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Retina Today

PART III

AMD DISEASE EDUCATION RESOURCE CENTER

A multipart case series presented by experts in the management and treatment of wet age-related macular degeneration.

Age-related macular degeneration (AMD) is a leading cause of blindness in adults in the developed world.[1] VEGF has been implicated as a major pathogenic factor in exudative AMD, as it stimulates angiogenesis and increases vascular permeability.[2] Treatment of AMD with anti-VEGF agents works well for the majority of patients with neovascular AMD and is thus the most popular option at present.

Retina specialists treating patients with AMD may initiate treatment with aflibercept (Eylea, Regeneron) or ranibizumab (Lucentis, Genentech), the two anti-VEGF drugs approved for this indication by the US Food and Drug Administration. Another option for physicians is off-label use of the anti-VEGF oncology drug bevacizumab (Avastin, Genentech). However, treatment with anti-VEGF therapy is not always straightforward. It is sometimes necessary to switch therapy in patients with treatment-resistant AMD.

In Part 3 of this series, David Eichenbaum, MD, a partner at Retina Vitreous Associates of Florida and an affiliate assistant professor of ophthalmology at the University of South Florida, shares two patient cases in which he had to change his treatment approach in order to achieve satisfactory results. A video of Dr. Eichenbaum presenting these cases can be viewed online in the AMD Resource Center at bit.ly/AMDresource.

1. Friedman DS, Katz J, Bressler NM, et al. Racial differences in the prevalence of age-related macular degeneration. *Ophthalmology*. 1999;106(6):1049-1055.
2. Aiello L, Avery RL, Arrigg PG, et al. Vascular endothelial growth factor in ocular fluid of patients with diabetic retinopathy and other retinal disorders. *N Engl J Med*. 1994;331(22):1480-1487.

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The Effect of Drug Selection on Outcomes in Patients With AMD

BY DAVID EICHENBAUM, MD

In this article I present the cases of two patients with age-related macular degeneration (AMD) and discuss how drug selection can affect outcomes over time.

CASE NO. 1

A 72-year-old man with an ophthalmic history of cataracts and dry AMD was referred to me by his general ophthalmologist. Medical history showed that he was fairly healthy, with some hypercholesterolemia. He has coronary artery disease and was taking the anticoagulant warfarin (Coumadin, Bristol-Myers Squibb) due to a previous stent placement. Visual acuity (VA) in his right eye (OD) was 20/32 at presentation His left eye (OS) had a VA of 20/40 and was symptomatic.

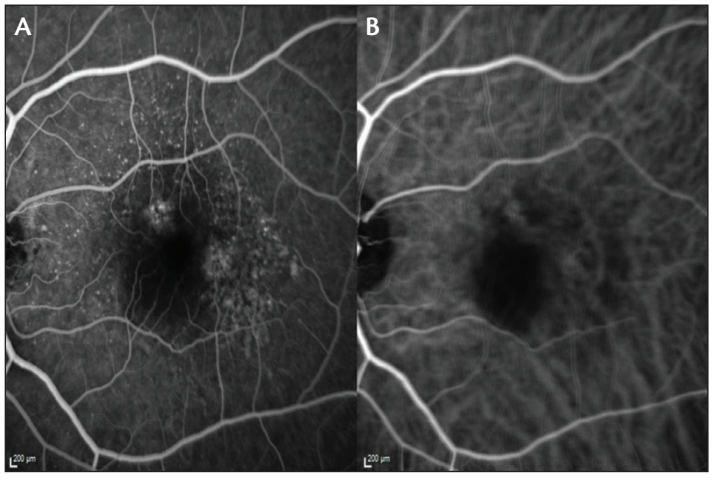

Figure 1. Case No. 1: Early intravenous FA (IVFA) performed on June 29, 2015, shows a choroidal neovascular membrane OS (A). Early ICGA shows a plaque within the subretinal space consistent with a vascularized PED (B).

