Optimizing Real-World Outcomes in Wet AMD
Reducing the Burden of Treatment With Longer-Acting Therapies

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The Real-World Burdens of Standard-of-Care Anti-VEGF Treatments for Wet AMD

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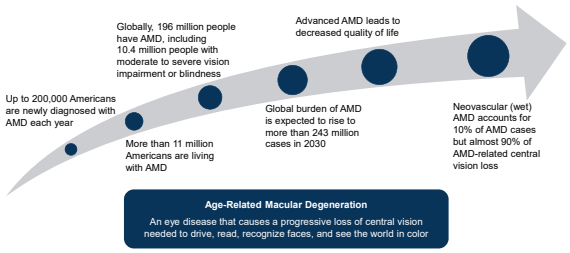
Prevalence and Burden of Age-Related Macular Degeneration (AMD)[1]



Age-Related Macular Degeneration

An eye disease that causes a progressive loss of central vision needed to drive, read, recognize faces, and see the world in color

1. https://www.ajmc.com/view/wet-agerelated-macular-degeneration-treatment-advances-to-reduce-the-injection-burden.

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Standard-of-Care Anti-VEGF Agents Used in Wet AMD[1-4]

Drug	Unlicensed Bevacizumab	Aflibercept	Ranibizumab	Brolucizumab
Format	Full antibody (IgG1)	VEGFR1/2-Fc fusion protein	Fab fragment	Single-chain antibody fragment
Molecular structure				
Molecular weight	149 kDa	97-115 kDa	48 kDa	26 kDa
Clinical dose	1.25 mg	2.0 mg	0.50 mg	6.0 mg
FDA-approved indications	Not FDA approved for ophthalmic use	Wet AMD, MEfRVO, DME, DR, ROP	Wet AMD, MEfRVO, DME, DR, myopic CNV	Wet AMD, DME
Dosing intervals for wet AMD	1.25 mg every 4 wk, based on literature	Loading dose of 3 injections at 4-wk intervals and then every 8 wk	0.5 mg every 4 wk	Loading dose of 3 injections at 4-wk intervals and then every 8 wk to 12 wk

1. https://eyewiki.aao.org/Bevacizumab. 2. Eylea (aflibercept) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/125387s075lbl.pdf.
3. Lucentis (ranibizumab injection) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/125156s117lbl.pdf.
4. Beovu (brolucizumab-dbll) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761125s020lbl.pdf.

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The Benefits and Burden of Intravitreal Anti-VEGF Therapies for the Treatment of Wet AMD

IVT anti-VEGF therapy is highly effective in clinical trials for wet AMD

Visual outcomes drop off in the real world

Visual outcomes correlate with treatment intensity (number of injections) in the real-world setting

The need for frequent monitoring and injections results in a high treatment burden, leading to poor treatment adherence

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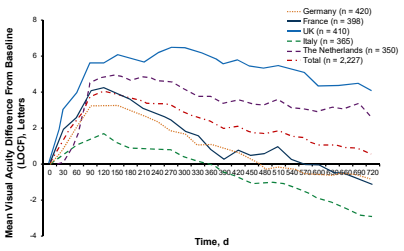
AURA Study: Real-Life Use of Anti-VEGF Therapy Associated With Poorer Outcomes Compared With Clinical Trial Outcomes[1]



1. Holz FG et al. *Br J Ophthalmol*. 2015;99:220-226.

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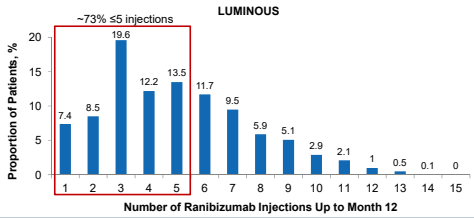
Real-World Data: Majority of Patients With Wet AMD Likely Undertreated During First Year of Management[1]



This translates to poor VA outcomes for patients if their disease is not controlled

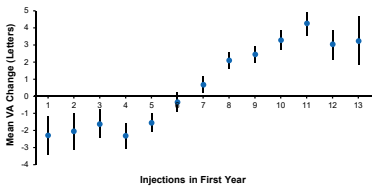
1. Holz FG et al. EURETINA 2017. Poster 17.54.

PeerView.com

Linear Relationship Between Change in VA and Number of Anti-VEGF Injections in First Year of Treatment[1]

Real-world analysis of 49,485 eyes found linear relationship between mean letters gained and mean number of injections, between 4 and 10 injections over 1 year

- ≤4 injections associated with loss of vision
- ≥10 injections associated with a plateau



1. Ciulla TA et al. *Ophthalmol Retina*. 2020;4:19-30.

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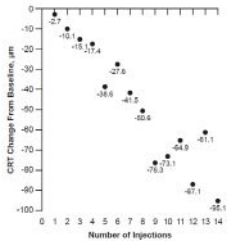
Magnitude of Change in CRT Inversely Correlated With Number of Anti-VEGF Injections Received in First Year[1]



1. Kiss S et al. *Ophthalmology*. 2020;127:1179-1188.

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Audience Polling Question

While intravitreal anti-VEGF therapy was usually highly effective in clinical trials for wet AMD, it is less effective in the real world, with many patients receiving little to no benefit. Which patient- or treatment-related factor is the best predictor of real-world benefit from anti-VEGF treatment in patients with wet AMD?

