Real-World Use of Aflibercept 8 mg in Eyes With Neovascular Age-Related Macular Degeneration (nAMD): Analysis of the IRIS® Registry (Illumin-8)

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Disclosures

- Dr Nguyen is a Scientific Advisory Board member for Genentech, Kriya, Osanni, and Regeneron Pharmaceuticals, Inc.
- Dr Leng has received funding from Astellas and served as a consultant for Astellas, Boehringer Ingelheim, Regeneron Pharmaceuticals, Inc., Roche/Genentech, Topcon, and Virtual Field
- Dr Sambhara is a consultant/advisor for 4DMT, AbbVie, Alcon, Adverum Biotechnologies, Alkeus, Annexon, ANI Pharmaceuticals, Apellis Pharmaceuticals, Astellas Pharma Inc, Coherus Biosciences, EyePoint Pharmaceuticals, Genentech, iDocSocial, Ocular Therapeutix, Opthea, Regeneron Pharmaceuticals, Inc., and Topcon; has received research funding from 4DMT, Adverum Biotechnologies, Annexon, Kodiak Biosciences, and Ocular Therapeutix; has served on steering committees for 4DMT, Ocular Therapeutix, and Regeneron Pharmaceuticals, Inc.; has received speaker fees from Apellis Pharmaceuticals, Astellas Pharma Inc, Heidelberg Engineering, and Regeneron Pharmaceuticals, Inc.; has received lecture fees from Evolve Medical, iDocSocial, MHJ Life Sciences, and Vindico Medical Education; and holds stock in Eclipse Life Sciences
- Dr Ferrone was a former part-time employee of Apellis; has acted as Principal Investigator or Sub-investigator with research grant support for 4DMT, Alexion, Alkeus, Apellis, Aviceda, Belite, Boehringer Ingelheim, Cognition, EyeBio, EyePoint, Genentech, Janssen, Ophthea, Outlook, Regeneron Pharmaceuticals, Inc., RegenXBio, and Resolute; and received honorarium for acting as consultant for 4DMT, AbbVie/Allergan, Alcon, Alkeus, Annexon, Apellis, Aviceda, Genentech, Neurotech, Ophthea, Regeneron Pharmaceuticals, Inc., and Zeiss; honorarium for Speaker fees from Regeneron Pharmaceuticals, Inc.; and travel grants from Alkeus and Regeneron Pharmaceuticals, Inc.
- Dr Do is a consultant to Boehringer Ingelheim, Genentech, Kodiak Sciences, Kriya, and Regeneron Pharmaceuticals, Inc.; has received research funding from Boehringer Ingelheim, Genentech, Kriya, and Regeneron Pharmaceuticals, Inc.; and has stock options from Kodiak Sciences
- Dana J. Murdock, Keran Moll, Eilish McCann, and Steven Sherman are employees of and hold stock/stock options in Regeneron Pharmaceuticals, Inc.
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Illumin-8

Background and Objective

- In the PULSAR trial, aflibercept 8 mg achieved similar BCVA outcomes to aflibercept 2 mg, with fewer injections in patients with nAMD through 96 weeks[1]
- Real-world evidence describing the use of aflibercept 8 mg in treatment-naive and previously treated patients with nAMD could inform clinical practice

Illumin-8 aims to describe real-world outcomes[a] in patients with nAMD from the AAO IRIS® Registry[2] who were:

- **Treatment-naive and initiated aflibercept 8 mg**
- **Previously treated with aflibercept 2 mg and switched to aflibercept 8 mg**

[a]Safety parameters were not assessed in this analysis.
nAMD, neovascular age-related macular degeneration; BCVA, best-corrected visual acuity.
1. Korobelnik JF et al. *Ophthalmology*. 2026;133:39-50. 2. Lee CS et al. *Ophthalmol Sci*. 2022;2:100112.

