Real-World Use of Aflibercept 8 mg in Eyes With nAMD or DME: Analysis of the American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight)

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ELARA Study Update

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Disclosures

- Diana V 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. Keran Moll, Dana Murdock, Eilish McCann, and Steven Sherman are employees and stockholders of Regeneron Pharmaceuticals, Inc.
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Background and Objectives

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- In the PULSAR and PHOTON trials, aflibercept 8 mg achieved similar BCVA outcomes to aflibercept 2 mg with fewer injections in patients with nAMD or DME, respectively, through 96 weeks[1–4]
- Real-world evidence describing the use of aflibercept 8 mg in treatment-naive and previously treated patients with nAMD or DME could be informative for clinical practice

This analysis (Illumin-8 study) aimed to describe real-world outcomes in patients with nAMD or DME in the American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight) database who received initial aflibercept 8 mg treatment or were previously treated with aflibercept 2 mg before switching to aflibercept 8 mg[a]

[a]Safety parameters were not accessed in this analysis.

BCVA, best corrected visual acuity; DME, diabetic macular edema; IRIS, Intelligent Research in Sight; nAMD, neovascular age-related macular degeneration.

1. Lanzetta P et al. *Lancet*. 2024;403:1141–1152. 2. Korobelnik J. Presented at: American Academy of Ophthalmology; November 3–6, 2023; San Francisco, CA. 3. Brown DM et al. *Lancet*. 2024;403:1153–1163. 4. Do D. Presented at: American Academy of Ophthalmology; November 3–6, 2023; San Francisco, CA.

Study Design

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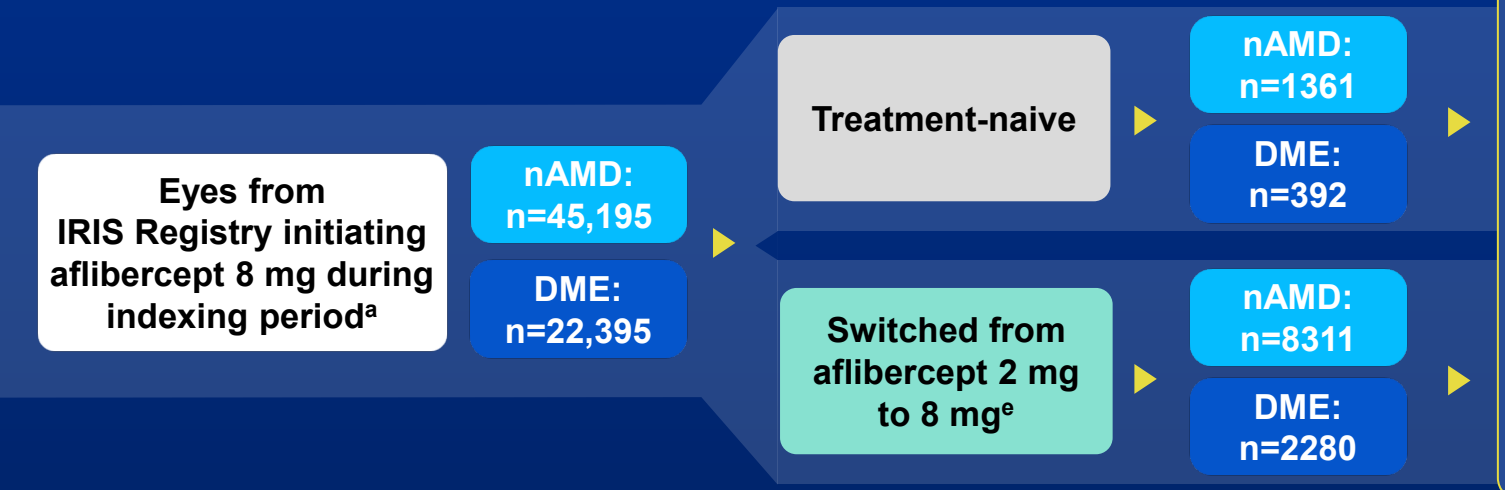
Eligibility criteria

- Aged ≥50 years with nAMD or ≥18 years with DME on index date[a]
- Initiated aflibercept 8 mg during indexing period,[b] and no other anti-VEGF or other treatments[c] on index date
- No diagnosis of DME/DR (for nAMD), nAMD (for DME), or RVO during baseline period[d] or on index date
- For patients with both eyes treated on index date and eligible for inclusion, 1 eye was randomly selected



Outcomes

Injection intervals

Treatment-naive:
Last assigned injection interval
Assessed in eyes receiving ≥1 aflibercept 8 mg injection(s) after initial dosing phase[f] with last injection >6 months post-index

Switchers: Change in last recorded injection intervals from pre-switch[g] to post-switch
Assessed in eyes receiving ≥1 post-initial dosing phase injection with last injection >6 months post-index, stratified by mean injection interval before switching[h]

Change in VA

Treatment-naive and switchers:
Change in VA from treatment initiation to last observed aflibercept 8 mg injection
Assessed in eyes with VA available at index date and >6 months post-index date, stratified by VA ≤20/50 or >20/50[i] at index date

[a]Index date: date of first aflibercept 8 mg injection. [b]Indexing period: August 18, 2023 to June 30, 2024. [c]Other treatments included intravitreal steroids and laser therapy. [d]Baseline period: 12 months prior to index date. [e]Eyes switched ≥16 weeks prior to index date with last pre-switch injection interval ≥6 weeks. [f]First 3 injections or 90 days, whichever occurred first. [g]Pre-switch phase was 12 months prior to index date. [h]Eyes were stratified by mean injection interval before switching (6 to ≤8 weeks, >8 to ≤10, >10 to ≤12, >12 to ≤16, and >16 weeks). [i]Equivalent to ≤65 or >65 ETDRS letters. DR, diabetic retinopathy; ETDRS, Early Treatment Diabetic Retinopathy Study; RVO, retinal vein occlusion; VA, visual acuity; VEGF, vascular endothelial growth factor.