1. I'm not sure
2. Anti-VEGF treatment selection (bevacizumab vs ranibizumab vs aflibercept)
3. Number of intravitreal injections performed
4. Patient's age
5. Patient's baseline visual acuity

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Factors Linked to Nonadherence With Intravitreal Anti-VEGF Injections

Shortcomings/ limitations of current anti-VEGF treatments

- Intensive therapy needed for maximum visual benefit
- Short duration of treatment effect
- Frequent injections and office visits
- Decreased ability to function on day of treatment
- Pain and discomfort from injection
- High out-of-pocket costs

Patient nonadherence to treatment

- Lack of knowledge about benefits of anti-VEGF therapy
- Loss of mobility
- Lack of transportation and burden on caregivers who provide rides to appointments
- Safety risk involved with office visits in the COVID era
- Fear of injections
- Fear of receiving a poor prognosis
- Serious comorbid illness taking priority
- Vacation or travel
- Financial concerns

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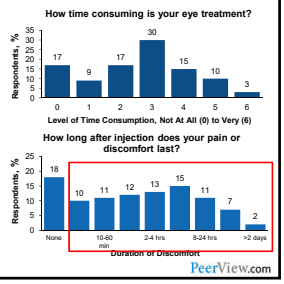
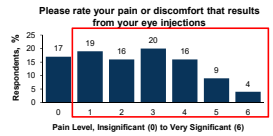
The Majority of Patients Experience Pain or Discomfort From Their Intravitreal Injections[1]

- Questionnaire developed to evaluate patient experience
- 142 patients participated
- Principal components analysis revealed five dimensions of patient burden:
  1. Disruption of normal routine
  2. Anxiety
  3. Frequency of visits
  4. Chronicity of disease
  5. Perceived treatment value/satisfaction





1. McClard CK et al. *BMJ Open Ophthalmol.* 2021;6:e000669.

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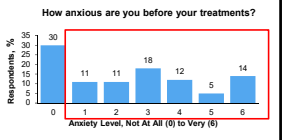
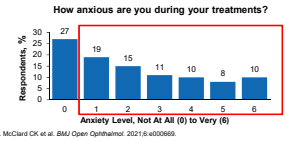
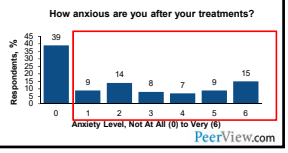
The Majority of Patients Experience Anxiety Before, During, and After Their Intravitreal Injections[1]







1. McClard CK et al. *BMJ Open Ophthalmol.* 2021;6:e000669.

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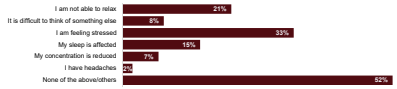
60% of Patients Experienced Anxiety on ≥1 Days Prior to Intravitreal Anti-VEGF Treatment[1]

- Survey of 130 Norwegian participants with wet AMD
- Patients received 9 injections per year on average
- 38% needed caregiver support for every treatment appointment
- 55% and 26% reported treatment was uncomfortable and somewhat painful, respectively
- Emotional impact of treatment burden

Reported Number of Days Patients Felt Anxious Prior to Latest Intravitreal Injection

How Anxiety About Intravitreal Injections Manifested in Patients



1. Reitan G et al. *Clin Ophthalmol*. 2023;17:1465-1474.

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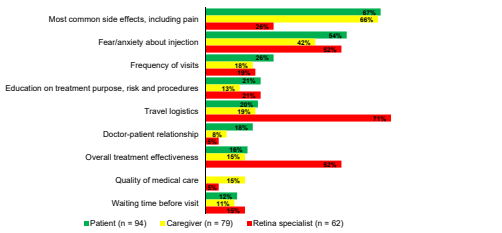
Retina Specialists and Patients/Caregivers Disagreed About Treatment Barriers That Most Impacted Treatment Adherence[1]

Treatment Barriers That Impacted Treatment Adherence Reported by Patients, Caregivers, and Retina Specialists



1. Giocanti-Auregan A et al. *Patient Prefer Adherence*. 2022;16:587-604.

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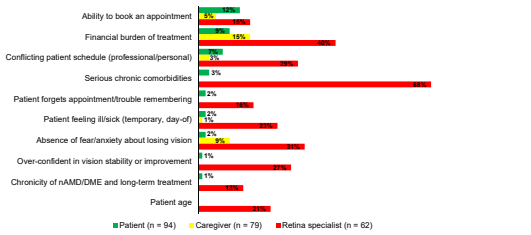
Retina Specialists and Patients/Caregivers Disagreed About Treatment Barriers That Most Impacted Treatment Adherence[1] (Cont'd)

Treatment Barriers Reported by Patients, Caregivers, and Retina Specialists



1. Giocanti-Auregan A et al. *Patient Prefer Adherence*. 2022;16:587-604.

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Audience Polling Question

Based on multiple recent studies examining patient-reported treatment burdens associated with anti-VEGF therapy, which of the following actions would you take to alleviate the treatment burden and/or reduce barriers to intravitreal anti-VEGF treatment for the most patients?