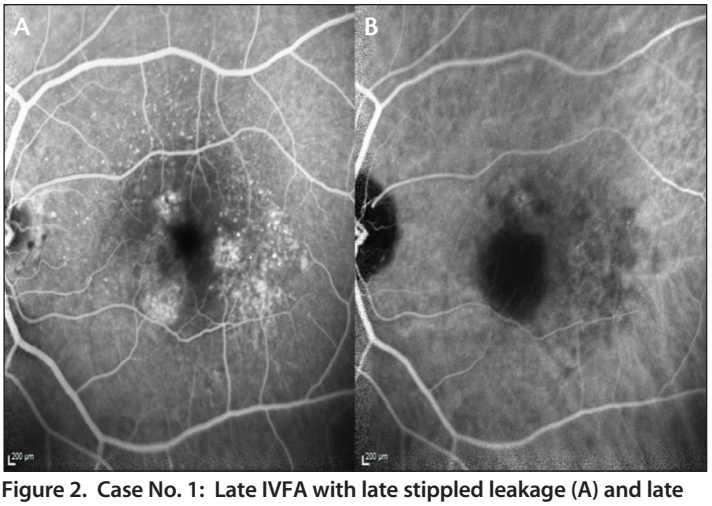

Figure 2. Case No. 1: Late IVFA with late stippled leakage (A) and late ICGA with temporal plaque (B), both performed on June 29, 2015.

Imaging and Treatment

At his first visit, on June 29, 2015, the patient's chief complaint was distortion of new onset. Fluorescein angiography (FA) OS showed a choroidal neovascular membrane with predominantly occult characteristics, and indocyanine green angiography (ICGA) showed a plaque within the subretinal space consistent with a vascularized pigment epithelial detachment (PED) (Figures 1 and 2).

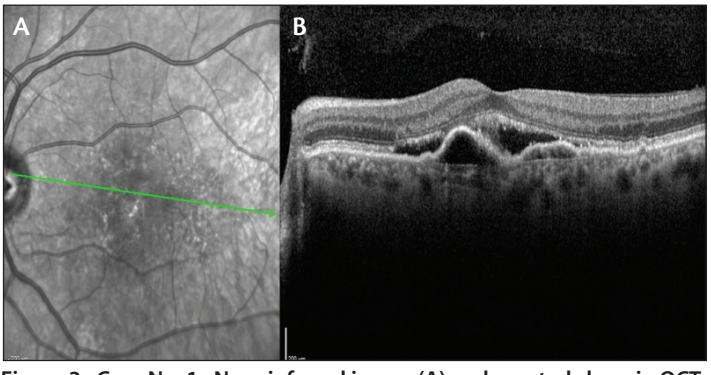

Figure 3. Case No. 1: Near-infrared image (A) and spectral-domain OCT (SD-OCT) with PED and subretinal fluid (B).

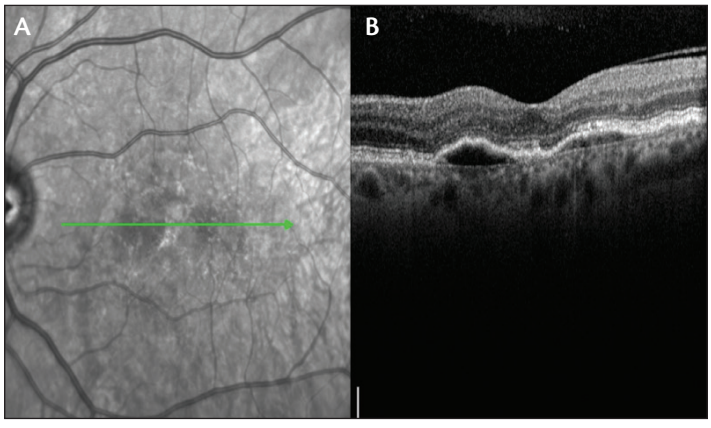

Figure 4. Case No. 1: Near-infrared photo taken on January 4, 2016 (A). SD-OCT shows decreased PED and no subretinal fluid (B).