Case Presentation

(managed by Diana V. Do, MD and Quan Dong Nguyen, MD, MSc)

68-year-old woman with blurry vision and nAMD in the left eye after multiple anti-VEGF injections

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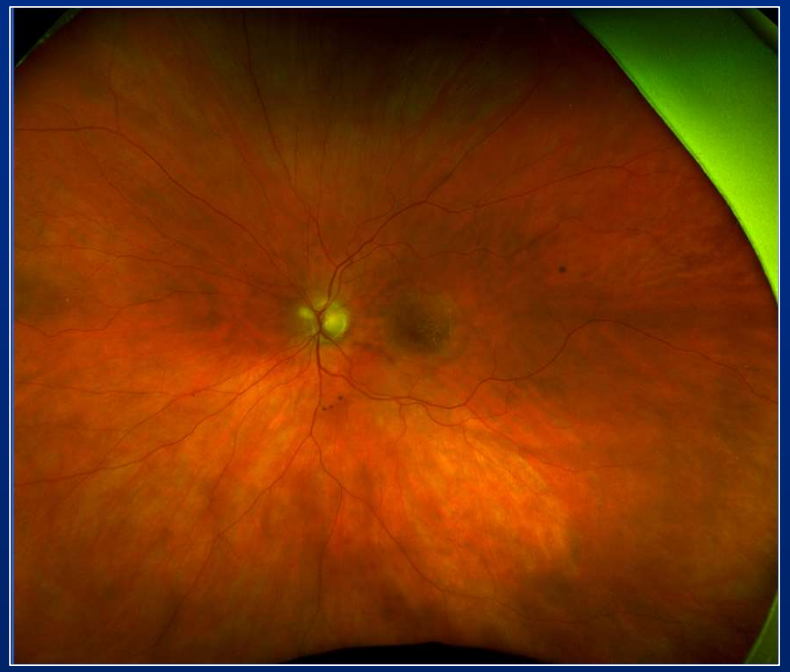

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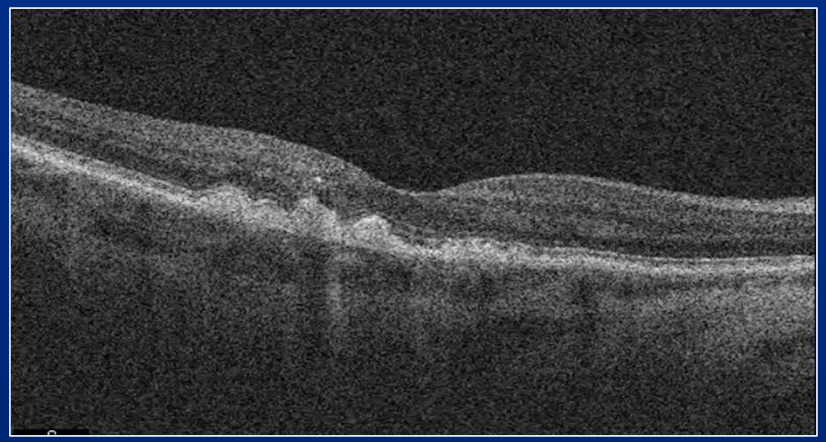
Case Presentation

(managed by Diana V. Do, MD and Quan Dong Nguyen, MD, MSc)

Left eye has received prior aflibercept 2 mg with 4-to-6-week intervals with persistent subretinal fluid. Last treatment was 6 weeks ago



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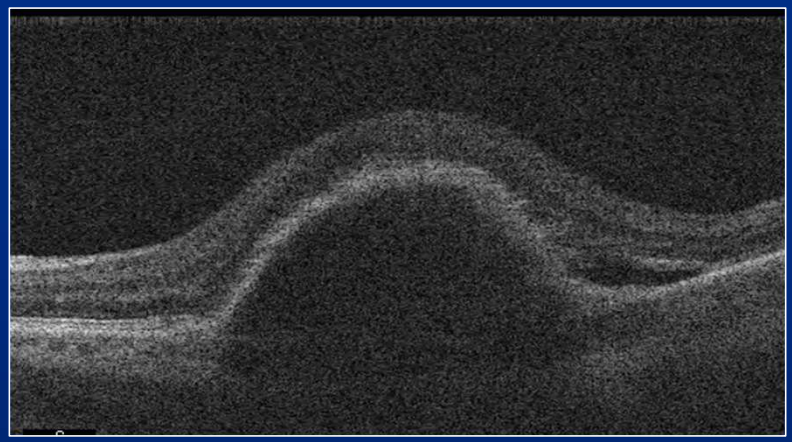

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What would you recommend?
Shorten interval?
Change anti-VEGF?