1. I'm not sure
2. Facilitate enrollment in patient assistance programs to reduce the financial burden of treatment
3. Improve the management of patients' other chronic health problems
4. Manage anxiety experienced by patients prior to their scheduled treatment
5. Reduce the wait time at the clinic before the patients' visit

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The Benefits and Limitations of Novel Wet AMD Therapies With Extended Dosing Intervals

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Novel Therapeutic Strategies Can Lower the Treatment Burden in Wet AMD by Extending the Dosing Interval[1-3]

Drug	Aflibercept (8 mg)	Ranibizumab Port Delivery System	Faricimab
Format	VEGFR1/2-Fc fusion protein	Fab fragment delivered via ocular implant	Bispecific Ang2/VEGF-A antibody
Molecular structure			
Molecular weight	97-115 kDa	48 kDa	150 kDa
Clinical dose	8.0 mg	2.0 mg	6.0 mg
FDA-approved indications	Wet AMD, DME, DR	Wet AMD	Wet AMD, DME, RVO
Dosing intervals for wet AMD	Loading dose of 3 injections at 4-wk intervals and then every 8-16 wk	Dose every 24 wk	Loading dose of 4 injections at 4-wk intervals and then every 8-16 wk

1. Eylea HD (aflibercept) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761355s000lbl.pdf.
2. Susvimo (ranibizumab injection) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761197s002lbl.pdf.
3. Vabysmo (faricimab-svoa) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761235s003lbl.pdf.

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PULSAR: Aflibercept 8 mg Phase 3 Trial in Wet AMD[1]

Aflibercept 8 mg was approved in August 2023 for treatment of wet AMD, DME, and DR

Multicenter, randomized, double-masked study in patients with treatment-naïve wet AMD
Randomized at baseline 1:1:1 (2Q8, 8Q2, 8Q16)

2Q8	8Q12	8Q16
Aflibercept 2 mg every 8 weeks after 3 initial monthly injections n = 336	Aflibercept 8 mg every 12 weeks after 3 initial monthly injections n = 335	Aflibercept 8 mg every 16 weeks after 3 initial monthly injections n = 338

Primary endpoint at week 48: Mean change in BCVA (noninferiority)

Key secondary endpoints:
Mean change in BCVA from baseline to week 60[a]
Proportion of patients without IRF and SRF in the center subfield at week 16

End of study at week 96 with optional 1-year extension through week 156

[a] For European Medicines Agency/Pharmaceuticals and Medical Devices Agency regulatory approval only.
1. https://clinicaltrials.gov/study/NCT04423718.

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PULSAR Dosing Schedule and Regimen Modifications to Shorten or Extend the Treatment Interval[1]

DRM: Interval Shortening During Years 1 and 2

Criteria for Interval Shortening
- >5-letter loss in BCVA compared with week 12 due to persistent or worsening wet AMD
AND
- >25-mcm increase in CST compared with week 12, or new-onset foveal neovascularization, or foveal hemorrhage

Patients Who Met the DRM Criteria Could Have Their Intervals Shortened at:
- Weeks 16 and 20: Patients on 8Q12 and 8Q16 to Q8
- Week 24: Patients on 8Q16 to Q12
- Weeks 32 and 44 for 8Q12 and week 40 for 8Q16: Intervals shortened by 4 weeks
- Week 52 onward: Patients on 8Q12 and 8Q16 will have dosing intervals shortened in 4-week intervals (to a minimum of Q8)

DRM: Interval Extension During Year 2

Criteria for Interval Extension
- <5-letter loss in BCVA compared with week 12
AND
- No fluid at the central subfield on OCT
AND
- No new foveal hemorrhage or foveal neovascularization

Patients Who Met the DRM Criteria Were Able to Extend at:
- Week 52 onward: Patients on 8Q12 and 8Q16 will have dosing intervals extended by 4-week increments; patients on 8Q16 can be extended to a maximum of Q20 and Q24 through weeks 60 and 96, respectively

1. https://clinicaltrials.gov/study/NCT04423718.