Patient Demographics and Ocular Characteristics at the Index Date[a]

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	Treatment-naive		Switchers	
	nAMD (n=1361)	DME (n=392)	nAMD (n=8311)	DME (n=2280)
Age, mean (SD), years	80.9 (6.8)	68.5 (10.3)	81.3 (6.9)	67.7 (10.3)
Male, n (%)	470 (35)	232 (59)	3177 (38)	1214 (53)
Race and ethnicity, n (%)				
Black or African American	14 (1)	43 (13)	80 (1)	213 (10)
Asian or Pacific Islander	21 (2)	15 (5)	165 (2)	59 (3)
Hispanic or Latino	19 (2)	35 (10)	124 (2)	123 (6)
White	1015 (87)	214 (64)	6423 (87)	1428 (70)
Other	102 (9)	28 (8)	634 (9)	217 (11)
Eyes with VA available, n (%)	1332 (98)	387 (99)	8282 (100)	2275 (100)
VA, mean (SD), ETDRS letters[b]	56.6 (22.7)	63.9 (2.6)	61.6 (3.2)	68.2 (3.4)
Bilateral nAMD[c] or DME[d], n (%)	449 (33)	355 (91)	4071 (49)	2102 (92)
Fellow eye also treated with aflibercept 8 mg on the index date, n (%)	167 (12)	127 (32)	1658 (20)	818 (36)

[a]Index date was date of first aflibercept 8 mg injection. [b]Measured during the 15 days before index date. [c]Patients with nAMD. [d]Patients with DME.

Treatment Exposure During Follow-Up

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	Treatment-naive		Switchers	
	nAMD (n=1361)	DME (n=392)	nAMD (n=8311)	DME (n=2280)
Duration of follow-up, weeks				
Median (Q1, Q3)	57.3 (50.9, 68.1)	56.0 (48.1, 67.1)	59.1 (50.3, 70.1)	57.0 (49.7, 67.1)
Mean (SD)	58.9 (12.8)	56.7 (13.8)	60.0 (13.4)	58.1 (12.7)
Number of aflibercept 8-mg injections during follow-up[a]				
Median (Q1, Q3)	7 (6, 8)	6 (5, 7)	6 (5, 8)	6 (5, 7)
Mean (SD)	7.0 (1.9)	6.1 (2.2)	6.6 (2.0)	6.1 (1.9)
Received ≥3 aflibercept 8 mg injections during initial dosing phase, n (%)[a]	916 (67.3)	392 (48.7)	6737 (81.1)	1744 (76.5)
Number of aflibercept 8-mg injections during initial dosing phase[a]				
Median (Q1, Q3)	3 (2, 3)	2 (2, 3)	2 (2, 2)	2 (2, 2)
Mean (SD)	2.6 (0.6)	2.3 (0.7)	2.2 (0.4)	2.2 (0.4)
Number of aflibercept 8-mg injections after initial dosing phase				
Median (Q1, Q3)	4 (3, 6)	4 (2, 5)	4 (3, 6)	4 (3, 5)
Mean (SD)	4.4 (1.7)	3.8 (1.9)	4.6 (1.8)	4.2 (1.7)

[a]Including the index date. Index date was the date of the first aflibercept 8 mg injection. Q, quartile.

Median Injection Interval and Change in VA >6 Months After Initiating Aflibercept 8 mg: Treatment-Naive

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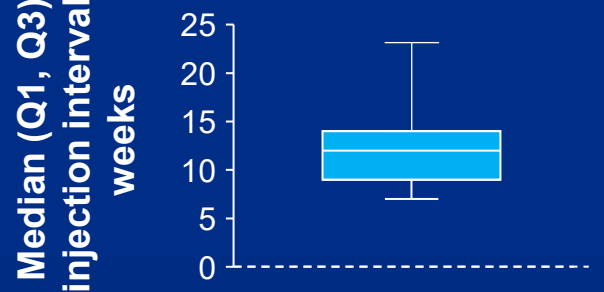
Last injection interval

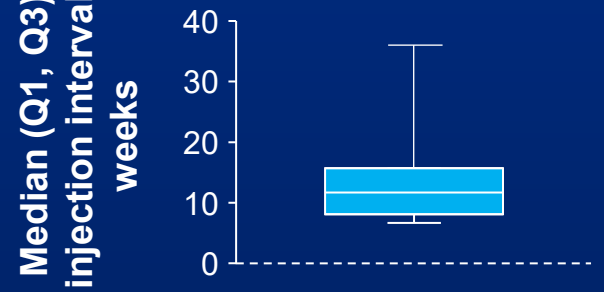
nAMD

Median (Q1, Q3): 12.0 (9.0, 14.0)



