolerance for the amount of subretinal fluid I'm willing to tolerate. It used to be about 50 microns but it's starting to ease up a little bit more particularly if a patient is doing well from a vision standpoint.

DR. BIRNHOLZ:
Fantastic. Well these have been great insights around VIEW 1, VIEW 2, the outcomes data, and of course insights from your own practice, but I'd like to put this into context for a few moments and maybe speak to a patient case or two that have important lessons to teach us about persistent fluid. Are there any that come to mind for you that you can share with us?

DR. KITCHENS:
Matt, I've got two great cases that I love to share. The first case is, uh, a gentleman who had persistent retinal fluid, 20/80 vision, had been receiving prior monthly anti-VEGF therapy and we really weren't seeing any improvement in his fluid. This is not your traditional VIEW 1 and VIEW 2 trial patient because those were all treatment-naïve patients, this is somebody who's already being treated with another anti-VEGF agent. I had another patient, this is my favorite patient, she's probably received more injections than anybody in my clinic, she presented with bilateral exudative age-related macular degeneration and received monthly treatments. In one eye she had recurrent intraretinal fluid, in the other eye she tended to have more subretinal fluid. She was a frequent flyer. She was somebody that required monthly injections to keep her retina dry. If we went beyond 28 days she would have subjective vision loss. But what was interesting is, is that I would see her every month and she would have persistent fluid. Even though she was receiving monthly EYLEA injections and had good vision and rarely had any subjective vision loss every time I would see her, she would have subretinal fluid in one eye and intraretinal fluid in the other eye. I think the last time I saw her she was 20/25 or 20/30. In her fellow eye, the one with the intraretinal fluid on majority of her visits once again it would dry up, in between these monthly visits, it actually had substantial atrophy. And even though her vision was still quite good at 20/50, 20/60 it's just interesting to see the difference in the potential different effect that we can see from subretinal fluid and intraretinal fluid in a patient like this, regardless of receiving monthly EYLEA injections.

DR. BIRNHOLZ:
Yeah, that's really interesting, Dr. Kitchens. Thank you for those great case samples. Well, we're almost out of time for today but I'd be remiss if I didn't ask, given everything that you've helped cover for us and the insights that you've provided whether there are any key take-aways that you'd like to leave with our audience today?

DR. KITCHENS:
Yeah Matt, I'll tell ya' there's a couple things. First of all, I love how we continue to dig back into these trials and garner important evidence for how to manage our patients. The second thing is when we look at that Year 2 data, we can see that these patients can do really well with extended intervals and to see that excellent maintenance of vision all the way out through Year 2, it's just very reassuring.

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DR. BIRNHOLZ:
Yeah. Fantastic take-aways, Dr. Kitchens. Thanks so much.

And now, let's review some additional important safety information and indications for EYLEA.

ANNOUNCER:
IMPORTANT SAFETY INFORMATION AND INDICATIONS

ADVERSE REACTIONS
Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with EYLEA including endophthalmitis and retinal detachment.

The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and intraocular pressure increased.

Patients may experience temporary visual disturbances after an intravitreal injection with EYLEA and the associated eye examinations. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

INDICATIONS
EYLEA® (aflibercept) Injection 2 mg (0.05 mL) is indicated for the treatment of patients with Neovascular (Wet) Age-related Macular Degeneration (AMD), Macular Edema following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), and Diabetic Retinopathy (DR).

Please see the full Prescribing Information for EYLEA.

DR. BIRNHOLZ:
Well, with those key take-aways in mind, Dr. Kitchens, it was wonderful speaking with you today, so many fantastic insights. Thanks again.

DR. KITCHENS:
Thanks Matt.

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