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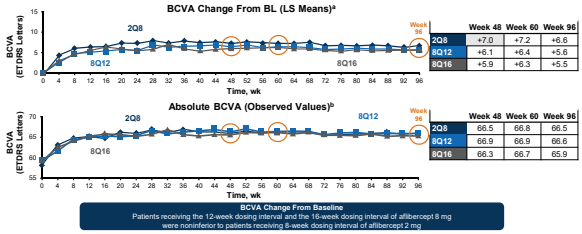
PULSAR: BCVA Outcomes at Week 96 With Aflibercept 8 mg



	Week 48	Week 60	Week 96
2Q8	+7.0	+7.2	+6.6
8Q12	+6.1	+6.4	+5.6
8Q16	+5.9	+6.3	+5.5

	Week 48	Week 60	Week 96
2Q8	66.5	66.8	66.5
8Q12	66.9	66.9	66.6
8Q16	66.3	66.7	65.9

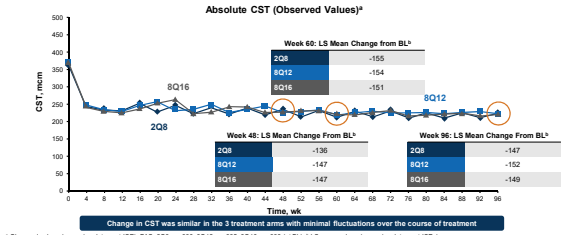
BCVA Change From Baseline

Patients receiving the 12-week dosing interval and the 16-week dosing interval of aflibercept 8 mg were noninferior to patients receiving 8-week dosing interval of aflibercept 2 mg

[a] LS mean values (censoring data post-ICE): FAS: 2Q8 n = 336; 8Q12 n = 335; 8Q16 n = 338 (at BL). LS means were generated using MMRM with BL BCVA measurement as a covariate, treatment group (aflibercept 2Q8, 8Q12, 8Q16), visit, and stratification variables (geographic region [Japan vs rest of world] and BL BCVA [<60 vs ≥60]) as fixed factory, and interaction terms for BL and visit and for treatment and visit. [b] Observed values (censoring data post-ICEs): FAS: 2Q8 n = 336; 8Q12 n = 335; 8Q16 n = 338 (at BL).

1. Lanzetta P. EURETINA 2023. Free Paper Session 3.

PULSAR: Central Subfield Thickness Through 96 Weeks[1]



Week 60: LS Mean Change from BL[b]	
2Q8	-155
8Q12	-154
8Q16	-151

Week 48: LS Mean Change From BL[b]	
2Q8	-136
8Q12	-147
8Q16	-147

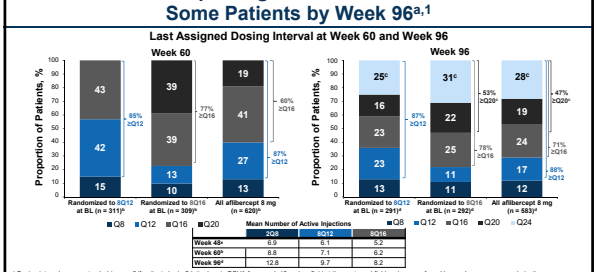
Week 96: LS Mean Change From BL[b]	
2Q8	-147
8Q12	-152
8Q16	-149

Change in CST was similar in the 3 treatment arms with minimal fluctuations over the course of treatment

[a] Observed values (censoring data post-ICE): FAS: 2Q8 n = 336; 8Q12 n = 335; 8Q16 n = 338 (at BL). [b] LS mean values (censoring data post-ICEs): FAS: 2Q8 n = 336; 8Q12 n = 335; 8Q16 n = 338 (at BL). LS mean values were generated using MMRM with BL CST measurement as a covariate, treatment group (aflibercept 2Q8, 8Q12, 8Q16), visit, and stratification variables (geographic region [Japan vs rest of world] and BL BCVA [<60 vs ≥60]) as fixed factory, and interaction terms for BL and visit and for treatment and visit.

1. Lanzetta P. EURETINA 2023. Free Paper Session 3.

PULSAR: Aflibercept 8 mg Is Able to Extend to 24 Weeks in Some Patients by Week 96[a,1]



Mean Number of Active Injections	2Q8	8Q12	8Q16
Week 48[a]	6.9	6.1	5.2
Week 60[b]	8.8	7.1	6.2
Week 96[d]	12.8	9.7	8.2

[a] Dosing intervals were extended in year 2 if patients had <5-letter loss in BCVA from week 12 and no fluid at the center subfield and no new foveal hemorrhage or neovascularization. [b] Patients completing week 60. [c] Patients were assigned to 24-week dosing intervals if they continue to meet extension criteria but did not have enough time to complete the interval within the 96-week study period. [d] Patients completing week 96. [e] Patients completing week 48. Values may not add up to 100% due to rounding.