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Study Design

Eligibility criteria

- Aged ≥50 years with nAMD on the index date[a,b]
- Initiated aflibercept 8 mg during the indexing period,[c] and no other anti-VEGF or other treatments[d] on the index date
- Received ≥1 aflibercept 8 mg injection(s) after the initial dosing phase,[e] with the last injection >12 months post-index date
- No diagnosis of DME or RVO during the baseline period[f] or on the index date

Eyes from the IRIS Registry initiating aflibercept 8 mg during the indexing period[c]

nAMD n=70,508

- **Treatment-naive[g]** → **nAMD n=1976**
- **Switched from aflibercept 2 mg to 8 mg[h]** → **nAMD n=9965**

Outcomes

Injection intervals	Change in VA
Treatment-naive: Last assigned injection interval	**Treatment-naive and switchers:** Change in VA from treatment initiation to last observed aflibercept 8 mg injection[j]
Switchers: Change in the last recorded injection intervals from pre-[f] to post-switch[i]	

[a]For patients with both eyes treated on the index date and eligible for inclusion, 1 eye was randomly selected. [b]Index date: date of the first aflibercept 8 mg injection. [c]Indexing period: August 18, 2023, to December 31, 2024. [d]Other treatments included intravitreal steroids and laser therapy. [e]First 3 injections or 90 days, whichever occurred first. [f]≥12 months prior to the index date. [g]Eyes that did not receive treatment with anti-VEGF, intravitreal steroid, or laser therapy during baseline period or on index date. [h]Eyes switched within 16 weeks prior to the index date with a last pre-switch injection interval ≥6 weeks. [i]Eyes were stratified by mean injection interval before switching (6 to ≤8, >8 to ≤10, >10 to ≤12, >12 to ≤16, and >16 weeks). [j]Assessed in eyes with VA available at the index date and at the last injection, stratified by VA ≤65 ETDRS letters or >65 ETDRS letters at the index date.

DME, diabetic macular edema; ETDRS, Early Treatment Diabetic Retinopathy Study; RVO, retinal vein occlusion; VA, visual acuity; VEGF, vascular endothelial growth factor.

Patient Demographics and Clinical Characteristics at Index Date

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	Treatment-naive (n=1976)	Switchers (n=9965)
Age, years, mean (SD)	80.5 (6.6)	80.8 (6.8)
Male, n (%)	673 (34.1)	3771 (37.8)
Race/Ethnicity, n (%)[a]		
White	1455 (87.5)	7464 (85.5)
Black or African American	19 (1.1)	93 (1.1)
Other[b]	166 (10.0)	1030 (11.8)
Hispanic or Latino	23 (1.4)	138 (1.6)
Bilateral nAMD, n (%)	590 (29.9)	4864 (48.8)
Functional VA category on index date, n (%)		
≤65 ETDRS letters	1153 (58.4)	4676 (46.9)
>65 ETDRS letters	813 (41.1)	5256 (52.7)

[a]Patients with missing values were excluded when calculating percentages. [b]Other includes Asian, Pacific Islander, or Other.
SD, standard deviation.

Follow-Up Information and Treatment Patterns with Aflibercept 8 mg

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	Treatment-naive (n=1976)	Switchers (n=9965)
Post-index follow-up, days, median (Q1, Q3)	519 (438, 603)	548 (470, 645)
Eyes that received ≥3 aflibercept 8 mg injections during the initial dosing phase,[a,b] n (%)	1393 (70.5)	1355 (13.6)
Number of aflibercept 8 mg injections during the initial dosing phase,[a,b] mean (SD)	2.6 (0.6)	1.9 (0.6)
Number of aflibercept 8 mg injections during the follow-up period,[a] mean (SD)	8.6 (2.3)	8.3 (2.4)

[a]Including the index date. Index date was the date of the first aflibercept 8 mg injection. [b]Initial dosing phase was defined as the first 3 injections or 90 days, whichever occurred first.
Q, quartile.