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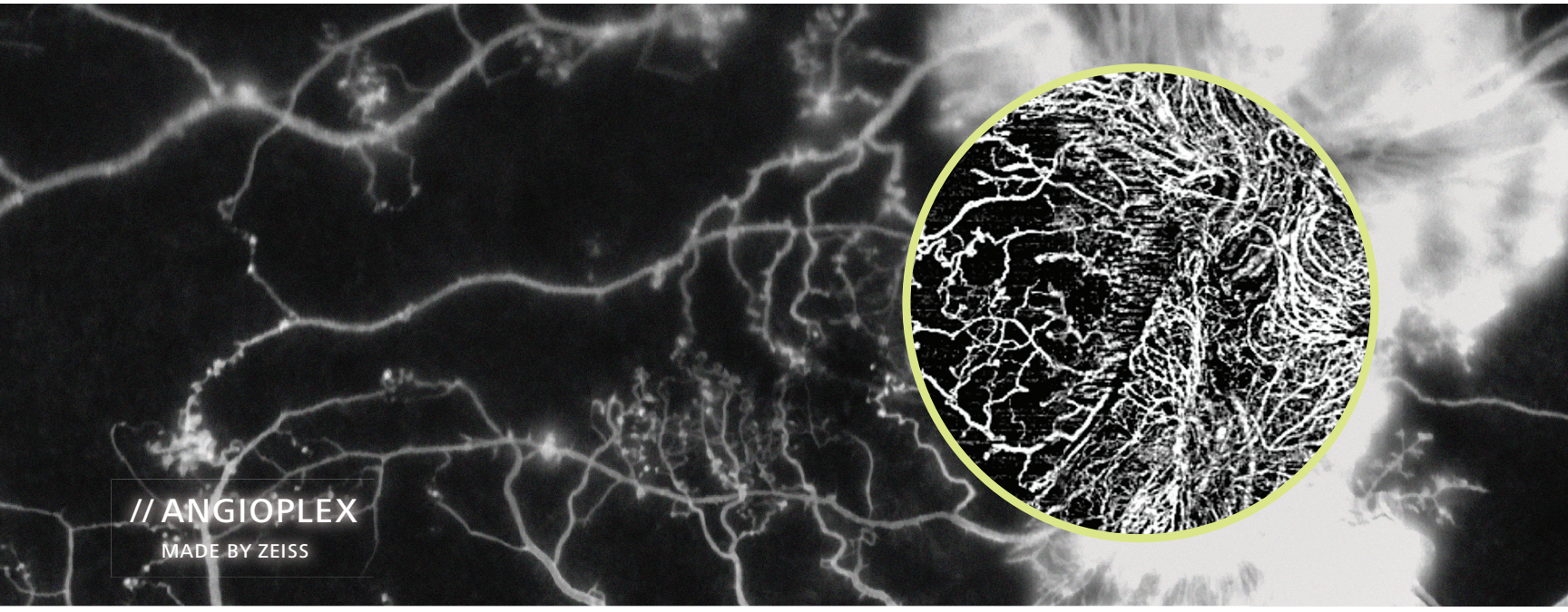

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An optical coherence tomography (OCT) scan taken at this visit showed subretinal fluid consistent with his symptomatic distortion (Figure 3). I injected intravitreal ranibizumab (Lucentis, Genentech) OS at this visit and scheduled a follow-up visit for 5 weeks later.

Follow-Up Course

On August 3, 2015, the patient returned and was a bit better symptomatically. His VA OS was unchanged, although an OCT scan showed a reduction in subretinal fluid. He received two more intravitreal injections of ranibizumab OS, one at this visit and another at a visit 1 month later. Although his VA improved slightly, he still had symptomatic distortion, and OCT showed a reaccumulation of fluid despite monthly ranibizumab treatment. After his third injection of ranibizumab, I chose to convert treatment to aflibercept (Eylea, Regeneron) in an effort to dry the subretinal space.

On November 23, 2015, the first visit after his first intravitreal injection of aflibercept, the patient's subretinal space was free of fluid OD, and the PED had decreased. Additionally, his VA had improved to 20/20 OS, and he reported a reduction in symptomatic distortion.

On January 4, 2016, I noted complete resorption of subretinal fluid, decrease of the PED, and reasonable VA of 20/25 OS (Figure 4). The patient remained on aflibercept treatment, although we slowly began to extend the intervals between treatment.

CASE NO. 2

This 85-year-old man also had an ophthalmic history of dry AMD. However, one notable difference between this patient and the patient described in Case No. 1 was that this patient had previously had cataract surgery OD and currently had a cataract OS. This patient had non–insulin-dependent diabetes that was well-controlled, with an HbA1C of 6.7. He also had well-controlled hypertension. His VA on presentation was 20/32 in the symptomatic pseudophakic eye (OD) and 20/25 in the nonsymptomatic eye (OS).

Imaging and Treatment

The patient presented on March 25, 2015, with the complaint of distorted and decreased visual acuity. FA revealed a choroidal neovascular membrane with predominantly occult characteristics. ICGA showed a plaque consistent with a choroidal neovascular membrane and what appeared to be some guttering of fluid, a sign that is consistent with an occult leak that has persisted for some time (Figures 5, 6, and 7). Interestingly, OCT appeared more benign than the angiography, with mild subretinal fluid in a shallow PED. A few days after this presentation, on March 30, 2015, I started the patient with an injection of ranibizumab.