1. Lanzetta P. EURETINA 2023. Free Paper Session 3.

PULSAR: Aflibercept 8 mg Safety Through Week 60[1]

	2Q8	8Q12	8Q16	All 8 mg
N (SAF)	336	335	338	673
Ocular safety				
Pts with ≥1 ocular TEAE,[a] %	45.2	42.4	42.3	42.3
Pts with ≥1 IOI TEAE, %	1.2	1.2	0.3	0.7
Pts with IOP ≥35 mmHg pre- or post-injection, %	0.3	0.9	0.3	0.6
Nonocular safety				
APTC events,[b] %	2.4	0.3	0.6	0.4
Hypertension events,[b] %	4.8	6.9	6.5	6.7
Nonocular SAEs,[b] %	15.8	12.2	12.1	12.2
Deaths,[c] %	1.5	0.9	0.6	0.7

- Ocular TEAEs occurring in ≥3% of patients in any treatment group were cataract, IOP increased,[d] SRF, retinal hemorrhage, visual acuity reduced, and vitreous floaters
- The safety profile of aflibercept 8 mg at week 96 is comparable to that at week 60 and also with aflibercept 2 mg

[a] In the study eye. [b] Treatment emergent. [c] All events. [d] Defined by preferred terms "intraocular pressure increased" and "ocular hypertension."
1. Lanzetta P. EURETINA 2023. Free Paper Session 3.

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Audience Polling Question

What were the 96-week outcomes findings from the phase 3 PULSAR trial?

1. I'm not sure
2. Aflibercept 8 mg was associated with noninferior visual acuity gains and higher intraocular pressure when administered every 8 weeks compared with aflibercept 2 mg administered every 8 weeks
3. Aflibercept 8 mg was associated with larger reductions in central subfield thickness and higher intraocular pressure when administered every 12 weeks compared with aflibercept 2 mg administered every 8 weeks
4. Aflibercept 8 mg was associated with noninferior visual acuity gains and similar adverse event rates when administered every 16 weeks compared with aflibercept 2 mg administered every 8 weeks
5. Aflibercept 8 mg was associated with larger reductions in central subfield thickness and similar adverse event rates when administered every 20 weeks compared with aflibercept 2 mg administered every 8 weeks

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5. Aflibercept 8 mg was associated with larger reductions in central subfield thickness and similar adverse event rates when administered every 20 weeks compared with aflibercept 2 mg administered every 8 weeks

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Ranibizumab Port Delivery System[1,2]

Phase 3 Archway Trial: 2-Year Results

Open-label randomized, visual acuity assessor–masked noninferiority and equivalence trial

- **Population:** Patients (N = 415) with wet AMD who were previously treated and responded to anti-VEGF injections
- **Treatment Arms:** 100 mg/mL ranibizumab PDS with **fixed 24-week refills** (Q24W), 0.5 mg/mL intravitreal ranibizumab injections Q4W

Primary Endpoint

Change in BCVA (ETDRS letters) score

Weeks Averaged	Difference in Adjusted Means	95% CI
44 and 48	-0.2	-1.8 to 1.3
60 and 64	0.4	-1.4 to 2.1
88 and 92	-0.5	-2.5 and 1.3

Secondary Endpoints

Change in BCVA score over time and change in CPT from baseline were generally the same between the two treatment arms

1. Holekamp NM et al. *Ophthalmol*. 2022;129:295-307. 2. Regillo C et al. *Ophthalmol*. 2023;130:735-747.

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Ranibizumab Port Delivery System: Safety Concerns Led to Voluntary Recall[1,2]

Endpoint	Ranibizumab IVT	Ranibizumab PDS
Adjusted mean CPT change from BL, mm	2.6	5.4
Ocular AEs of special interest, %		
Vitreous hemorrhage	2.4	5.2
Endophthalmitis	0	1.6
Retinal detachment	0	0.8
Conjunctival erosion	0	2.4
Conjunctival retraction	0	2.0

Most ocular AEs in the PDS arm occurred within 1 month of implantation

In late 2022, the ocular implant and insertion tool assembly (including the drug vial and initial fill needle) for ranibizumab PDS were voluntarily recalled due to septum dislodgment; this did not include the refill vial and needle

1. Holekamp NM et al. *Ophthalmol*. 2022;129:295-307. 2 https://www.ophthalmologytimes.com/view/genentech-recalling-ranibizumab-injection-ocular-implant-in-us.

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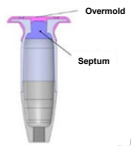
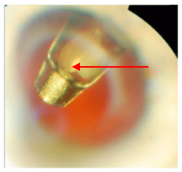
Implant Septum Dislodgement[1]

Normal Position of the Septum in PDS





2.3% (33 cases in 1,419 implants) as of August 31, 2022

1. https://eyewiki.org/Port_Delivery_System.

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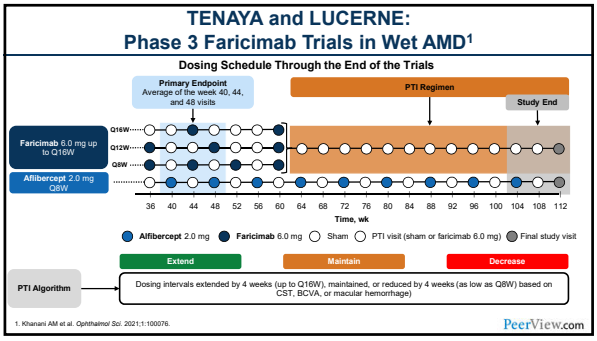
TENAYA and LUCERNE: Phase 3 Faricimab Trials in Wet AMD[1]