Treatment-Naive nAMD: Injection Interval and Change in VA at >12 Months with Aflibercept 8 mg

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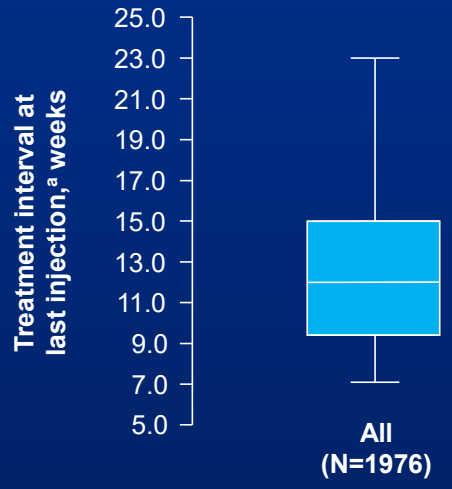
- The last observed injection interval after initiating aflibercept 8 mg was 12.0 weeks
- VA at index date was maintained during follow-up

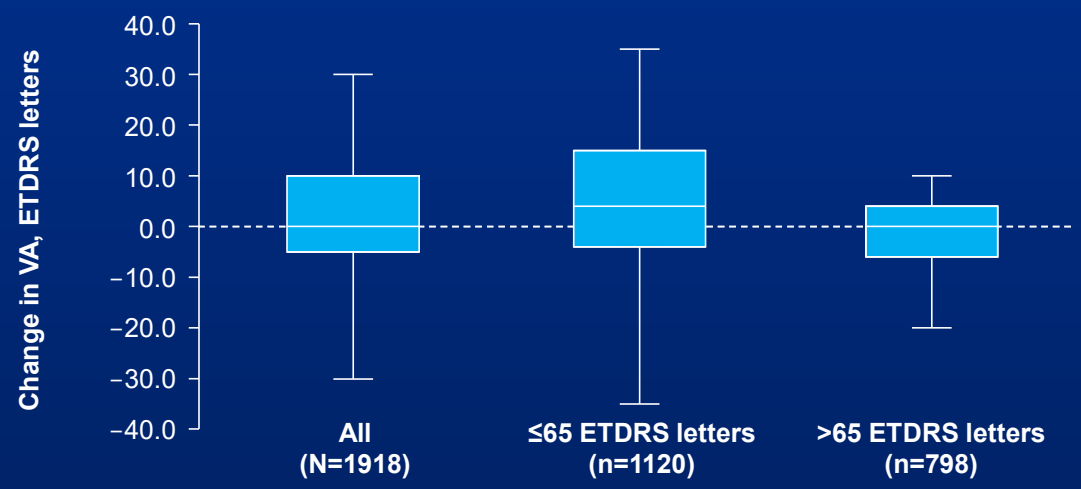
Last Injection Interval

	All (N=1976)
Median (Q1, Q3)	12.0 (9.4, 15.0)
Mean (SD)	13.7 (8.5)



Change in VA in the Overall Cohort and by Baseline VA Subgroups[b]

	All (N=1918)	≤65 ETDRS letters (n=1120)	>65 ETDRS letters (n=798)
Median (Q1, Q3)	0 (−5, 10)	4 (−4, 15)	0 (−6, 4)
Mean (SD)	1.3 (18.1)	4.4 (21.0)	−2.9 (11.7)



Boxes show median (middle line) and Q1 and Q3 (upper and lower bounds); whiskers show the 5% and 95% percentiles.
[a]>12 months post-index date. [b]From the index date to last injection.