Follow-Up Course

Four weeks after receiving the first intravitreal injection of ranibizumab, the patient returned with a dry retina, flattening of his PED, slight worsening of VA (20/40+), and no change in symptoms. After receiving a second intravitreal injection of ranibizumab at our center in Florida, this seasonal resident returned to his home in New York, where he received less frequent injections of an unspecified agent (one on July 16, 2015, and another on September 1, 2015).

The patient returned to my office in October complaining of

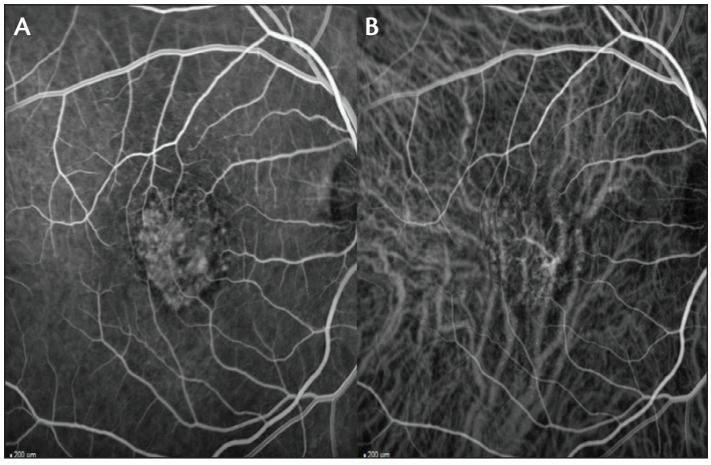

Figure 5. Case No. 2: Transit IVFA (A) and early ICGA (B).

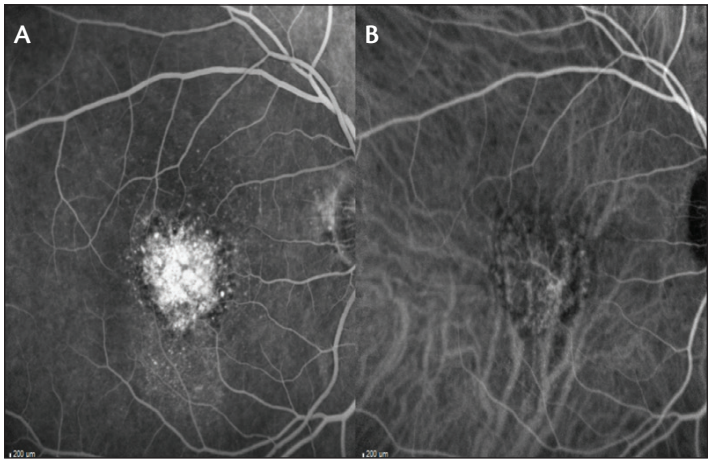

Figure 6. Case No. 2: Late IVFA shows late leakage (A). Late ICGA shows early subfoveal plaque (B).

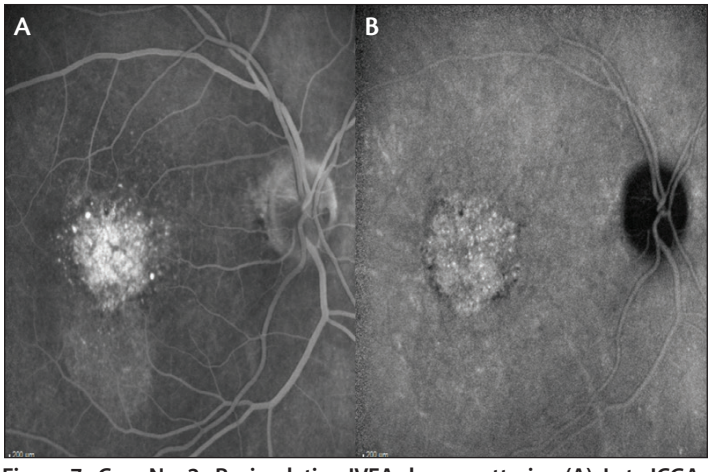

Figure 7. Case No. 2: Recirculation IVFA shows guttering (A). Late ICGA shows plaque (B).

Discover Strength in efficacy

As demonstrated in phase 3 clinical trials in patients with Wet AMD, Macular Edema following RVO, DME, and DR in patients with DME

Choose EYLEA® (aflibercept) Injection from the start

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INDICATIONS AND IMPORTANT SAFETY INFORMATION

INDICATIONS

- EYLEA® (aflibercept) Injection 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) in Patients with DME.