1. Khanani AM et al. *Ophthalmol Sci*. 2021;1:100076.

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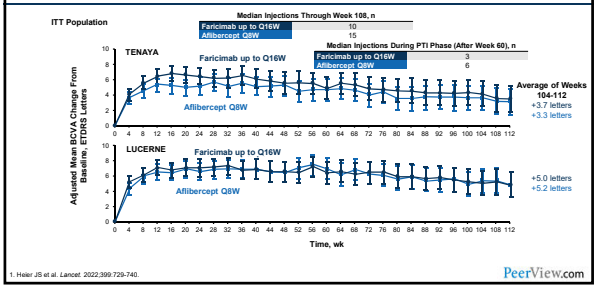
Faricimab Phase 3 Trials: Mean Change in BCVA From Baseline to Week 112[1]



1. Heier JS et al. *Lancet*. 2022;399:729-740.

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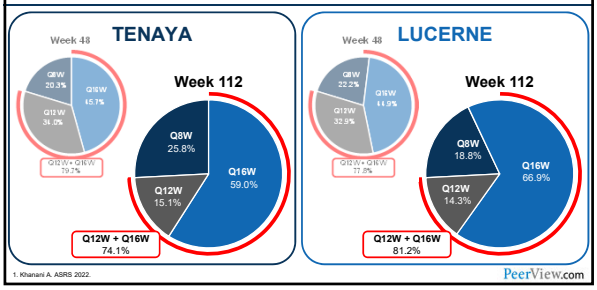
Faricimab Treatment Intervals at Weeks 48 and 112 in Wet AMD[1]



1. Khanani A. ASRS 2022.

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Faricimab Pooled TENAYA and LUCERNE Safety Data[1]

Exposure-Adjusted Incidence Rates of AEs Through Week 48, events/100 patient-years	Faricimab (n = 665)	Aflibercept (n = 664)
IOI events (95% CI)	2.68 (1.53-4.35)	1.52 (0.69-2.88)
Iritis	0.50	0.51
Uveitis	0.50	0.34
Keratic precipitates	0.17	0.0
Vitritis	0.50	0.17
Iridocyclitis	0.84	0.34
Chorioretinitis	0.17	0.0
Postprocedural inflammation	0.0	0.17
Endophthalmitis events	0.0	0.17
Retinal vasculitis events	0.0	0.0

1. Guymer R et al. Angiogenesis, Exudation, and Degeneration-Virtual Edition; Bascom Palmer Eye Institute, University of Miami Health System; February 11-12, 2022; Miami, FL.

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FARETINA-AMD: Faricimab Real-World Data[1]

Ongoing real-world data study utilizing data from the IRIS registry (AAO EHR registry); 17,500 eyes included, of which 6.2% were treatment-naïve

Best documented VA ≥20/40 in 49% treatment-experienced and 37% treatment-naïve eyes

Treatment-naïve eyes gained mean 2 letters VA; treatment-experienced eyes remained relatively stable

69% of previously treated eyes achieved an extended interval, of which 55% extended after 1-2 injections of faricimab

66% of treatment-naïve eyes, the analysis showed extended the interval, of which 43% extended after 1-2 injections

1. Leng T et al. ASRS 2023.

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Audience Polling Question

What was a major difference between the FARETINA-AMD real-world study compared with the faricimab clinical trials?

1. I'm not sure
2. Most of the patients in FARETINA-AMD had been previously treated for wet AMD, while all of the ongoing and completed clinical trials evaluating faricimab in patients with wet AMD focused on treatment-naïve patients
3. Faricimab was associated with greater visual acuity outcomes among treatment-naïve patients in the real-world study compared with the clinical trials
4. Patients who were switched from aflibercept experienced a temporary loss of visual acuity, and this was not demonstrated in the clinical trials
5. Patients were allowed to extend the dosing interval after 1 or 2 monthly faricimab injections rather than requiring 4 monthly injections before extending the dosing interval

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Applying Personalized Treatment Strategies to Optimize Outcomes Based on Patient Needs and Preferences

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First-Line Treatment Options in Wet AMD: Optimizing Treatment Outcomes Within the Current System

Approved and off-label anti-VEGF treatment options

- Bevacizumab (off-label)
- Ranibizumab
- Aflibercept 2 mg
- Ranibizumab-eqrn (biosimilar)
- Ranibizumab-nuna (biosimilar)
- Brolucizumab
- Faricimab
- Aflibercept 8 mg

How do you select the most appropriate first-line therapy out of these options for your patients with wet AMD?

Are there any constraints put on physicians when selecting first-line therapy (eg, do payers require step therapy?)

How does this impact patient care?

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Biosimilars Can Provide a More Affordable Option for Intravitreal Anti-VEGF Therapies[1-3]

What are biosimilars?