Switching From Aflibercept 2 mg to 8 mg: Injection Interval and Change in VA at >12 Months

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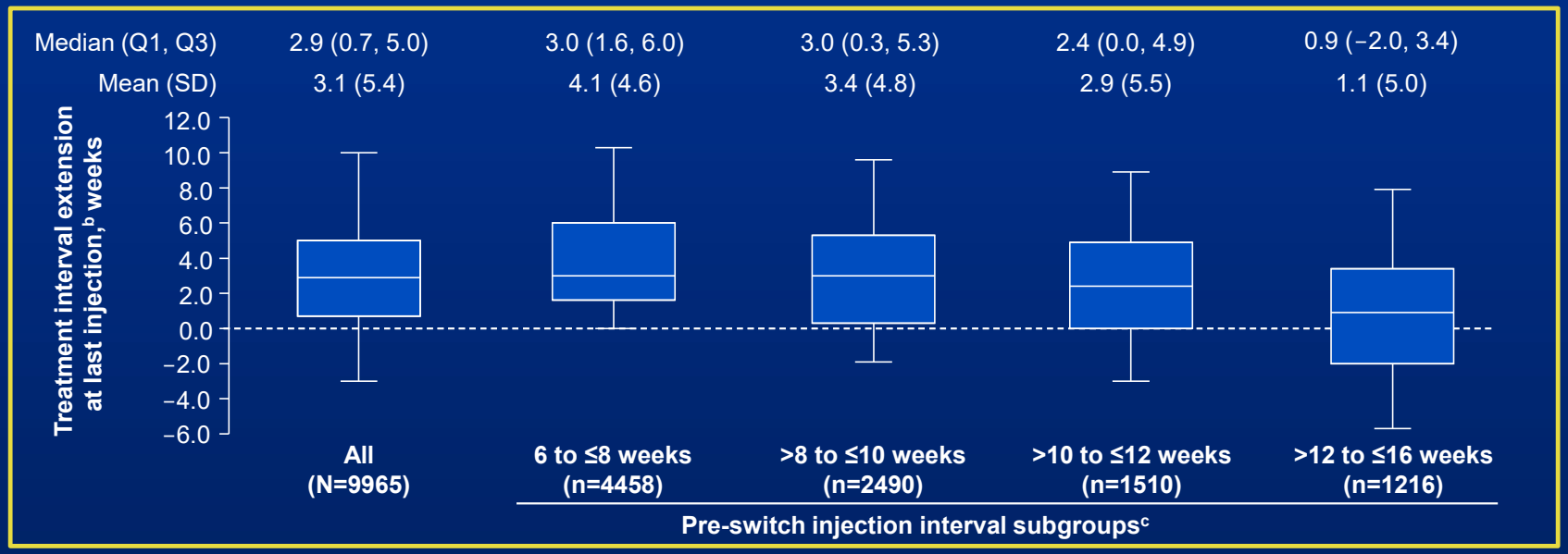
- **Median duration of the last treatment interval in eyes switched from aflibercept 2 mg to 8 mg was 12.0 weeks**
- **The finding represents an extension of 2.9 weeks versus the last pre-switch interval**
- **VA was maintained during follow-up[a]**

Change in Injection Interval in the Overall Cohort and by Pre-Switch Injection Interval Subgroups



Boxes show median (middle line) and Q1 and Q3 (upper and lower bounds); whiskers show the 5% and 95% percentiles.
[a]The median (Q1, Q3) change in VA from the index date to last injection was 0 (–6, 4) letters in the overall cohort of eyes switched to aflibercept 8 mg from 2 mg, and 0 (–7, 5) and 0 (–6, 0) letters in VA subgroups with ≤65 and >65 ETDRS letters, respectively. [b]>12 months post-index date. [c]The number of eyes in each subgroup do not add up to the number of all eyes, because 291 patients had a pre-switch interval of >16 weeks. This subgroup is not shown on the figure.