CONTRAINDICATIONS

- EYLEA® (aflibercept) Injection 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. 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.

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 floaters, intraocular pressure increased, and vitreous detachment.

Please see brief summary of full Prescribing Information on the following page.

EYLEA®
(aflibercept) Injection
For Intravitreal Injection

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EYLEA is a registered trademark of Regeneron Pharmaceuticals, Inc.

REGENERON

01/2016
US-LEA-1648

EYLEA®
(aflibercept) Injection
For Intravitreal Injection

BRIEF SUMMARY OF FULL PRESCRIBING INFORMATION

For complete details, see Full Prescribing Information.

1 INDICATIONS AND USAGE

EYLEA® (aflibercept) Injection 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) in Patients with DME.

2 DOSAGE AND ADMINISTRATION

2.1 Important Injection Instructions. For ophthalmic intravitreal injection. EYLEA must only be administered by a qualified physician.

2.2 Neovascular (Wet) Age-Related Macular Degeneration (AMD). The recommended dose for EYLEA is 2 mg (0.05 mL or 50 microliters) administered by intravitreal injection every 4 weeks (monthly) for the first 12 weeks (3 months), followed by 2 mg (0.05 mL) via intravitreal injection once every 8 weeks (2 months). Although EYLEA may be dosed as frequently as 2 mg every 4 weeks (monthly), additional efficacy was not demonstrated when EYLEA was dosed every 4 weeks compared to every 8 weeks.

2.3 Macular Edema Following Retinal Vein Occlusion (RVO). The recommended dose for EYLEA is (0.05 mL or 50 microliters) administered by intravitreal injection once every 4 weeks (monthly).

2.4 Diabetic Macular Edema (DME). The recommended dose for EYLEA is (0.05 mL or 50 microliters) administered by intravitreal injection every 4 weeks (monthly) for the first 5 injections followed by 2 mg (0.05 mL) via intravitreal injection once every 8 weeks (2 months). Although EYLEA may be dosed as frequently as 2 mg every 4 weeks (monthly), additional efficacy was not demonstrated when EYLEA was dosed every 4 weeks compared to every 8 weeks.

2.5 Diabetic Retinopathy (DR) in Patients with DME. The recommended dose for EYLEA is 2 mg (0.05 mL or 50 microliters) administered by intravitreal injection every 4 weeks (monthly) for the first 5 injections, followed by 2 mg (0.05 mL) via intravitreal injection once every 8 weeks (2 months). Although EYLEA may be dosed as frequently as 2 mg every 4 weeks (monthly), additional efficacy was not demonstrated when EYLEA was dosed every 4 weeks compared to every 8 weeks.

2.6 Preparation for Administration. EYLEA should be inspected visually prior to administration. If particulates, cloudiness, or discoloration are visible, the vial must not be used. Using aseptic technique, the intravitreal injection should be performed with a 30-gauge x ½-inch injection needle. For complete preparation for administration instructions, see full prescribing information.

2.7 Injection Procedure. The intravitreal injection procedure should be carried out under controlled aseptic conditions, which include surgical hand disinfection and the use of sterile gloves, a sterile drape, and a sterile eyelid speculum (or equivalent). Adequate anesthesia and a topical broad–spectrum microbicide should be given prior to the injection.

Immediately following the intravitreal injection, patients should be monitored for elevation in intraocular pressure. Appropriate monitoring may consist of a check for perfusion of the optic nerve head or tonometry. If required, a sterile paracentesis needle should be available.

Following intravitreal injection, patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment (e.g., eye pain, redness of the eye, photophobia, blurring of vision) without delay (*see Patient Counseling Information*).

Each vial should only be used for the treatment of a single eye. If the contralateral eye requires treatment, a new vial should be used and the sterile field, syringe, gloves, drapes, eyelid speculum, filter, and injection needles should be changed before EYLEA is administered to the other eye. After injection, any unused product must be discarded.

3 DOSAGE FORMS AND STRENGTHS

Single-use, glass vial designed to provide 0.05 mL of 40 mg/mL solution (2 mg) for intravitreal injection.

4 CONTRAINDICATIONS

EYLEA is contraindicated in patients with

- Ocular or periocular infections
- Active intraocular inflammation
- Known hypersensitivity to aflibercept or any of the excipients in EYLEA. Hypersensitivity reactions may manifest as severe intraocular inflammation

5 WARNINGS AND PRECAUTIONS

5.1 Endophthalmitis and Retinal Detachments. Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments (*see Adverse Reactions*). 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 (*see Dosage and Administration and Patient Counseling Information*).