- Molecules that are "highly similar" to existing reference biologic products
- Provide comparable physiochemical properties, pharmacokinetics, pharmacodynamics, immunogenicity, safety, efficacy

Current and emerging biosimilars for the treatment of AMD

- Byooviz (ranibizumab-nuna): First ophthalmology biosimilar approved in 2021 for wet AMD, macular edema from VO, myopic CNV
- Cimerli (ranibizumab-eqrn): Second ophthalmology biosimilar approved in 2022 for wet AMD, RVO, DME, DR, and mCNV
- FYB203 (aflibercept 2 mg biosimilar): BLA submitted to the US FDA in June 2023 following trial in patients with nAMD

1. Woo SJ et al. *JAMA Ophthalmol.* 2021;139:68-76. 2. Holtz FG et al. *Ophthalmol.* 2022;129:54-63.
3. https://www.biosimilardevelopment.com/doc/formycon-announces-submission-of-the-biologics-license-u-s-food-and-drug-administration-fda-0001.

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Addressing Treatment Burden With New Patients With AMD

- **It's important to address potential burdens and barriers upfront, before patients become resistant to treatment**
- **Many issues can be solved simply through patient education**

- For financial/insurance/Medicare concerns, it's helpful to have information about available patient resources prepared ahead of time
- It's important to educate patients about the serious consequences of not adhering to their treatment regimen (eg, loss of vision)
- Address potential factors that could lead to treatment nonadherence (eg, needing assistance with transportation)

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Patient-Centered Dosing Strategies for Wet AMD[1,2]

Fixed Dosing vs PRN vs Treat-and-Extend

Fixed Dosing

Advantages
- Consistent treatment
- Predictable outcomes
- Less frequent imaging

Disadvantages
- Nonindividualized
- Overtreatment
- High treatment burden
- Higher cost

PRN

Advantages
- Lower treatment burden
- Cost effective
- More personalized

Disadvantages
- Fluid fluctuations
- Allows for recurrent disease
- Risk of irreversible damage
- Inconsistent response
- Frequent monitoring

Treat-and-Extend

Best of Both
Treat-and-extend combines aspects of both
- Continuous regimen with a "PRN" or variable interval approach that avoids disadvantages of each method

Benefits
Individualized treat-and-extend regimens have been shown to …
- Increase treatment adherence
- Achieve VA gains nearly comparable to clinical trials

Individualized treatment approaches can also be used with longer-acting treatment options (eg, aflibercept 8 mg, faricimab) to further reduce treatment burden and optimize vision outcomes

1. Volkmann I et al. *BMC Ophthalmol.* 2020;20:122. 2. Gallardo M et al. *Ophthalmol Retina.* 2021;5:604-624.

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Patient Cases

Patient 1: Treatment-Naïve Wet AMD[1]

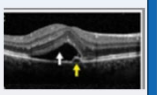
Patient History

- 78-year-old woman with wet AMD, OS
- Diagnosed in November 2022
- Medical history includes hypertension, severe osteoarthritis limits her mobility

Fluorescein angiography shows neovascular membranes that appear as hyperfluorescent lesions in the retina (arrow)

Baseline Ocular Features

- Baseline BCVA: 20/100
- Baseline CST: 375 mcm
- Patient also had SRF and PED



SD-OCT shows subretinal fluid (white arrow), and a small adjacent pigment epithelial detachment (yellow arrow)

1. Images from Yonekawa Y et al. *J Clin Med*. 2015;4:343-359.

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Patient 1: Patient-Centered Treatment Planning

Patient History and Baseline Ocular Features

- 78-year-old woman with newly diagnosed bilateral wet AMD
- Baseline BCVA: 20/100
- Also has significant CST, SRF, and PED

Treatment Planning and Shared Decision-Making With Patient

- Discussed the importance of treating wet AMD early with intravitreal anti-VEGF injections to optimize visual outcomes and explained that outcomes are correlated with number of injections in first year of treatment
- Patient can no longer drive due to her severe osteoarthritis, so she is dependent on her daughter, who drives her to her appointments; patient lives 60 miles away, and the drive takes approximately 90 minutes each way
- She understands the need for treatment, and is willing to give it a try, but she is worried that monthly clinic appointments for injections will be too burdensome for her and her daughter, who works full-time, to participate in long term

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Audience Polling Question

What would you recommend for this patient's initial treatment?

1. I'm not sure
2. First-generation anti-VEGF treatment (eg, ranibizumab, aflibercept, bevacizumab)
3. Anti-VEGF biosimilar
4. Brolucizumab
5. Aflibercept 8 mg
6. Faricimab
7. Something else

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Patient 1 Case Discussion: What Treatment Approach Would You Recommend?

- Patient would be a good candidate for a treatment option with an extended dosing interval (eg, aflibercept 8 mg or faricimab)
  - After 3-4 monthly treatments, she may be able to extend the dosing interval more quickly with these agents, since they can be extended by up to 4 weeks at every visit once the disease has been controlled
  - Is there any evidence at this time to support the selection of one over the other for this patient?
    - 96-week PULSAR outcomes showed that a significant proportion of patients taking aflibercept 8 mg can extend intervals out to 24 weeks
- What if her insurance mandates step therapy (eg, requiring use of bevacizumab in first line)? How would your treatment plan change?
- What if she has bilateral wet AMD? Would that change your treatment approach?
- Any other issues to address with this patient case?