Limitations

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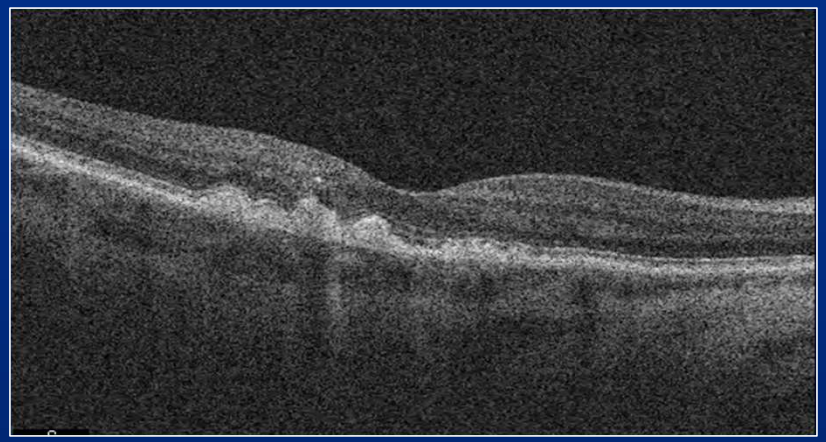
- Electronic medical records were used (not claims data), which may not reflect complete medical history
- Analysis represents early real-world experience with aflibercept 8 mg
- VA data reported were not always BCVA
- Analysis only included eyes with at least 12 months of aflibercept 8 mg treatment

Case Presentation

(managed by Diana V. Do, MD and Quan Dong Nguyen, MD, MSc)

Left eye has received prior aflibercept 2 mg with 4-to-6-week intervals with persistent subretinal fluid. Last treatment was 6 weeks ago



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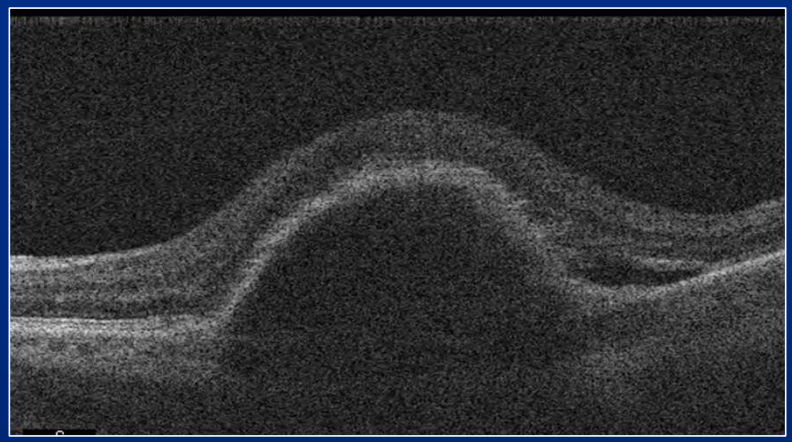

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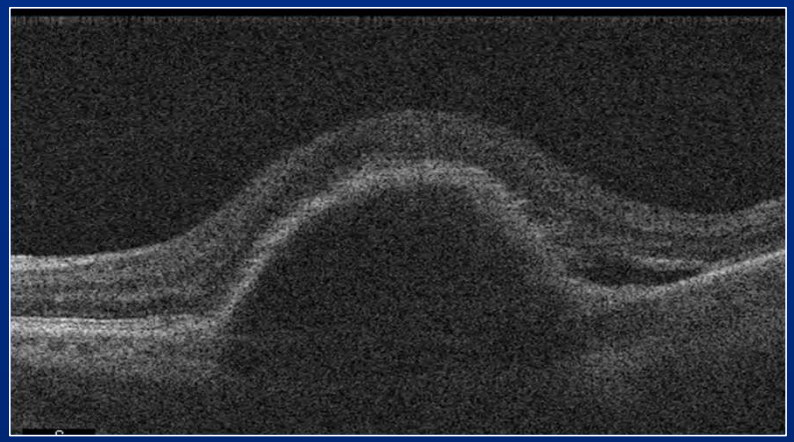
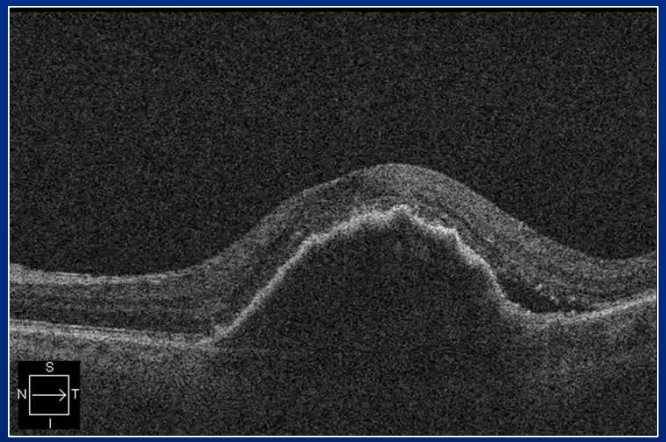
What would you recommend?
Shorten interval?
Change anti-VEGF?