5.2 Increase in Intraocular Pressure. Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA (*see Adverse Reactions*). Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with vascular edothelial growth factor (VEGF) inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately (*see Dosage and Administration*).

5.3 Thromboembolic Events. 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. 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.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in the *Warnings and Precautions* section of the labeling:

- Endophthalmitis and retinal detachments
- Increased intraocular pressure
- Thromboembolic events

6.1 Clinical Trials Experience. Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in other clinical trials of the same or another drug and may not reflect the rates observed in practice.

A total of 2711 patients treated with EYLEA constituted the safety population in seven phase 3 studies. Among those, 2110 patients were treated with the recommended dose of 2 mg. 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 floaters, intraocular pressure increased, and vitreous detachment.

Neovascular (Wet) Age-Related Macular Degeneration (AMD). The data described below reflect exposure to EYLEA in 1824 patients with wet AMD, including 1223 patients treated with the 2-mg dose, in 2 double-masked, active-controlled clinical studies (VIEW1 and VIEW2) for 12 months.

Table 1: Most Common Adverse Reactions (≥1%) in Wet AMD Studies

Adverse Reactions	EYLEA (N=1824)	Active Control (ranibizumab) (N=595)
Conjunctival hemorrhage	25%	28%
Eye pain	9%	9%
Cataract	7%	7%
Vitreous detachment	6%	6%
Vitreous floaters	6%	7%
Intraocular pressure increased	5%	7%
Ocular hyperemia	4%	8%
Corneal epithelium defect	4%	5%
Detachment of the retinal pigment epithelium	3%	3%
Injection site pain	3%	3%
Foreign body sensation in eyes	3%	4%
Lacrimation increased	3%	1%
Vision blurred	2%	2%
Intraocular inflammation	2%	3%
Retinal pigment epithelium tear	2%	1%
Injection site hemorrhage	1%	2%
Eyelid edema	1%	2%
Corneal edema	1%	1%

Less common serious adverse reactions reported in <1% of the patients treated with EYLEA were hypersensitivity, retinal detachment, retinal tear, and endophthalmitis.

Macular Edema Following Retinal Vein Occlusion (RVO). The data described below reflect 6 months exposure to EYLEA with a monthly 2 mg dose in 218 patients following CRVO in 2 clinical studies (COPERNICUS and GALILEO) and 91 patients following BRVO in one clinical study (VIBRANT).

Table 2: Most Common Adverse Reactions (≥1%) in RVO Studies

Adverse Reactions	CRVO		BRVO	
	EYLEA (N=218)	Control (N=142)	EYLEA (N=91)	Control (N=92)
Eye pain	13%	5%	4%	5%
Conjunctival hemorrhage	12%	11%	20%	4%
Intraocular pressure increased	8%	6%	2%	0%
Corneal epithelium defect	5%	4%	2%	0%
Vitreous floaters	5%	1%	1%	0%
Ocular hyperemia	5%	3%	2%	2%
Foreign body sensation in eyes	3%	5%	3%	0%
Vitreous detachment	3%	4%	2%	0%
Lacrimation increased	3%	4%	3%	0%
Injection site pain	3%	1%	1%	0%
Vision blurred	1%	<1%	1%	1%
Intraocular inflammation	1%	1%	0%	0%
Cataract	<1%	1%	5%	0%
Eyelid edema	<1%	1%	1%	0%

Less common adverse reactions reported in <1% of the patients treated with EYLEA in the CRVO studies were corneal edema, retinal tear, hypersensitivity, and endophthalmitis.

Diabetic Macular Edema (DME). The data described below reflect exposure to EYLEA in 578 patients with DME treated with the 2-mg dose in 2 double-masked, controlled clinical studies (VIVID and VISTA) from baseline to week 52 and from baseline to week 100.