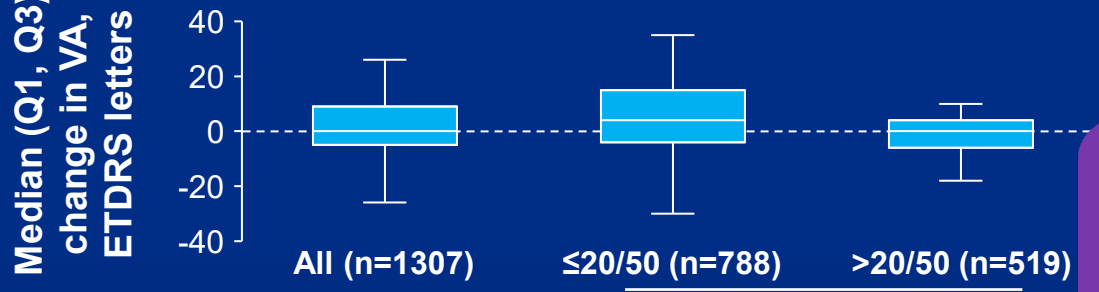
DME

Median (Q1, Q3): 11.7 (8.1, 15.7)



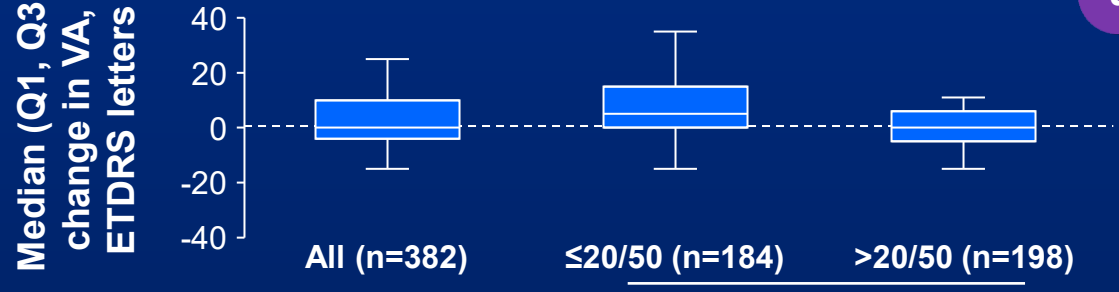
Change in VA from index date to last injection

nAMD



Median (Q1, Q3) VA at the index date, ETDRS letters: 61 (45, 76) | 50 (35, 61) | 76 (70, 80)

DME



Median (Q1, Q3) VA at the index date, ETDRS letters: 70 (58, 76) | 58 (41, 65) | 76 (70, 80)

Injection interval of ~12 weeks in both nAMD and DME

Box plot whiskers indicate medians (middle line), Q1 and Q3 (upper and lower bounds of the boxes) and 5% and 95% percentiles (whiskers). nAMD: mean (SD) injection interval: 12.9 (6.8) weeks. Mean (SD) change in VA: 1.5 (17.7) letters for all eyes, 4.6 (19.9) letters for eyes with VA ≤20/50 at index date, and −3.3 (12.1) letters for those with VA >20/50 at index date. DME: mean (SD) injection interval: 14.3 (10.3) weeks. Mean (SD) change in VA: 2.7 (15.1) letters for all eyes, 6.4 (17.5) letters for eyes with VA ≤20/50 at index date, and −0.8 (11.4) letters for those with VA >20/50 at index date.

Change in Median Injection Interval >6 Months After Initiating Aflibercept 8 mg: Switched to Aflibercept 8 mg From 2 mg