Case Presentation

(managed by Diana V. Do, MD and Quan Dong Nguyen, MD, MSc)



Aflibercept 2 mg
Shortened interval
4 weeks



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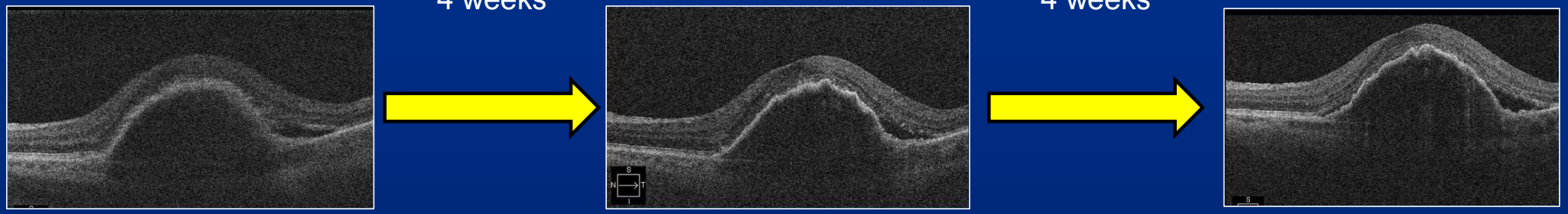
What would you recommend?
Should we stay on every 4-week aflibercept 2 mg?

Case Presentation

(managed by Diana V. Do, MD and Quan Dong Nguyen, MD, MSc)

Continued Aflibercept 2 mg but shortened interval to 4 weeks



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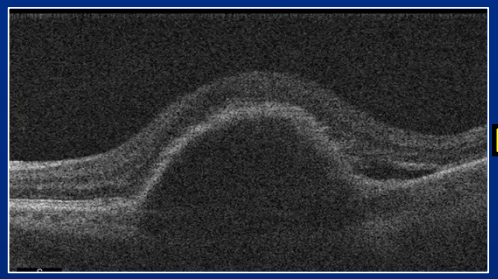
What would you recommend?
Switch anti-VEGF?

Case Presentation

(managed by Diana V. Do, MD and Quan Dong Nguyen, MD, MSc)

Switched to Aflibercept 8 mg and patient returned 8 weeks later

Aflibercept 2 mg
4 weeks



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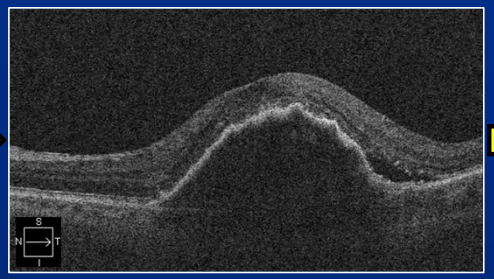
Aflibercept 2 mg
4 weeks