Table 3: Most Common Adverse Reactions (≥1%) in DME Studies

Adverse Reactions	Baseline to Week 52		Baseline to Week 100	
	EYLEA (N=578)	Control (N=287)	EYLEA (N=578)	Control (N=287)
Conjunctival hemorrhage	28%	17%	31%	21%
Eye pain	9%	6%	11%	9%
Cataract	8%	9%	19%	17%
Vitreous floaters	6%	3%	8%	6%
Corneal epithelium defect	5%	3%	7%	5%
Intraocular pressure increased	5%	3%	9%	5%
Ocular hyperemia	5%	6%	5%	6%
Vitreous detachment	3%	3%	8%	6%
Foreign body sensation in eyes	3%	3%	3%	3%
Lacrimation increased	3%	2%	4%	2%
Vision blurred	2%	2%	3%	4%
Intraocular inflammation	2%	<1%	3%	1%
Injection site pain	2%	<1%	2%	<1%
Eyelid edema	<1%	1%	2%	1%

Less common adverse reactions reported in <1% of the patients treated with EYLEA were hypersensitivity, retinal detachment, retinal tear, corneal edema, and injection site hemorrhage.

6.2 Immunogenicity. As with all therapeutic proteins, there is a potential for an immune response in patients treated with EYLEA. The immunogenicity of EYLEA was evaluated in serum samples. The immunogenicity data reflect the percentage of patients whose test results were considered positive for antibodies to EYLEA in immunoassays. The detection of an immune response is highly dependent on the sensitivity and specificity of the assays used, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to EYLEA with the incidence of antibodies to other products may be misleading.

In the wet AMD, RVO, and DME studies, the pre-treatment incidence of immunoreactivity to EYLEA was approximately 1% to 3% across treatment groups. After dosing with EYLEA for 24-100 weeks, antibodies to EYLEA were detected in a similar percentage range of patients. There were no differences in efficacy or safety between patients with or without immunoreactivity.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy. Pregnancy Category C. Aflibercept produced embryo-fetal toxicity when administered every three days during organogenesis to pregnant rabbits at intravenous doses ≥3 mg per kg, or every six days at subcutaneous doses ≥0.1 mg per kg. Adverse embryo-fetal effects included increased incidences of postimplantation loss and fetal malformations, including anasarca, umbilical hernia, diaphragmatic hernia, gastroschisis, cleft palate, ectrodactyly, intestinal atresia, spina bifida, encephalomeningocele, heart and major vessel defects, and skeletal malformations (fused vertebrae, sternebrae, and ribs; supernumerary vertebral arches and ribs; and incomplete ossification). The maternal No Observed Adverse Effect Level (NOAEL) in these studies was 3 mg per kg. Aflibercept produced fetal malformations at all doses assessed in rabbits and the fetal NOAEL was less than 0.1 mg per kg. Administration of the lowest dose assessed in rabbits (0.1 mg per kg) resulted in systemic exposure (AUC) that was approximately 10 times the systemic exposure observed in humans after an intravitreal dose of 2 mg. There are no adequate and well-controlled studies in pregnant women. EYLEA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers. It is unknown whether aflibercept is excreted in human milk. Because many drugs are excreted in human milk, a risk to the breastfed child cannot be excluded. EYLEA is not recommended during breastfeeding. A decision must be made whether to discontinue nursing or to discontinue treatment with EYLEA, taking into account the importance of the drug to the mother.

8.4 Pediatric Use. The safety and effectiveness of EYLEA in pediatric patients have not been established.

8.5 Geriatric Use. In the clinical studies, approximately 76% (2049/2701) of patients randomized to treatment with EYLEA were ≥65 years of age and approximately 46% (1250/2701) were ≥75 years of age. No significant differences in efficacy or safety were seen with increasing age in these studies.

17 PATIENT COUNSELING INFORMATION

In the days following EYLEA administration, patients are at risk of developing endophthalmitis or retinal detachment. If the eye becomes red, sensitive to light, painful, or develops a change in vision, advise patients to seek immediate care from an ophthalmologist (*see Warnings and Precautions*). Patients may experience temporary visual disturbances after an intravitreal injection with EYLEA and the associated eye examinations (*see Adverse Reactions*). Advise patients not to drive or use machinery until visual function has recovered sufficiently.

REGENERON

Manufactured by:
Regeneron Pharmaceuticals, Inc.
777 Old Saw Mill River Road
Tarrytown, NY 10591-6707

U.S. License Number 1760

Issue Date: March 2015
Initial U.S. Approval: 2011

Regeneron U.S. Patents 7,070,959; 7,303,746; 7,303,747; 7,306,799; 7,374,757; 7,374,758; 7,531,173; 7,608,261; 7,972,598; 8,029,791; 8,092,803; 8,647,842; and other pending patents.

LEA-0721

> "It is important to monitor patients' unique responses over time and to try to optimize treatment for each individual case.