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Patient 2: Persistent Wet AMD on Ranibizumab[1]

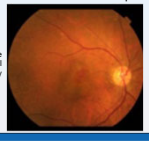
Patient History

- 66-year-old man with wet AMD, OD
- Persistent fluid and inadequate BCVA despite 2 years of ranibizumab injections, although he has missed several appointments over the time period

Current Ocular Features

- BCVA: 20/80
- CST: 350 mcm
- Patient also has SRF and PED

Fundus photograph reveals the presence of polypoidal choroidal vasculopathy



SD-OCT shows slight SRF and prominent subfoveal PED

1. Images from Hirakata T et al. *Clin Ophthalmology*. 2016;10:969-977.

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Patient 2: Patient-Centered Treatment Planning

Patient History and Current Ocular Features

- 66-year-old man with wet AMD who was diagnosed 2 years ago and has been receiving ranibizumab injections, but disease persists
- BCVA: 20/80
- Also has significant CST, SRF, and PED

Treatment Planning and Shared Decision-Making With Patient

- Reviewed patient's treatment history, noting that he missed 7 appointments over past 2 years, and explained that it is important to come in for all scheduled visits to ensure that we are keeping the disease under control, since fluctuating fluid can cause cumulative damage
- Patient shared that he has struggled to remain adherent to treatment because the frequent intravitreal injections are very unpleasant and stressful to deal with
- He was frustrated to hear that his eye was not responding to the treatment, and said he didn't think it was worth it to continue getting the shots, so he was considering quitting treatment altogether

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Audience Polling Question

What would you recommend this patient do next?

1. I'm not sure
2. Discontinue treatment
3. Maintain current ranibizumab treatment and dosing interval
4. Reduce ranibizumab dosing interval
5. Switch to a ranibizumab biosimilar
6. Switch to aflibercept 2 mg
7. Switch to aflibercept 8 mg
8. Switch to faricimab
9. Something else

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Patient 2 Case Discussion: What Treatment Approach Would You Recommend?

- Patient would be a good candidate to switch to a treatment option with an extended dosing interval (eg, aflibercept 8 mg or faricimab)
  - Although he wants to quit treatment, that would be a bad idea because it would greatly increase his risk for losing sight in that eye; he is still relatively young and may have many more years ahead of him, so maintaining good visual acuity should be a top priority
  - Since he is having difficulty remaining adherent to treatment because of anxiety related to the shots, reducing the overall number of shots that he needs to undergo would improve his QOL
- What other issues should be addressed for this case?

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Summary

- Wet AMD is a major cause of visual impairment and blindness with increasing prevalence as the population ages
- Anti-VEGF treatments have been a game-changer for patients with wet AMD for over 15 years
- More durable and longer-acting treatments that reduce injection frequency and treatment burden are now available
- Treatment needs to be individualized to address patients' needs and preferences

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Audience Q&A

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Please remember to complete and submit your Post-Test and Evaluation for CE credit.

PeerView.com/AMD-Survey-BPZ

Thank you, and have a good day.

PeerView Live

Scan to access the post-test and evaluation

Abbreviations

2Q8: 2 mg every 8 weeks
8Q12: 8 mg every 12 weeks
8Q16: 8 mg every 16 weeks
AAO: American Academy of Ophthalmology
AMD: age-related macular degeneration
ANG2: angiopoetin-2
Anti-VEGF: anti–vascular endothelial growth factor
APTC: Anti-Platelet Trialists' Collaboration
BCVA: best corrected visual acuity
BL: baseline
CNV: choroidal neovascularization
COVID: coronavirus disease
CPT: center point retinal thickness
CRT: central retinal thickness
CST: central subfield thickness
DME: diabetic macular edema
DR: diabetic retinopathy
EHR: electronic health record
ETDRS: Early Treatment Diabetic Retinopathy Study
EURETINA: European Society of Retina Specialists
FAS: full analysis set
ICE: intercurrent event
IgGI: immunoglobin GI
IOI: intraocular inflammation
IOP: intraocular pressure
IRF: intraretinal fluid
IRIS: Intelligent Research in Sight
IVT: intravitreal anti–vascular endothelial growth factor therapy
LS: least squares
MEfRVO: macular edema following retinal vein occlusion
MMRM: mixed model for repeated measures
nAMD: neovascular age-related macular degeneration
OCT: optical coherence tomography
PTI: personalized treatment intervals
Q8W: every 8 weeks
Q12W: every 12 weeks
Q16W: every 16 weeks
ROP: retinopathy of prematurity
RVO: retinal vein occlusion
SAE: serious adverse event
SAF: safety analysis set
TEAE: treatment-emergent adverse event
SRF: subretinal fluid
VA: visual acuity
VEGF-A: vascular endothelial growth factor A
VEGFR1: vascular endothelial growth factor receptor 1