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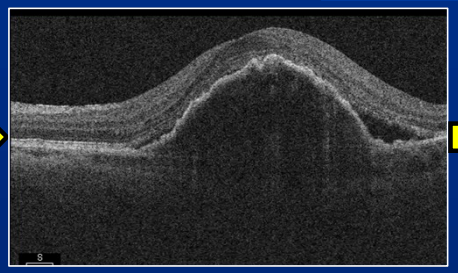
Aflibercept 8 mg
8 weeks



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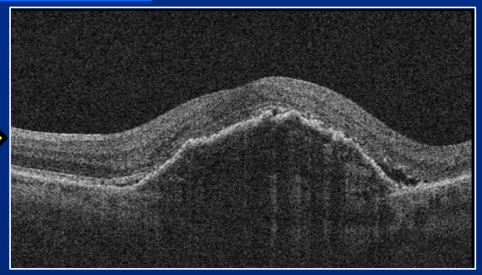

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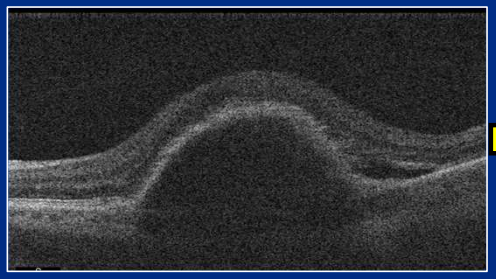
Less fluid,
Longer interval with
aflibercept 8 mg

Case Presentation

(managed by Diana V. Do, MD and Quan Dong Nguyen, MD, MSc)

Aflibercept 2 mg
4 weeks



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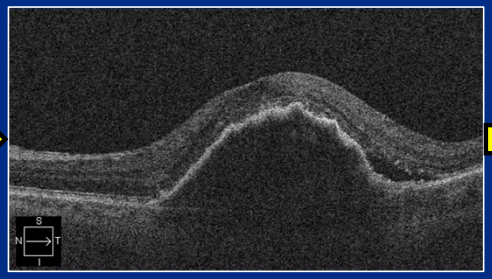
Aflibercept 2 mg
4 weeks



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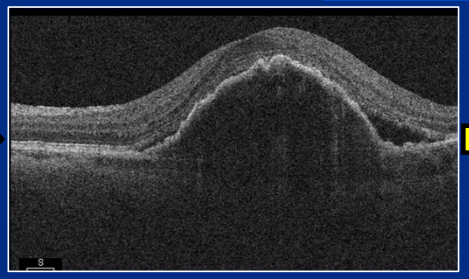

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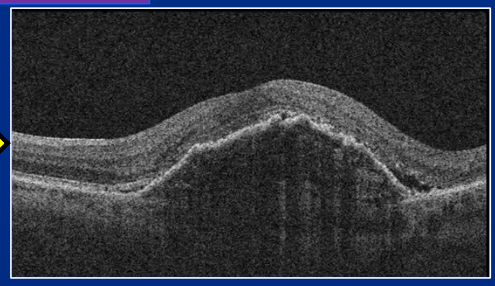
Aflibercept 8 mg
8 weeks



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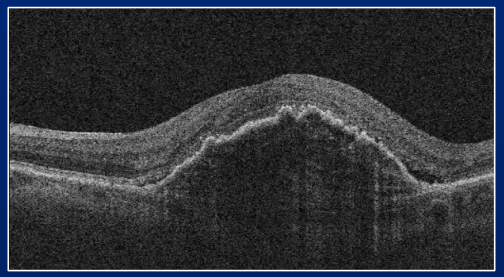
Aflibercept 8 mg
8 weeks



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- **Less fluid after switching to aflibercept 8 mg**
- **Longer interval with aflibercept 8 mg**
- **Would you extend the next visit to 10 weeks or longer?**

Conclusions

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- In treatment-naive and previously treated eyes, the median last observed injection interval beyond 1 year was 12.0 weeks, with VA maintained overall
  - In previously treated eyes, switching to aflibercept 8 mg from 2 mg resulted in an extension of 2.9 weeks in the injection interval compared with the last pre-switch treatment interval
  - Treatment-naive eyes with low baseline VA (≤65 ETDRS letters) showed the greatest visual improvement