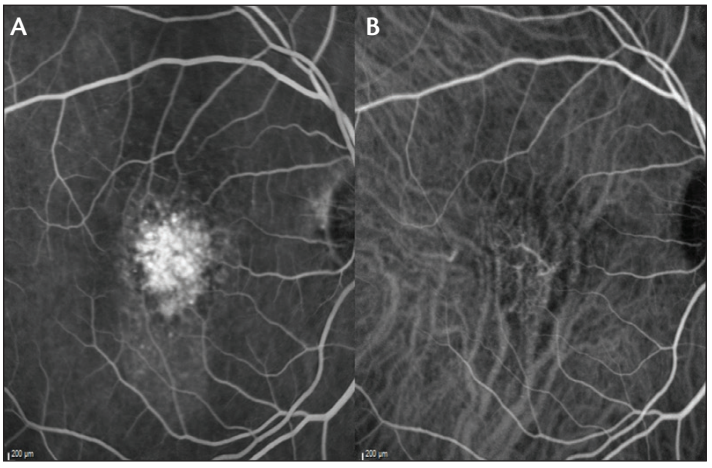

Figure 9. Case No. 2: Late IVFA with staining (A). Late ICGA with reduction of plaque (B).

additional distortion, and OCT showed a reaccumulation of fluid since his last injection of ranibizumab in New York. I reinitiated treatment with ranibizumab because the patient had done well with it previously, but when he returned 5 weeks later I noted persistent subretinal fluid, persistent distortion, and stable but suboptimal VA (Figure 8).

At this point I chose to convert the patient to treatment with intravitreal aflibercept, and at the next visit after this first injection I noted drying. His VA OD improved to 20/32 4 weeks after the first injection, he reported less distortion, and his macula was dry with a stable, shallow PED. I administered a second intravitreal injection of aflibercept, and the patient's macula continued to remain dry.

Interestingly, the patient returned 6 weeks after his third intravitreal injection of aflibercept OD reporting symptoms in the contralateral eye. His visual acuity OS was 20/50, and I observed a new choroidal neovascular membrane OS. FA showed a hyperfluorescent, almost polypoid appearance, as though the patient had a retinal angiomatous proliferation–type lesion OS, and ICGA corroborated this.

Persistence of the choroidal neovascular membrane OD was seen on FA and ICGA similar to presentation, with perhaps a slight reduction in leakage and hyperfluorescence (Figure 9). The macula OD remained dry since his third injection of aflibercept.

I initiated monthly intravitreal aflibercept treatment OS on March 14, 2016, and I continued to offer the patient a less frequent treatment interval OD, due to his success with less-than-monthly aflibercept in this eye.

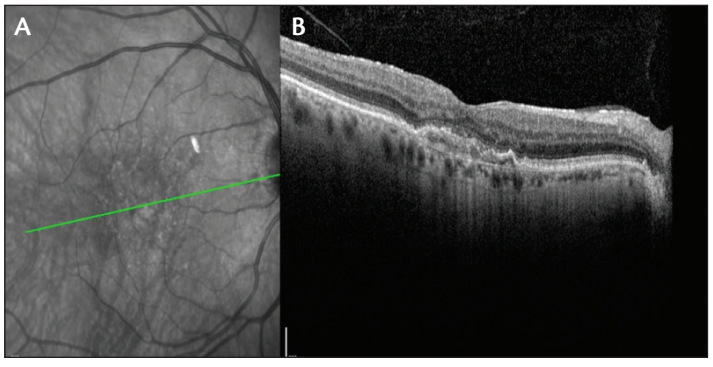

Figure 8. Case No. 2: Near-infrared photo (A). Reaccumulation of mild subretinal fluid (B).

CONCLUSION

It is reasonable to start patients on any commercially available anti-VEGF agent, as there are robust data supporting the safety and efficacy of bevacizumab, ranibizumab, and aflibercept. It is important to monitor patients' unique responses over time and to try to optimize treatment for each individual case. Ongoing examination, periodic imaging, and switching agents when there is suboptimal response are important techniques to employ in day-to-day practice. Although there are minimal prospective, randomized, controlled data guiding the techniques for drug switching, it is reasonable to try the various commercially available agents if one sees that the anatomy and vision can be further optimized. One may see some inter-individual variation in drug response in certain patients. Assessing genetic biomarkers to predict a patient's response to intravitreal therapy will be a focus in our field going forward. For now, in the absence of that data, each physician can use exam and imaging findings in an effort to customize individual treatment. ■

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