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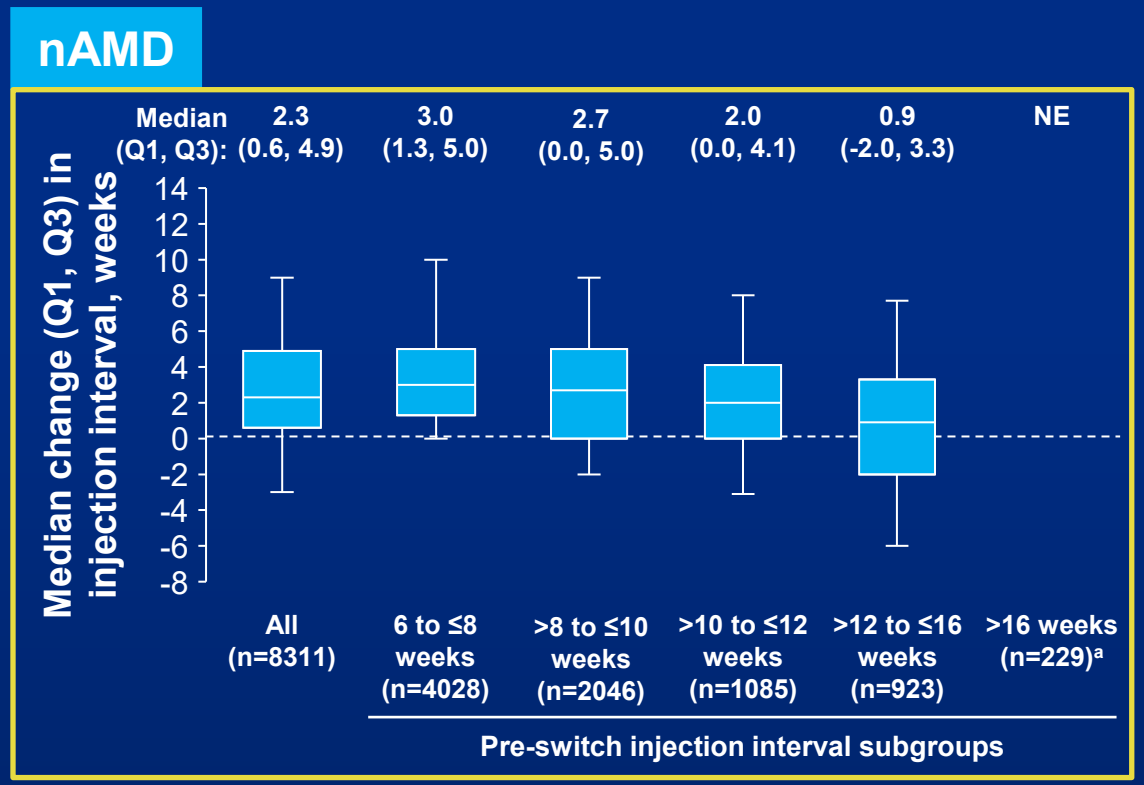
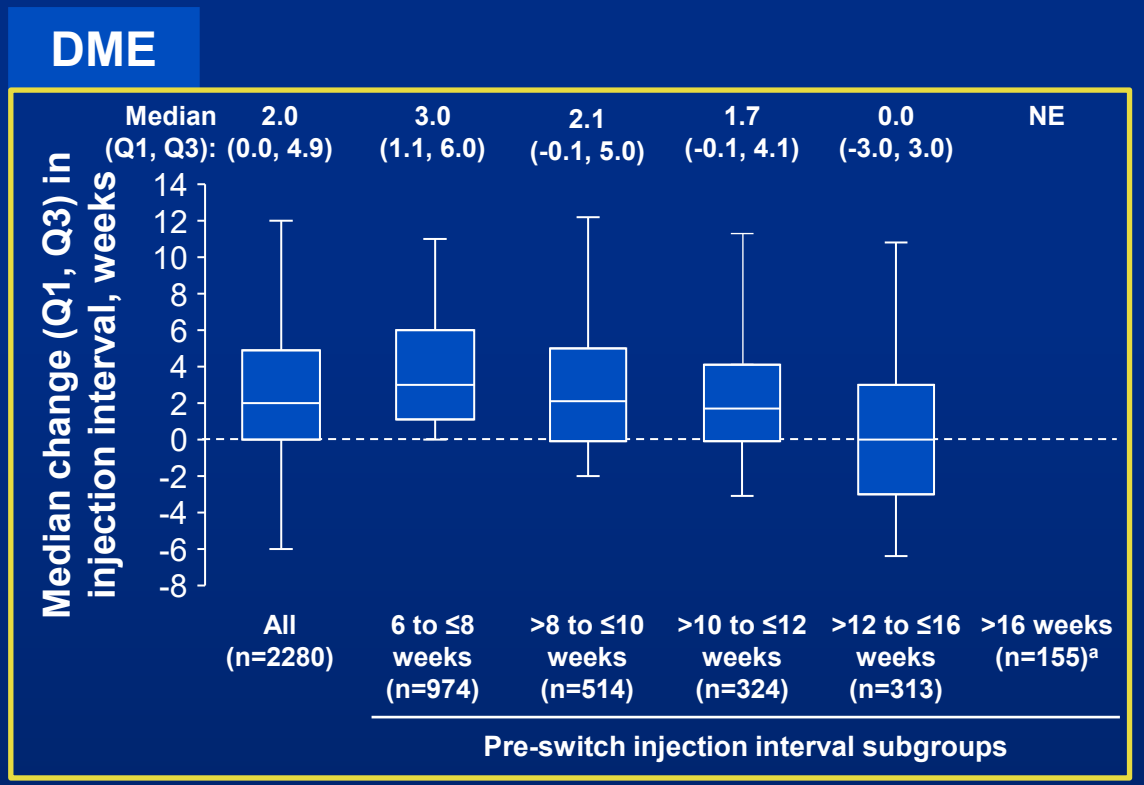
Change in injection interval by pre-switch injection interval subgroups





Injection interval extensions of ~2 weeks were achieved after switching to aflibercept 8 mg while VA was maintained

Box plot whiskers indicate medians (middle line), Q1 and Q3 (upper and lower bounds of the boxes) and 5% and 95% percentiles (whiskers). nAMD: mean (SD) change in injection interval: 2.8 (5.1) weeks (for all eyes). DME: mean (SD) change in injection interval: 2.5 (7.1) weeks (for all eyes). All interval extensions were achieved with no change in VA.

[a]This subgroup was NE. NE, not evaluated.

Limitations

- Electronic medical records used
  - May not reflect complete medical and ocular history
- Analysis represents early real-world experience with aflibercept 8 mg with a limited follow-up period
- Routine clinical VA testing used
  - Not as accurate as best corrected VA used in clinical trials
- Patients switching or discontinuing aflibercept 8 mg treatment prior to 6 months are not reflected in the analysis of treatment-naive patients
- A subset of patients who had ≥2 injections prior to switching to aflibercept 8 mg from other anti-VEGF therapies were included in the analysis, which may not represent the wider population treated with aflibercept 8 mg

Conclusions

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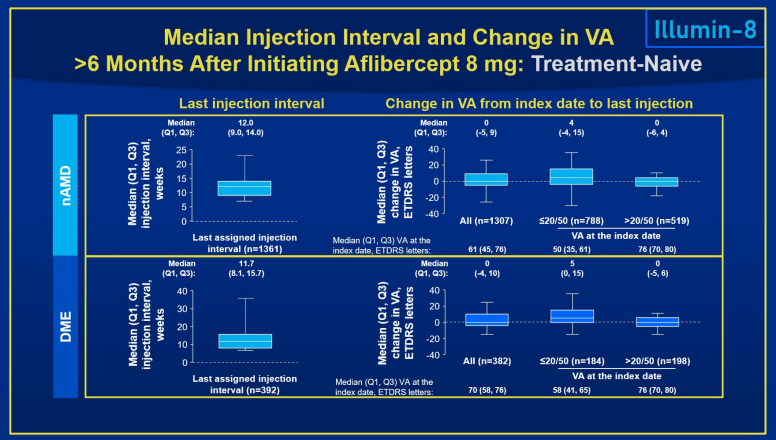
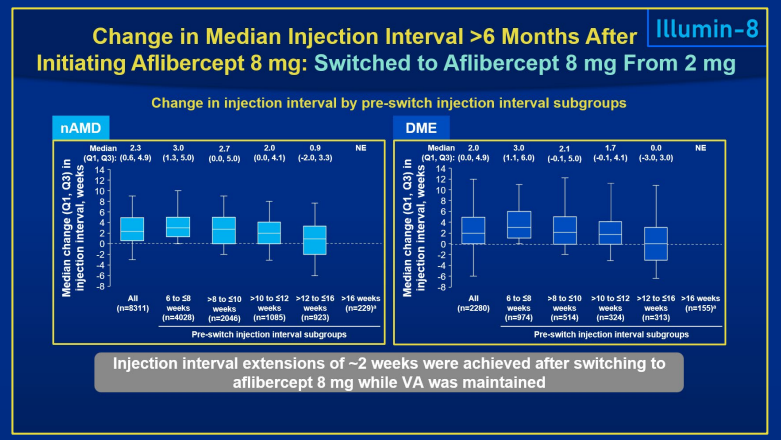




- In this early real-world analysis of the IRIS Registry database, after 6 months, **treatment-naive patients with nAMD or DME achieved injection intervals of 12 weeks, with VA gains among eyes with index VA ≤20/50**
- **Aflibercept 8 mg extended injection intervals for patients with nAMD or DME who switched from aflibercept 2 mg by ~2 weeks with maintained VA**
- Additional analyses with longer follow-up periods are ongoing to assess the long-term effectiveness and durability of aflibercept 8 mg in treatment-naive and previously-treated patients with nAMD or DME in the real world

ELARA Study Design

ELARA is an ongoing, multicenter, single-arm, Phase 3b, 96-week trial evaluating the efficacy and safety of aflibercept 8 mg in previously treated patients with nAMD or DME

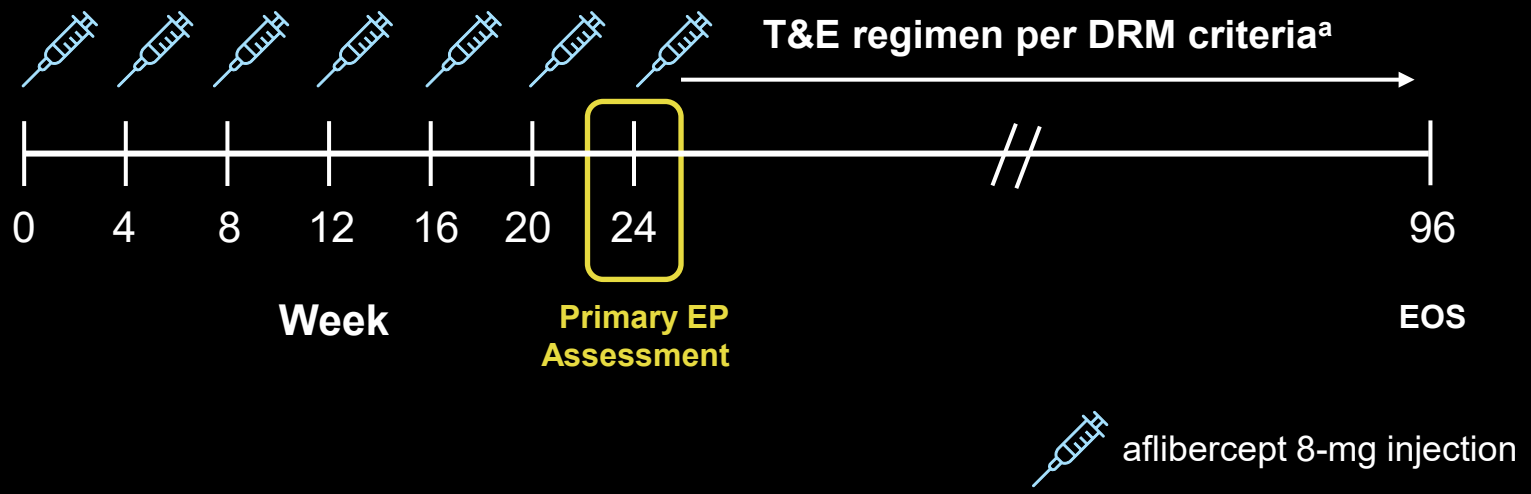
Study eyes (n=417) previously treated with ≥3 intravitreal anti-VEGF injections within 5 months prior to study start in:

nAMD (n=242)

Patients aged ≥50 years with CNV lesions due to nAMD

DME (n=175)

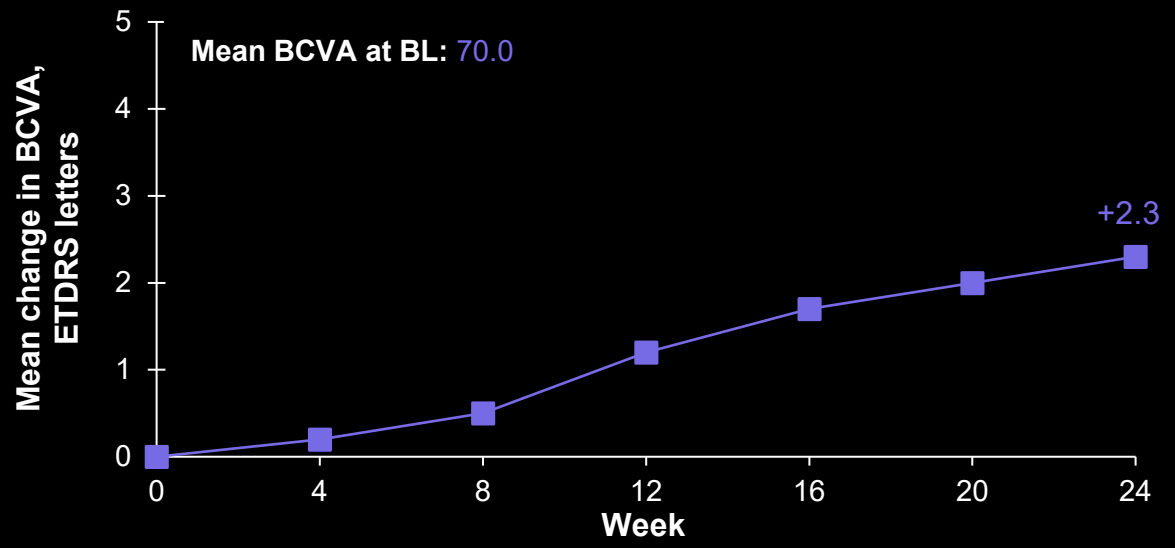
Patients aged ≥18 years with center-involved DME



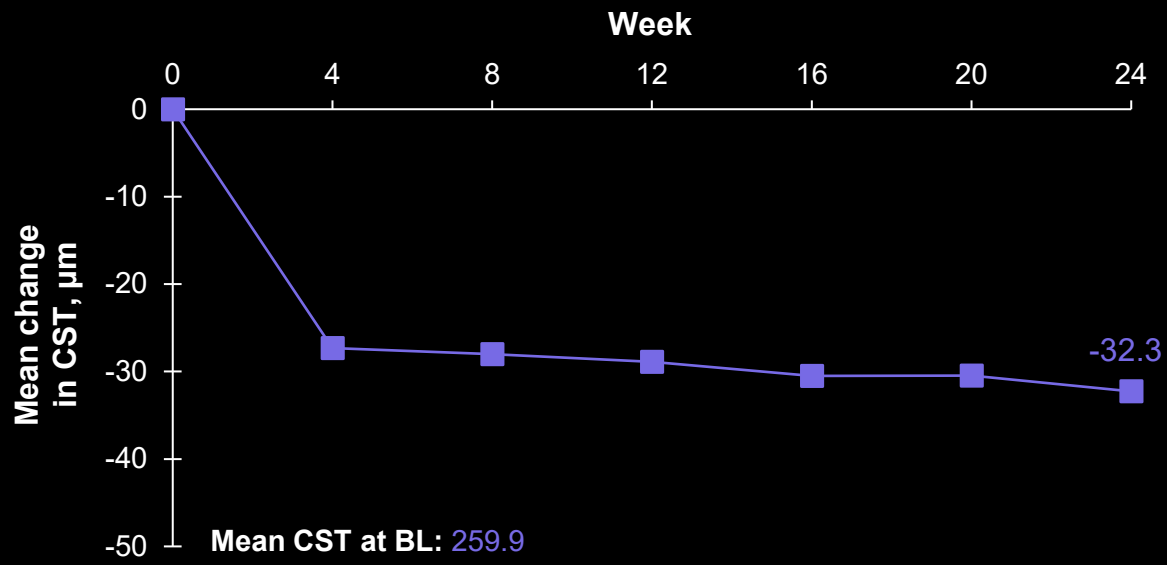
[a]Dosing intervals of patients meeting prespecified DRM criteria were shortened or extended.
CNV, choroidal neovascularization; DME, diabetic macular edema; DRM, dose regimen modification; EOS, end of study; EP, endpoint; nAMD, neovascular age-related macular degeneration; T&E, treat and extend; VEGF, vascular endothelial growth factor.

Preliminary 24-Week Results From ELARA: nAMD cohort

Mean change in BCVA



Mean change in CST

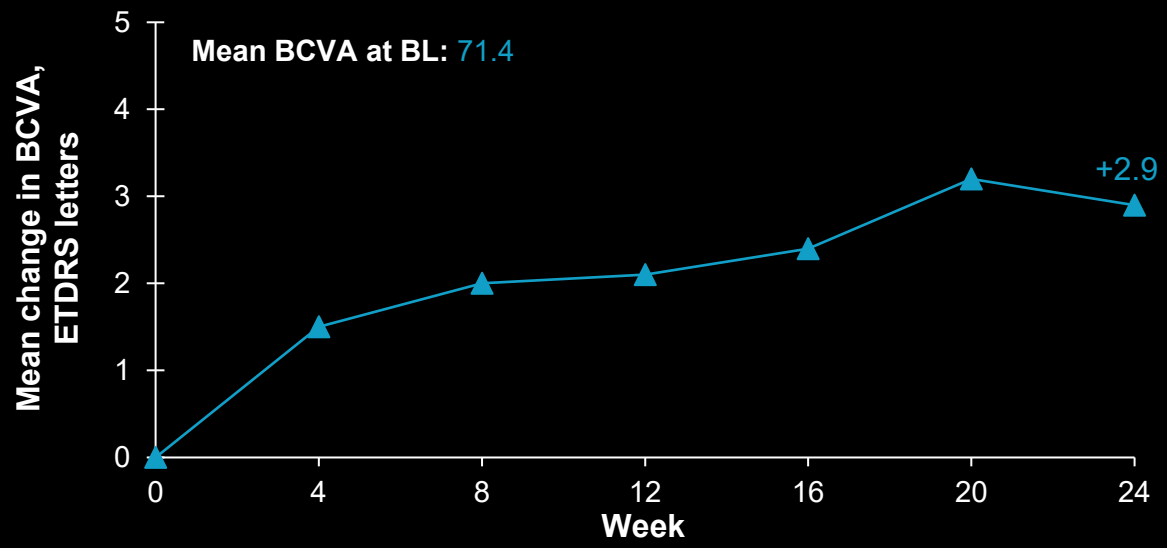


Observed cases.
nAMD: n=242 for mean change in BCVA, n=236 for mean change in CST.
BCVA, best-corrected visual acuity; BL, baseline; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study.

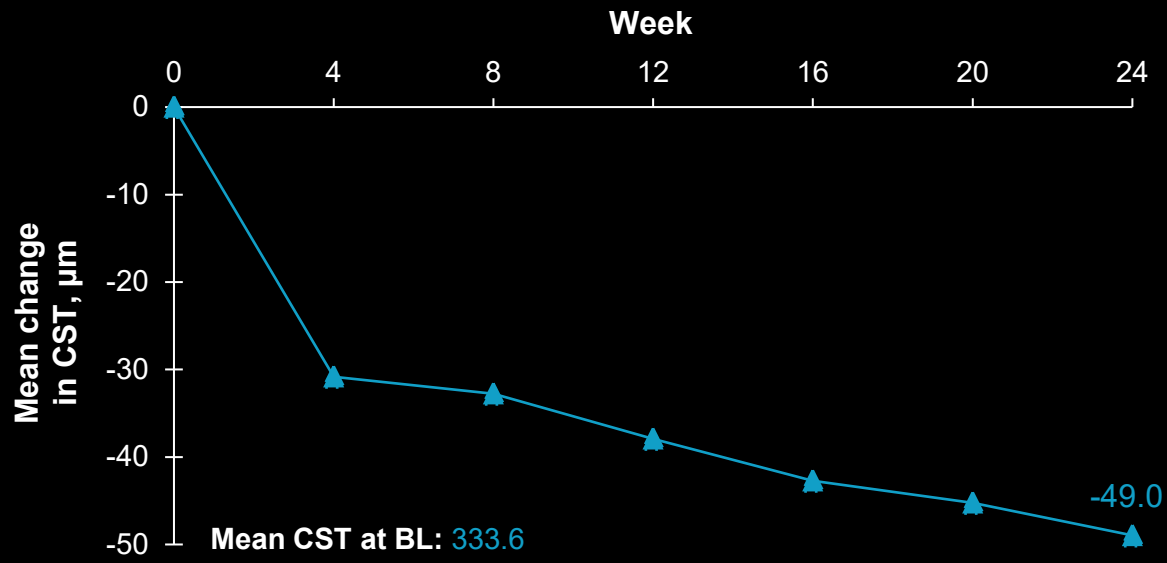
Preliminary 24-Week Results From ELARA: DME cohort

ELARA

Mean change in BCVA



Mean change in CST



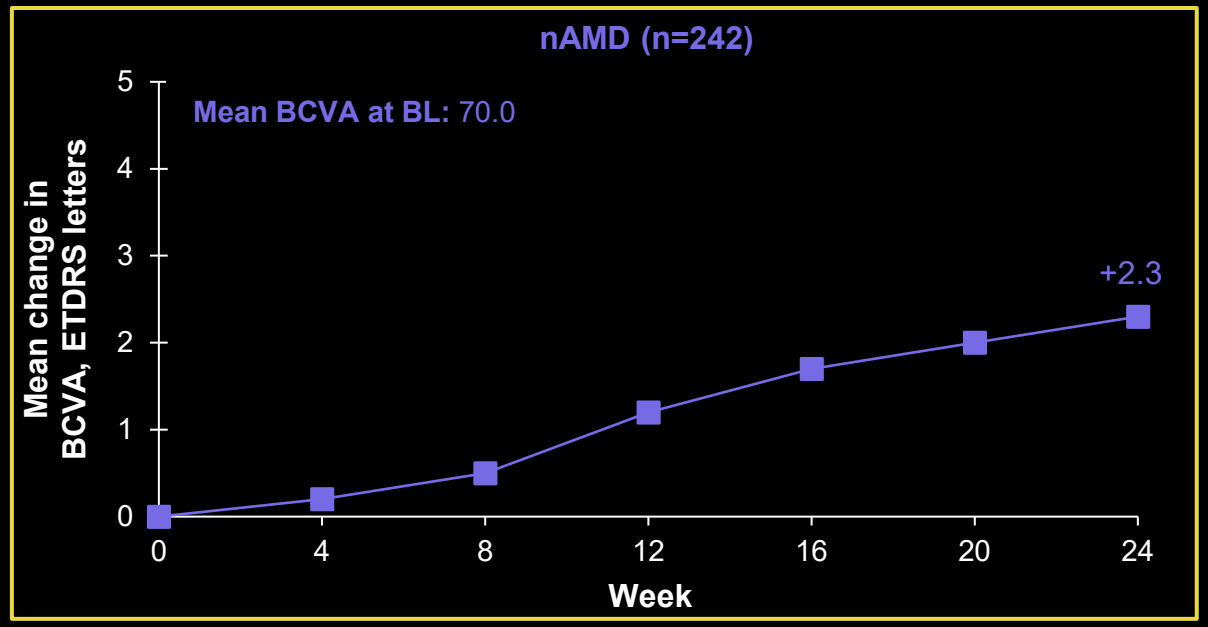
Observed cases.
DME: n=175 for both mean change in BCVA and CST.

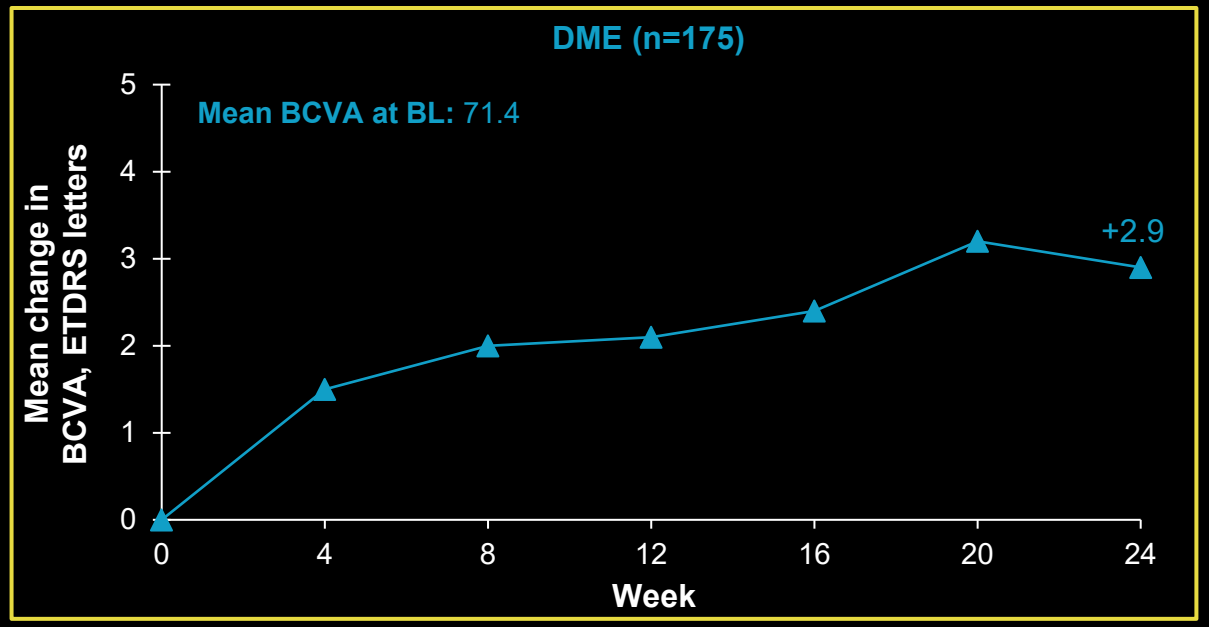
Preliminary 24-Week Results From ELARA

Preliminary findings from 417 patients with nAMD or DME indicate:

- Aflibercept 8q4 achieved meaningful improvements in BCVA and CST at Week 24 in previously treated patients
- The safety profile of aflibercept 8q4 through Week 24 was consistent with the established safety profile of both aflibercept 2 mg and 8 mg
  - Ocular TEAEs in the study eye were reported in 19.4% of patients; the most common ocular TEAEs were conjunctival hemorrhage and cataract

Mean Change in BCVA Through Week 24





Observed cases.
TEAE, treatment-emergent adverse event.